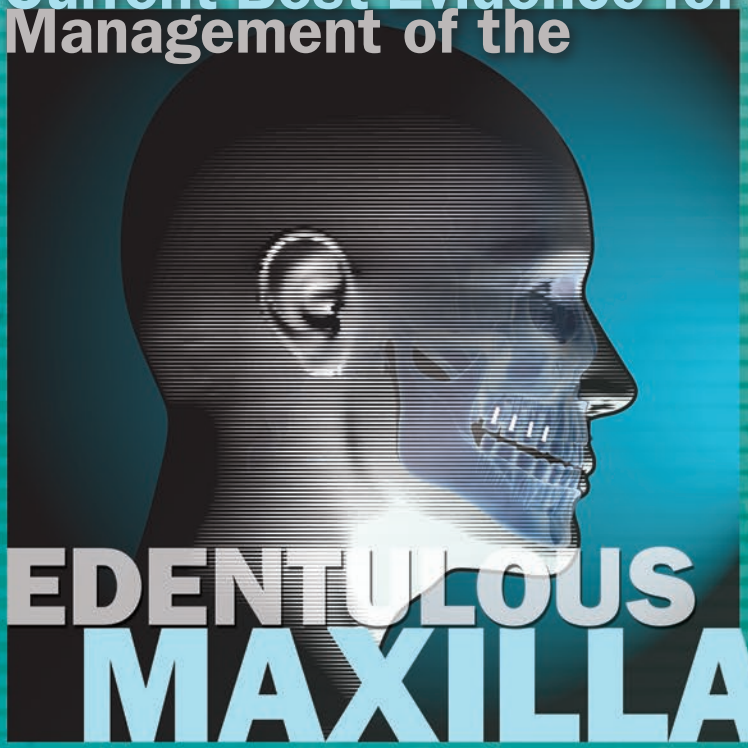
Volume 31 • 2016
SUPPLEMENT

JOMI

The International Journal of ORAL & MAXILLOFACIAL IMPLANTS

Current Best Evidence for Management of the EDENTULOUS MAXILLA



ACADEMY OF OSSEOINTEGRATION 2014 SUMMIT

QUINTESSENCE PUBLISHING

2014 SUMMIT

The Academy of Osseointegration thanks the following corporate partners for their support of the 2014 Summit

Nobel Biocare®

DENTSPLY IMPLANTS

oraPHARMA

HENRY SCHEIN®
DENTAL | SURGICAL SOLUTIONS

OSSEOINTEGRATION FOUNDATION

OSTEOGENICS
BIOMEDICAL

QUINTESSENCE PUBLISHING

straumann®

ZIMMER BIOMET
Your progress. Our promise.™

Academy of Osseointegration 2014 Summit:

Current Best Evidence for Management of the Edentulous Maxilla

August 7–9, 2014 • Oak Brook, Illinois

Current Best Evidence for Management of the Edentulous Maxilla

As new technologies make implant therapy possible for a growing number of patients, the responsibilities for clinicians also multiply. The profession is ultimately charged with providing the best available patient care. However, new materials and techniques are developed faster than can be objectively evaluated. The resulting lack of consensus burdens individual clinicians, who still remain responsible for providing treatment based on current best evidence.

The decision-making process for clinical management of the edentulous maxilla requires familiarity with current best evidence on far-reaching topics including bone augmentation for implant site development, implant system design, advanced imaging procedures, biologics, and an interdisciplinary approach to prosthetic management.

In addition to considering parameters of patient care, clinicians must answer critical questions about each specific patient. What is the maxillary/mandibular ridge relationship? What is the quality and quantity of available hard and soft tissue? Can the patient maintain adequate oral hygiene? Do habits or disease put this patient in an at-risk category?

Today, there are many new ways to manage distinct clinical situations and an array of treatment options requiring advanced training and experience. To assist dentists in making choices that best utilize current research to improve the quality and efficiency of patient care, the Academy of Osseointegration in August 2014 brought together more than 120 of the world's leading scientists and clinicians. Their mutual goal was to expand current clinical practice guidelines to include management of the edentulous maxilla. Based on a systematic review of the current literature, clinical information, and accepted treatment approaches, the resulting guidelines will serve as an educational tool for dentists and facilitate their ability to communicate about treatment planning with patients.

There is no doubt that technology will continue its rapid pace in providing dentistry with enhanced diagnostic tools, improved materials, and better prosthetic options for managing the edentulous maxilla. Subsequently, up-to-date guidelines, as proposed by the worldwide leaders in the field, will enable all dentists to make judicious use of current best evidence and ongoing advances for their patients.

— Clark M. Stanford, Co-Chair

JOMI
The International Journal of
ORAL & MAXILLOFACIAL IMPLANTS
Table of Contents
ISSN 0882-2786 (print) • ISSN 1942-4434 (online)
Volume 31 • Supplement • 2016

Academy of Osseointegration 2014 Summit:

Current Best Evidence for Management of the Edentulous Maxilla

Introduction

Group 1 Role of Bone Augmentation for Implant Placement

Group 2 Role of Implant Design and Systems

Group 3 Role of Imaging to Guide Implant Placement

Publisher
H. W. Haase

Executive Vice President
William G. Hartman

Director, Journal Publications
Lori A. Bateman

Managing Editor
Julie Rule

Production Manager
Diane Curran

Production
Susan Moulton

For information contact:
Quintessence Publishing Co, Inc,
4350 Chandler Drive, Hanover Park, IL 60133
Telephone: (630) 736-3600
Toll Free: (800) 621-0387 • Fax: (630) 736-3633
Web site: www.quintpub.com

The International Journal of Oral & Maxillofacial Implants is indexed and/or abstracted in Index Medicus, Science Citation Index, Current Contents/Clinical Medicine, MEDLINE, Index to the Dental Literature, and CINAHL database.

The International Journal of Oral & Maxillofacial Implants (ISSN 0882-2786 [print]; ISSN 1942-4434 [online]) is published bimonthly by Quintessence Publishing Co, Inc, 4350 Chandler Drive, Hanover Park, Illinois 60133, to disseminate current information related to the management of patients utilizing implant modalities and to report the results of basic and clinical research by investigators whose studies embrace the implant concept. Printed in USA.

Postmaster: Send address changes to Quintessence Publishing Co, Inc, 4350 Chandler Drive, Hanover Park, Illinois 60133.

Academy of Osseointegration's Summit on Clinical Practice Guidelines for the Edentulous Maxilla: Overview, Process, and Outcomes—Changing the Face of Implant Dentistry

Clark M. Stanford, DDS, PhD[1]

Purpose: *Starting in 2012, the Academy of Osseointegration initiated the planning process for an AO Summit to develop clinical practice guidelines (CPGs) for management of the edentulous maxilla.* ***Materials and Methods:*** *A planning committee led by Professor Clark Stanford and Dr Ole Jensen created a work plan based on five domain areas to be addressed by the summit. The five domain areas were defined as: (1) role of grafting for ridge development for implant placement, (2) role of implant design and systems in management of the edentulous maxilla, (3) role of imaging to guide implant placement, (4) role of biologics to assist in ridge development, and (5) role of prosthetic management.* ***Results:*** *The summit was held in August 2014, and the results are presented in this overview. All of the supporting systematic reviews and the detailed CPGs are presented in this special edition of JOMI.* ***Conclusion:*** *While the evidence was observed to be weak in regard to the literature for most of the systematic reviews, the summit strived to establish the current best evidence and practical CPGs that will assist clinicians in practice.* Int J Oral Maxillofac Implants 2016;31(suppl):s6–s15. doi: 10.11607/jomi.16suppl.ovw

Keywords: *consensus conference, edentulous maxilla, clinical practice guidelines*

The rehabilitation of the edentulous maxilla can present with a range of challenges and risks. Whereas the conventional complete denture has been a favored option for more than 100 years, the development of implant therapy and the deployment of various approaches to utilize implants in the rehabilitation of the edentulous maxilla have presented new challenges to the rehabilitation team. As a part of its strategic plan, the Academy of Osseointegration (AO) defined priority areas for the development of consensus guidelines.

The concept of clinical practice guidelines (CPGs) has been evident in medicine for some time, with a number of approaches used in their development along with commentary about the role of these by the Institute of Medicine.[1] An important aspect of CPGs is to weigh the evidence but also try to establish what the current best evidence is and then to frame any proposed CPGs within the framework of the limitations of the evidence. Rosenfeld and Shiffman[2] presented a process manual for the development of CPGs, which is used by the American Academy of Otolaryngology–Head and Neck Surgery, that detailed a specific process for the development of CPGs including:

- Introduction Statement: overview, purpose, target diagnosis, or issue with definition of terms
- Guideline Purpose: state why this is being proposed, target audience, guideline exclusion
- Health Care Burden: comment on the cost, remake rate, quality of life (QoL)
- Methods: describe the methods of the literature search, methodology to grade the studies (SORT Criteria)
- Guideline Key Action Statements: list in a summary table the explicit statements along with supporting text and graded evidence
- Implementation Considerations: dissemination of the CPG, anticipated barriers
- Disclaimers: based on disclosed conflict of interest (CoI)
- Acknowledgments: funding source, etc
- Authors and conflict of interest disclosures and references

[1]UIC Distinguished Professor and Dean, The University of Illinois at Chicago, Chicago, Illinois, USA.

Correspondence to: Dr Clark M. Stanford, The University of Illinois at Chicago, College of Dentistry, 801 South Paulina St (MC621), Chicago, IL 60612, USA.

An important aspect of the CPG statements is the level or strength of the recommendation, grounded in the level of evidence (or ethical/moral position) supporting the statement. For instance, in the process of considering the statement, one should consider the following aspects:

- When: when is the CPG to be applied (specifically, what type of patient is presenting the condition)?
- Who: specifically to what type of dentist (usually, CPGs define "who" as the clinician)?
- Level of Obligation: "Must," "Should," or "May"? Must: ethical imperative and/or very strong evidence; Should: qualifies a strength of the evidence, usually strong evidence; May: used when the evidence is weak or the benefit/harm relationship is not clear
- Do What (define the exact intervention)?
- To Whom?

The edentulous maxilla often presents with a range of challenges as well as a range of solutions. The purpose of this consensus summit was to define the issues, develop a process, and use this model for implant dentistry as a model for our health profession.

MATERIALS AND METHODS

Starting in 2012, the Academy of Osseointegration initiated the planning process for an AO Summit to develop clinical practice guidelines (CPGs) for management of the edentulous maxilla. Through the work of a planning committee led by Professor Clark Stanford and Dr Ole Jensen, plans were created to divide the work into five domain areas to be addressed by the summit, recognizing that some related areas, while important, were either already recently addressed by CPGs (Cite Radiology CPG) or were felt to have insufficient evidence at this time to warrant attention by the planning or task groups. The five domain areas were defined as *(1)* role of grafting for ridge development for implant placement, *(2)* role of implant design and systems in management of the edentulous maxilla, *(3)* role of imaging to guide implant placement, *(4)* role of biologics to assist in ridge development, and *(5)* role of prosthetic management. For planning purposes, two cochairs were named for each task group. These were for task group 1: Drs Tara Aghaloo and Craig Misch; group 2: Drs George Romanos and Paulo Coelho; group 3: Drs Kent Knoernschild and Trishul Allareddy; group 4: Drs Gustavo Avila and Daniel Spagnoli; and group 5: Drs Lyndon Cooper and James Taylor. For each task group, approximately 15 clinicians, clinician scientists, or research faculty were assigned to help in the development of defined questions to address the assigned topics (three to five questions in a PICO format), and systematic review(s) were undertaken by each group. As the systematic reviews were nearing completion, each group then worked on creating a proposed set of CPGs that address the issues and aspects framed within a format that addresses the range of training and education needed to apply the CPG at the level of evidence presented in the systematic review. To assist in understanding and communication of the CPGs, this was framed with three patient scenarios that could be considered from "Green" to "Yellow" to "Red," much like a traffic signal defines, to proceed with caution; slow, pause, and reevaluate; or caution, stop, and reevaluate. These case presentations were held at the summit meeting. The summit was held in Chicago, Illinois (USA) in early August 2014, and all participants attended the 3-day summit. All participants declared signed Conflict of Interest (CoI) statements prior to the summit. The summit had two plenary speakers (Drs Palo Malo on Day 1 and Peter Moy on Day 2). Following the plenary talk, each group cochair presented the proposed CPGs developed prior to the summit and presented supporting evidence from the systematic review(s). Intermixed with this presentation were three short patient presentations intended to frame what the task group considered to be a "Green," "Yellow," or "Red" patient case based on risk factors given the domain of the task group's assignment. Each presentation was in sequence with the group chair 1 presentation followed by a chair from another group acting in the role as a provocateur, or devil's advocate. There was then a general audience discussion for about 45 minutes. All five groups presented in this format over the first 2 days. During the end of day 2, each group went into seclusion and refined or revised the proposed CPG based on the comments from the discussions. On day 3, using an electronic Audience Response System (Turning Pointe, Option Technology), the modified CPGs were presented to the entire audience. Following further discussion and debate, the audience was then asked to score the strength or enthusiasm of:

1. Score #1: What is the current best evidence? If the evidence is weak or does not exist, we need to outline gaps in our knowledge, and weigh the strength of our recommendations.
2. Score #2: Current clinical practice guidelines, developed though a rigorous process and scored by the evidence that supports them.
3. Score #3: Based on these current clinical guidelines, score the strength of the evidence based on the clinical skill level needed to achieve the documented outcome (subjective).

Table 1 Level of Support for Group 1 CPG #1

	Responses	
	Percent	Count
Supportive	76.74%	66
Neutral	5.81%	5
Not Supportive	17.44%	15
Totals	100%	86

Table 2 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 1 CPG #1 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	60.47%	52
A well-trained and skilled clinical team and support staff with some experience	36.05%	31
A trained and skilled clinical team and support staff with limited experience	3.49%	3
Totals	100%	86

Table 3 Level of Support for Group 1 CPG #2

	Responses	
	Percent	Count
Supportive	82.76%	72
Neutral	5.75%	5
Not supportive	11.49%	10
Totals	100%	87

Table 4 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 1 CPG #2 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	41.38%	36
A well-trained and skilled clinical team and support staff with some experience	57.47%	50
A trained and skilled clinical team and support staff with limited experience	1.15%	1
Totals	100%	87

RESULTS

Outcomes of the Voting Process

In the initial voting period, it was observed that most of the evidence was at a Grade Level C, and the audience was not comfortable making a vote based on the evidence as presented in the presentation format. The decision was therefore for each systematic review to stand as the supporting evidence as of the summit. The attendees then proceeded to score each of the CPGs and the level of clinical skill needed to carry out the CPG on day 3 of the summit.

The scores for each of the groups are as follows.

Group 1: Role of Bone Augmentation for Implant Placement

CPG #1: When there is inadequate bone in the edentulous maxilla for placement of the preferred implant size in the planned position for esthetics, prosthetic support, and long-term stability, bone augmentation must be considered (Tables 1 and 2).

The consensus was that bone augmentation procedures should be undertaken with caution (yellow) to a high degree of caution (red).

CPG #2: When there is inadequate vertical bone height in the posterior aspect of the edentulous maxilla for dental implant placement of the preferred size in the planned position for esthetics, prosthetic support, and long-term stability, surgeons should consider sinus bone augmentation procedures (Tables 3 and 4).

Consensus discussion noted that there are conditions that may alter the rating from yellow to red including anatomical conditions, benign sinus pathology, bone height below the sinus, planned prosthesis, and management of adverse events.

CPG #3: When there is inadequate bone width in the edentulous maxilla for dental implant placement of the preferred size in the planned position for esthetics, prosthetic support, and long-term stability, surgeons should consider horizontal bone augmentation procedures (Tables 5 and 6).

Consensus discussion indicated that there are conditions that may alter the rating from yellow to red, including staged augmentation for implant placement, or a narrow ridge without adequate bone for the implant chosen. Retreatment of a failed augmentation or the need for an extraoral donor site harvest would move the rating from yellow to red.

CPG #4: When there is inadequate bone height in the edentulous maxilla for dental implant placement of

Table 5 Level of Support for Group 1 CPG #3

	Responses	
	Percent	Count
Supportive	78.82%	67
Neutral	8.24%	7
Not supportive	12.94%	11
Totals	100%	85

Table 6 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 1 CPG #3 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	43.53%	37
A well-trained and skilled clinical team and support staff with some experience	49.41%	42
A trained and skilled clinical team and support staff with limited experience	7.06%	6
Totals	100%	85

Table 7 Level of Support for Group 1 CPG #4

	Responses	
	Percent	Count
Supportive	60.47%	52
Neutral	19.77%	17
Not supportive	19.77%	17
Totals	100%	86

Table 8 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 1 CPG #4 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	91.86%	79
A well-trained and skilled clinical team and support staff with some experience	5.81%	5
A trained and skilled clinical team and support staff with limited experience	2.33%	2
Totals	100%	86

the preferred size in the planned position for esthetics, prosthetic support, and long-term stability, surgeons should consider vertical bone augmentation procedures (Tables 7 and 8).

Consensus discussion noted that all vertical augmentation procedures, other than sinus augmentation, would be rated red, as vertical atrophy is the most challenging condition and surgical procedures for vertical augmentation are complex. Retreatment of a failed bone augmentation and/or the need for an extraoral donor site harvest would add further complexity to the procedure.

Group 2: Role of Implant Design and Systems

CPG #1: Clinicians may use threaded parallel or tapered implants, with or without surface treatment, varied thread design, varied implant-abutment connections, with a length and diameter appropriate to available bone volume (Tables 9 and 10).

The consensus discussion indicated the implant system can assist the average clinician (green), and implant therapy should be considered for the edentulous maxilla. The alveolar bone does not require any bone augmentation, and there is adequate prosthetic jaw relationship (vertical and horizontal space) for the desired definitive restoration. Additional patient characteristics include lack of history of periodontal disease or previous implant failure, no bruxism, low smile line, and no smoking (or only socially) habit. Patient preferences are treatment with removable prostheses (eg, overdentures).

CPG #2: Clinicians may use tilted threaded parallel or tapered implants, with or without surface treatment, varied thread design, varied implant-abutment connections, length, and diameter appropriate to available bone volume. Immediate, early, and delayed loading protocols may be applied (Tables 11 and 12).

The consensus discussion indicated a high level of disagreement regarding the perceived use of tilted implants. The discussion was framed around the caution needed to implement this approach but included a discussion on the use of tilted implants to improve implant stability with splinting and immediate loading. It also included the use of four unsplinted implants with immediate loading and a removable fixed prosthesis or more implants in low-density bone (grafted bone or soft bone). A well-experienced surgical team, undersizing of the osteotomies during implant placement, and use of implants to condense the bone at the insertion time may improve the clinical outcomes after many years of treatment.

Table 9 Level of Support for Group 2 CPG #1

	Responses	
	Percent	Count
Supportive	81.40%	70
Neutral	10.47%	9
Not supportive	8.14%	7
Totals	100%	86

Table 10 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 2 CPG #1 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	2.35%	2
A well-trained and skilled clinical team and support staff with some experience	43.53%	37
A trained and skilled clinical team and support staff with limited experience	54.12%	46
Totals	100%	85

Table 11 Level of Support for Group 2 CPG #2

	Responses	
	Percent	Count
Supportive	49.40%	41
Neutral	18.07%	15
Not supportive	32.53%	27
Totals	100%	83

Table 12 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 2 CPG #2 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	21.18%	18
A well-trained and skilled clinical team and support staff with some experience	71.76%	61
A trained and skilled clinical team and support staff with limited experience	7.06%	6
Totals	100%	85

CPG #3: Clinicians may use threaded parallel or tapered implants, with or without surface treatment, varied thread design, varied implant-abutment connections, and with length and diameter appropriate to available bone volume. Solid implants below 3 mm in diameter are not included in this recommendation. Simultaneous bone grafting, axial and/or tilted implants in alveolar bone, pterygomaxilla, or zygomatic bone may be utilized as a surgical approach. Immediate, early, and delayed loading protocols may be applied (Tables 13 and 14).

A consensus discussion indicated a fair agreement that patients with an edentulous maxilla receive implants to support fixed or removable prostheses. Patients with alveolar bone height < 8 mm and width < 4 mm have poor bone quality (according to Lekholm and Zarb, 1985)[3] during osteotomy drilling (type IV). The alveolar bone requests simultaneous bone augmentation (fresh extraction sockets, vertical or horizontal). All vertical or horizontal unfavorable jaw relationships may be included. Additional patient characteristics may include history of periodontal disease or previous implant failure, bruxism, high smile line, and heavy smoking. Patient preferences may be treatment with fixed or removable prostheses and immediate loading protocols.

Group 3: Role of Imaging to Guide Implant Placement

CPG #1: All acquired radiographic volumetric datasets must be evaluated for pathosis and anatomical constraints. Referral to a person who is trained in advanced interpretation techniques in radiology may be necessary (Tables 15 and 16).

Consensus discussion indicated agreement that when imaging is used for implant treatment planning, the studies need to be diagnostically evaluated for all potential pathologic conditions.

CPG #2: Computer-generated static guides may enhance the communication within the clinical team (Tables 17 and 18).

CPG #3: Competent clinical application of guided surgery should depend upon the design and fabrication of computer-generated static guides based on effective clinician diagnosis, and clinical prosthetic planning with a scanning template when appropriate. For implant placement accuracy, clinicians must have competence in guide workflow with understanding of sources of error (Tables 19 and 20).

In the consensus discussion, there was fair support for experience to understand the workflow and especially the sources of error that can occur in the digital workflow.

Table 13 Level of Support for Group 2 CPG #3

	Responses	
	Percent	Count
Supportive	67.06%	57
Neutral	9.41%	8
Not supportive	23.53%	20
Totals	100%	85

Table 14 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 2 CPG #3 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	97.56%	80
A well-trained and skilled clinical team and support staff with some experience	2.44%	2
A trained and skilled clinical team and support staff with limited experience	0.00%	0
Totals	100%	82

Table 15 Level of Support for Group 3 CPG #1

	Responses	
	Percent	Count
Supportive	88.37%	76
Neutral	3.49%	3
Not supportive	8.14%	7
Totals	100%	86

Table 16 Which of the Following Best Describes The Clinical Education, Training, and Experience to Implement Group 3 CPG #1 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	34.09%	30
A well-trained and skilled clinical team and support staff with some experience	51.14%	45
A trained and skilled clinical team and support staff with limited experience	14.77%	13
Totals	100%	88

Table 17 Level of Support for Group 3 CPG #2

	Responses	
	Percent	Count
Supportive	80.46%	70
Neutral	5.75%	5
Not supportive	13.79%	12
Totals	100%	87

Table 18 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 3 CPG #2 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	15.29%	13
A well-trained and skilled clinical team and support staff with some experience	58.82%	50
A trained and skilled clinical team and support staff with limited experience	25.88%	22
Totals	100%	85

CPG #4: A computer-generated static surgical guide (bone supported or soft tissue supported) may lead to prosthetic and implant survival and success, and patient satisfaction (Tables 21 and 22).

The consensus discussion indicated a level of disagreement that imaging and its application directly impacted implant survival.

Group 4: Role of Biologics to Assist in Ridge Development

Group 4 was limited by almost no evidence as it directly applied to biologics exclusive to the edentulous maxilla. Due to this limitation, they applied logic to consider various applications using the data at hand, but the outcomes are not directed at the edentulous maxilla alone.

CPG #1: For maxillary buccal wall extraction socket defects, the evidence suggests that rhBMP-2/ACS may be considered to promote bone repair and to facilitate implant placement (Tables 23 and 24).

Consensus discussion indicated that while there was fair support for this application of one proteomic for the potential for ridge preservation, the procedure itself can be performed by most clinicians.

CPG #2: Limited evidence suggests that autologous stem cell delivery in a gelatin foam may be considered

Table 19 Level of Support for Group 3 CPG #3

	Responses	
	Percent	Count
Supportive	67.82%	59
Neutral	11.49%	10
Not supportive	20.69%	18
Totals	100%	87

Table 20 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 3 CPG #3 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	31.40%	27
A well-trained and skilled clinical team and support staff with some experience	65.12%	56
A trained and skilled clinical team and support staff with limited experience	3.49%	3
Totals	100%	86

Table 21 Level of Support for Group 3 CPG #4

	Responses	
	Percent	Count
Supportive	60.23%	53
Neutral	13.64%	12
Not supportive	26.14%	23
Totals	100%	88

Table 22 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 3 CPG #4 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	16.67%	14
A well-trained and skilled clinical team and support staff with some experience	71.43%	60
A trained and skilled clinical team and support staff with limited experience	11.90%	10
Totals	100%	84

Table 23 Level of Support for Group 4 CPG #1

	Responses	
	Percent	Count
Supportive	53.93%	48
Neutral	14.61%	13
Not supportive	31.46%	28
Totals	100%	89

Table 24 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 4 CPG #1 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	9.41%	8
A well-trained and skilled clinical team and support staff with some experience	57.65%	49
A trained and skilled clinical team and support staff with limited experience	32.94%	28
Totals	100%	85

to accelerate bone formation and minimize ridge height reduction to enable implant placement in extraction sockets (Tables 25 and 26).

Consensus discussion indicated that while there was fair support for this application, there is a level of complexity in management of the construct that may warrant enhanced training and education.

CPG #3: Limited evidence suggests that rhPDGF-BB combined with FDBA or ß-TCP may be considered to accelerate bone formation in extraction sockets (Tables 27 and 28).

Consensus discussion indicated that while there was fair support for this application of one proteomic for the potential for ridge preservation, the procedure itself can be performed by most clinicians with some experience.

CPG #4: For maxillary sinus floor augmentation, evidence supports that rhBMP-2 + ACS should be considered as an alternative to bone autografts in promoting bone formation to enable implant placement and reduce patient morbidity associated with graft harvest (Tables 29 and 30).

Consensus discussion indicated that while there was only fair support of one proteomic in this application, as a sinus augmentation procedure, there was the need for advanced training and education for its application.

Table 25 Level of Support for Group 4 CPG #2

	Responses	
	Percent	Count
Supportive	42.05%	37
Neutral	18.18%	16
Not supportive	39.77%	35
Totals	100%	88

Table 26 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 4 CPG #2 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	32.53%	27
A well-trained and skilled clinical team and support staff with some experience	46.99%	39
A trained and skilled clinical team and support staff with limited experience	20.48%	17
Totals	100%	83

Table 27 Level of Support for Group 4 CPG #3

	Responses	
	Percent	Count
Supportive	52.87%	46
Neutral	16.09%	14
Not supportive	31.03%	27
Totals	100%	87

Table 28 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 4 CPG #3 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	26.74%	2 3
A well-trained and skilled clinical team and support staff with some experience	55.81%	48
A trained and skilled clinical team and support staff with limited experience	17.44%	15
Totals	100%	86

Table 29 Level of Support for Group 4 CPG #4

	Responses	
	Percent	Count
Supportive	53.33%	48
Neutral	4.44%	4
Not supportive	42.22%	38
Totals	100%	90

Table 30 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 4 CPG #4 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	47.13%	41
A well-trained and skilled clinical team and support staff with some experience	48.28%	42
A trained and skilled clinical team and support staff with limited experience	4.60%	4
Totals	100%	87

Group 5: Role of Prosthetic Management

CPG #1: The therapeutic team must identify local, systemic, anatomical (especially vertical restorative space), and patient-specific factors influencing treatment choices. Based on observed diagnostic information, the selected treatment will match the treatment capacity of the therapeutic team (Tables 31 and 32).

Consensus opinion was strong in supporting this, and there was an important recognition of the role of careful diagnosis before any therapy is considered.

CPG #2: The complete maxillary denture is the minimal treatment afforded to the maxillary edentulous patient. Prosthodontists and restorative dentists should provide all patients with immediate, interim, or complete dentures when patients will become or are edentulous.

A maxillary denture provides rehabilitation without implants and represents a treatment choice when complex restorative needs cannot be met by the professional team or addressed financially by the patient.

Dentures provide functional and esthetic diagnostic guidance for further implant-supported prostheses.

Dentures not meeting therapeutic goals (eg, esthetic, phonetic, mastication, hygiene) should be replaced, or alternative reconstruction using implants should be considered (Tables 33 and 34).

Table 31 Level of Support for Group 5 CPG #1

	Responses	
	Percent	Count
Supportive	100.00%	33
Neutral	0.00%	0
Not supportive	0.00%	0
Totals	100%	33

Table 32 Which of the Following Best Describes the Clinical Education, Training and Experience to Implement Group 5 CPG #1 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	10.34%	9
A well-trained and skilled clinical team and support staff with some experience	51.72%	45
A trained and skilled clinical team and support staff with limited experience	37.93%	33
Totals	100%	87

Table 33 Level of Support for Group 5 CPG #2

	Responses	
	Percent	Count
Supportive	88.37%	76
Neutral	4.65%	4
Not supportive	6.98%	6
Totals	100%	86

Table 34 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 5 CPG #2 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience	8.05%	7
A well-trained and skilled clinical team and support staff with some experience	24.14%	21
A trained and skilled clinical team and support staff with limited experience	67.82%	59
Totals	100%	87

Table 35 Level of Support for Group 5 CPG #3

	Responses	
	Percent	Count
Supportive	86.21%	75
Neutral	9.20%	8
Not supportive	4.60%	4
Totals	100%	87

Table 36 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 5 CPG #3 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience.	16.47%	14
A well-trained and skilled clinical team and support staff with some experience	75.29%	64
A trained and skilled clinical team and support staff with limited experience	8.24%	7
Totals	100%	85

There was a clear consensus that at least a complete denture is needed for the edentulous maxilla. It is interesting to note that the majority felt this was not a complex procedure.

CPG #3: Clinicians can provide a maxillary overdenture as a stabilized removable solution for the edentulous patient that provides increased patient satisfaction and oral health-related quality of life.

The maxillary overdenture may be provided with four to six implants using splinted or solitary implant concepts.

The provision of implants cannot interfere with or preclude the provision of phonetics, mastication, and esthetics.

Both the patient and clinical team are willing and able to provide long-term care including surveillance, intervention, maintenance, repair, or replacement (Tables 35 and 36).

The consensus noted strong support for the use of overdenture therapy and the need for experience when this is used.

CPG #4: Maxillary implant-stabilized fixed complete denture or prosthesis (ISFP) can be provided minimally with four implants. More implants are used when there is increased risk of implant failure or the prosthetic concept requires it (eg, segmentation).

Table 37 Level of Support for Group 5 CPG #4

	Responses	
	Percent	Count
Supportive	89.77%	79
Neutral	5.68%	5
Not supportive	4.55%	4
Totals	100%	88

Table 38 Which of the Following Best Describes the Clinical Education, Training, and Experience to Implement Group 5 CPG #4 at the Level of the Evidence?

	Responses	
	Percent	Count
A well-trained and skilled clinical team and support staff with extensive experience.	43.68%	38
A well-trained and skilled clinical team and support staff with some experience	55.17%	48
A trained and skilled clinical team and support staff with limited experience	1.15%	1
Totals	100%	87

ISFP therapy should be informed by the provision or presence of an ideal provisional or prototypic denture.

Patients and clinicians must accept lifelong responsibility for biologic and prosthetic management, maintenance, and/or replacement. Thus, ISFP design should favor maintenance, retrievability, repair, or replacement (reproduction) (Tables 37 and 38).

Consensus indicated the added complexity of a fixed-style approach to rehabilitation is favored, but it brings an added level of complexity that necessitates additional training and education above the novice level.

DISCUSSION

The edentulous maxilla often presents with a range of challenges as well as a range of solutions. The purpose of this consensus summit was to define the issues, develop a process, and use this model for implant dentistry as a model for our health profession. Unfortunately, in the process of developing the systematic reviews, the level of evidence was often weak, and this created issues in establishing CPGs and separating these from clinical opinion. As such, the entire working team worked many hours in developing the reviews, crafting the CPGs, and debating these before, at, and after the summit. The scoring reported is a snapshot of the summit's participants after hearing all the data, the proposed CPGs, and reviewing the clinical cases used as examples of how the CPGs could be applied. The CPGs that are presented are essentially the best recommendations the summit participants could make for the profession and represent a position at one point in time. As guidelines, the profession should consider these as guideposts along the development of best clinical care, and as with all reference points, these will evolve as our science develops and we continue our process of understanding the role of patient- and clinician-oriented risk factors in providing the very best in patient care.

REFERENCES

1. Clinical Practice Guidelines We Can Trust. Graham R, Mancher M, Miller Wolman D, Greenfield S, Steinberg E, eds. Committee on Standards for Developing Trustworthy Clinical Practice Guidelines; Institute of Medicine IOM Report 2011. ISBN 978-0-309-16422-1.
2. Rosenfeld RM and Shiffman RN. Clinical practice guideline development manual: A quality-driven approach for translating evidence into action. Otolaryngol Head Neck Surg 2009;140:S1–S43.
3. Lekholm u, Zarb GA. Patient selection and Preparation. In: Bråne-mark PI, Zarb GA, Albrektsson T (eds). Tissue Integrated Prostheses. Osseointegration in Clinical Dentistry. Chicago:Quintessence, 1985:199–209.

Management of the Edentulous Maxilla

Tara L. Aghaloo, DDS, MD, PhD[1]

Why is treatment of the edentulous maxilla a current/hot topic?

Treatment of the edentulous maxilla is such a hot topic today because many things have changed and many things have stayed the same. A comprehensive diagnostic workup followed by careful treatment planning is still the most important aspect of treating edentulous patients, no matter how complicated the surgery or restorative procedures are. We have patients who are able to receive fixed prostheses on implants in a number of hours; we have new digital tools to give us significantly improved views of our patients' bone quality and quantity, vital structures, and potential pathology; and we have a tremendous selection of new prosthetic and surgical materials to aid in making almost every patient a candidate for dental implants.

What makes the clinical management of the edentulous maxilla so complex and controversial?

This topic is controversial because treatment is often seen as "one size fits all." What I mean is that some clinicians want to give everyone immediately loaded fixed prostheses on tilted implants, other clinicians want to perform bone augmentation to place implants into a classically healed ridge, and still others are somewhere in between. The issue is that technology is advancing so rapidly that we do not have time to evaluate the techniques and materials that we are utilizing in an objective way. In other words, by the time we have long-term studies on one technique or material, new and likely better ones have become available. However, this does not excuse the profession from researching these new technologies before we widely offer them to our patients. Herein lies the controversy.

[1]Professor and Assistant Dean for Clinical Research, Division of Diagnostic and Surgical Sciences, University of California–Los Angeles School of Dentistry, Los Angeles, California, USA.

Why are clinical practice guidelines so important for dentistry?

Clinical practice guidelines are so important for dentistry, especially for implant dentistry, because there are so many ways to manage specific clinical situations. Some treatment options require advanced training and skill, and should not be performed by less experienced clinicians, at least not without the proper training. The recent Academy of Osseointegration Summit on the Edentulous Maxilla proposed Clinical Practice Guidelines (CPGs), which were developed based on a systematic review of the current dental literature, clinical information, and accepted approaches to the treatment of the edentulous atrophic maxilla. These guidelines are intended to provide practicing clinicians with current thoughts and recommendations for several topics, including the role of bone augmentation for implant site development, the role of implant design and surgical approaches, the role of advanced imaging for more minimally invasive procedures, the role of tissue engineering in hard and soft tissue reconstruction, and an interdisciplinary approach to prosthetic management of the edentulous maxilla. The guidelines can also be used as an educational tool to assist dentists in treatment choices, to improve the quality and efficiency of patient care, and to explain treatment options to patients.

What are some key diagnostic criteria to consider when weighing treatment options?

When evaluating different treatment options, we must consider maxillary/mandibular ridge relationship, quality and quantity of available hard and soft tissue, lip support, ability to maintain adequate oral hygiene, presence of pathology, and evidence of parafunctional habits.

How have advances in imaging/technology impacted the diagnosis/treatment of the edentulous maxilla?

Advanced imaging, mostly referring to cone-beam computed tomography (CBCT) scans, is essential in both the diagnostic and treatment phases of treating patients with an edentulous maxilla. Not only can it help us determine if there is adequate bone for implant placement, visualize maxillary anatomy,

and diagnose the degree of osseous atrophy, but it can help identify anatomical variations and the presence of pathology. Utilizing CBCT scans to digitally plan an implant case before it is actually performed on a patient is an extremely valuable tool, both for the novice and experienced clinician. Having a "test run" on each individual patient, where potential difficulties or challenges can be identified and overcome, cannot be overstated. This can help determine position or angulation of implants, number of implants, prefabricated surgical guides, or provisional and sometimes final prosthesis fabrication. The role of advanced imaging will only continue to increase in the future.

Highlight the various treatment options that should be considered.

Treatment options that should be considered for the edentulous maxilla were covered very well in the AO Summit. After discussing the patient's chief complaint, doing a complete history, physical exam, diagnostic casts, and appropriate radiographs, these options can be discussed. A maxillary complete denture is always an option, especially if it is well made and can meet the esthetic, phonetic, and functional requirements. If it cannot, a prosthesis utilizing implants should be considered. A removable implant-assisted overdenture is an option that has been shown to increase a patient's satisfaction and quality of life. However, this treatment option requires surgery, increased cost, and must be evaluated regularly for maintenance, repair, and/or replacement. Another option is an implant-supported fixed prosthesis, which generally requires more complicated surgery and increased cost. Again, if this is the option that fits the esthetic, prosthetic, and functional requirements of an individual patient, and the clinician and patient are willing to undergo regular maintenance, repair, or replacement, then the fixed prosthesis should be chosen.

At this stage, it is extremely important to consider the training and skill of the treating clinician. If there is an option that may be considered for a patient, but the treating clinician is not comfortable with it, that patient should be referred to another clinician who can provide those options. Clinicians should not perform procedures or recommend treatment options that they do not have the training or skills to perform.

How important is patient communication in treatment planning?

Patient communication is the most vital aspect involved in diagnosis and treatment planning. We have to remember why patients seek our consultation: They want teeth! It is up to us to inform them of their attributes and limitations to resolving their chief complaint. Whether it is a complicated medical history, inadequate available bone, unrealistic expectations, or financial limitations, any treatment performed will fail without proper communication.

What does the future look like for the management of the edentulous maxilla?

The future is extremely bright in management of the edentulous maxilla, whether it is severely atrophic or not. It is apparent that technology will continue to improve and provide us with enhanced diagnostic tools, improved materials to augment deficient tissues via less invasive procedures, better prosthetic options for both provisional and definitive restorations, and implants that can be loaded sooner and can be used in more compromised sites

Role of Bone Augmentation for Implant Placement

Group Co-Chairs

Tara L. Aghaloo, DDS, MD, PhD
Craig Misch, DDS, MDS

Group Participants

Susan Cutler, DMD
C. Edgar Davila, DDS, MS, CDT
Vincent J. Iacono, DMD
Hideaki Katsuyama, DDS, PhD
Fouad Khoury, DMD, PhD
Bach Le, DDS, MD
Jay P. Malmquist, DMD
William Martin, DMD, MS
Ed McGlumphy, DDS, MS
Pablo Galindo Moreno, DDS, PhD
Dean Morton, BDS, MS
Peter Moy, DMD
Michael A. Pikos, DDS
Edward Sevetz, DMD
Istvan Urban, DMD, MD, PhD
Stephen Wallace, DDS
Hom-Lay Wang, DDS, MSD, PhD

Bone Augmentation of the Edentulous Maxilla for Implant Placement: A Systematic Review

Tara L. Aghaloo, DDS, MD, PhD[1]/Craig Misch, DDS, MDS[2]/Guo-Hao Lin, DDS[3]/
Vincent J. Iacono, DMD[4]/Hom-Lay Wang, DDS, MS, PhD[5]

Purpose: *Multiple bone augmentation techniques are available to allow implant placement in the atrophic maxilla. However, questions remain, regarding which methods are most predictable and have the best dental implant survival rate (SR) in grafted bone. The aim of this systematic review was to evaluate literature from the last 30 years to determine predictability of bone grafting of the edentulous maxilla for implant placement as well as for implant SR.* ***Materials and Methods:*** *A systematic review was performed of studies conducted during the period 1980 to 2014, specifically focusing on the edentulous maxilla and bone grafting. Surgical techniques discussed in the publications included were guided bone regeneration (GBR), sinus augmentation, onlay bone grafting, nasal floor grafting, and Le Fort I interpositional grafting. All identified articles were evaluated and screened to meet strict inclusion criteria of at least 10 patients, complete maxillary edentulism, 1-year follow-up, and information regarding implant SR. A total of 974 articles were identified with electronic and manual searches. On further evaluation of the titles and abstracts, 44 articles were excluded. Full texts of the articles that met the inclusion criteria were reviewed, of which 40 articles were included in the systematic review.* ***Results:*** *For onlay bone grafting, 16 studies were included and analyzed, and the weighted mean implant SR was 85.2%. For the GBR technique, two studies were included, with a reported SR ranging from 96.1% to 100%. For Le Fort I interpositional grafting, 11 studies were included, with a weighted mean SR of 89.6%. For the sinus augmentation technique, 12 studies were investigated and the weighted mean SR was 91.5%. For the combination technique, six studies were analyzed and the weighted mean SR was 93.6%.* ***Conclusions:*** *All five treatment modalities discussed—onlay bone grafting, GBR, Le Fort I interpositional grafting, maxillary sinus augmentation, and/or nasal floor inlay grafting or the combination approach—can be successfully used to augment edentulous maxillary ridge with high implant SRs.* Int J Oral Maxillofac Implants 2016;31(suppl):s19–s30. doi: 10.11607/jomi.16suppl.g1

Key words: *bone augmentation, GBR, Le Fort I interpositional grafting, nasal floor grafting, onlay bone grafting, sinus augmentation*

[1]Professor and Assistant Dean for Clinical Research, Division of Diagnostic and Surgical Sciences, University of California–Los Angeles School of Dentistry, Los Angeles, California, USA.
[2]Clinical Associate Professor, Department of Implant Dentistry, New York University College of Dentistry, New York, NY, USA.
[3]Resident, Graduate Periodontics, Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, Michigan, USA.
[4]Professor and Chair, Department of Periodontology, School of Dental Medicine, Stony Brook University, Stony Brook, New York, USA.
[5]Professor and Program Director, Graduate Periodontics, Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, Michigan, USA.

Correspondence to: Dr Tara L. Aghaloo, UCLA School of Dentistry, 10833 Le Conte Ave, Box 951668, Los Angeles, CA 90095-1668, USA.

Dental implant placement for edentulous patients has become a common and well-accepted treatment modality. When implant-supported prosthetic alternatives are considered, the clinician must evaluate the patient for adequate bone volume for implant placement in the desired locations. The success of implant procedures and maintenance of long-term stability are directly related to the quality and quantity of the supporting bone. Restoring the edentulous maxilla poses significant challenges for the treating clinician, especially in situations of severe ridge resorption.[1–8] Alveolar bone resorption may result from trauma, periodontal disease, pathology, congenital deformities, ill-fitting prostheses, or disuse atrophy from long-term edentulism.[5,9–12] It is now extremely uncommon to tell patients that they are not candidates for dental implants, even when their remaining bone is of inadequate quality or quantity. When

the residual ridge lacks the necessary bone volume for proper implant placement, bone augmentation procedures are one option to be used.

Various grafting procedures and materials are available to aid the implant surgeon in providing the ideal foundation for prosthetic rehabilitation.[1,8,13,14] However, the edentulous maxilla is particularly challenging with regard to augmentation because of anatomic limitations, such as the nasal floor, maxillary sinus, resorption pattern, and interarch relationship.[4,5] Implant survival rates (SRs) are generally lower in the maxilla than in the mandible, especially in the posterior maxilla where bone quality can be poor.[10,15–20] In terms of maxillary augmentation techniques, sinus augmentation is the most predictable and documented procedure to support implants, in both short- and long-term studies.[21–24] In addition, many longer-term studies (> 5 years) report high SRs and implant stability when more extensive grafting is performed in the edentulous maxilla to support implants,[6,10,13,25,26] with an improvement in quality of life, esthetics, and function.[6,27] In comparison, the management of the severely resorbed edentulous maxilla, without grafting to support implants, is a more recent technique requiring adequate bone in the anterior maxilla. These tilted implants, as well as zygomatic and short implant alternatives to avoid grafting, may result in less favorable prosthetic designs such as long cantilevers as well as speech, hygiene, or esthetic issues.[28–31] Although anectodally or preliminarily, implants in the edentulous maxilla without bone grafting demonstrate high SRs, they are not without technical difficulties and side effects. [32–34] It is apparent that more studies are needed to document those results with confidence and to establish long-term follow-up data.

Augmentation facilitates improved placement for prosthetic support and contour, the ability to place a greater number of implants, longer- and/or wider-diameter implants, and less prosthetic cantilever.[10,35] In cases with shorter implants, higher failure rates have been reported.[36–40] More recent studies demonstrate similar SRs when no grafting is performed, using short or narrow implants.[41,42] However, long-term implant success and prosthetic outcomes in the edentulous maxilla are still largely unknown.[43–45] Much of the increased failure rates observed when extensive bone grafts are performed is directly related to the quality and quantity of bone and use of machined surface implants.[36] Variations in surgical technique, augmentation materials, and published outcomes makes it difficult to compare studies or to combine results in a meaningful manner, especially when focusing on the edentulous maxilla. Therefore, the aim of this systematic review was to evaluate literature from the last 30 years to determine predictability for bone augmentation in the edentulous maxilla for implant placement as well as implant survival.

MATERIALS AND METHODS

Inclusion and exclusion criteria were defined by the authors before beginning the study (Table 1).

Focus Question

The focus question developed using the PICO (population, intervention, comparison, outcome) format was related to grafting of the edentulous maxilla.

Study Type

Only clinical studies in humans and published in English were accepted for this systematic review. The clinical study had to include a minimum of 10 completely edentulous patients, irrespective of the number of treated patients for a given therapeutic option. Case reports, review articles, technical notes, and experimental studies were excluded from the systematic review.

Type and Area of Intervention

Horizontal, vertical, Le Fort I interpositional and nasal floor grafting, or sinus bone augmentation had to be performed in the completely edentulous maxilla.

Outcome Parameters and Follow-up Period

Studies were included provided they reported data about implant success and/or SRs of implants that were placed in conjunction with data on horizontal, vertical, Le Fort I procedure, nasal floor grafting, or sinus augmentation and that the implants had been loaded for a minimum period of 1 year.

Search Strategy

A PubMed electronic search was conducted to identify the potential articles for inclusion in this systematic review. The search included articles from 1980 to 2014. In addition, the following journals were hand searched for potential relevant articles: Clinical Oral Implant Research and International Journal of Oral and Maxillofacial Implants. Articles were selected using the following search terms: ("Edentulous" OR "Atrophic") AND "Maxilla" AND "Augmentation" AND "Sinus" "NOT" Partial. This search was combined with search terms: "Horizontal" and "Vertical." Duplicates were removed from the search. The authors individually screened the titles of the articles based on the inclusion criteria. If the title or abstract did not allow a clear decision to be made about inclusion, the full article was obtained. Based on the preselection, the full-text articles were then analyzed as to whether they met the inclusion criteria, and mutual agreement on the final selection of studies was obtained. Furthermore, the references of included studies were searched for publications that had not been identified electronically.

Search Combination

Search terms included the following: ((“Jaw, Edentulous”[Mesh:NoExp] OR edentulous[text word] OR atrophic[text word]) AND (“Maxilla”[Mesh] OR maxilla[text word])) AND (“Oral Surgical Procedures”[Mesh] OR graft*[text word] OR “bone regeneration”[text word] OR “guided bone regeneration”[text word] OR transplantation[MESH] OR transplantation[subheading]) OR ((bone[text word] OR vertical[text word] OR sinus[text word] OR “horizontal”[text word]) AND augmentation*[text word])) NOT partial* NOT (animals[mh] NOT humans[mh].

Data Extraction

Articles were evaluated exactly as published, and no additional reference or contact with authors was sought. The two reviewers independently extracted the data from the selected publications. The following information was collected from the publications:

- Study design
- Comparison group
- Randomization
- Masking (single, double, not possible)
- Time of follow-up
- Number of patients
- Number of patients with edentulous maxillae
- Number of subject dropouts
- Number of implants
- Number of implants in edentulous maxillae
- Health condition
- Grafting technique
- Implant length
- Implant diameter
- Implant system
- Type of prosthesis
- Healing period
- SR
- Data analyses and statistics

The method used for meta-analysis in this article was previously reported by another systematic review.[46] The primary outcome was the implant SR. The pooled weighted mean and the 95% confidence interval (CI) of each technique were estimated using a computer program (Comprehensive Meta-analysis Version 2, Biostat). Random-effects meta-analyses of the selected studies were applied to minimize potential bias caused by methodologic differences among studies. Forest plots were produced to graphically represent weighted mean and 95% CI for primary outcomes in the studies included. The number of implants placed was used as the analysis unit for primary outcome. In addition, heterogeneity among studies was assessed with the chi-square test, with a value of $P < .05$ representing significant heterogeneity. The reporting of these meta-analyses adhered to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement.[47]

Table 1 The Systematic Search Strategy Used in the Current Review

Focus question: Grafting the edentulous maxilla	
Search strategy	Population: Patients with completely edentulous maxilla
	Intervention or exposure: Vertical ridge augmentation, horizontal ridge augmentation, sinus augmentation; implants; grafting materials
	Comparison: Grafting techniques; implant survival vs none
	Outcome: Survival rate
	Filters(language): English
Database search	Electronic: PubMed (English)
	Hand searched: Clinical Oral Implant Research and International Journal of Oral and Maxillofacial Implants
Selection criteria	Inclusion criteria
	10 patients
	Implants placed with 12 months of follow-up
	Human studies only
	English language
	Exclusion criteria
	Animal studies
	< 10 patients
	< 12 months of follow-up

RESULTS

Of the 89 studies evaluated based on titles and abstracts, 44 were excluded because of lack of 12-month follow-up, lack of reporting of implant SRs, inclusion of a large number of partially edentulous patients, or duplicate patients from previous studies (Fig 1). After full-text screening, another five studies were further excluded for data extraction and meta-analysis because of insufficient data reported. When evaluating the level of evidence for articles included, most were retrospective case series, or level II-3 studies without a concurrent or historical control group.[48] Many of these studies, however, had large numbers of patients, collected clinically relevant information, and reported patient-centered outcomes. Some studies also included control or nongrafting groups, conducted split-mouth studies, or randomized treatment allocation (Fig 2).

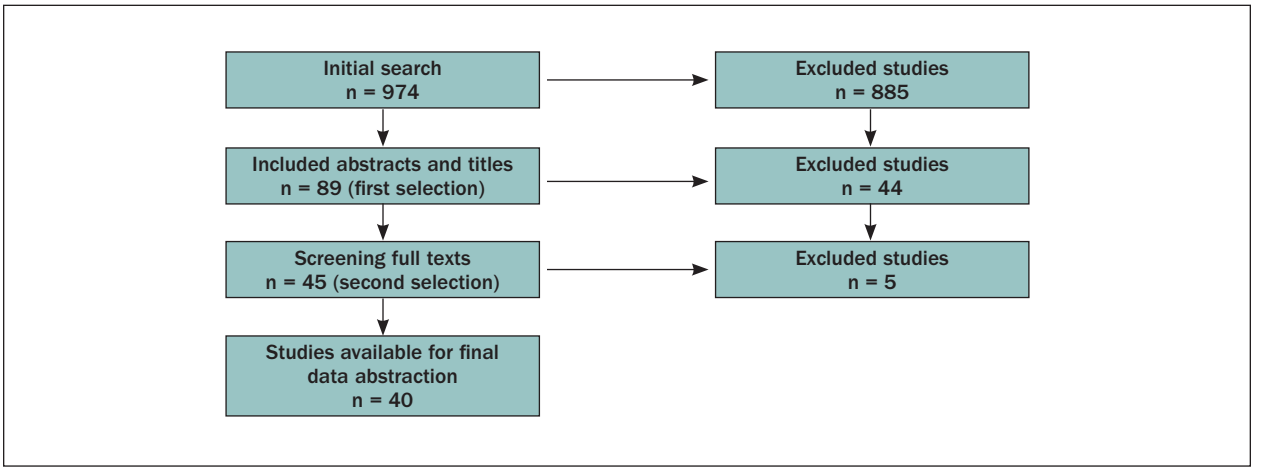


Fig 1 Flow chart showing the selection process of the current review.

Much importance has been placed on validating current therapies, especially with regard to implant dentistry. An increasing number of studies are now available to evaluate grafting success rate as well as implant survival. This is demonstrated in the distribution of studies from 1990 to the present (Fig 3). The number of studies has been increasing overall, especially those with very long-term follow-up. A detailed examination of the articles included revealed that few studies included patients with sinus augmentation as the only grafting technique. Most of the completely edentulous patients requiring sinus grafting also had severe anterior maxillary atrophy, which required either an onlay graft or a nasal floor (or inlay) graft. This is not surprising, because the length of time for which the patients were edentulous in these studies was often greater than 10 to 20 years. A combination of techniques was by far the most common, such as Le Fort I interpositional grafts that were combined with onlay grafts, or buccal guided bone regeneration (GBR) that was combined with sinus augmentation or nasal inlay grafts (Fig 4).

Onlay Bone Grafting

Scientific evidence for onlay bone grafting of the completely edentulous maxilla was provided by 16 (12 retrospective, 3 prospective, and 1 concurrent controlled) studies.[3,8,13,14,36,38,49–59] These clinical studies included data from 515 patients in which 2,446 implants were placed. The follow-up period ranged from 1 to 12 years. The studies were heterogenous in nature including various graft donor sites, simultaneous and staged implant placement, machine and textured implant surface types, and prosthetic designs. The majority of maxillae were reconstructed with iliac bone grafts but cranial and rib grafts were also used. The reported SRs of implants in maxillary onlay bone grafts ranged from 73.3% to 100%. Lower implant survival was associated with a machined implant surface (73.3%–91%) or simultaneous graft-implant placement (73.8%–91%) compared with a staged approach (85.7%–100%) or textured surface implants (88.9%–100%). The prosthesis stability ranged from 75% to 100%. The marginal bone levels around the implants ranged from 1.49 to 4.80 mm.[3,13,36,49,51,52] Greater bone loss was associated with simultaneous implant placement and long conical neck machined implants.

Of the 16 studies included, which used the onlay bone augmentation technique for ridge augmentation, the weighted mean SR was 85.2% (95% confidence interval [CI] = 80.8%–88.8%, Fig 5). The *P* value was .01 with the chi-square test, which represented a moderate to high heterogeneity among studies.

GBR

Only two studies included scientific evidence for GBR. One study[60] included 14 patients with 75 implants. After 1 year of loading, an SR of 100% was seen in all groups (no graft, autogenous bone with anorganic bovine bone, or autogenous bone with bone ceramic). The other study[14] was a retrospective one including 26 patients with 5-year follow-up data, which compared iliac crest bone graft with demineralized freeze-dried bone allograft. The SR in iliac crest bone grafts was 96.1% compared with a 98.7% SR in demineralized freeze-dried bone allografts, with the differences between the two graft materials not significant.

These two studies that used the GBR technique were not included in the meta-analysis because their limited number precluded a meaningful meta-analysis.

Le Fort I Interpositional Grafting

Scientific evidence for Le Fort I interpositional grafting was included in 11 studies (seven retrospective case series, three prospective case series, and one prospective concurrent controlled study). These clinical studies included data from 250 patients with edentulous maxillae. Here, 1,588 implants with a follow-up of 1

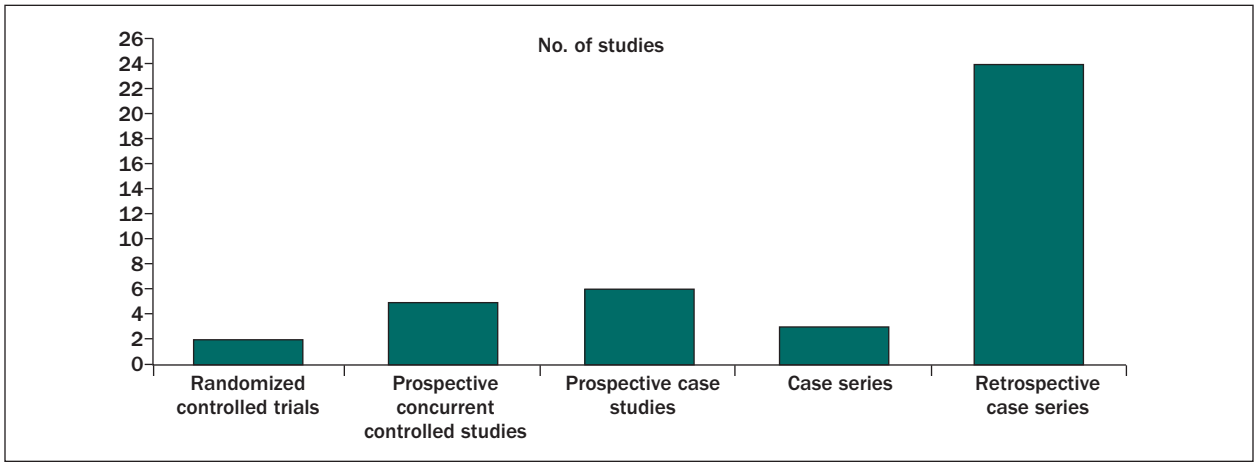


Fig 2 Bar chart representing the design of the studies included.

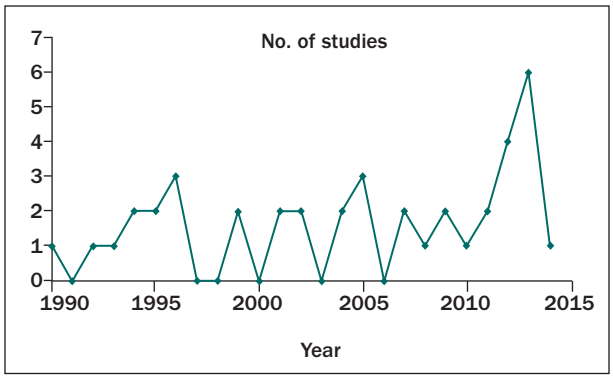


Fig 3 Line chart representing the year of publication of the studies included.

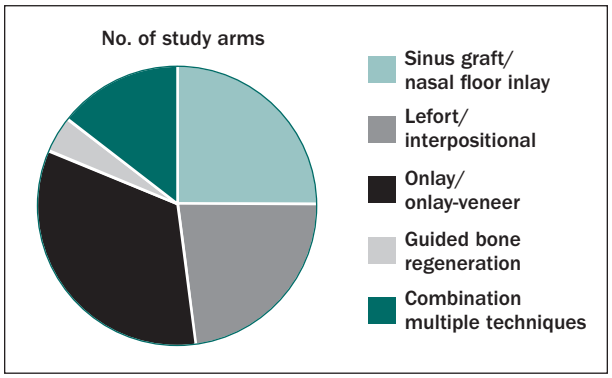


Fig 4 Circle chart representing the techniques studied in the current review.

to 12 years demonstrated an SR between 68.3% and 96.6%.[5–7,10,13,26,37,61–66] One study reported that greater implant failure rate was associated with shorter implant length.[37] Three studies compared the implant SR between the Le Fort I grafting technique and combination (onlay and sinus augmentation) technique, of which two studies[7,66] reported a higher implant SR for the combination technique. The prosthesis stability ranged from 75% to 100%. The marginal bone levels around the implants ranged from 0.3 to 3.1 mm.[5,10,61,64,65]

For studies using the Le Fort I interpositional grafting technique for ridge augmentation, the weighted mean SR was 89.6% (95% CI = 85.5%–92.7%; Fig 6). $P = .24$ with the chi-square test, which represented a low heterogeneity among studies.

Sinus Augmentation/Nasal Floor Inlay Grafting

Scientific evidence for sinus augmentation[18,31,43,56,67–71]/nasal floor inlay grafting[50,54,72] was provided by 12 studies. These clinical studies included data from 561 patients with edentulous maxillae with 4,860 implants. The follow-up period ranged from 1 to 11.5 years, and the implant SR ranged from 75.2% to 99.1%. The marginal bone level changes around the implants ranged from 0.43 to 4.2 mm.[43,67,69,71] Two studies compared implants placed in grafted vs nongrafted bone.[18,43] Of these two studies, Pieri et al[43] reported that grafted (posterior) vs native bone (anterior) comparisons showed 98.7% survival and success at 1 year (97.7% test and 100% control implants). Johansson et al[18] reported a cumulative implant success rate of 75.3% in grafted areas and 82.2% in nongrafted sites. Rickert et al[71] compared anorganic bovine bone with either bone marrow aspirate or autogenous bone and reported an implant SR of 91% vs 100%, respectively.[71] Another comparative study with anorganic bovine bone vs native bone demonstrated a 98.7% survival in the posterior maxilla (graft) compared with a 100% survival in the anterior maxilla (native bone).[31] Zinser et al[70] performed a regression analysis and summarized that significant implant failure predictors include the graft material used, residual crestal bone height, American Society of Anesthesiologists class, surgical technique, implant proximity, smoking, and age.

For the 12 studies using sinus augmentation and/or nasal floor inlay grafting techniques, the weighted mean SR was 91.5% (95% CI = 86.4%–94.8%; Fig 7). $P = .43$ with the chi-square test, which represented a low heterogeneity among studies.

Study	N	SR (%)	Lower Limit	Upper Limit	Weight %
Adell et al (1990)[49]	124	75.0	66.6	81.8	8.70
Isaksson (1994)[50]	47	83.0	69.5	91.3	6.40
Jemt and LeKholm (1995)[36]	801	85.9	83.3	88.1	9.76
Astrand et al (1996)[51]	92	75.0	65.2	82.8	8.28
Köndell et al (1996)[52]	75	73.3	62.2	82.1	8.03
Keller et al (1999)[39]	204	86.3	80.9	90.4	8.74
Widmark et al (2001)[53]	101	79.2	70.2	86.0	8.23
Becktor et al (2002)[54]	145	80.7	73.5	86.3	8.66
Nystrom et al (2002)[13]	177	74.6	67.7	80.5	9.10
Thor et al (2005)[55]	152	98.7	94.9	99.7	3.39
Wiltfang et al (2005)[56]	235	91.5	87.2	94.5	8.37
Contar et al (2009)[57]	51	100.0	86.3	100.0	1.17
Dahlin and Johansson (2011)[14]	13	96.1	59.8	99.8	1.13
Sbordone et al (2012)[3]	31	100.0	74.2	100.0	0.74
Mertens et al (2013a)[58]	99	88.9	81.1	93.7	7.26
Mertens et al (2013b)[59]	99	99.0	93.2	99.9	2.04
All	2,446	85.2	80.8	88.8	100.0

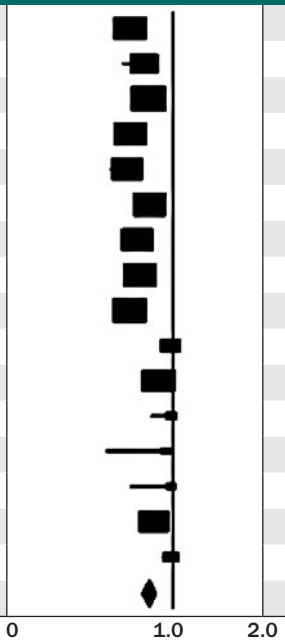


Fig 5 Forest plot representing the weighted mean SR of 85.2% (95% CI = 80.8%–88.8%) for the onlay bone grafting technique.

Study	N	SR (%)	Lower Limit	Upper Limit	Weight %
Isaksson et al (1993)[62]	41	w	52.7	80.6	9.65
Karekmanov (1995)[37]	225	86.6	81.5	90.5	11.85
Li et al (1996)[63]	139	82.0	74.7	87.5	11.48
Yerit et al (2004)[64]	324	91.0	87.4	93.7	11.87
Hallman et al (2005)[65]	156	90.4	84.7	94.1	10.69
Chiapasco et al (2007)[5]	281	94.5	91.1	96.6	10.85
Sjöström et al (2007)[10]	29	96.6	79.2	99.5	2.89
Nyström et al (2009)[61]	167	85.0	78.7	89.7	11.54
van der Mark et al (2011)[7]	54	94.4	84.1	98.2	6.06
De Santis et al (2012)[6]	124	95.2	89.7	97.8	8.32
Rasmusson et al (2012)[66]	48	95.8	84.8	98.9	4.80
All	1,588	89.6	85.5	92.7	100.0

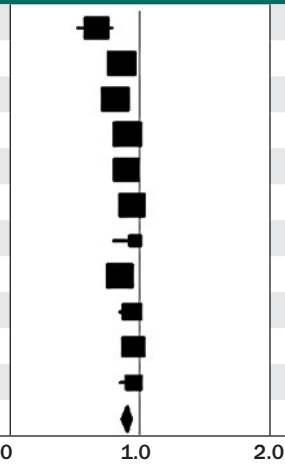


Fig 6 Forest plot representing the weighted mean SR of 89.6% (95% CI = 85.5%–92.7%) for Le Fort I interpositional grafting.

Combination Grafting

Scientific evidence for onlay-sinus graft or GBR-sinus graft was provided by six studies (three retrospective case series, two case series, and one prospective concurrent controlled study). These clinical studies included data from 166 patients who had edentulous maxillae with 963 implants and had follow-up periods of 19 to 72 months.

The reported implant SRs in the six studies ranged from 75.1% to 100%. One study reported[8] that implant SR in the grafted sites was 75.1% compared with 84% in nongrafts. Higher failure of implants was seen after onlay grafting (37%) compared with inlay grafting (24.9%), with a marginal bone loss of 3.3 mm in grafted bone vs 2.9 mm in native bone.[8] Another study[66] included three study groups that received the Le Fort I technique, onlay bone grafting in combination with sinus augmentation, and GBR in combination with sinus augmentation, and reported implant SRs of 95.8%, 94.7%, and 100%, respectively.

The meta-analysis of SR excluded the study group that received GBR in combination with sinus augmentation[66] because of the different study designs. The weighted mean SR was 93.6% (95% CI = 84.6%–97.5%; Fig 8). $P = .26$ with the chi-square test, which represented low heterogeneity among studies.

Study	N	SR (%)	Lower Limit	Upper Limit	Weight %
Isaksson (1994)[50]	36	86.1	70.7	94.1	7.49
Jensen et al (1994)[72]	152	88.8	82.7	92.9	9.01
Johansson et al (1999)[18]	129	75.2	67.0	81.9	9.29
Hising et al (2001)[67]	231	80.5	74.9	85.1	9.45
Becktor et al (2002)[54]	353	80.5	76.0	84.3	9.57
Wiltfang et al (2005)[56]	349	94.6	91.7	96.5	9.12
Chiapasco et al (2008)[68]	2,037	96.6	95.7	97.3	9.61
Scarano et al (2010)[69]	264	94.3	90.8	96.5	8.96
Pieri et al (2012)[43]	90	97.7	91.5	99.4	5.91
Hernández-Alfaro et al (2003)[31]	108	99.1	93.7	99.9	4.12
Zinser et al (2013)[70]	1,045	93.3	91.6	94.7	9.61
Rickert et al (2014)[71]	66	91.0	81.3	95.9	7.87
All	4,860	91.5	86.4	94.8	100.0

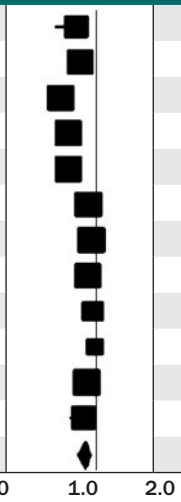


Fig 7 Forest plot representing the weighted mean SR of 91.5% (95% CI = 86.4%–94.8%) for sinus augmentation and/or nasal floor inlay grafting.

Study	N	SR (%)	Lower Limit	Upper Limit	Weight %
Becktor et al (2004)[8]	437	75.1	70.8	78.9	23.92
Sjöström et al (2007)[10]	163	88.3	82.4	92.4	22.88
van der Mark et al (2011)[7]	86	97.7	91.2	99.4	16.12
Rasmusson et al (2012)[66]	38	94.7	81.2	98.7	16.05
Castanga (2013)[111]	120	100.0	90.1	100.0	4.80
Cordaro et al (2013)[86]	81	97.5	90.6	99.4	16.23
All	925	93.6	84.6	97.5	100.0

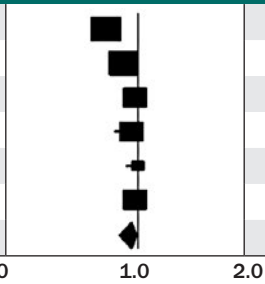


Fig 8 Forest plot representing the weighted mean SR of 93.6% (95% CI = 84.6%–97.5%) for the combination technique.

DISCUSSION

Systematic reviews carry the highest level of evidence to evaluate specific treatment protocols, and serve to make sense of a large body of literature.[48] In this review, implant survival was evaluated after bone grafting procedures were performed in edentulous maxillae for implant site development. Although a large body of literature exists, studies were not included if they were case reports, had fewer than 10 patients, or had follow-up periods of less than 1 year after implant loading.

Studies that met the inclusion criteria included those that performed sinus augmentation, onlay bone grafting, GBR, nasal floor grafting and Le Fort I interpositional grafting procedures. Most studies reported implant SRs comparable to those seen when bone grafting was not performed. Although dental implant survival was used in this systematic review to determine bone augmentation success, this evaluation criterion has several limitations. Implant failure can occur independent of augmentation success. Often the baseline situation of the patient (degree of atrophy, bone quality) is not identified in the study. As such, patients who require more complex augmentation techniques (severe atrophy) may have implant SRs that are lower than less demanding procedures. If the result of the augmentation is compromised, the implant size may have been modified to accommodate the conditions, unknown to the reader. If the graft failed, then no implants would have been placed. If the implant surface is not identified (eg, machined), a lower implant SR may be interpreted as having low augmentation success. In addition, implant survival may be a function of the residual native bone supporting the implant rather than the grafted bone.[73] Although there are disadvantages in relying on implant survival to measure augmentation success, this is one of the few parameters that gets consistently reported to allow comparison between studies.

Additional information determined from many studies included implant success, graft resorption, prosthetic success, marginal bone measurements, mean bone gain or loss after grafting, implant stability, patient satisfaction, cost analysis, surgical complications, medical risk factors, and peri-implant parameters such as bleeding, plaque index, and pocket depths. A large amount of data was obtained and analyzed, but few studies directly compared specific treatment protocols or grafting techniques, or had control groups. This makes it difficult to generalize to large patient populations or draw definitive conclusions.

It is well accepted that survival is higher when implants are placed in native bone.[8,17,43,74–76] However, when inadequate bone does not allow implants to be placed in the proper prosthetic position or even to be placed at all, it is unclear whether implant survival in those cases will be similar to implants placed in grafted bone. Even in cases with enough bone for implant placement, GBR may be performed on the buccal side of the ridge to augment a thin cortex or implant dehiscences or to improve esthetic outcomes.[43,60] A dehiscence or thin buccal plate can lead to bone resorption and soft tissue recession.[43]

The most predictable and well-documented bone grafting technique is maxillary sinus augmentation.[22–24,73] In the edentulous maxilla, pneumatization of the maxillary sinuses is common. In these cases, sinus augmentation can be performed alone or in combination with anterior grafting procedures such as onlay grafting and nasal floor augmentation.[8,37,67,71,77–79] Implant SRs in edentulous maxillae after sinus grafting are high, regardless of whether autogenous bone is used alone, in combination with xenograft, or xenograft alone.[9,67,71,77] This approach avoids the significant posterior cantilever of tilted anterior implants, the technical difficulties and complications of zygomatic and pterygoid implants, and the concern for lack of long-term data for both procedures.[28–30,53,80–82]

Maxillary sinus grafting and horizontal bone augmentation are predictable techniques associated with high implant SRs. Vertical ridge augmentation poses greater challenges. Although there are several methods for vertical augmentation, this review only investigated onlay bone grafting and interpositional grafts. Surgical complexity, donor site morbidity, graft stability under denture loading, graft resorption, and the degree of long-term fixation of implants in residual native bone are factors that need to be considered.[1,3,52] The use of a denture during onlay graft healing can cause wound dehiscence, graft displacement, graft resorption, and implant failure. Minimal use of the denture and a soft diet is encouraged until the graft becomes incorporated after 4 months. Higher implant failure has been observed when the edentulous maxilla is grafted against opposing natural dentition.[79]

Several factors may affect the amount of graft resorption during healing. Autogenous bone graft remodeling is necessary for incorporation to the osseous recipient site. Bone grafts inserted between osteotomized segments (interpositional grafts) resorb less than onlay grafts placed outside the bone contour.[83] Vertical bone grafts are more technically demanding and subject to greater volume loss than horizontal augmentations.[84] The osseous microarchitecture of the graft will also influence graft healing. Denser cortical grafts, from the calvarium or mandible, tend to resorb less than those containing a greater cancellous component, such as the iliac crest.[58,85,86] When using iliac bone, it may be prudent to overbuild the reconstructed ridge in anticipation of volume loss on healing. Reconstruction of the atrophic maxilla is usually staged with implant placement after graft healing to allow for remodeling. Enough time should elapse for graft incorporation, but implants should be inserted early enough to stimulate and maintain the regenerated bone.[87] Most studies report that the majority of the resorption occurs within the first year and is low thereafter.[85,88–90] Although the degree of iliac bone resorption can be variable and in some cases significant, it does not appear to be detrimental to long-term dental implant survival.[1,3,88,89,91] Several studies document minimal marginal bone loss after implant placement and loading in grafted sites.[53,92] This may be a factor of implant surface and/or design.[91,93]

The use of a barrier membrane, titanium mesh, or slow resorbing bone substitute has been suggested to protect onlay bone grafts from resorption. Although some studies have found that membranes have a positive influence on graft healing, others dispute their significance.[94,95] Titanium mesh maintains space but is usually used with particulate cancellous bone for ridge augmentation.[96] Bovine hydroxyapatite has been found to reduce graft loss when placed over and around autograft blocks.[97] As previously discussed, it is also important to limit graft loading by the upper complete or partial denture during graft healing.

Vertical augmentation continues to be one of the most challenging problems in implant dentistry today. Therefore alternative therapies continue to be investigated to avoid classic onlay grafting, such as distraction osteogenesis, interpositional graft, and growth factors with titanium mesh or other rigid scaffolds. Several studies on maxillary onlay autogenous bone grafts report lower implant SRs. Several variables can account for this finding. The most significant is the use of machined surface dental implants. During the developmental and early routine periods of reconstructing the severely atrophic maxilla, machined surface implants (Brånemark) were used with iliac bone grafts.[25,36] The lower survival of machined surface implants in the

maxilla and poorer quality bone is well documented.[19,36,98] The use of textured surface implants in onlay bone grafts can provide implant SRs similar to those seen in native bone.[99] Along with implant survival, crestal bone resorption also varies in machined vs enhanced implant surfaces. Studies show large variability, ranging from 0.04 to 2.7 mm with different implant macro- and microdesigns.[9,100,101] Most crestal bone loss occurs within the first year of function, and may be lower with rough surface implants.[98,102]

Simultaneous placement of dental implants in maxillary block autografts also has a much lower SR than staged insertion after graft healing (79.3% vs 93.4%).[103] This approach was used initially in an attempt to fix the bone graft, decrease the number of surgeries, and shorten treatment length. A staged technique is preferred, allowing the bone graft to remodel and incorporate before implant insertion. The type of bone graft and its inherent quality can also influence implant survival. Bone harvested from the iliac crest has a thin outer cortex and a thicker cancellous layer. Bone grafts from the calvarium or mandibular donor sites are mainly cortical and denser. Implant survival in calvarial and mandibular bone grafts is often higher than iliac bone augmentations.[58,99] Many of the early studies on maxillary reconstruction used machined implants placed simultaneous with iliac bone grafts—a combination of variables that often produced poor results. Contemporary protocols for managing the atrophic maxilla typically involve onlay bone grafting followed by the placement of moderately rough surface implants 4 to 6 months later.

Onlay grafting has been shown to improve implant survival in long-term studies.[36] Depending on the skeletal relationship and maxillary resorption pattern, onlay or inlay (interpositional) grafts may be performed.[26] Le Fort I interpositional grafting addresses both bone volume and interarch relationship problems that are common in the long-term edentulous patient, but pose significant challenges such as hospitalization, long operating time, general anesthesia, and usually a secondary site for autogenous bone harvest.[104] In addition, implant SRs are often less than ideal, ranging from 81% to 98.5%.[6,10,36,49,104] These higher SRs may be the result of enhanced implant surfaces.[6,9,105,106]

Results from the present systematic review demonstrate the challenges in treating the atrophic edentulous maxilla. Bone grafting, including all techniques described herein, is an effective way to provide adequate support for prosthetically driven implant placement. Although studies from almost 30 years ago exist, some with long-term follow-up, it is still difficult to draw definitive conclusions. Several additional surgical procedures did not have adequate publications that fit the inclusion criteria. Bone augmentation may also be performed with protected bone regeneration using scaffold techniques (ie, titanium mesh grafting), horizontal ridge expansion (splitting), and distraction osteogenesis. One major limitation of this systematic review is the lack of uniform data reporting in published studies. In general, implant SR per implant is reported rather than implant survival per patient. With this method of reporting, each implant is counted individually, whereas each patient should be counted individually. Of course this would significantly decrease the SR, and would make it difficult to compare results with those found in existing literature. However, it would give a more accurate and statistically meaningful representation of implant failure. Moreover, most studies still report implant survival and not success. Just as previous systematic reviews on bone grafting for implant placement have concluded, implant survival that shows the implant to be simply in the mouth is not adequate information for clinicians or patients. Increased demands on marginal bone levels, function, and esthetics, just to mention a few parameters, are generally not included in the literature.[73] It is important to go beyond survival to include basic success criteria, such as absence of pain, dysesthesia, paresthesia, subjective complaints, absence of infection with suppuration, absence of implant mobility, absence of continuous radiolucency around the implant, and bone loss of less than 1.5 mm in the first year followed by 0.2 mm per year.[107,108]

Follow-up data are also extremely important when evaluating the implant literature. Many studies, especially those describing the more recently developed techniques, do not have the same stringent criteria or follow-up time. Because most of the bone graft resorption associated with many grafting techniques occurs during the first 12 to 24 months,[10,26,79] a 12-month period was chosen as the minimum implant follow-up point. As we delved more into the full texts of the articles included, it was often difficult to decipher which patients and which implants failed in the specific treatment groups. This was especially challenging when studies included both completely and partially edentulous patients. These methodologic issues are well known in the implant literature, and have previously been identified.[73,109,110] Many studies followed patients for several years and contained important information on long-term implant survival. However, because these implants were placed in the 1980s, 1990s, or early 2000s, machined surface implants were used. Most implants placed today contain enhanced or roughened surfaces, therefore the results may not apply directly to our current practices. This is not surprising, however, because the field of implant dentistry and related technology and procedures are always evolving.

CONCLUSIONS

Within the limitations of this systematic review and analysis, all five treatment modalities discussed here, such as onlay bone grafting, GBR, Le Fort I interpositional grafting, maxillary sinus augmentation, and/or nasal floor inlay grafting or the combination approach can be successfully used to augment edentulous maxillary ridge with high implant SRs.

ACKNOWLEDGMENTS

The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the article. The authors reported no conflicts of interest related to this study.

REFERENCES

1. Dasmah A, Thor A, Ekestubbe A, Sennerby L, Rasmusson L. Particulate vs. block bone grafts: Three-dimensional changes in graft volume after reconstruction of the atrophic maxilla, a 2-year radiographic follow-up. J Craniomaxillofac Surg 2012;40:654–659.
2. Acocella A, Bertolai R, Ellis E 3rd, Nissan J, Sacco R. Maxillary alveolar ridge reconstruction with monocortical fresh-frozen bone blocks: A clinical, histological and histomorphometric study. J Craniomaxillofac Surg 2012;40:525–533.
3. Sbordone C, Toti P, Guidetti F, et al. Volume changes of iliac crest autogenous bone grafts after vertical and horizontal alveolar ridge augmentation of atrophic maxillas and mandibles: A 6-year computerized tomographic follow-up. J Oral Maxillofac Surg 2012;70:2559–2565.
4. Jemt T, Johansson J. Implant treatment in the edentulous maxillae: A 15-year follow-up study on 76 consecutive patients provided with fixed prostheses. Clin Implant Dent Relat Res 2006;8:61–69.
5. Chiapasco M, Brusati R, Ronchi P. Le Fort I osteotomy with interpositional bone grafts and delayed oral implants for the rehabilitation of extremely atrophied maxillae: A 1-9-year clinical follow-up study on humans. Clin Oral Implants Res 2007;18:74–85.
6. De Santis D, Trevisiol L, D'Agostino A, et al. Guided bone regeneration with autogenous block grafts applied to Le Fort I osteotomy for treatment of severely resorbed maxillae: A 4- to 6-year prospective study. Clin Oral Implants Res 2012;23:60–69.
7. van der Mark EL, Bierenbroodspot F, Baas EM, de Lange J. Reconstruction of an atrophic maxilla: Comparison of two methods. Br J Oral Maxillofac Surg 2011;49:198–202.
8. Becktor JP, Isaksson S, Sennerby L. Survival analysis of endosseous implants in grafted and nongrafted edentulous maxillae. Int J Oral Maxillofac Implants 2004;19:107–115.
9. De Bruyn H, Bouvry P, Collaert B, et al. Long-term clinical, microbiological, and radiographic outcomes of Brånemark implants installed in augmented maxillary bone for fixed full-arch rehabilitation. Clin Implant Dent Relat Res 2013;15:73–82.10.
10. Sjöström M, Sennerby L, Nilson H, Lundgren S. Reconstruction of the atrophic edentulous maxilla with free iliac crest grafts and implants: A 3-year report of a prospective clinical study. Clin Implant Dent Relat Res 2007;9:46–59.
11. Tallgren A. The continuing reduction of the residual alveolar ridges in complete denture wearers: A mixed-longitudinal study covering 25 years. J Prosthet Dent 1972;27:120–132.
12. Cawood JI, Howell RA. A classification of the edentulous jaws. Int J Oral Maxillofac Surg 1988;17:232–236.
13. Nyström E, Ahlqvist J, Legrell PE, Kahnberg KE. Bone graft remodelling and implant success rate in the treatment of the severely resorbed maxilla: A 5-year longitudinal study. Int J Oral Maxillofac Surg 2002;31:158–164.
14. Dahlin C, Johansson A. Iliac crest autogenous bone graft versus alloplastic graft and guided bone regeneration in the reconstruction of atrophic maxillae: A 5-year retrospective study on cost-effectiveness and clinical outcome. Clin Implant Dent Relat Res 2011;13:305–310.
15. Moy PK, Medina D, Shetty V, Aghaloo TL. Dental implant failure rates and associated risk factors. Int J Oral Maxillofac Implants 2005;20:569–577.
16. Jemt T, Book K, Linden B, Urde G. Failures and complications in 92 consecutively inserted overdentures supported by Brånemark implants in severely resorbed edentulous maxillae: A study from prosthetic treatment to first annual check-up. Int J Oral Maxillofac Implants 1992;7:162–167.
17. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. Eur J Oral Sci 1998;106:721–764.
18. Johansson B, Wannfors K, Ekenbäck J, Smedberg JI, Hirsch J. Implants and sinus-inlay bone grafts in a 1-stage procedure on severely atrophied maxillae: Surgical aspects of a 3-year follow-up study. Int J Oral Maxillofac Implants 1999;14:811–818.
19. Jaffin RA, Berman CL. The excessive loss of Brånemark fixtures in type IV bone: A 5-year analysis. J Periodontol.1991;62:2–4.
20. Cawood JI, Howell RA. Reconstructive preprosthetic surgery. I. Anatomical considerations. Int J Oral Maxillofac Surg 1991;20:75–82.
21. Yamamichi N, Itose T, Neiva R, Wang HL. Long-term evaluation of implant survival in augmented sinuses: A case series. Int J Periodontics Restorative Dent 2008;28:163–169.
22. Jensen OT, Shulman LB, Block MS, Iacono VJ. Report of the Sinus Consensus Conference of 1996. Int J Oral Maxillofac Implants 1998;13 Suppl:11–45.
23. Wallace SS, Froum SJ. Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review. Ann Periodontol 2003;8:328–343.
24. Del Fabbro M, Testori T, Francetti L, Weinstein R. Systematic review of survival rates for implants placed in the grafted maxillary sinus. Int J Periodontics Restorative Dent 2004;24:565–577.
25. Nystrom E, Kahnberg KE, Gunne J. Bone grafts and Brånemark implants in the treatment of the severely resorbed maxilla: A 2-year longitudinal study. Int J Oral Maxillofac Implants 1993;8:45–53.
26. Nyström E, Nilson H, Gunne J, Lundgren S. A 9–14 year follow-up of onlay bone grafting in the atrophic maxilla. Int J Oral Maxillofac Surg 2009;38:111–116.
27. Cricchio G, Lundgren S. Donor site morbidity in two different approaches to anterior iliac crest bone harvesting. Clin Implant Dent Relat Res 2003;5:161–169.
28. Shackleton JL, Carr L, Slabbert JC, Becker PJ. Survival of fixed implant-supported prostheses related to cantilever lengths. J Prosthet Dent 1994;71:23–26.
29. Rosén A, Gynther G. Implant treatment without bone grafting in edentulous severely resorbed maxillas: A long-term follow-up study. J Oral Maxillofac Surg 2007;65:1010–1016.
30. Maló P, Rangert B, Nobre M. All-on-4 immediate-function concept with Brånemark System implants for completely edentulous maxillae: A 1-year retrospective clinical study. Clin Implant Dent Relat Res 2005;7 Suppl 1:S88–S94.
31. Hernández-Alfaro F, Sancho-Puchades M, Guijarro-Martinez R. Total reconstruction of the atrophic maxilla with intraoral bone grafts and biomaterials: A prospective clinical study with cone beam computed tomography validation. Int J Oral Maxillofac Implants 2013;28:241–251.
32. Chrcanovic BR, Abreu MH. Survival and complications of zygomatic implants: A systematic review. Oral Maxillofac Surg.2013;17:81–93.
33. Monje A, Chan HL, Fu JH, et al. Are short dental implants (<10 mm) effective? A meta-analysis on prospective clinical trials. J Periodontol 2013;84:895–904.
34. Monje A, Fu JH, Chan HL, et al. Do implant length and width matter for short dental implants (<10 mm)? A meta-analysis of prospective studies. J Periodontol 2013;84:1783–1791.

35. Herrmann I, Lekholm U, Holm S, Kultje C. Evaluation of patient and implant characteristics as potential prognostic factors for oral implant failures. Int J Oral Maxillofac Implants 2005;20:220–230.
36. Jemt T, Lekholm U. Implant treatment in edentulous maxillae: A 5-year follow-up report on patients with different degrees of jaw resorption. Int J Oral Maxillofac Implants 1995;10:303–311.
37. Krekmanov L. A modified method of simultaneous bone grafting and placement of endosseous implants in the severely atrophic maxilla. Int J Oral Maxillofac Implants 1995;10:682–688.
38. Keller EE, Tolman DE, Eckert S. Surgical-prosthodontic reconstruction of advanced maxillary bone compromise with autogenous onlay block bone grafts and osseointegrated endosseous implants: A 12-year study of 32 consecutive patients. Int J Oral Maxillofac Implants 1999;14:197–209.
39. Keller EE, Tolman DE, Eckert SE. Maxillary antral-nasal inlay autogenous bone graft reconstruction of compromised maxilla: A 12-year retrospective study. Int J Oral Maxillofac Implants 1999;14:707–721.
40. Sennerby L, Roos J. Surgical determinants of clinical success of osseointegrated oral implants: A review of the literature. Int J Prosthodont 1998;11:408–420.
41. Arisan V, Bölükbaşi N, Ersanli S, Ozdemir T. Evaluation of 316 narrow diameter implants followed for 5–10 years: A clinical and radiographic retrospective study. Clin Oral Implants Res 2010;21:296–307.
42. Neldam CA, Pinholt EM. State of the art of short dental implants: A systematic review of the literature. Clin Implant Dent Relat Res 2012;14:622–632.
43. Pieri F, Aldini NN, Fini M, Marchetti C, Corinaldesi G. Immediate fixed implant rehabilitation of the atrophic edentulous maxilla after bilateral sinus floor augmentation: A 12-month pilot study. Clin Implant Dent Relat Res 2012;14 Suppl 1:e67–e82.
44. Renouard F, Nisand D. Short implants in the severely resorbed maxilla: A 2-year retrospective clinical study. Clin Implant Dent Relat Res 2005;7 Suppl 1:S104–S110.
45. Corrente G, Abundo R, des Ambrois AB, Savio L, Perelli M. Short porous implants in the posterior maxilla: A 3-year report of a prospective study. Int J Periodontics Restorative Dent.2009;29:23–29.
46. Khoshkam V, Chan HL, Lin GH, et al. Reconstructive procedures for treating peri-implantitis: A systematic review. J Dent Res 2013;92:131S–138S.
47. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. J Clin Epidemiol 2009;151:W65–W94.
48. Grimes DA, Schulz KF. An overview of clinical research: The lay of the land. Lancet 2002;359:57–61.
49. Adell R, Lekholm U, Gröndahl K, et al. Reconstruction of severely resorbed edentulous maxillae using osseointegrated fixtures in immediate autogenous bone grafts. Int J Oral Maxillofac Implants 1990;5:233–246.
50. Isaksson S. Evaluation of three bone grafting techniques for severely resorbed maxillae in conjunction with immediate endosseous implants. Int J Oral Maxillofac Implants 1994;9:679–688.
51. Astrand P, Nord PG, Brånemark PI. Titanium implants and onlay bone graft to the atrophic edentulous maxilla: A 3-year longitudinal study. Int J Oral Maxillofac Surg 1996;25:25–29.
52. Köndell PA, Nordenram A, Moberg LE, Eliasson S, Nyberg B. Reconstruction of the resorbed edentulous maxilla using autogenous rib grafts and osseointegrated implants. Clin Oral Implants Res 1996;7:286–290.
53. Widmark G, Andersson B, Carlsson GE, Lindvall AM, Ivanoff CJ. Rehabilitation of patients with severely resorbed maxillae by means of implants with or without bone grafts: A 3- to 5-year follow-up clinical report. Int J Oral Maxillofac Implants 2001;16:73–79.
54. Becktor JP, Eckert SE, Isaksson S, Keller EE. The influence of mandibular dentition on implant failures in bone-grafted edentulous maxillae. Int J Oral Maxillofac Implants 2002;17:69–77.
55. Thor A, Wannfors K, Sennerby L, Rasmusson L. Reconstruction of the severely resorbed maxilla with autogenous bone, platelet-rich plasma, and implants: 1-year results of a controlled prospective 5-year study. Clin Implant Dent Relat Res 2005;7:209–220.
56. Wiltfang J, Schultze-Mosgau S, Nkenke E, et al. Onlay augmentation versus sinuslift procedure in the treatment of the severely resorbed maxilla: A 5-year comparative longitudinal study. Int J Oral Maxillofac Surg 2005;34:885–889.
57. Contar CM, Sarot JR, Bordini J Jr, et al. Maxillary ridge augmentation with fresh-frozen bone allografts. J Oral Maxillofac Surg 2009;67:1280–1285.
58. Mertens C, Decker C, Seeberger R, et al. Early bone resorption after vertical bone augmentation--a comparison of calvarial and iliac grafts. Clin Oral Implants Res.2013;24:820–825.
59. Mertens C, Steveling HG, Seeberger R, Hoffmann J, Freier K. Reconstruction of severely atrophied alveolar ridges with calvarial onlay bone grafts and dental implants. Clin Implant Dent Relat Res 2013;15:673–683.
60. Van Assche N, Michels S, Naert I, Quirynen M. Randomized controlled trial to compare two bone substitutes in the treatment of bony dehiscences. Clin Implant Dent Relat Res 2013;15:558–568.
61. Nyström E, Nilson H, Gunne J, Lundgren S. Reconstruction of the atrophic maxilla with interpositional bone grafting/Le Fort I osteotomy and endosteal implants: A 11–16 year follow-up. Int J Oral Maxillofac Surg 2009;38:1–6.
62. Isaksson S, Ekfeldt A, Alberius P, Blomqvist JE. Early results from reconstruction of severely atrophic (Class VI) maxillas by immediate endosseous implants in conjunction with bone grafting and Le Fort I osteotomy. Int J Oral Maxillofac Surg 1993;22:144–148.
63. Li KK, Stephens WL, Gliklich R. Reconstruction of the severely atrophic edentulous maxilla using Le Fort I osteotomy with simultaneous bone graft and implant placement. J Oral Maxillofac Surg 1996;54:542–546; discussion 547.
64. Yerit KC, Posch M, Hainich S, et al. Long-term implant survival in the grafted maxilla: Results of a 12-year retrospective study. Clin Oral Implants Res 2004;15:693–699.
65. Hallman M, Mordenfeld A, Strandkvist T. A retrospective 5-year follow-up study of two different titanium implant surfaces used after interpositional bone grafting for reconstruction of the atrophic edentulous maxilla. Clin Implant Dent Relat Res 2005;7:121–126.
66. Rasmusson L, Thor A, Sennerby L. Stability evaluation of implants integrated in grafted and nongrafted maxillary bone: A clinical study from implant placement to abutment connection. Clin Implant Dent Relat Res 2012;14:61–66.
67. Hising P, Bolin A, Branting C. Reconstruction of severely resorbed alveolar ridge crests with dental implants using a bovine bone mineral for augmentation. Int J Oral Maxillofac Implants 2001;16:90–97.
68. Chiapasco M, Zaniboni M, Rimondini L. Dental implants placed in grafted maxillary sinuses: A retrospective analysis of clinical outcome according to the initial clinical situation and a proposal of defect classification. Clin Oral Implants Res 2008;19:416–428.
69. Scarano A, Piattelli A, Assenza B, et al. Porcine bone used in sinus augmentation procedures: A 5-year retrospective clinical evaluation. J Oral Maxillofac Surg 2010;68:1869–1873.
70. Zinser MJ, Randelzhofer P, Kuiper L, Zöller JE, De Lange GL. The predictors of implant failure after maxillary sinus floor augmentation and reconstruction: A retrospective study of 1045 consecutive implants. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;115:571–582.
71. Rickert D, Vissink A, Slot WJ, et al. Maxillary sinus floor elevation surgery with BioOss(R) mixed with a bone marrow concentrate or autogenous bone: Test of principle on implant survival and clinical performance. Int J Oral Maxillofac Surg 2014;43:243–247.
72. Jensen J, Sindet-Pedersen S, Oliver AJ. Varying treatment strategies for reconstruction of maxillary atrophy with implants: Results in 98 patients. J Oral Maxillofac Surg 1994;52:210–216; discussion 216–218.
73. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? Int J Oral Maxillofac Implants 2007;22 Suppl:49–70.

74. Lekholm U, Wannfors K, Isaksson S, Adielsson B. Oral implants in combination with bone grafts. A 3-year retrospective multicenter study using the Brånemark implant system. Int J Oral Maxillofac Surg 1999;28:181–187.
75. Pjetursson BE, Tan K, Lang NP, et al. A systematic review of the survival and complication rates of fixed partial dentures (FPDs) after an observation period of at least 5 years. Clin Oral Implants Res 2004;15:625–642.
76. Haas R, Polak C, Fürhauser R, et al. A long-term follow-up of 76 Bränemark single-tooth implants. Clin Oral Implants Res 2002;13:38–43.
77. Lorenzoni M, Pertl C, Wegscheider W, et al. Retrospective analysis of Frialit-2 implants in the augmented sinus. Int J Periodontics Restorative Dent 2000;20:255–267.
78. Belträo GC, de Abreu AT, Belträo RG, Finco NF. Lateral cephalometric radiograph for the planning of maxillary implant reconstruction. Dentomaxillofac Radiol 2007;36:45–50.
79. Becktor JP, Rebellato J, Becktor KB, et al. Transverse displacement of the proximal segment after bilateral sagittal osteotomy. J Oral Maxillofac Surg 2002;60:395–403.
80. Fernández H, Gómez-Delgado A, Trujillo-Saldarriaga S, Varón-Cardona D, Castro-Núñez J. Zygomatic implants for the management of the severely atrophied maxilla: A retrospective analysis of 244 implants. J Oral Maxillofac Surg 2014;72:887–891.
81. Goiato MC, Pellizzer EP, Moreno A, et al. Implants in the zygomatic bone for maxillary prosthetic rehabilitation: A systematic review. Int J Oral Maxillofac Surg 2014;43:748–757.
82. Bidra AS, Huynh-Ba G. Implants in the pterygoid region: A systematic review of the literature. Int J Oral Maxillofac Surg 2011;40:773–781.
83. Motoki DS, Mulliken JB. The healing of bone and cartilage. Clin Plast Surg 1990;17:527–544.
84. Rocchietta I, Fontana F, Simion M. Clinical outcomes of vertical bone augmentation to enable dental implant placement: A systematic review. J Clin Periodontol 2008;35:203–215.
85. Carinci F, Farina A, Zanetti U, et al. Alveolar ridge augmentation: A comparative longitudinal study between calvaria and iliac crest bone grafts. J Oral Implantol 2005;31:39–45.
86. Cordaro L, Torsello F, Mirisola di Torresanto V, Baricevic M. Rehabilitation of an edentulous atrophic maxilla with four unsplinted narrow diameter titanium-zirconium implants supporting an overdenture. Quintessence Int 2013;44:37–43.
87. Nelson K, Ozyuvaci H, Bilgic B, Klein M, Hildebrand D. Histomorphometric evaluation and clinical assessment of endosseous implants in iliac bone grafts with shortened healing periods. Int J Oral Maxillofac Implants 2006;21:392–398.
88. Schmitt CM, Moest T, Lutz R, Neukam FW, Schlegel KA. Anorganic bovine bone (ABB) vs. autologous bone (AB) plus ABB in maxillary sinus grafting. A prospective non-randomized clinical and histomorphometrical trial. Clin Oral Implants Res 2014. (epub ahead of print).
89. Reinert S, König S, Bremerich A, Eufinger H, Krimmel M. Stability of bone grafting and placement of implants in the severely atrophic maxilla. Br J Oral Maxillofac Surg 2003;41:249–255.
90. Johansson B, Grepe A, Wannfors K, Hirsch JM. A clinical study of changes in the volume of bone grafts in the atrophic maxilla. Dentomaxillofac Radiol 2001;30:157–161.
91. Nyström E, Ahlqvist J, Gunne J, Kahnberg KE. 10-year follow-up of onlay bone grafts and implants in severely resorbed maxillae. Int J Oral Maxillofac Surg 2004;33:258–262.
92. Barone A, Toti P, Quaranta A, Derchi G, Covani U. The Clinical Outcomes of Immediate Versus Delayed Restoration Procedures on Immediate Implants: A Comparative Cohort Study for Single-Tooth Replacement. Clin Implant Dent Relat Res 2014.(epub ahead of print).
93. Chiapasco M, Casentini P, Zaniboni M. Implants in reconstructed bone: A comparative study on the outcome of Straumann tissue level and bone level implants placed in vertically deficient alveolar ridges treated by means of autogenous onlay bone grafts. Clin Implant Dent Relat Res 2014;16:32–50.
94. Gielkens PF, Bos RR, Raghoebar GM, Stegenga B. Is there evidence that barrier membranes prevent bone resorption in autologous bone grafts during the healing period? A systematic review. Int J Oral Maxillofac Implants 2007;22:390–398.
95. Heberer S, Ruhe B, Krekeler L, et al. A prospective randomized split-mouth study comparing iliac onlay grafts in atrophied edentulous patients: Covered with periosteum or a bioresorbable membrane. Clin Oral Implants Res 2009;20:319–326.
96. Louis PJ, Gutta R, Said-Al-Naief N, Bartolucci AA. Reconstruction of the maxilla and mandible with particulate bone graft and titanium mesh for implant placement. J Oral Maxillofac Surg 2008;66:235–245.
97. Cordaro L, Torsello F, Morcavallo S, di Torresanto VM. Effect of bovine bone and collagen membranes on healing of mandibular bone blocks: A prospective randomized controlled study. Clin Oral Implants Res 2011;22:1145–1150.
98. Adell R, Lekholm U, Rockler B, Brånemark PI. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg 1981;10:387–416.
99. Chiapasco M, Casentini P, Zaniboni M. Bone augmentation procedures in implant dentistry. Int J Oral Maxillofac Implants 2009;24 Suppl:237–259.
100. Blanes RJ, Bernard JP, Blanes ZM, Belser UC. A 10-year prospective study of ITI dental implants placed in the posterior region. I: Clinical and radiographic results. Clin Oral Implants Res 2007;18:699–706.
101. Cehreli MC, Karasoy D, Kökat AM, Akça K, Eckert S. A systematic review of marginal bone loss around implants retaining or supporting overdentures. Int J Oral Maxillofac Implants.2010;25:266–277.
102. Schwarz F, Herten M, Bieling K, Becker J. Crestal bone changes at nonsubmerged implants (Camlog) with different machined collar lengths: A histomorphometric pilot study in dogs. Int J Oral Maxillofac Implants 2008;23:335–342.
103. Chiapasco M, Zaniboni M, Boisco M. Augmentation procedures for the rehabilitation of deficient edentulous ridges with oral implants. Clin Oral Implants Res 2006;17 Suppl 2:136–159.
104. Chiapasco M, Zaniboni M, Rimondini L. Autogenous onlay bone grafts vs. alveolar distraction osteogenesis for the correction of vertically deficient edentulous ridges: A 2-4-year prospective study on humans. Clin Oral Implants Res.2007;18:432–440.
105. Pinholt EM. Brånemark and ITI dental implants in the human bone-grafted maxilla: A comparative evaluation. Clin Oral Implants Res 2003;14:584–592.
106. Cosyn J, Vandenbulcke E, Browaeys H, Van Maele G, De Bruyn H. Factors associated with failure of surface-modified implants up to four years of function. Clin Implant Dent Relat Res 2012;14:347–358.
107. Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: A review and proposed criteria of success. Int J Oral Maxillofac Implants 1986;1:11–25.
108. Weyant RJ, Burt BA. An assessment of survival rates and within-patient clustering of failures for endosseous oral implants. J Dent Res 1993;72:2–8.
109. Coulthard P, Esposito M, Jokstad A, Worthington HV. Interventions for replacing missing teeth: Bone augmentation techniques for dental implant treatment. Cochrane Database Syst Rev 2003:CD003607.
110. Esposito M, Coulthard P, Worthington HV, Jokstad A. Quality assessment of randomized controlled trials of oral implants. Int J Oral Maxillofac Implants 2001;16:783–792.
111. Castagna, L, Polido WD, Soares LG, Tinoco EM. Tomographic evaluation of iliac crest bone grafting and the use of immediate temporary implants to the atrophic maxilla. Int J Oral Maxillofac Surg 2013;42:1067–1072.

Clinical Practice Guidelines: Role of Bone Augmentation for Implant Placement in the Edentulous Maxilla

INTRODUCTION

The management of edentulous patients with dental implants has become a common and well-accepted treatment modality.[1] When implant-supported prosthetic alternatives are considered, the clinician must evaluate the patient for adequate bone volume for implant placement in the desired locations. The success of implant procedures and maintenance of long-term stability are directly related to the quality and quantity of the supporting bone.[2] When the residual ridge lacks the necessary bone volume for proper implant placement, bone augmentation procedures may be employed. A variety of surgical procedures and augmentation materials have been developed and utilized to manage osseous deficiencies.

The edentulous maxilla may pose unique anatomical challenges for the clinician. Following tooth extraction, the greatest loss of bone in the maxilla occurs facially.[3,4] As a result, the atrophic residual ridge is often palatal to the prosthetic tooth position. Efforts to reconstruct the atrophic maxilla to its original form will often require buccal bone augmentation. The patient's use of a complete denture will contribute to continuing medial resorption as well as loss of vertical bone height over time.[5] After years of denture wear, the atrophic ridge may not have adequate bone volume for dental implant placement. Maxillary ridge resorption may also create unfavorable transverse relationships with the opposing mandibular dentition. In addition to atrophy, bone may be lost from severe periodontitis, infection, trauma, congenital deformities, impacted teeth, pathology, and even dental implant failures. Pneumatization of the maxillary sinuses can compromise the amount of available bone for implant placement in the posterior maxilla. The nasal cavity and nasopalatine canal may limit anterior implant insertion. The maxillary bone is often less dense than the mandible, especially in the posterior regions below the sinuses.[6]

It is important to define the prosthetic goals of treatment prior to the maxillary reconstruction. The design of the final prosthesis determines the number of implants required and their ideal positions. If there is inadequate available bone for implant placement in the preferred locations, then bone augmentation is considered. The choice of a particular augmentation technique will depend on several factors, including the degree of bone loss, the size and morphology of the osseous defect, the location in the mouth, the design of the prosthesis, and clinician or patient preferences. The surgeon should strive to select a method that offers predictable results for the presenting clinical situation and provides osseous support for long-term implant and prosthetic function.

PURPOSE

These Clinical Practice Guidelines were developed by a volunteer task force group of the Academy of Osseointegration. Group 1 specifically examined the topic of bone augmentation for dental implant site development in the edentulous atrophic maxilla. The Clinical Practice Guidelines were based on a systematic review of the current dental literature, clinical information, and accepted approaches to the treatment of the edentulous atrophic maxilla with bone augmentation techniques. These Clinical Practice Guidelines are intended to provide clinicians with current thoughts and recommendations on the management of the edentulous atrophic maxilla requiring bone augmentation for dental implant placement. The guidelines may also be used as an educational tool to assist dentists and students in treatment choices, and is an effort to improve the quality and efficiency of patient care. These guidelines can assist practitioners not only in making clinical decisions about their patients, but also in describing to patients why the chosen treatment represents the preferred course of action.

TARGET CONDITIONS

This document focuses on the edentulous atrophic maxilla requiring bone augmentation for dental implant placement. A clinical and radiographic examination is necessary to assess the atrophic maxilla. Computed tomography is an invaluable tool to visualize maxillary anatomy and three-dimensionally

doi: 10.11607/jomi.16suppl.g1.cpg

diagnose the degree of osseous atrophy.[7] There have been several classification systems proposed to describe the progressive stages of atrophy of the edentulous jaws.[3,6,8,9] Although some of these classifications centered around osseous conditions for implant treatment, they have limitations as dental implant designs and surgical approaches to the atrophic jaw have evolved.[8,9] The Cologne Classification of Alveolar Ridge Defects is an anatomical- and therapeutic-based system for making treatment decisions regarding bone augmentation.[10] Another recent site and jaw classification has been proposed for immediate implant placement and loading based on specific cortical bone sites in the facial skeleton.[11]

It is somewhat difficult to define specific dimensions that constitute insufficient bone volume for dental implant placement and need for bone augmentation. Dental implants are available in various diameters, lengths, and designs. When reduced bone dimensions are present, the surgeon may select a smaller diameter or shorter implant to accommodate these conditions or even place fewer implants. However, maxillary ridge resorption may create unfavorable transverse relationships with the opposing mandibular dentition. In the edentulous maxilla, the clinician must weigh concerns for adequate biomechanical support as well as long-term implant and prosthetic stability. Although there is usually less need for bone augmentation to address esthetic demands in the edentulous maxilla, this may also be a concern in some cases. Therefore, inadequate available bone may be defined as the inability to place the preferred implant size in the planned position for esthetics, prosthetic support, and/or long-term function.

These guidelines may not apply to patients with medical conditions or local factors that may contraindicate surgery and/or compromise wound healing. Systemic conditions may include uncontrolled diabetes, immunodeficiency, advanced renal or hepatic disease, blood dyscrasias, and severe bleeding disorders, as well as others.[12,13] Recent myocardial infarction, cerebral vascular incident, or Class IV status (American Society of Anesthesiologists) may contraindicate surgery.[14] Patients receiving antiresorptive (bisphosphonates) or antiangiogenic therapy, chemotherapy, or immunosuppressive drugs may also be poor candidates for bone augmentation procedures.[12,15] In addition, noncompliant patients with psychologic or mental disorders and patients with present drug or alcohol abuse problems may not be good candidates for surgical therapy.[12] There may be reluctance to recommend more complex reconstructive procedures on patients of advanced age.[16] A history of radiation treatment to the maxillary region requires further investigation as to the dosage, area involved, and risk of tumor recurrence.[12] Smoking and other forms of tobacco use are local factors that can complicate healing and compromise bone augmentation outcomes.[17–21] Sinus bone graft patients may tolerate smoking better than those undergoing horizontal or vertical augmentation, but implant survival may be reduced.[17,22] Sinus pathology may complicate sinus bone augmentation procedures.[23,24] A history of untreated periodontitis in the mandibular dentition may adversely affect long-term implant success.[25] The retreatment of a failed bone augmentation procedure is more complex, as there often is poor quality tissue (scar, thin mucosa) and compromised vascularity. In addition, patient management can be stressful since there are added costs and longer treatment.

TARGET PROCEDURES

Several bone augmentation techniques have been developed to manage the edentulous atrophic maxilla.[26–30] Methods used for bone augmentation may be categorized into sinus, horizontal, and vertical bone augmentation. Surgical methods for sinus bone augmentation include lateral window sinus bone grafting, transcrestal sinus bone grafting (osteotome or antral balloon), and osteotome sinus floor elevation (simultaneous implant placement without grafting). Horizontal bone augmentation may be performed using guided bone regeneration (GBR), onlay bone grafting, protected bone regeneration using scaffold techniques (ie, titanium mesh grafting) or ridge expansion (splitting). Vertical bone augmentation techniques include GBR, onlay bone grafting, protected bone regeneration using scaffold techniques (ie, titanium mesh grafting), interpositional grafting (osteoperiosteal flap), Lefort I osteotomy with interpositional grafting, distraction osteogenesis, and nasal bone grafting. Procedures may be combined to address anatomical deficiencies and three-dimensional defects requiring both horizontal and vertical augmentation. For example, sinus bone augmentation may be combined with onlay block grafting in the anterior maxilla. Even when protocols for reduced implant numbers are utilized, bone augmentation may still be indicated.[32,33] Dental implant placement may be performed with the augmentation procedure or staged after the area has healed. This may depend on the ability to achieve primary implant stability in native bone. However, when more severe atrophy is present or significant augmentation gains are required, a delayed approach to implant placement after site development may be preferred.

There are several types of biomaterials utilized for bone augmentation procedures. Autogenous bone

grafts are harvested directly from the patient and transplanted to the deficient area. Autogenous bone has been considered the gold standard of graft materials, as it has superior biologic properties.[34,35] Various donor sites have been used for ridge augmentation, including local or intraoral areas and remote or extraoral regions such as the tibia, calvarium, or ilium. The iliac crest has been used most often for extensive onlay augmentation.[36,37] Intraoral block bone grafts may be more suitable for moderate atrophy and width augmentation.[37–41] Autogenous bone may not be necessary for sinus bone grafting.[26,42] Bone substitutes such as allografts, xenografts, and alloplastic materials have also been utilized for maxillary augmentation. Allografts are obtained from human donors and are processed by tissue banks to reduce antigenicity and risk of disease transmission. They are offered in fresh-frozen, mineralized, and demineralized forms. The osteoinductive capacity of these types of grafts has come under question.[43,44] Xenografts are derived from a different animal species such as bovine, porcine, or coral sources. The animal bone is processed to remove the organic component, leaving an osteoconductive hydroxylapatite product. Alloplastic materials are synthetic bone substitutes. They include hydroxylapatite, calcium phosphates, calcium sulfates, and bioactive glasses. These may provide an osteoconductive scaffold for bone formation. Bone substitutes may be mixed with autogenous bone, used alone or in combinations. They are currently offered in block or particulate forms but may be customized using CAD/CAM techniques. Recently, much interest has been focused on the use of growth factors and stem cells in combination with traditional materials or as a replacement for autogenous bone grafts. However, this document will not address the use of tissue engineering products for bone augmentation, as this topic is covered by Group 4. Surgeons should appreciate that no single clinical technique or biomaterial is optimum for every augmentation procedure. Instead, one should consider the advantages and disadvantages of each alternative in a given clinical situation, and select the material with lowest overall cost and morbidity, and the highest likelihood of success.[35]

OUTCOMES MEASURED

There are a number of parameters that can be used to assess the outcome of ridge augmentation procedures, including graft success, amount of bone gain, patient satisfaction, and dental implant success/survival. An augmentation procedure would be deemed successful if the surgeon was able to place the preferred implant size in the planned position without the need for additional bone repair. The majority of clinical studies only report graft failure without commenting on less satisfactory outcomes that compromised implant placement. Some articles do discuss the need to regraft at implant placement.[45] The amount of bone gained would provide valuable information to understand which techniques are most successful in regenerating bone volume. However, most studies do not perform preoperative measurements of the ridge or report how much bone was actually formed by a technique.[46] Patient assessment of bone augmentation surgery usually focuses on postoperative morbidity (pain, loss of function), but some questionnaires inquire about satisfaction with the surgery.[47] Patients who have also completed prosthetic treatment have been surveyed on function and quality-of-life impact.[48]

Dental implant survival was used in the systematic review to determine bone augmentation success. . Implant failure can occur independently of augmentation success. Often the baseline situation of the patient (degree of atrophy, bone quality) is not identified in the study.[46] As such, patients who require more complex augmentation techniques (severe atrophy) may have implant survival rates that are lower than less-demanding procedures. If the result of the augmentation is compromised, unknown to the reader, the implant size may have been modified to accommodate the conditions. If the graft failed, then no implants would have been placed. If the implant surface is not identified (machined), a decreased implant survival rate may be interpreted as low augmentation success. In addition, implant survival may be a function of the residual native bone supporting the implant rather than the grafted bone.[26] Although there are disadvantages in relying on implant survival to measure augmentation success, this is one of the parameters that gets consistently reported to allow comparison between studies.

TARGET AUDIENCE

These guidelines are intended for use by dental implant surgeons and implant restorative dentists (oral and maxillofacial surgeons, periodontists, prosthodontists, general practitioners) managing edentulous patients with maxillary atrophy. It should be noted that bone augmentation procedures may be more technique and operator-experience-sensitive.[26] Most of the clinical studies reviewed were performed by experienced clinicians, many of whom were specifically trained in oral and maxillofacial surgery or periodontics. The reported clinical results may not be achieved by less skillful practitioners.[49] Clinicians performing

these surgical augmentation techniques should have completed additional education and training.[50,51] Referral to an experienced surgical specialist should be considered for more complicated cases and complex augmentation procedures (ie, severe maxillary atrophy, vertical bone augmentation).[50,52]

METHODS

The Clinical Practice Guidelines were based on a systematic review of the current dental literature, clinical information, and accepted approaches to the treatment of the edentulous atrophic maxilla with bone augmentation techniques. A systematic review was performed between 1980 and 2014, specifically focusing on the edentulous maxilla and bone augmentation. All identified articles were evaluated and screened to meet strict inclusion criteria of at least 10 patients, complete maxillary edentulism, 1 year follow-up, and information regarding implant survival rate. Surgical techniques from these studies included are GBR, sinus augmentation, onlay grafting, nasal floor bone grafting, and Lefort I interpositional grafting. There are additional augmentation procedures that are in routine clinical use, including distraction osteogenesis, protected bone regeneration, or scaffold techniques such as titanium mesh grafting, ridge expansion (splitting), and osteoperiosteal flaps. Where information from the literature is sparse or lacking, the work group will develop opinion statements.

GUIDELINE KEY ACTION STATEMENTS

These Guideline Key Action Statements are based on PICO questions and a systematic evidence review that addressed the following key questions related to the treatment of the edentulous maxilla with bone augmentation:

1. For patients with an atrophic edentulous maxilla who desire implant-supported prostheses but have inadequate bone in the posterior maxilla, how does sinus bone augmentation affect implant survival?
2. For patients with an atrophic edentulous maxilla who desire implant-supported prostheses but have inadequate bone, how does bone augmentation affect implant survival?
3. For patients with an atrophic edentulous maxilla who desire implant-supported prostheses but need ridge augmentation, which techniques are most successful?

CASE SCENARIO/LEVEL OF EVIDENCE/ RECOMMENDATIONS

The various clinical situations and applied therapies discussed below (Case Scenarios) will be rated as green, yellow, or red. These ratings describe the management of the case by the clinician based on their training, skill, and experience and not necessarily the patient conditions. The available evidence where these guidelines are based was graded according to the Strength of Recommendation Taxonomy (SORT). Evidence was rated using a three-point scale based on the quality, quantity, and consistency. Clinical recommendations were ranked as follows:

A: Consistent and good-quality patient-oriented evidence.
B: Inconsistent or limited-quality patient-oriented evidence.
C: Consensus, usual practice, opinion, disease-oriented evidence, case series.

A: Maxillary Atrophy with Inadequate Bone for Dental Implants

When there is inadequate bone in the edentulous maxilla for placement of the preferred implant size in the planned position for esthetics, prosthetic support, and long-term stability, bone augmentation procedures should be considered.

- **Case Scenario:** Yellow or Red
- **Level of Evidence:** B, C

B: Inadequate Vertical Bone Height in the Edentulous Posterior Maxilla (Moderate to Severe Maxillary Atrophy and/or Pneumatization of the Maxillary Sinus)

When there is inadequate vertical bone height in the posterior aspect of the edentulous maxilla for placement of the preferred implant size in the planned position for esthetics, prosthetic support, and long-term stability, surgeons should consider sinus bone augmentation procedures.

- **Case Scenario:** Yellow to Red. Conditions may alter the rating from Yellow to Red including sinus anatomy (septae), benign sinus pathology, bone height below the sinus, planned prosthesis, and management of postoperative adverse events.
- **Level of Evidence:** B

C: Inadequate Bone Width in the Edentulous Maxilla (Moderate Maxillary Atrophy)

When there is inadequate bone width in the edentulous maxilla for placement of the preferred implant size in the planned position for esthetics, prosthetic support, and long-term stability, surgeons should consider horizontal bone augmentation procedures.

- **Case Scenario:** Yellow to Red.
  Conditions may alter the rating from Yellow to Red including simultaneous augmentation and implant placement and very narrow ridge without adequate bone for the implant chosen. Retreatment of a failed augmentation would move the rating from Yellow to Red. The need for an extraoral donor site harvest would move the rating to Red. Retreatment of a failed bone augmentation would move the rating to Red.
- **Level of Evidence:** C

D: Inadequate Bone Height in the Edentulous Maxilla (Severe Maxillary Atrophy)

When there is inadequate bone height in the edentulous maxilla (excluding the sinus region) for placement of the preferred implant size in the planned position for esthetics, prosthetic support, and long-term stability, surgeons should consider vertical bone augmentation procedures.

- **Case Scenario:** Red.
  All vertical augmentation procedures would be rated Red, as severe atrophy is the most challenging condition, and surgical procedures for vertical augmentation are complex. Retreatment of a failed bone augmentation would add further complexity to the procedure.
- **Level of Evidence:** C

BURDEN OF CONDITION

Complete edentulism is a debilitating and chronic condition. Although the incidence of edentulism has diminished over the last decade, this problem remains a major health burden throughout the world, especially in the older population.[53–55] The prevalence of complete tooth loss in different countries can vary based on economics, education, dental health knowledge, and attitudes to dental care.[54] The number of completely edentulous people in the United States is approximately 9 million, and 25% of those over the age of 60 years are without teeth.[56] Edentulism contributes to functional, physical, psychologic, and social impairment. With progressive atrophy from denture wear, the use of a removable prosthesis becomes even more challenging for the edentulous patient.

Compared with a mandibular denture, many patients can adapt to and tolerate wearing a maxillary prosthesis. As denture use contributes to maxillary bone loss, the effect of ridge resorption may not become evident to the patient until significant reduction has occurred.[58] The use of denture adhesive can mask the unfavorable anatomy for denture retention. By the time the patient is motivated to seek treatment, there may not be adequate bone for implant placement, and bone augmentation procedures may well be needed. The need for bone augmentation procedures may discourage patients from accepting implant treatment.[59] Maxillary denture wearers should be educated about continued ridge resorption over time and the greater difficulty in treating their condition with advancing bone loss.

HEALTH CARE BURDEN

The advancements in implant dentistry have significantly improved the quality of life of the denture wearer. However, the cost of dental implant treatment is significantly greater than conventional removable prostheses. When bone augmentation is needed to allow implant placement, this invariably increases the overall costs of treatment. Global sales of dental bone graft materials reached $130 million in 2006, and the use of bone grafts was projected to more than double by 2012 with revenues reaching $266 million.[60] In addition to surgical costs, there may be added patient expenses including diagnostic radiographs (computed tomography [CT] scans, stereolithographic models), anesthesia, adjunctive materials (aseptic technique, platelet preparations, growth factors), and associated prosthetic procedures (templates, provisional prosthesis, relines). Complex maxillary reconstructions, such as Lefort I osteotomies or extraoral bone harvest, are usually performed in an operating room under general anesthesia and may require hospitalization, which significantly increases costs.[60–62] Some major graft procedures may be covered by medical insurance, especially if there is a history of trauma or pathology causing the need for maxillary reconstruction. Although more dental insurance carriers are covering dental implant replacement, they may not include bone augmentation procedures. In addition, the lower annual maximum benefit of dental insurance will often be exceeded by the cost of grafting and adjunctive procedures. Most augmentation procedures for dental implant placement require added out-of-pocket expenses for the patient. In some cases, dental implant treatment may be cost prohibitive due to this additional financial burden.[59]

BENEFITS AND HARMS

Bone augmentation of the edentulous maxilla can offer several benefits for the patient and clinician. In some cases, maxillary atrophy is so severe that dental implants cannot be inserted. Bone augmentation can make these handicapped patients candidates for implant therapy. Enhancing bone volume can allow the surgeon to select an appropriate implant size for the intended site. An adequate number and distribution of implants may be placed for long-term biomechanical support of the prosthesis.[64] This may better distribute loads and reduce prosthetic complications.[65,66] Sinus bone augmentation can reduce or eliminate long prosthetic cantilevers.[67,68] Even when the "All on Four" protocol is utilized, sinus bone augmentation may still be beneficial.[32,33] As the maxillary ridge resorbs medially, the potential implant sites become more palatal to the prosthetic tooth positions. This creates an unfavorable transverse relationship with the opposing mandibular dentition (buccal cantilever). Palatal implant positions may cause phonetic problems.[69,70] They may also create prosthetic contours that compromise oral hygiene and possibly lead to periimplant bone loss.[70–72] Horizontal bone augmentation can correct this discrepancy, improving biomechanical loading of the implants, access to home care, and prosthetic contours. Unfavorable crown-to-implant ratios can be corrected with vertical bone augmentation.[64,73,74] Augmentation of the ridge is sometimes needed for esthetics to develop proper prosthetic contours, pontic form, and tooth length. It can also provide added lip support when a flange is not present.[75]

Bone augmentation of the edentulous atrophic maxilla can have unique challenges. When severe atrophy is present, the upper denture has much less stability and retention. It can be difficult to modify the already-unstable denture to avoid graft loading yet provide the patient a suitable prosthesis for use during healing. Improper use of the denture during onlay graft healing can cause wound dehiscence, graft resorption, or implant failure. Minimizing wearing of the denture and a soft diet is encouraged until graft incorporation has occurred.[76] Provisional small-diameter implants can be used to support a provisional prosthesis to minimize graft loading.[77,78] Higher implant failure has been observed when the edentulous maxilla is grafted against opposing natural dentition.[79]

Most treatments are associated with some potential risks, especially invasive and operative treatments. Compared with dental implant placement, bone augmentation procedures may increase the risk of morbidity for the patient with the added possibility of failure. A discussion of available treatment options and applicable procedures for a patient's condition relies on mutual communication between the patient and surgeon, weighing the potential risks and benefits for that patient.

In general, bone augmentation surgeries can result in pain, swelling, bleeding, bruising, infection, and temporary loss of function. There may be a greater need to follow strict aseptic technique with augmentation procedures compared with routine dental implant surgery.[80] Specific surgical procedures have inherent related risks. Although the incidence is low, sinus bone augmentation can result in postoperative sinusitis.[23,81,82] Ridge expansion can cause fracture of cortical plates and bone resorption.[27,83–85] Distraction osteogenesis has been associated with vector control problems, resorption of the transported ossicle, device function/instability, and dehiscence[86,87] Any surgical technique that augments bone volume by placing a graft material over the ridge necessitating flap advancement for primary closure will risk the complication of wound dehiscence. Clinicians must have the surgical skills in flap manipulation, especially for vertical augmentation. Membrane exposure, infection, and/or membrane degradation can occur with GBR.[88–91] Early titanium mesh exposure usually results in graft failure but may be tolerated if it occurs after initial wound healing (2 to 3 weeks).[63, 92] Wound dehiscence of block bone grafts is detrimental to their incorporation and can cause increased resorption and/or failure.[19,93]

The harvesting of autogenous bone grafts will add surgical time and can also contribute to additional complications. However, each donor site has specific anatomical risks and associated degree of morbidity (minimal to severe). The procurement of local autograft from the maxilla adds minimal morbidity. Small block bone grafts or particulate bone may be harvested from the palate, zygomatic buttress, or tuberosity.[37,94] The mandibular ramus also has very low incidence of postoperative complications, and as such, has become a preferred donor site.[93,95–99] The mandibular symphysis has much greater morbidity, including neurosensory changes in the lip, chin, and teeth and greater pain.[40,93,95,99–102] The majority of sensory disturbances are temporary.[103] In the evaluation of extraoral donor sites, the calvarium has the lowest incidence of postoperative problems.[104,105] However, use of this site requires an operating room with general anesthesia, and many patients are reluctant to undergo cranial bone harvest. The proximal tibia can provide large amounts of cancellous bone for grafting with a low incidence of significant complications.[106,107] They may include hematoma formation, wound dehiscence, infection, and rarely fracture. The iliac crest provides the greatest source of bone for arch reconstruction but also has the greatest morbidity of any donor site.[93] Postoperative pain from the hip is usually the most common problem.[108] Although acute postoperative pain can be significant, the use of a local anesthesia-infusion device can provide exceptional pain control that exceeds the duration of pharmacologic activity.[109,110] Preemptive use of analgesics is also beneficial for patient comfort.

Chronic pain of the donor site has been reported.[111] Temporary gait disturbances may require ambulatory assistance for a week or longer. Patients must refrain from exercise and heavy lifting for at least 6 weeks after surgery. There is a low incidence of hematoma formation. Cutaneous paresthesia of the thigh area has been reported with an anterior approach to the iliac crest, but this is usually temporary.[104,111] Although it is usually covered by underwear, some patients may object to the appearance of a scar. Anterior iliac spine fractures are rare.[111] Although some surgeons have found that the posterior iliac crest may produce less morbidity, this requires turning the patient over while anesthetized after bone harvest.[112,113] Modifications in the iliac harvest technique have significantly reduced complications and postoperative morbidity.[108,114,115]

Patients undergoing maxillary grafting with mandibular bone grafts (chin, ramus) were highly satisfied with treatment but noted significantly less discomfort and greater satisfaction with the ramus donor site.[98,99,116] Assessment studies on patients who had iliac bone grafting of the maxilla found low morbidity and high patient acceptance, supporting its use.[108,115,117,118] Undoubtedly, most patients would prefer not to undergo bone harvest, and efforts are continuing to find a suitable replacement for autogenous bone.

It should also be noted that bone augmentation procedures will often increase the overall length of treatment. This is especially the case when site development is staged, allowing for the augmented area to heal before implants are placed. This can add several months to the overall timeline. Implant healing in grafted bone may also require extended time for integration in some cases.

Current clinical trends attempt to reduce the morbidity of maxillary bone augmentation surgery. The transcrestal osteotome approach to sinus bone grafting is less invasive but may not be as successful when there is minimal bone below the sinus.[119] Bone substitutes have proven to be effective for sinus bone grafting, but there are some concerns with treating the enlarged pneumatized sinus with minimal residual bone height.[26,120–122] The use of rhBMP-2 for sinus bone grafting has produced questionable outcomes and lower implant survival rates compared with autograft and/or bone substitutes.[42,123–126] As the management of the posterior maxilla has become more routine and predictable, attention has been directed at simplifying anterior augmentation. The treatment of horizontal bone deficiencies using ridge expansion has a low incidence of complications with favorable implant survival but does require adequate initial bone width for splitting (> 3.0 mm).[83,127–130] Ultrasonic bone surgery has simplified this technique.[131] Another option for width augmentation is to use autogenous bone grafts from donor sites with low morbidity, such as the mandibular ramus.[76,132] An alternative to autograft is the use of allogeneic bone blocks.[130,133] However, there are higher costs, and allografts require longer healing, the routine use of barrier membranes, and may be less predictable than autogenous bone.[134,135] Titanium mesh with particulate autograft and bone substitutes, with or without growth factors, offers another approach.[92,136] The application of GBR techniques using tenting screws, bone substitutes, and are absorbable membranes can achieve modest bone gains.[137–140] For the severely atrophic maxilla, there may still be a need for the harvest of iliac bone grafts. However, the use of rhBMP-2 composite grafts with titanium mesh has shown promise in treating this condition.[63] An alternative to the Lefort I osteotomy is an osteoperiosteal flap performed below the nasal cavity and using rhBMP-2 for the interpositional graft.[141] The option of using shorter implants can reduce the amount of vertical bone augmentation needed.[142] The above proposed new approaches offer less trauma and patient morbidity while achieving high success rates. Future efforts should focus on the long-term follow-up of these techniques.

RESEARCH NEEDS

The systematic review of the current literature on bone augmentation of the edentulous maxilla exposed many areas of deficiency. With the exception of sinus bone grafting, several ridge augmentation procedures that are routinely used in practice have not been well documented with clinical studies. However, one could argue that much of the augmentation research from partially edentulous patients or other areas of the arches is applicable to treatment of the edentulous maxilla. Many reports found favorable results of the augmentation outcome but lacked information on dental implant survival and/or long-term follow-up of the patients. Including information on the baseline conditions and bone augmentation gains in the data would be useful for surgeons to determine which techniques are best suited for particular situations.

ACKNOWLEDGMENTS

A volunteer task force group of the Academy of Osseointegration developed these clinical practice guidelines based on a systematic review of the current dental literature, clinical information, and accepted approaches to the treatment of the edentulous atrophic maxilla with bone augmentation techniques. These clinical practice guidelines are not intended for use as a fixed protocol, as some patients may be served by different treatment approaches. Given the individual patient's clinical circumstances, treatment should be based on a clinician's independent judgment. These guidelines and the systematic review upon which it is based were funded exclusively by the Academy of Osseointegration. All group members gave full disclosure of conflicts of interest prior to participating in the development of these guidelines.

REFERENCES

1. Papaspyridakos P, Chen CJ, Chuang SK, Weber HP. Implant loading protocols for edentulous patients with fixed prostheses: A systematic review and meta-analysis. Int J Oral Maxillofac Implants 2014;29 (suppl):256–270
2. Jemt T, Lekholm U. Implant treatment in edentulous maxillae: A 5-year follow-up report on patients with different degrees of jaw resorption. Int J Oral Maxillofac Implants 1995;10:303–311.
3. Cawood JI, Howell RA. A classification of the edentulous jaws. Int J Oral Maxillofac Surg 1988;17:232–236
4. Schropp L, Wenzel A, Kostopoulos L, Karring T. Bone healing and soft tissue contour changes following single-tooth extraction: A clinical and radiographic 12-month prospective study. Int J Periodontics Restorative Dent 2003;23:313–323.
5. Tallgren A. The continuing reduction of the residual alveolar ridges in complete denture wearers: A mixed-longitudinal study covering 25 years. J Prosthet Dent 1972;27:120–132.
6. Lekholm U, Zarb GA. Patient selection and preparation. In: Tissue-integrated Prostheses: Osseointegration in Clinical Dentistry. Brånemark P-I, Zarb GA, Albrektsson T (eds). Chicago: Quintessence, 1985:199–209.
7. Katsoulis J, Enkling N, Takeichi T, Urban IA, Mericske-Stern R, Avrampou M. Relative bone width of the edentulous maxillary ridge. Clinical implications of digital assessment in presurgical implant planning. Clin Implant Dent Relat Res 2012;14(suppl 1):e213–23.e2
8. Misch CE. Divisions of available bone in implant dentistry. Int J Oral Implantol 1990;7:9–17.
9. Jensen OT. Site classification for osseointegrated implant. J Prosthet Dent 1989;61:228–234.
10. Cologne Classification for Alveolar Ridge Defects. 8th European Consensus Conference of BDIZ EDI. February 2013: http://www.bdiz.eu/pdf/Konsensus-Leitfaden-0_engl.pdf
11. Jensen OT. Complete arch site classification for all-on-4 immediate function. J Prosthet Dent 2014 May 13 [Epub ahead of print]
12. Davis CL. Medical factors affecting treatment planning. In: Fonseca R, Davis HW (eds). In: Reconstructive Preprosthetic Oral and Maxillofacial Surgery, ed 2. Philadelphia: W.B. Saunders, 1995:127–134.
13. Hwang D, Wang HL. Medical contraindications to implant therapy: Part I: Absolute contraindications. Implant Dent 2006;15:353–360.
14. Miller TJ, Jeong HS, Davis K, et al. Evaluation of the American Society of Anesthesiologists Physical Status classification system in risk assessment for plastic and reconstructive surgery patients. Aesthet Surg J 2014;34:448–456.
15. American Association of Oral and Maxillofacial Surgeons 2014 Position Paper on Medication-related Osteonecrosis of the Jaw (MRONJ): http://www.aaoms.org/docs/position_papers/mronj_position_paper.pdf?pdf=MRONJ-Position-Paper
16. Betts N, Barber HD. The pathophysiology of aging. In: Fonseca R, Davis HW (eds). Reconstructive Preporosthetic Oral and Maxillofacial Surgery, ed 2. Philadelphia: W.B. Saunders Co., 1995: 3–18
17. Levin L, Herzberg R, Dolev E, Schwartz-Arad D. Smoking and complications of onlay bone grafts and sinus lift operations. Int J Oral Maxillofac Implants 2004;19:369–373.
18. Bunyaratavej P. Smoking increased the risk of major complications of onlay bone graft. J Evid Based Dent Pract 2005;5:96–97.
19. Li J, Wang HL. Common implant-related advanced bone grafting complications: Classification, etiology, and management. Implant Dent 2008;17:389–401.
20. Lindfors LT, Tervonen EA, Sándor GK, Ylikontiola LP. Guided bone regeneration using a titanium-reinforced ePTFE membrane and particulate autogenous bone: The effect of smoking and membrane exposure. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109:825–830.
21. Misch CM. Complications of autogenous bone grafting. In: Froum SJ (ed). Dental Implant Complications: Etiology, Prevention and Treatment. Ames, Iowa: Wiley-Blackwell,2010:227–255.
22. Testori T, Weinstein RL, Taschieri S, Del Fabbro M. Risk factor analysis following maxillary sinus augmentation: A retrospective multicenter study. Int J Oral Maxillofac Implants 2012;27:1170–1176.
23. Pikos MA. Complications of maxillary sinus augmentation. In: Jensen OT (ed). The Sinus Bone Graft. Chicago: Quintessence 2006,103–114.
24. Chan HL, Wang HL. Sinus pathology and anatomy in relation to complications in lateral window sinus augmentation. Implant Dent. 2011;20:406–412.
25. Roccuzzo M, Bonino F, Aglietta M, Dalmasso P. Ten-year results of a three arms prospective cohort study on implants in periodontally compromised patients. Part 2: clinical results. Clin Oral Implants Res 2012;23:389-395.
26. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? Int J Oral Maxillofac Implants 2007;22(suppl):49–70.
27. Donos N, Mardas N, Chadha V. Clinical outcomes of implants following lateral bone augmentation: Systematic assessment of available options (barrier membranes, bone grafts, split osteotomy). J Clin Periodontol 2008;35(8 suppl):173–202.
28. Rocchietta I, Fontana F, Simion M. Clinical outcomes of vertical bone augmentation to enable dental implant placement: A systematic review. J Clin Periodontol 2008;35(suppl 8):203–215.
29. Chiapasco M, Casentini P, Zaniboni M. Bone augmentation procedures in implant dentistry. Int J Oral Maxillofac Implants 2009;24:237–259.
30. Zakhary IE, El-Mekkawi HA, Elsalanty ME. Alveolar ridge augmentation for implant fixation: Status review. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;114(5 suppl):S179–S189.
31. Hinze M, Vrielinck L, Thalmair T, Wachtel H, Bolz W. Zygomatic implant placement in conjunction with sinus bone grafting: The "extended sinus elevation technique." A case-cohort study. Int J Oral Maxillofac Implants 2013;28:e376–e385.
32. Jensen OT, Adams MW. Anterior sinus grafts for angled implant placement for severe maxillary atrophy as an alternative to zygomatic implants for full arch fixed restoration: Technique and report of 5 cases. J Oral Maxillofac Surg 2014;72:1268–1280.
33. Jensen OT, Kuhlke KL, Leopardi A, Adams MW, Ringeman JL. BMP-2/ACS/allograft for combined maxillary alveolar split/sinus floor grafting with and without simultaneous dental implant placement: Report of 21 implants placed into 7 alveolar split sites followed for up to 3 years. Int J Oral Maxillofac Implants 2014;29:e81–e94.
34. Misch CM. Autogenous bone: is it still the gold standard? Implant Dent 2010;19:361.
35. Rogers GF, Greene AK. Autogenous bone graft: Basic science and clinical implications. J Craniofac Surg 2012;23:323–327.
36. Adell R, Lekholm U, Grondahl K, Bränemark PI, Lindstrom J, Jacobsson M. Reconstruction of severely resorbed edentulous maxillae using osseointegrated fixtures in immediate autogenous bone grafts. Int J Oral Maxillofac Implants 1990;5:233–246.
37. Misch CM. Autogenous bone grafting for dental implants. In: Fonseca RJ, Turvery TA, Marciani RD (eds). Oral and Maxillofacial Surgery, ed 2, Volume 1. Philadelphia: W.B. Saunders Co. 2008:344–370.
38. Misch CM. Ridge augmentation using mandibular ramus bone grafts for the placement of dental implants: Presentation of a technique. Pract Periodont Aesthet Dent 1996;8:127–135.
39. Pikos MA. Block autografts for localized ridge augmentation: Part I. The posterior maxilla. Implant Dent 1999;8:279–285.
40. Pikos MA. Mandibular block autografts for alveolar ridge augmentation. Atlas Oral Maxillofac Surg Clin North Am 2005;13:91–107.
41. Cordaro L, Boghi F, Mirisola di Torresanto V, Torsello F. Reconstruction of the moderately atrophic edentulous maxilla with mandibular bone grafts. Clin Oral Implants Res 2013;24:1214–1221.
42. Del Fabbro M, Wallace SS, Testori T. Long-term implant survival in the grafted maxillary sinus: a systematic review. Int J Periodontics Restorative Dent 2013;33:773–783.
43. Blum B, Moseley J, Miller L, Richelsoph K, Haggard G. Measurement of bone morphogenetic proteins and other growth factors in demineralized bone matrix. Orthopedics 2004:27:s161–s165.
44. Boyan BD, Ranly DM, McMillan J, Sunwoo M, Roche K, Schwartz Z. Osteoinductive ability of human allograft formulations. J Periodontol 2006;77:1555–1563.
45. Jensen SS, Terheyden H. Bone augmentation procedures in localized defects in the alveolar ridge: Clinical results with different bone grafts and bone-substitute materials. Int J Oral Maxillofac Implants 2009;24:218–236.

46. Milinkovic I, Cordaro L. Are there specific indications for the different alveolar bone augmentation procedures for implant placement? A systematic review. Int J Oral Maxillofac Surg 2014;43:606–625.
47. Falkensammer N, Kirmeier R, Arnetzl C, Wildburger A, Eskici A, Jakse N. Modified iliac bone harvesting—Morbidity and patients' experience. J Oral Maxillofac Surg 2009;67:1700–1705.
48. Gunne J, Nyström E, Kahnberg KE. Bone grafts and implants in the treatment of the severely resorbed maxillae: A 3-year follow-up of the prosthetic restoration. Int J Prosthodont 1995;8:38-45.
49. Da Silva JD, Kazimiroff J, Papas A, et al. Outcomes of implants and restorations placed in general dental practices: A retrospective study by the Practitioners Engaged in Applied Research and Learning (PEARL) Network. J Am Dent Assoc 2014;145:704–713.
50. 2010 Guidelines of the Academy of Osseointegration for the Provision of Dental Implants and Associate Patient Care. Int J Oral Maxillofac Implants 2010;25:620–627.
51. Rees J. Medicolegal implications of dental implant therapy. Prim Dent J 2013;2:34–38.
52. Eckert SE. Does anyone really benefit from turf wars? Int J Oral Maxillofac Implants 2013;28:651–652.
53. Douglass CW, Shih A, Ostry L. "Will there be a need for complete dentures in the United States in 2020?" Journal of Prosthetic Dentistry 2002;87:5–8.
54. Müller F, Naharro M, Carlsson GE. What are the prevalence and incidence of tooth loss in the adult and elderly population in Europe? Clin Oral Implants Res 2007;18 (suppl 3): 2–14.
55. Wu B, Liang J, Plassman BL, Remle C, Luo X. Edentulism trends among middle-aged and older adults in the United States: Comparison of five racial/ethnic groups. Community Dent Oral Epidemiol 2012;40:145–153.
56. Beltrán-Aguilar ED, Barker LK, Canto MT, et al. Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis--United States, 1988-1994 and 1999-2002. MMWR Surveill Summ 2005;54:1–43.
57. Allen PF, McMillan AS. A review of the functional and psychosocial outcomes of edentulousness treated with complete replacement dentures. J Canadian Dent Assoc 2003;69:662–668.
58. Divaris K, Ntounis A, Marinis A, Polyzois G, Polychronopoulou A. Loss of natural dentition: Multi-level effects among a geriatric population. Gerodontology 2012;29:e192–e199.
59. Korsch M, Robra BP, Walther W. Implant counseling and information: Questions, predictors, and decision-making of patients before implant therapy. Clin Oral Implants Res 2014 Jan 20 [Epub ahead of print]
60. Dental Tribune, U.S. Edition, Dental Tribune America, New York, NY, 2010;March:2B.
61. Dahlin C, Johansson A. Iliac crest autogenous bone graft versus alloplastic graft and guided bone regeneration in the reconstruction of atrophic maxillae: A 5-year retrospective study on cost-effectiveness and clinical outcome. Clin Implant Dent Relat Res 2011;13:305–310.
62. Truedsson A, Hjalte K, Sunzel B, Warfvinge G. Maxillary sinus augmentation with iliac autograft - a health-economic analysis. Clin Oral Implants Res 2013;24:1088–1093.
63. Marx RE, Armentano L, Olavarria A, Samaniego J. rhBMP-2/ACS grafts versus autogenous cancellous marrow grafts in large vertical defects of the maxilla: An unsponsored randomized open-label clinical trial. Int J Oral Maxillofac Implants 2013;28:e243–251.
64. Misch CE. Stress factors: influence on treatment planning. In: Misch CE (ed). Dental implant prosthetics. St. Louis: Mosby Inc, 2005;71–90.
65. Salvi GE, Brägger U. Mechanical and technical risks in implant therapy. Int J Oral Maxillofac Implants 2009;24(suppl):69-85.
66. Baggi L, Pastore S, Di Girolamo M, Vairo G. Implant-bone load transfer mechanisms in complete-arch prostheses supported by four implants: A three-dimensional finite element approach. J Prosthet Dent 2013;109:9–21.
67. Zurdo J, Romão C, Wennström JL. Survival and complication rates of implant-supported fixed partial dentures with cantilevers: a systematic review. Clin Oral Implants Res 2009;20(suppl 4):59–66.
68. Aglietta M, Siciliano VI, Zwahlen M, et al. A systematic review of the survival and complication rates of implant supported fixed dental prostheses with cantilever extensions after an observation period of at least 5 years. Clin Oral Implants Res 2009;20:441–451.
69. Goodacre CJ, Bernal G, Rungcharassaeng K, Kan JY. Clinical complications with implants and implant prostheses. J Prosthet Dent 2003;90:121–132.
70. Sartori EM, Padovan LE, de Mattias Sartori IA, Ribeiro PD Jr, Gomes de Souza Carvalho AC, Goiato MC. Evaluation of satisfaction of patients rehabilitated with zygomatic fixtures. J Oral Maxillofac Surg 2012;70:314–349.
71. Abi Nader S, Eimar H, Momani M, Shang K, Daniel NG, Tamimi F. Plaque Accumulation Beneath Maxillary All-on-4™ Implant-Supported Prostheses. Clin Implant Dent Relat Res 2014 Jan 27 [Epub ahead of print]
72. Vázquez Álvarez R, Pérez Sayáns M, Gayoso Diz P, García García A. Factors affecting peri-implant bone loss: A post-five-year retrospective study. Clin Oral Implants Res 2014 Jun 30 [Epub ahead of print]
73. Quaranta A, Piemontese M, Rappelli G, Sammartino G, Procaccini M. Technical and biological complications related to crown to implant ratio: A systematic review. Implant Dent 2014;23:180-187.
74. Garaicoa-Pazmiño C, Suarez F, Monje A, et al. Influence of Crown-Implant Ratio Upon Marginal Bone Loss. A Systematic Review. J Periodontol 2014;85:1214–1221.
75. Calvani L, Michalakis K, Hirayama H. The influence of full-arch implant-retained fixed dental prostheses on upper lip support and lower facial esthetics: Preliminary clinical observations. Eur J Esthet Dent 2007;2:420–428.
76. Misch CM. Maxillary autogenous bone grafting. Oral Maxillofac Surg Clin North Am 2011;23:229–238
77. Wang HL, Okayasu K, Fu JH, Hamerink HA, Layher MG, Rudek IE. The success rate of narrow body implants used for supporting immediate provisional restorations: A pilot feasibility study. Implant Dent 2012;21:467–473.
78. Castagna L, Polido WD, Soares LG, Tinoco EM. Tomographic evaluation of iliac crest bone grafting and the use of immediate temporary implants to the atrophic maxilla. Int J Oral Maxillofac Surg 2013;42:1067–1072.
79. Becktor JP, Eckert SE, Isaksson S, Keller EE. The influence of mandibular dentition on implant failures in bone-grafted edentulous maxillae. Int J Oral Maxillofac Implants 2002;17:69–77.
80. Scharf DR, Tarnow DP. Success rates of osseointegration for implants placed under sterile versus clean conditions. J Perio 1993;64:954–956.
81. Timmenga NM, Raghoebar GM, van Weissenbruch R, Vissink A. Maxillary sinusitis after augmentation of the maxillary sinus floor: A report of 2 cases. J Oral Maxillofac Surg 2001;59:200–204.
82. Barone A, Santini S, Sbordone L, Crespi R, Covani U. A clinical study of the outcomes and complications associated with maxillary sinus augmentation. Int J Oral Maxillofac Implants 2006;21:81–85.
83. Misch CM. Implant site development using ridge splitting techniques. Oral Maxillofac Surg Clin North Am 2004;16:65–74.
84. Chiapasco M, Casentini P, Zaniboni M. Bone augmentation procedures in implant dentistry. Int J Oral Maxillofac Implants 2009;24 (suppl);237–259.
85. Jensen OT, Cullum DR, Baer D. Marginal bone stability using 3 different flap approaches for alveolar split expansion for dental implants: A 1-year clinical study. J Oral Maxillofac Surg 2009;67:1921–1930.
86. Saulacic N, Zix J, Iizuka T. Complication rates and associated factors in alveolar distraction osteogenesis: A comprehensive review. Int J Oral Maxillofac Surg 2009;38:210–217.
87. Ettl T, Gerlach T, Schüsselbauer T, Gosau M, Reichert TE, Driemel O. Bone resorption and complications in alveolar distraction osteogenesis. Clin Oral Investig 2010;14:481–489.

88. Lang NP, Hammerle CH, Bragger U, Lehmann B, Nyman SR. Guided tissue regeneration in jawbone defects prior to implant placement. Clin Oral Implants Res 1994;5:7–92.
89. Rocchietta I, Fontana F, Simion M. Clinical outcomes of vertical bone augmentation to enable dental implant placement: A systematic review. Int J Periodontics Restorative Dent 2008;28:601–607.
90. Tal H, Kozlovsky A, Artzi Z, et al. Cross-linked and non-cross-linked collagen barrier membranes disintegrate following surgical exposure to the oral environment: A histological study in the cat. Clin Oral Implants Res 2008;19:760–766.
91. Chiapasco M, Zaniboni M. Clinical outcomes of GBR procedures to correct peri-implant dehiscences and fenestrations: a systematic review. Clin Oral Implants Res 2009;20 (suppl 4):113–123.
92. Louis PJ, Gutta R, Said-Al-Naief N, Bartolucci AA. Reconstruction of the maxilla and mandible with particulate bone graft and titanium mesh for implant placement. J Oral Maxillofac Surg 2008;66:235–245.
93. Misch CM. Re: "distance between external cortical bone and mandibular canal for harvesting ramus graft: A human cadaver study". J Periodontol 2010;81:1103–1104.
94. Sittitavornwong S, Gutta R. Bone graft harvesting from regional sites. Oral Maxillofac Surg Clin North Am 2010;22:317–330
95. Misch CM. Comparison of intraoral donor sites for onlay grafting prior to implant placement. Int J Oral Maxillofac Implants 1997;12:767-776.
96. Peleg M, Garg AK, Misch CM, Mazor Z. Maxillary sinus and ridge augmentations using a surface-derived autogenous bone graft. J Oral Maxillofac Surg 2004;62:1535–1544.
97. Carlsen A, Gorst-Rasmussen A, Jensen T. Donor site morbidity associated with autogenous bone harvesting from the ascending mandibular ramus. Implant Dent 2013;22:503–506.
98. Scheerlinck LM, Muradin MS, van der Bilt A, Meijer GJ, Koole R, Van Cann EM. Donor site complications in bone grafting: Comparison of iliac crest, calvarial, and mandibular ramus bone. Int J Oral Maxillofac Implants 2013;28:222–227.
99. Nkenke E, Neukam FW. Autogenous bone harvesting and grafting in advanced jaw resorption: Morbidity, resorption and implant survival. Eur J Oral Implantol 2014;7:203–217.
100. Nkenke E, Schulze-Mosgau S, Radespiel M. Morbidity of harvesting of chin grafts: A prospective study. Clin Oral Implant Res 2001;12:495–502.
101. Misch CM. Autogenous bone: Is it still the gold standard? Implant Dent 2010;19:361.
102. Raghoebar GM, Louwerse C, Kalk WWI. Morbidity of chin bone harvesting. Clin Oral Implants Res 2001;12:503–507.
103. Nóia CF, Ortega-Lopes R, Ricardo de Albergaria Barbosa J, Barbeiro RH, Mazzonetto R. Evaluation of patients' perceptions of alterations after chin bone graft harvesting. Implant Dent 2012;21:411–414.
104. Zouhary KJ. Bone graft harvesting from distant sites: Concepts and techniques. Oral Maxillofac Surg Clin North Am 2010;22:301–316.
105. Touzet S, Ferri J, Wojcik T, Raoul G. Complications of calvarial bone harvesting for maxillofacial reconstructions. J Craniofac Surg 2011;22:178–181.
106. Mazock JB, Schow SR, Triplett RG. Proximal tibia bone harvest: Review of technique, complications, and use in maxillofacial surgery. Int J Oral Maxillofac Implants 2004;19:586–593.
107. Chen YC, Chen CH, Chen PL, Huang IY, Shen YS, Chen CM. Donor site morbidity after harvesting of proximal tibia bone. Head Neck 2006;28:496–500.
108. Cricchio G, Lundgren S. Donor site morbidity in two different approaches to anterior iliac crest bone harvesting. Clin Implant Dent Relat Res 2003;5:161–169.
109. Hahn M, Dover MS, Whear NM, Moule I. Local bupivacaine infusion following bone graft harvest from the iliac crest. Int J Oral Maxillofac Surg 1996;25:400–401.
110. Hoard MA, Bill TJ, Campbell RL. Reduction in morbidity after iliac crest bone harvesting: the concept of preemptive analgesia. J Craniofac Surg 1998;9:448–451.
111. Almaiman M, Al-Bargi HH, Manson P. Complication of anterior iliac bone graft harvesting in 372 adult patients from May 2006 to May 2011 and a literature review. Craniomaxillofac Trauma Reconstr 2013;6:257–266.
112. Ahlmann E, Patzakis M, Roidis N, Shepherd L, Holtom P. Comparison of anterior and posterior iliac crest bone grafts in terms of harvest-site morbidity and functional outcomes. J Bone Joint Surg Am 2002;84-A:716–720.
113. Marx RE, Morales MJ. Morbidity from bone harvest in major jaw reconstruction: A randomized trial comparing the lateral anterior and posterior approaches to the ilium. J Oral Maxillofac Surg 1988;46:196–203.
114. Sàndor GK, Rittenberg BN, Clokie CM, Caminiti MF. Clinical success in harvesting autogenous bone using a minimally invasive trephine. J Oral Maxillofac Surg 2003;61:164–168.
115. Falkensammer N, Kirmeier R, Arnetzl C, Wildburger A, Eskici A, Jakse N. Modified iliac bone harvesting: Morbidity and patients' experience. J Oral Maxillofac Surg 2009;67:1700–1705
116. Andersson L. Patient self-evaluation of intra-oral bone grafting treatment to the maxillary frontal region. Dent Traumatol 2008;24:164–169.
117. Kalk WW, Raghoebar GM, Jansma J, Boering G. Morbidity from iliac crest bone harvesting. J Oral Maxillofac Surg. 1996;54(12):1424-9
118. Fasolis M, Boffano P, Ramieri G. Morbidity associated with anterior iliac crest bone graft. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;114:586–591.
119. Călin C, Petre A, Drafta S. Osteotome-mediated sinus floor elevation: A systematic review and meta-analysis. Int J Oral Maxillofac Implants 2014;29:558–576.
120. Jang HY, Kim HC, Lee SC, Lee JY. Choice of graft material in relation to maxillary sinus width in internal sinus floor augmentation. J Oral Maxillofac Surg 2010;68:1859–1868.
121. Klijn RJ, Meijer GJ, Bronkhorst EM, Jansen JA. Sinus floor augmentation surgery using autologous bone grafts from various donor sites: a meta-analysis of the total bone volume. Tissue Eng Part B Rev 2010;16:295–303.
122. Soardi CM, Spinato S, Zaffe D, Wang HL. Atrophic maxillary floor augmentation by mineralized human bone allograft in sinuses of different size: An histologic and histomorphometric analysis. Clin Oral Implants Res 2011;22:560–566.
123. Triplett RG, Nevins M, Marx RE, et al. Pivotal, randomized, parallel evaluation of recombinant human bone morphogenetic protein-2/absorbable collagen sponge and autogenous bone graft for maxillary sinus floor augmentation. J Oral Maxillofac Surg 2009;67:1947–1960.
124. Voss P, Sauerbier S, Wiedmann-Al-Ahmad M, et al. Bone regeneration in sinus lifts: comparing tissue-engineered bone and iliac bone. Br J Oral Maxillofac Surg 2010;48:121-126.
125. Kao DW, Kubota A, Nevins M, Fiorellini JP. The negative effect of combining rhBMP-2 and Bio-Oss on bone formation for maxillary sinus augmentation. Int J Periodontics Restorative Dent. 2012;32:61–67.
126. Froum SJ, Wallace S, Cho SC, et al. Histomorphometric comparison of different concentrations of recombinant human bone morphogenetic protein with allogeneic bone compared to the use of 100% mineralized cancellous bone allograft in maxillary sinus grafting. Int J Periodontics Restorative Dent 2013;33:721–730.
127. Scipioni A, Bruschi GB, Calesini G.The edentulous ridge expansion technique: A five-year study. Int J Periodontics Restorative Dent 1994;14:451–459.
128. Sethi A, Kaus T. Maxillary ridge expansion with simultaneous implant placement: 5-year results of an ongoing clinical study. Int J Oral Maxillofac Implants 2000;15:491–499.
129. Demetriades N, Park JI, Laskarides C. Alternative bone expansion technique for implant placement in atrophic edentulous maxilla and mandible. J Oral Implantol 2011;37:463–471.
130. Fu J, Wang HL. Horizontal bone augmentation: The decision tree. Int J Periodontics Rest Dent 2011;31:429–436.

131. Blus C, Szmukler-Moncler S, Vozza I, Rispoli L, Polastri C. Split-crest and immediate implant placement with ultrasonic bone surgery (piezosurgery): 3-year follow-up of 180 treated implant sites. Quintessence Int 2010;41:463–469.
132. Cordaro L, Boghi F, Mirisola di Torresanto V, Torsello F. Reconstruction of the moderately atrophic edentulous maxilla with mandibular bone grafts. Clin Oral Implants Res. 2013;24(11):1214-21.
133. Acocella A, Bertolai R, Ellis E, 3rd Nissan J, Sacco R. Maxillary alveolar ridge reconstruction with monocortical fresh-frozen bone blocks: A clinical, histological and histomorphometric study. J Craniomaxillofac Surg 2012;40:525–533.
134. Keith JD Jr, Petrungaro P, Leonetti JA, Elwell CW, Zeren KJ, Caputo C, Nikitakis NG, Schöpf C, Warner MM. Clinical and histologic evaluation of a mineralized block allograft: Results from the developmental period (2001-2004). Int J Periodontics Restorative Dent 2006;26:321–327.
135. Waasdorp J, Reynolds MA. Allogeneic bone onlay grafts for alveolar ridge augmentation: A systematic review. Int J Oral Maxillofac Implants 2010;25:525–531.
136. Her S, Kang T, Fien MJ. Titanium mesh as an alternative to a membrane for ridge augmentation. J Oral Maxillofac Surg 2012;70:803–810.
137. Park SH, Lee KW, Oh TJ, Misch CE, Shotwell JL, Wang H-L. Effect of absorbable membranes on sandwich bone augmentation. Clin Oral Implants Res 2008;19:32–41.
138. Le B, Rohrer MD, Prasad HS. Screw "tent-pole" grafting technique for reconstruction of large vertical alveolar ridge defects using human mineralized allograft for implant site preparation. J Oral Maxillofac Surg 2010;68:428–435.
139. Fu JH, Oh TJ, Benavides E, Rudek I, Wang HL. A randomized clinical trial evaluating the efficacy of the sandwich bone augmentation technique in increasing buccal bone thickness during implant placement surgery: I. Clinical and radiographic parameters. Clin Oral Implants Res 2014;25:458–467.
140. Urban IA, Nagursky H, Lozada JL. Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: A prospective case series in 22 patients. Int J Oral Maxillofac Implants 2011;26:404–414.
141. Jensen OT, Cottam JR, Ringeman JL. Experience with bone morphogenetic protein-2 and interpositional grafting of edentulous maxillae: A comparison of Le Fort I downfracture to full-arch (horseshoe) segmental osteotomy done in conjunction with sinus floor grafting. Int J Oral Maxillofac Implants 2013;28:e331-e348.
142. Monje A, Chan HL, Fu JH, Suarez Lopez del Amo F, Galindo-Moreno P, Wang H-L. Are short dental implants (< 10 mm) effective? A meta-anaylsis on prospective clinical trials. J Periodontol 2013;84:895–904.

Role of Implant Design and Systems

Group Co-Chairs

Georgios E. Romanos, DDS, DMD, PhD
Paulo Coelho, DDS, MS, PhD

Group Participants

Edward Amet, DDS, BS, MSD
Francesco Bassi, MD, DDS
Ed Bedrossian, DDS
Asbjørn Jokstad, DDS, PhD
Liran Levin, DMD
Thomas McGarry, DDS
Luiz Meirelles, DDS, PhD
Takahiro Ogawa, DDS, PhD
Franck Renouard, DDS
Mariano Sanz, DDS, PhD
Paul A. Schnitman, DDS, MSD
Ann Wennerberg, DDS, PhD
Haibo Wen, PhD
Ben Wu, DDS, PhD

A Systematic Review of the Role of Implant Design in the Rehabilitation of the Edentulous Maxilla

Asbjørn Jokstad, DDS, PhD[1]/Mariano Sanz, DDS, PhD[2]/
Takahiro Ogawa, DDS, PhD[3]/Francesco Bassi, MD, DDS[4]/Liran Levin, DMD[5]/
Ann Wennerberg, DDS, PhD[6]/Georgios E. Romanos, DDS, PhD, DMD[7]

Purpose: *To identify and critically appraise scientific publications evaluating the possible effect of implant design on treatment outcomes in the rehabilitation of patients with a fully edentulous maxilla.* ***Materials and Methods****: Scientific reports were sought in three electronic bibliographic databases, combined with searches for meeting abstracts, and in the grey literature. English, German, or Scandinavian scientific publications on prospective or retrospective longitudinal studies with effects of an implant design or feature on the treatment outcomes were eligible. Minimum requirement for inclusion was at least 10 study participants who were followed up for at least 2 years after implant loading. The PRISMA guidelines were followed for selecting data to extract from the individual studies. These were characteristics of the individual studies, risk of bias within individual studies, and the results of individual studies. Three editorial teams independently identified and extracted the data.* ***Results:*** *The search resulted in 998 primary studies, of which 525 met the inclusion criteria and were read in full text. Of these, 105 studies were included in qualitative syntheses. Seventeen studies were designed with an objective to assess effects of implant design or feature on outcomes, 23 studies described tilted implants to enable placement of longer implants, 30 studies reported effects of implants placed in zygomatic bone with or without additional alveolar implants, and 9 studies reported effects of implants placed in pterygoid bone or other bony buttresses with or without additional alveolar implants. Sixteen articles reported bone augmentation with simultaneous or delayed implant placement in patients with a predominantly Cawood-Howell bone class V and VI maxilla. Ten papers reported effects of implant design on outcomes, despite the lack of an a priori stated objective to assess a particular implant design or feature. There is a lack of compelling data to state that one particular implant system or design feature stands out amidst others, when applied to restoring the fully edentulous maxilla with implant-retained prostheses.* ***Conclusion:*** *This systematic review failed to identify compelling evidence to conclude that any particular implant or feature affects the treatment outcome in patients with a fully edentulous maxilla.* Int J Oral Maxillofac Implants 2016;31(suppl):s43–s99. doi: 10.11607/jomi.16suppl.g2

Keywords: *bibliographic, databases, humans, prospective studies, retrospective studies, treatment outcome, zygoma*

[1]Professor, Department of Clinical Dentistry, Faculty of Health Sciences, UiT The Arctic University of Norway, Tromsø, Norway.
[2]Professor, Complutense University of Madrid, Estomatologia III, Madrid, Spain.
[3]Professor, Weintraub Center for Reconstructive Biotechnology and Division of Advanced Prosthodontics, UCLA School of Dentistry, Los Angeles, California, USA.
[4]Professor, University of Turin, Department of Surgical Sciences Dental School, Torino, Italy.
[5]Professor, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Canada.
[6]Professor, Department of Prosthodontics, Faculty of Odontology, Malmö University, Sweden.
[7]Professor, Department of Periodontology, Stony Brook University School of Dental Medicine, Stony Brook, New York, USA.

This study was presented at a plenary session of the Academy of Osseointegration Summit Meeting, August 7, 2014, Chicago, Illinois, USA.

Correspondence to: Dr Asbjørn Jokstad, UiT The Arctic University of Norway, N-9037 Tromsø, Norway. Fax: +47 776 44900. Email: Asbjorn.Jokstad@uit.no

Individuals with a fully edentulous maxilla frequently report low social self-confidence and related low quality of life because of compromised oral functions and poor esthetics. Most may benefit from the relatively low-cost technical solution of a correctly designed removable dental prosthesis individually fitted to the remaining oral tissues, which can restore both oral functions as well as the facial and oral appearance to a certain level.[1] Many, however, are unable to adapt to a more or less removable dental prosthesis. This could be attributed to specific conditions of general or oral health, compromised local anatomy that impedes optimal prosthesis design, or psychological barriers.[2] The introduction of endosseous titanium dental implants has provided a more predictable alternative than a conventional removable prosthesis to restore the patient's facial appearance and oral functions with a dental device retained or supported by these root-analogues.[3]

With implant-supported prostheses having a high predictability of re-establishing oral functions and esthetics, new dental implant designs and material compositions have increased rapidly. There were 45 dental implant systems available in the market in 1988,[4] 98 systems in 2000,[5] 225 systems from 78 manufacturers in 2002,[6] and 600 systems from 146 manufacturers in 2008.[7] Currently, there are at least 364 dental implant manufacturers producing an estimate of 1,600 different implant systems. Distinct minorities of these implant manufacturers have undertaken basic, animal, and human research when designing new or altering the components of existing implant systems. Consequently, many currently commercially available dental implants have insufficient, questionable, or simply totally lacking scientific justification of the product designs and material compositions. This is even more profound when looking for high-quality long-term evidence. Potential alterations of the implant design include both its macro-geometry as well as its surface microtopography, which transforms surface chemical and biochemical properties, corrosion characteristics and wear debris release, surface energy, and wettability as well as topography on micrometer and nanometer scales.[8–10]

It is uncertain whether one particular implant design is optimal for the fully edentulous maxilla. It is also doubtful whether one may extrapolate data from other clinical scenarios, such as in single implants or implant-supported small fixed dental prostheses in partial edentate jaws. The main objective of this systematic review was to identify and critically appraise scientific publications to evaluate the possible effect of implant design on treatment outcomes in the rehabilitation of the fully edentulous maxilla. A secondary objective was to provide the basis for the development of evidence-based clinical guidelines for best management of patients with a fully edentulous maxilla. (See separate sections in the IJOMI supplement.)

MATERIALS AND METHODS

Protocol and Registration

The Academy of Osseointegration 2014 summit organizing committee determined the topic for this systematic review in July 2013 and established a task group to develop the PICO question (population, intervention, comparison, and outcome) and the criteria for study eligibility, and to conduct the reviewing process. An intranet website hosted by the University of Iowa served for sharing all relevant evidence and as the communication tool for the task group.

Focused Question

The task group developed the following PICO question: "For patients with a fully edentulous maxilla who desire an implant-supported prosthesis, does the implant design affect the following outcomes: crestal bone loss or implant failure; patient satisfaction; and biological and technical adverse events of implant and prosthesis, including surgical complications, maintenance needs, and cost aspects?"

Eligibility Criteria

The authors considered all scientific publications reporting longitudinal studies that included the use of more than one implant system as eligible. Also eligible were reports with abstracts suggesting any effect of an implant design feature on the treatment outcomes. The minimum requirement for inclusion was that the report had to describe at least 10 study participants with a fully edentulous maxilla restored with an implant-retained or -supported prosthesis and followed for at least 2 years after their rehabilitation. The selected minimum follow-up time and cohort size was determined as a trade-off between the required time and resource allocation for conducting this systematic review compared with the clinical relevance of the length of the follow-up time. The authors considered both prospective and retrospective study designs published in full publications and/or meeting abstracts in the scientific and grey literature. These reports were restricted for logistical reasons to English, German, and Scandinavian languages (Danish, Norwegian, and Swedish).

The authors read the identified reports in full if the abstracts did not clearly state whether the general term "edentulous" encompassed study participants with a fully edentulous maxilla. Reports were not included for consideration if the research focus was on postrestoration interventions of adverse treatment outcomes, eg, of peri-implantitis, dehiscence, fenestration, repairs, etc, or preimplant augmentation interventions with no further reporting of outcomes of implants or supraconstruction. Moreover, this review did not include patients undergoing reconstructions related to extensive loss of oromaxillofacial tissues, eg, caused by trauma, cancer, or congenital defects.

Information Sources

Scientific reports were sought in three electronic bibliographic databases: MEDLINE through Pubmed (www.pubmed.com, National Library of Medicine), The Cochrane Central Registry of Controlled Trials (www.thecochranelibrary.com, Wiley Blackwell), and EMBASE via OVID (www.embase.com, Elsevier). The authors searched for clinical research not yet published in full text, or remaining unpublished in the abstract database of the International Association for Dental

Research (iadr.confex.com/iadr/search.epl). They also searched for potential clinical studies published in the grey literature or elsewhere through Google Scholar. The most recent search date was June 30, 2014, and went back to 1965, or the earliest records of the electronic bibliographic databases.

Search Strategy

The authors adopted the key words and MESH terms from a recent systematic review on the prosthetic rehabilitation of patients with edentulous jaws conducted by the Swedish Council on Health Technology Assessment (Table 1).[11] The search strategy was modified to fit the appropriate formats applicable to the different electronic bibliographic databases.

Reviews of the reference lists found in the relevant systematic reviews supplemented the search through the electronic databases (Tables 2a and 2b). The authors further hand searched recent issues of relevant scientific journals not yet recorded in the electronic databases. In addition, they used a personal indexed database of clinical studies related to oral implants and prosthetics built by the lead author containing over 4,500 references. Finally, the individual experts of the task group were asked to provide missing studies after having received tentative lists of identified publications for inclusion in the systematic review.

Study Selection

Three independent teams, each consisting of two or three coinvestigators, focused on one specific aspect of the implant design. The first focused on studies reporting on the role of overall implant body shape and thread design for the rehabilitation of the edentulous maxilla in healthy and medically compromised patients. The second focused on the role of implant length and diameter and the implant-abutment connection, while the third appraised the role of implant surface. Each team screened for study eligibility independently by using a common form and after completion, the teams swapped the topics and verified the previous search until they reached a consensus. The authors planned to resolve potential disagreements by forced decision by the task group chairs, but no such situations arose.

Data Collection Process

The three teams also collected data independently and resolved discrepancies by consensus. The authors of the primary publications were not contacted to obtain further data or to confirm extracted data.

Reports were excluded if the outcomes of the individual implants were presented as a function of their lengths or diameters, when these implants supported a prosthetic restoration jointly with other implants having different geometries. The authors also excluded studies in which the outcomes specific to a fully edentulous maxilla were not identified as a function of the implant design characteristic, if subsequent follow-up data could replace the earlier data, or if the full text of the report was inaccessible.

In situations with multiple publications from a single clinical study, the report with the longest follow-up was selected for data extraction. If particular details about materials and methods were lacking in the primary report, then the earlier reports were appraised.

Extracted Data Items

The authors followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines for selecting relevant data to extract from the individual studies. These were characteristics of the individual studies, risk of bias within the individual studies, and the results of individual studies, that is, items 18 to 20 in the PRISMA checklist.[12] Characteristics of the individual studies included identification of the lead author and description of the study participants' condition, including the anatomy of the maxilla with regard to remaining bone (Fig 1).[13] Moreover, the years when the implants were placed and whether the study was conducted in a single or multiple university, public health, or private practice settings were recorded. The number of study participants and implants placed with the follow-up time was supplemented with a description of implant-type(s) with diameters and lengths. Details of the actual intervention included: *(1)* status of the pre–implant surgery situation, *(2)* implant surgery details, *(3)* the protocols for immediate, early, or delayed implant loading, and *(4)* type of supraconstruction. Details of the treatment outcome included clinical as well as patient-relevant outcomes such as satisfaction with esthetics and function and quality of life (Table 3).

Risk of Potential Bias in Individual Studies

Elements that possibly could limit the study internal and external validity included the study's main objective and design methodology selected, the number of participants and accrued number of implants, follow-up time in years, drop-out numbers, statistical tests, and reported funding source.

Potential bias was assessed by comparing contents against a list of criteria (Table 4) compiled from two quality-assessment tools used in recent systematic reviews.[14,15] These in turn were derived from the Dutch Cochrane Centre and the Newcastle-Ottawa Scale.[16] The authors separated publications that reported an a priori intention to appraise effects of any aspect of implant design on treatment outcomes from those containing no reference to this study objective, but still reported such findings. It was considered likely that the observations made this latter category of studies spurious,

Table 1 Search Strategy for MEDLINE through PubMed*

(“Dental Implants”[MeSH:noexp] OR “Dental Implantation, Endosseous”[MeSH:noexp] OR “Blade Implantation”[MeSH] OR ((“Dentistry”[MeSH] OR “dental”[Title/Abstract])
AND
(“Osseointegration”[MeSH] OR “osseointegration”[Title/Abstract])) OR (“dental”[Title/Abstract]
AND
(“implant”[Title/Abstract] OR “implants”[Title/Abstract] OR “implantation”[Title/Abstract]))
AND
(“Denture, Overlay”[MeSH] OR “Denture, Complete”[MeSH] OR “Denture, Partial, Removable”[MeSH] OR “Dental Prosthesis, Implant-Supported”[MeSH] OR “Denture, Fixed”[MeSH:noexp] OR “denture”[Title/Abstract] OR “prosthesis”[Title/Abstract])
AND
(“Edentulous”[Title/Abstract] OR “Jaw, Edentulous”[MeSH:noexp] OR “Mouth, Edentulous”[MeSH:noexp] OR “edentulism”[Title/Abstract]) NOT “partially edentulous”[Title/Abstract]
AND
“Maxilla” [MeSH]

*Adapted from Swedish Council on Health Technology Assessment.[11]

Table 2a Systematic Reviews Published Since 2009 With a Focus on Rehabilitation of the Fully Edentulous Maxilla Using Different Surgical Strategies or With a Focus on Assessing the Patient-Relevant Outcomes

Study (y)	Title	Source	Aim
Bassi et al (2013)	Economic outcomes in prosthodontics	Int J Prosthodont 2013;26:465–469	To identify the types of economic measures currently used in implant prosthodontics and determine the degree to which cost of care is considered in the context of any positive outcome of the care provided
Bassi et al (2013)	Functional outcomes for clinical evaluation of implant restorations	Int J Prosthodont 2013;26:411–418	To identify functional assessments of speech, swallowing, mastication, nutrition, sensation, and motor function as they relate to dental implant therapies
Bassi et al (2013)	Psychologic outcomes in implant prosthodontics	Int J Prosthodont 2013;26:429–434	To identify psychologic outcomes with properties deemed critical to meet clinical trial and clinical practice needs for the future
Bidra and Huynh-Ba (2011)	Implants in the pterygoid region: A systematic review of the literature	Int J Oral Maxillofac Surg 2011; 40:773–781	To identify clinical studies on the short- and long-term survival of implants placed in the pterygoid region
Bozini et al (2011)	A meta-analysis of prosthodontic complication rates of implant-supported fixed dental prostheses in edentulous patients after an observation period of at least 5 years	Int J Oral Maxillofac Implants 2011; 26:304–318	To systematically review clinical studies on prosthodontic complication rates of implant-fixed dental prostheses in edentulous patients after an observation period of at least 5 years
Cehreli et al (2010)	A systematic review of marginal bone loss around implants retaining or supporting overdentures	Int J Oral Maxillofac Implants 2010; 25:266–277	To evaluate, through a systematic review of the literature, the effects of implant design and attachment type on marginal bone loss in implant-retained/supported overdentures
Cehreli et al (2010)	Systematic review of prosthetic maintenance requirements for implant-supported overdentures	Int J Oral Maxillofac Implants 2010;25:163–180	To evaluate prosthetic maintenance requirements for implant-retained/supported overdentures via a review of the literature
Chrcanovic and Abreu (2012)	Survival and complications of zygomatic implants: A systematic review	Oral Maxillofac Surg 2013; 17:81–93	To answer the focused questions: “What is the survival rate of zygomatic implants (zis)?” and “What are the most common complications related to surgery of zygomatic implants?”

Table 2a ***Continued*** **Systematic Reviews Published Since 2009 With a Focus on Rehabilitation of the Fully Edentulous Maxilla Using Different Surgical Strategies or With a Focus on Assessing the Patient-Relevant Outcomes**

Study (y)	Title	Source	Aim
Chung et al (2011)	Immediate loading in the maxillary arch: Evidence-based guidelines to improve success rates—A review	J Oral Implantol 2011;37:610–621	To investigate the status of immediate loading of dental implants in the maxilla to determine its predictability as a treatment option for partial and complete maxillary edentulism
Corbella et al (2013)	Long-term outcomes for the treatment of atrophic posterior maxilla: A systematic review of literature	Clin Implant Dent Relat Res 2014;17:120–132	To estimate the implant survival rate in different types of techniques for the rehabilitation of posterior atrophic maxilla, after at least 3 years of follow-up
Del Fabbro and Ceresoli (2014)	The fate of marginal bone around axial vs tilted implants: A systematic review	Eur J Oral Implantol 2014;7:171–189	To compare the crestal bone level change around axially placed vs tilted implants supporting fixed prosthetic reconstructions for the rehabilitation of partially and fully edentulous jaws, after at least 1 year of function
Del Fabbro et al (2012-2010e)	Tilted implants for the rehabilitation of edentulous jaws: a systematic review	Clin Implant Dent Relat Res 2012;14:612–621	To evaluate the survival rate of upright and tilted implants supporting fixed prosthetic reconstructions for the immediate rehabilitation of partially and fully edentulous jaws, after at least 1 year of function
Dellavia et al (2014)	Functional jaw muscle assessment in patients with a full fixed prosthesis on a limited number of implants: A review of the literature	Eur J Oral Implantol 2014;7:155–169	To assess the function of jaw muscles in edentulous patients restored with full fixed prostheses on a limited number (≤ 6) of implants, compared with dentate subjects and edentulous subjects wearing dentures, implant-supported overdentures, or full fixed prostheses supported by more than six implants
Esposito and Worthington (2013)	Interventions for replacing missing teeth: Dental implants in zygomatic bone for the rehabilitation of the severely deficient edentulous maxilla	Cochrane Database Syst Rev CD004151 2013(p3) Update of: 2005(p2), 2003(p1)	To test the hypothesis of no difference in outcomes between zygomatic implants without bone augmenting procedures in comparison with conventional dental implants in augmented bone for severely resorbed maxillae
Esposito et al (2014)	Interventions for replacing missing teeth: Augmentation procedures for the maxillary sinus	Cochrane Database Syst Rev 2014;5:CD008397	To determine whether and when augmentation of the maxillary sinus is necessary and which are the most effective augmentation techniques for rehabilitating patients with implant-supported prostheses
Gallucci et al (2009)	Loading protocols for dental implants in edentulous patients	Int J Oral Maxillofac Implants 2009;24 (suppl 1):132–146	To present the current scientific and clinical evidence related to implant-supported rehabilitations for the edentulous mandible and maxilla
Goiato et al (2014)	Implants in the zygomatic bone for maxillary prosthetic rehabilitation: A systematic review	Int J Oral Maxillofac Surg 2014;43:748–757	To evaluate clinical studies on the follow-up survival of implants inserted in the zygomatic bone for maxillary rehabilitation
Heydecke et al (2012)	What is the optimal number of implants for fixed reconstructions: A systematic review	Clin Oral Implants Res 2012; 23(suppl 6): 217–228	To assess the 5- and 10-year survival and complication rates of implant-supported fixed reconstructions in partially and totally edentulous patients with regard to the optimal number and distribution of dental implants
Kotsakis et al (2014)	A systematic review of observational studies evaluating implant placement in the maxillary jaws of medically compromised patients	Clin Implant Dent Relat Res 2015;17:598–609	To evaluate the survival of implants placed in the maxillary jaws of medically compromised patients

Table 2a ***Continued*** **Systematic Reviews Published Since 2009 With a Focus on Rehabilitation of the Fully Edentulous Maxilla Using Different Surgical Strategies or With a Focus on Assessing the Patient-Relevant Outcomes**

Study (y)	Title	Source	Aim
Lambert et al (2009)	Descriptive analysis of implant and prosthodontic survival rates with fixed implant-supported rehabilitations in the edentulous maxilla	J Periodontol 2009; 80:1220–1230	To review the 1- to 15-year survival rates of fixed implant rehabilitations in the edentulous maxilla
McGrath et al (2012)	An evidence-based review of patient-reported outcome measures in dental implant research among dentate subjects	J Clin Periodontol 2012;39:193–201	To conduct an evidence-based review of patient-reported outcome measures in dental implant research among dentate patients so as to gain an understanding of the use of such measures, and the potential evidence that can be gleaned from such studies
Menini et al (2012)	Tilted implants in the immediate loading rehabilitation of the maxilla: A systematic review	J Dent Res 2012;91:821–827	To evaluate the outcomes of upright and tilted implants supporting full-arch fixed dentures for the immediate rehabilitation of edentulous maxillae, after at least 1 year of function
Mericske-Stern and Worni (2014)	Optimal number of oral implants for fixed reconstructions: A review of the literature	Eur J Oral Implantol 2014;7:133–153	To review best evidence for the preferred or best number of implants to be used for the support of a fixed prosthesis in the edentulous maxilla or mandible
Monje et al (2012)	Marginal bone loss around tilted implants in comparison to straight implants: A meta-analysis	Int J Oral Maxillofac Implants 2012;27:1576–1583	To compare the amount of marginal bone loss around tilted and straight implants, and to compare the incidence of biomechanic complications as the secondary aim
Ohkubo and Baek (2010)	Does the presence of antagonist remaining teeth affect implant overdenture success? A systematic review	J Oral Rehabil 2010;37:306–312	To clarify the correlation between existing teeth and the survival/success rate of maxillary and mandibular implant overdentures
Papaspyridakos et al (2012)	A systematic review of biologic and technical complications with fixed implant rehabilitations for edentulous patients	Int J Oral Maxillofac Implants 2012;27:102–110	To assess the incidence and types of biologic and technical complications associated with implant-supported fixed complete dental prostheses for edentulous patients
Patzelt et al (2014-2013e)	The all-on-four treatment concept: A systematic review	Clin Implant Dent Relat Res 2014;16:836–855	To evaluate the all-on-four treatment concept with regard to survival rates of oral implants, applied fixed dental prostheses and temporal changes in proximal bone levels
Pommer et al (2014)	Patients' preferences towards minimally invasive treatment alternatives for implant rehabilitation of edentulous jaws	Eur J Oral Implantol 2014; 7:91–109	To evaluate patient satisfaction, oral health–related quality of life, and patients' preferences toward minimally invasive treatment options for graftless rehabilitation of complete edentulism by means of dental implants
Raghoebar et al (2014)	A systematic review of implant-supported overdentures in the edentulous maxilla, compared to the mandible: How many implants?	Eur J Oral Implantol 2014;7:191–201	To review the treatment outcome of concepts used for implant-supported maxillary overdentures, focusing on the survival of implants, survival of maxillary overdentures, and condition of the implant surrounding hard and soft tissues after a mean observation period of at least 1 year
Roccuzzo et al (2012)	What is the optimal number of implants for removable reconstructions? A systematic review on implant-supported overdentures	Clin Oral Implants Res 2012;23 (suppl 6):229–237	To assess the optimal number of implants for removable reconstructions

Table 2a ***Continued*** **Systematic Reviews Published Since 2009 With a Focus on Rehabilitation of the Fully Edentulous Maxilla Using Different Surgical Strategies or With a Focus on Assessing the Patient-Relevant Outcomes**

Study (y)	Title	Source	Aim
Sánchez-Ayala et al (2010)	Nutritional effects of implant therapy in edentulous patients: A systematic review	Implant Dent 2010;19:196–207	To present all the relevant studies that have evaluated the possible physical and nutrient intake improvements of edentulous subjects rehabilitated with removable and supported or retained implant dentures
Schley and Wolfart (2011)	Which prosthetic treatment concepts present a reliable evidence-based option for the edentulous maxilla related to number and position of dental implants?	Eur J Oral Implantol 2011;4:31–47	To answer the following questions: Which prosthetic treatment concept related to implant number and position presents a reliable evidence-based option for the edentulous maxilla?
Slot et al (2010)	A systematic review of implant-supported maxillary overdentures after a mean observation period of at least 1 year	J Clin Periodontol 2010;37:98–110	To assess the survival of implants, survival of maxillary overdentures, and the condition of surrounding hard and soft tissues after a mean observation period of at least 1 year
Vogel et al (2013)	Evaluating the health economic implications and cost-effectiveness of dental implants: A literature review	Int J Oral Maxillofac Implants 2013;28:343–356	To review the available literature on the costs and cost-effectiveness of dental implant-supported or -retained prostheses vs tooth-supported fixed partial denture restorations or mucosa-borne conventional complete or partial dentures

Table 2b **Systematic Reviews Published Since 2009 With a Focus on Effects of Characteristics of Implant***

Study (y)	Title	Source	Aim
Abrahamsson and Berglundh (2009)	Effects of different implant surfaces and designs on marginal bone-level alterations: A review	Clin Oral Implants Res 2009;20(suppl 4): 207–215	To evaluate the effect of different implant surfaces and designs on marginal bone-level alterations
Al-Nsour et al (2012)	Effect of the platform-switching technique on preservation of peri-implant marginal bone: A systematic review	Int J Oral Maxillofac Implants 2012; 27:138–145	To systemically review the effect of platform switching on preserving implant marginal bone
Aloy-Prósper et al (2011)	Marginal bone loss in relation to the implant neck surface: An update	Med Oral Patol Oral Cir Bucal 2011; 16:e36 5–e368	To appraise publications on the marginal bone loss of implants with a polished neck, rough neck with microthreading, and rough neck without microthreading
Alsabeeha et al (2012)	Hydroxyapatite-coated oral implants: A systematic review and meta-analysis	Int J Oral Maxillofac Implants 2012;27:1123–1130	To evaluate treatment outcomes of hydroxyapatite-coated implants in comparison to nonhydroxyapatite-coated implants
Andreiotelli et al (2009)	Are ceramic implants a viable alternative to titanium implants? A systematic literature review	Clin Oral Implants Res 2009;20(suppl 4): 32–47	To locate animal and clinical data on bone-implant contact and clinical survival/success that would help to answer the question "Are ceramic implants a viable alternative to titanium implants?"
Annibali et al (2011)	Short dental implants: A systematic review	J Dent Res 2012;91:25–32	To systematically evaluate clinical studies of implants < 10 mm in length, to determine short implant-supported prosthesis success in the atrophic jaw

*Characteristics such as material, surface, dimension including diameter or length, one- or two-piece, implant-abutment connection on outcomes.

Table 2b ***Continued*** **Systematic Reviews Published Since 2009 With a Focus on Effects of Characteristics of Implant***

Study (y)	Title	Source	Aim
Annibali et al (2012)	Peri-implant marginal bone level: A systematic review and meta-analysis of studies comparing platform switching versus conventionally restored implants	J Clin Periodontol 2012;39:1097–1113	To systematically review the literature to compare implant survival and marginal bone loss around platform-switched vs conventionally restored platform-matching dental implants
Atieh et al (2010)	Platform switching for marginal bone preservation around dental implants: A systematic review and meta-analysis	J Periodontol 2010;81:1350–1366	To systematically review radiographic marginal bone level changes and the survival of platform-switched implants compared with conventional platform-matched implants
Atieh et al (2012)	Survival of short dental implants for treatment of posterior partial edentulism: A systematic review	Int J Oral Maxillofac Implants 2012;27:1323-1331	To systematically review studies concerning dental implants of ≤ 8.5 mm placed in the posterior maxilla and/or mandible to support fixed restorations
Barrachina-Díez et al (2013)	Long-term outcome of one-piece implants. Part I: Implant characteristics and loading protocols–A systematic literature review with meta-analysis	Int J Oral Maxillofac Implants 2013;28:503–518	To evaluate the long-term clinical performance of one-piece implants
Barrachina-Díez et al (2013)	Long-term outcome of one-piece implants. Part II: Prosthetic outcomes–A systematic literature review with meta-analysis	Int J Oral Maxillofac Implants 2013; 28:1470–1482	To evaluate the long-term clinical performance of prosthetic reconstructions on one-piece implants, with a focus on technical and biological complications
Bateli et al (2011)	Implant neck configurations for preservation of marginal bone level: A systematic review	Int J Oral Maxillofac Implants 2011;26:290–303	To evaluate the effectiveness of various implant neck configurations in the preservation of marginal bone level as well as to identify the available scientific evidence
Bishti et al (2014-2013e)	Effect of the implant-abutment interface on peri-implant tissues: A systematic review	Acta Odontol Scand 2014;72:13–25	To determine the peri-implant tissue response to different implant abutment materials and designs available and to assess the impact of tissue biotype
Depprich et al (2014-2012e)	Current findings regarding zirconia implants	Clin Implant Dent Relat Res 2014;16:124–137	To analyze the available clinical data on the survival and success rate of dental zirconia implants
Elangovan et al (2013)	Quality assessment of systematic reviews on short dental implants	J Periodontol 2013;84:758–767	To analyze the quality of published systematic reviews focused on short dental implants using established checklists such as the assessment of multiple systematic reviews
Esposito et al (2014)	Interventions for replacing missing teeth: Different types of dental implants	Cochrane Database Syst Rev CD003815 2014(p4) Update of: 2007(p4), 2005(p3), 2003(p2), 2002(p1)	To test the null hypothesis of no difference in clinical performance between various root-formed osseointegrated dental implant types
Gracis et al (2012)	Internal vs. external connections for abutments/ reconstructions: A systematic review	Clin Oral Implants Res 2012;23(suppl 6):202–216	(1) To evaluate the accuracy of implant-level impressions in cases with internal and external connection abutments/reconstructions, and (2) to evaluate the incidence of technical complications
Junker et al (2009)	Effects of implant surface coatings and composition on bone integration: A systematic review	Clin Oral Implants Res 2009;20(suppl 4):185–206	To evaluate the bone integration efficacy of recently developed and marketed oral implants as well as experimental surface alterations

*Characteristics such as material, surface, dimension including diameter or length, one- or two-piece, implant-abutment connection on outcomes.

Table 2b ***Continued*** **Systematic Reviews Published Since 2009 With a Focus on Effects of Characteristics of Implant***

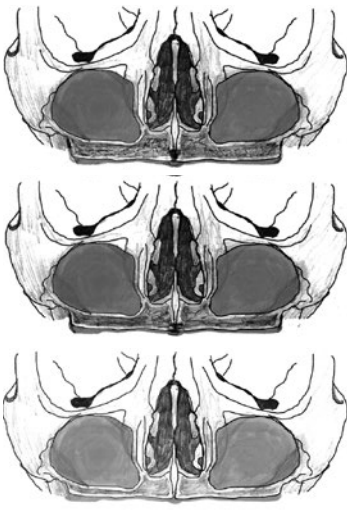
Study (y)	Title	Source	Aim
Kotsovilis et al (2009)	A systematic review and meta-analysis on the effect of implant length on the survival of rough-surface dental implants	J Periodontol 2009; 80:1700–1718	To address the focused question "Is there a significant difference in survival between short (or = 10 mm) rough-surface dental implants placed in (1) totally or (2) partially edentulous patients?"
Laurell and Lundgren (2011-2009e)	Marginal bone level changes at dental implants after 5 years in function: A meta-analysis	Clin Implant Dent Relat Res 2011;13:19–28	To compile and compare data on peri-implant marginal bone level changes from prospective studies that have registered the peri-implant marginal bone level radiographically after 5 years of follow-up for implant systems currently available on the market
Menchero-Cantalejo et al (2011)	Meta-analysis on the survival of short implants	Med Oral Patol Oral Cir Bucal 2011;16:e546–e551	To evaluate the success and failure rates of short implants (10 mm or less) for oral rehabilitations in cases of limited bone height
Monje et al (2013a)	Are short dental implants (< 10 mm) effective? A meta-analysis on prospective clinical trials	J Periodontol 2013; 84:895–904	To compare the survival rate of short (< 10 mm) and standard (≥ 10 mm) rough-surface dental implants under functional loading.
Monje et al (2013b)	Do implant length and width matter for short dental implants (< 10 mm)? A meta-analysis of prospective studies	J Periodontol 2013;84:1783–1791	To determine the effects of dental implant length and width on implant survival rate of short (6-9 mm) implants
Neldam and Pinholt (2012)	State of the art of short dental implants: A systematic review of the literature	Clin Implant Dent Relat Res 2012;14:622–632	To evaluate publications on short dental implants, defined as an implant with a length of ≤ 8 mm, installed in the maxilla or in the mandible with special reference to implant type, survival rate, location of implant site, and observation time
Pommer et al (2011)	Impact of dental implant length on early failure rates: A meta-analysis of observational studies	J Clin Periodontol 2011;38:856–863	To test the null hypothesis of no difference in failure rates of short (minimum length: 7 mm) and longer dental implants (≥ 10 mm) in a meta-analysis of prospective observational trials
Renvert et al (2011)	How do implant surface characteristics influence peri-implant disease?	J Clin Periodontol 2011;38(suppl 11):214–222	To review the literature on how implant surface characteristics influence peri-implant disease
Romeo et al (2010)	The use of short dental implants in clinical practice: Literature review	Minerva Stomatol 2010; 59:23–31	To evaluate the differences in survival rate and the rational use of short implants
Rungruanganunt et al (2013)	The effect of static load on dental implant survival: A systematic review	Int J Oral Maxillofac Implants 2013;28:1218–1225	To systematically review the current evidence related to the effects of static loading on the long-term stability of the osseointegrated interface
Schmitt et al (2013)	Performance of conical abutment (Morse Taper) connection implants: A systematic review	J Biomed Mater Res A 2014;102:552–574	To compare conical vs nonconical implant-abutment connection systems in terms of their in vitro and in vivo performances
Sohrabi et al (2012)	How successful are small-diameter implants? A literature review	Clin Oral Implants Res 2012;23:515–524	To determine (1) the survival of narrow diameter implants, (2) whether survival is dependent on whether these implants are placed using a flap or flapless approach, and (3) whether there is a relationship between length and implant survival in short dental implants
Srinivasan et al (2012)	Efficacy and predictability of short dental implants (< 8 mm): A critical appraisal of the recent literature	Int J Oral Maxillofac Implants 2012;27:1429–1437	To evaluate the predictability of treatment outcomes with short dental implants, implants shorter than 8 mm

*Characteristics such as material, surface, dimension including diameter or length, one- or two-piece, implant-abutment connection on outcomes.

Table 2b ***Continued*** **Systematic Reviews Published Since 2009 With a Focus on Effects of Characteristics of Implant***

Study (y)	Title	Source	Aim
Srinivasan et al (2013)	Survival rates of short (6 mm) micro-rough surface implants: A review of literature and meta-analysis	Clin Oral Implants Res 2014;25:539–545	To test the hypothesis that 6 mm micro-rough short Straumann implants provide predictable survival rates and verify that most failures occurring are early failures
Sun et al (2011)	Failure rates of short (≤ 10 mm) dental implants and factors influencing their failure: A systematic review	Int J Oral Maxillofac Implants 2011;26:816–825	To evaluate the long-term failure rates of short dental implants (≤ 10 mm) and to analyze the influence of various factors on implant failure
Telleman et al (2011)	A systematic review of the prognosis of short (< 10 mm) dental implants placed in the partially edentulous patient	J Clin Periodontol 2011;38:667–676	To evaluate, through a systematic review of the literature, the estimated implant survival rate of short (< 10 mm) dental implants placed in partially edentulous patients.
van Oirschot et al (2013-2012e)	Long-term survival of calcium phosphate-coated dental implants: A meta-analytical approach to the clinical literature	Clin Oral Implants Res 2013;24:355–362 [Epub 2012]	To systematically appraise and to conduct a meta-analysis of long-term survival data of calcium phosphate–coated dental implants in clinical trials
Vouros et al (2012)	Systematic assessment of clinical outcomes in bone-level and tissue-level endosseous dental implants	Int J Oral Maxillofac Implants 2012;27:1359–1374	To address the clinical and radiographic outcomes of bone-level implants vs tissue-level implants after restoration with dental prostheses
Wennerberg and Albrektsson (2009)	Effects of titanium surface topography on bone integration: A systematic review	Clin Oral Implants Res 2009;20(suppl 4):172–184	To analyze possible effects of titanium surface topography on bone integration

*Characteristics such as material, surface, dimension including diameter or length, one- or two-piece, implant-abutment connection on outcomes.



Cawood Howell–Anatomy

Class	Ridge form	Height	Width	Comment
II				Post extraction
III	Round	Adequate (> 10 mm)*	Adequate (> 4 mm)*	*
IV	Knife edge	Adequate (> 10 mm)	Inadequate (< 4 mm)	
V	Flat	Inadequate (< 10 mm)	Inadequate (< 4 mm)	
VI	Depression			Some loss of basal bone evident

*mm not described in original paper.

Fig 1 Illustration of approximate remaining maxillary bone according to the Cawood-Howell bone classification system.[13] Note that the authors did not state the dimensions in millimeters in their original study.

and the article therefore probably more prone to bias than the studies designed for the purposes of appraising implant design effects.

The statistical method was appraised for appropriateness, in light of the stated study objective, with particular emphasis on statistical test assumptions and choice of statistical unit. In addition, the authors recorded whether a formal ethics board or committee had approved the study protocol, and whether the authors declared a funding source of the study. Both

Table 3 Treatment Outcomes in Edentulous Maxilla
Immediate
Surgical complications
Prosthodontic complications
Late
Dissatisfaction with function
Speech/chewing ability/other (eg, saliva spray)
Dissatisfaction with appearance
Prominent chin ("bulge")
Sunken profile (posterior medial modiolus, large nasolabial angle, marked nasolabial fold)
Teeth not showing
Upper lip not showing (orbicularis oris collapse)
Transition line prosthesis: tissue visible upon smiling
Occlusally related
Even functional occlusion (articulation)
Overclosure
Pain in temporomandibular joint, possibly because of incorrect vertical dimension of occlusion
Biological adverse outcome
Ulcers/soreness/bleeding, possibly because of lack of oral health access
Inflammatory peri-implant diseases
Technical adverse outcome
Supraconstruction
Ill-fit supraconstruction to implants
Implant system components wear and break down
Cost/fiduciary aspects
Maintenance needs

Table 4 Appraisal of Risk of Potential Bias in Individual Studies				
1.	Is there a clearly stated study objective that matches the reported outcome?	1	?	0
2.	Is the study design appropriate with respect to the stated study objective?	1	?	0
3.	Has an ethics board approved the study?	1	?	0
4.	Are the characteristics of the study participants clearly described?	1	?	0
5.	Is there a risk of selection bias – are the inclusion and exclusion criteria clearly described?	1	?	0
6.	Are all steps of the intervention clearly described – if comparative, are all participants treated according to the same intervention (apart from factor of interest)?	1	?	0
7.	Are the outcomes clearly described – are adequate methods used to assess these outcomes?	1	?	0
8.	Has blinding been used when outcomes have been assessed?	1	?	0
9.	Is the follow-up rate satisfactory?	1	?	0
10.	Are all participants accounted for?	1	?	0
11.	Can selective loss to follow-up likely be excluded?	1	?	0
12.	Are the most important confounders or prognostic factors identified and are these taken into consideration with respect to the study design and analysis?	1	?	0
13.	Are the statistical analyses appropriate in light of the study objective, test assumptions, and choice of statistical unit?	1	?	0
14.	Is the funding source for the study declared?	1	?	0

1 = yes, 0 = no, ? = unclear

criteria were associated with a lower risk of potential bias. Formal statistical assessment to assess publication bias was not applied.

Summary Measures

The authors planned this systematic review to present primarily descriptive data as a basis for the development of clinical practice guidelines following the process described by Rosenfeld and Shiffman.[17] They considered using RevMan 5 (Nordic Cochrane Centre) for conducting meta-analyses, if possible. Unfortunately, the yield of the literature search was limited, and the reports too heterogeneous with regard to study methods as well as clinical procedures and variables. Hence, no forest or funnel plots were generated in this review. The authors recommend that the reader appraise the systematic reviews listed in Tables 2a and 2b for meta-analytic data.

RESULTS

Study Selection

Approximately 1,000 studies were identified initially. After screening the abstracts, about half of these (n = 473) were not eligible according to the a priori inclusion criteria. The predominant reason was a follow-up period of less than 2 years (n = 340) or fewer than 10 study participants (n = 91) or lacking both criteria (n = 34)

(Fig 2). The heterogeneous formats of the abstract and reporting of clinical outcomes precluded conclusive decisions about inclusion and exclusion so the full text of the remaining 525 articles were scrutinized. About one fifth of these reports were selected for data extraction (n = 105). The major reason for exclusion was that the outcomes as a function of implant design aspects specific to a rehabilitated edentulous maxilla could not be identified in the report (n = 382) (Fig 2). Further details on the nonincluded and excluded reports, including reasons for decision are located on the website of the Academy of Osseointegration (www.osseo.org).

Within the overall PICO, the authors identified six subcategories by an amalgamation of the preimplant surgery characteristics of the study participants, combined with the complexity level and sequence of interventions (Table 5 and Figs 3–7).

Study Characteristics

Studies Designed to Assess Effects of Implant Design or Particular Feature on Outcomes (Fig 3). The literature search identified 196 reports, of which 77 were not included and 102 were excluded (Table 6)[18–31]. As many as 34 reports were from one study cohort, that is, the extensive Dental Implant Clinical Research Group (DICRG) study undertaken by 30 Veterans Affairs Medical Centers across the United States.[32] The predominant reason for noninclusion was reported observation period less than 2 years (n = 77), while the dominant reason for study exclusion was that outcomes as a function of aspects of implant design specific to a rehabilitated edentulous maxilla could not be identified in the article (n = 79). A common experience was that reports with focus on "maxillary posterior atrophy," with or without sinus grafting often failed to describe whether the study participants were partially or fully edentulous. The authors selected 17 reports published between 1995 and 2013 for data extraction.[18–34]

The studies selected for data extraction included study participant cohorts that encompassed all categories of patient conditions[23,26,32] or only participants with edentulous jaws or an edentulous maxilla. Four studies included study participants with terminal teeth, who received immediate postextraction implants.[19,25,30,31]

The 17 reports presented results based on 3,205 study participants with 12,599 implants placed between 1987[34,35] and 2008.[19] The study settings were single private (n = 6), university (n = 6), public (n = 2), or multicenter (n = 3). The study cohorts ranged between 12 and 829[32] participants with 72 to 2,955[32] implants, which were followed up from 2 to 15[21] years. The prevailing implant systems used were manufactured by Nobel Biocare (n = 10), Astra Tech and Biomet 3i (n = 3), Straumann (n = 2), and Lifecore (n = 1), Camlog (n = 1), Dentsply (n = 1), and CoreVent (n = 1). Two studies did not report the name of the implant manufacturer.

Studies Reporting the Effects of Tilted Implants to Enable Placement of Longer Implants (Fig 4). The literature search identified 46 reports, of which 21 were not included and 2 were excluded because cylindrical implants were placed in healed sites, whereas tapered implants were placed in all postextraction sites. The most predominant reason for noninclusion was lack of an observation period longer than 2 years (n = 18). Twenty-three reports remained for data extraction, primarily with the intent of comparing the outcome of the axial vs (invariably longer) tilted implants (Table 7).[35–57]

The studies selected for data extraction were published between 1999[57] and 2014,[35–37] and included study participant cohorts that encompassed partially edentate or fully edentulous maxilla. Some of the studies focused on patients with a general or posterior maxillary atrophy. Twelve reports included study participants with terminal teeth, who received immediate postextraction implants, either axially placed or tilted or both. It was often difficult to judge whether some of the reports described outcomes of the same or separate study participant cohorts.

The 23 reports presented results based on 1,516 study participants with 6,681implants placed between 1991[55] and 2012.[38] The study settings were single private (n = 8), university (n = 8), not reported (n = 4), public (n = 1), or multicenter (n = 2). The study cohorts ranged between 15 and 242 participants with 68 to 995 implants, followed up from 2 to 12 years. The prevailing implant systems used were manufactured by Nobel Biocare (n = 15), Biomet 31 (n = 2), and one each by Zimmer, Sweden & Martina, and Friatec/Friadent.Three studies did not report the name of the implant manufacturer. Separate outcomes as a function of different types or features of implants could be extracted from five reports.[42,46–48,52]

Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 5). The literature search identified 56 reports, of which 26 were not included because either the observation period was less than 2 years or the study population was less than 10. Thirty reports remained for data extraction, primarily with the intent to compare the intrapatient outcome of the zygoma vs conventional implants (Table 8).[58–87]

The studies selected for data extraction were published between 2002[87] and 2014[58–60] and included study participant cohorts that encompassed partially edentate or fully edentulous maxilla. Most of the studies reported that there was general or posterior atrophy, but few described the actual Cawood-Howell classifications.[13] None of the studies included participants with terminal teeth, who received immediate

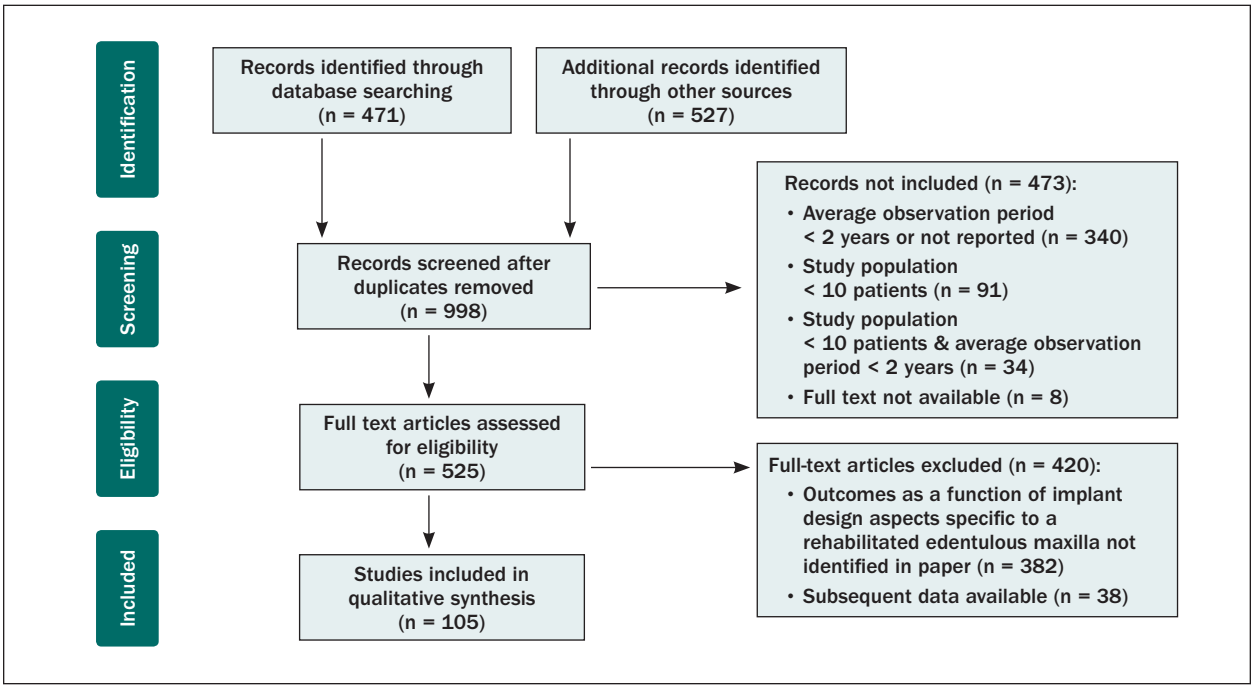


Fig 2 PRISMA flow-chart.[12] Reports of studies describing implant-supported prosthesis in fully edentulous maxilla.

Table 5 Subcategories of Reports Based on Characteristics of Study Design as well as Strategy for Surgical Intervention

Study Objective	Identified	Not Included	Excluded	Included
To assess effects of implant design or feature on outcomes (all categories of the Cawood-Howell bone classification system)[18–34]	196	77	102	17
To report effects of tilted implants to enable placement of longer implants (all categories of the Cawood-Howell bone classification system)[35–57]	46	21	2	23
To report effects of implants placed in zygomatic bone with or without additional alveolar implants (predominantly Cawood-Howell bone class V and VI)[58–87]	56	26	0	30
To report effects of implants placed in pterygoid bone or other bony buttresses with or without additional alveolar implants (predominantly Cawood-Howell bone class V and VI)[88–96]	13	4	0	9
To report bone augmentation with simultaneous or delayed implant placement (predominantly Cawood-Howell bone class V and VI)[97–112]	165	92	57	16
No a priori stated objective to assess a particular implant design or feature (all categories of the Cawood-Howell bone classification system)[113–122]	522	253	259	10
Total	998	473	420	105

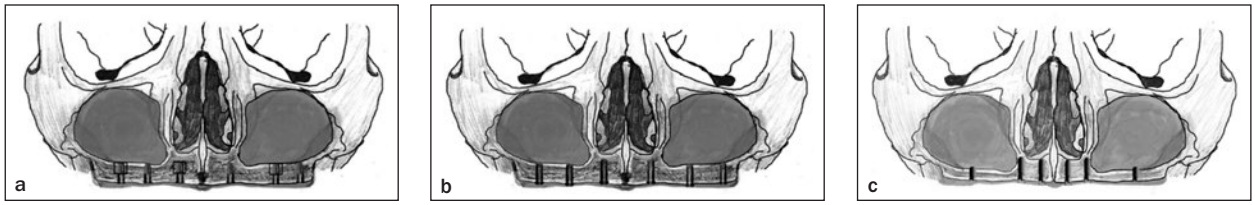


Fig 3 Examples of variations in study designs applied to appraise effects of implant design features, beyond parallel study cohort comparisons.[21] *(a)* Placement of implants in random locations, in this case, Brånemark implants with two different tap relief profiles.[34] *(b)* Split-mouth study, eg, comparing effects of different CoreVent implants.[32] *(c)* Comparing short Straumann implants placed in limited bone distally, with longer implants placed anteriorly in study participants with Cawood-Howell class IV maxilla.[22]

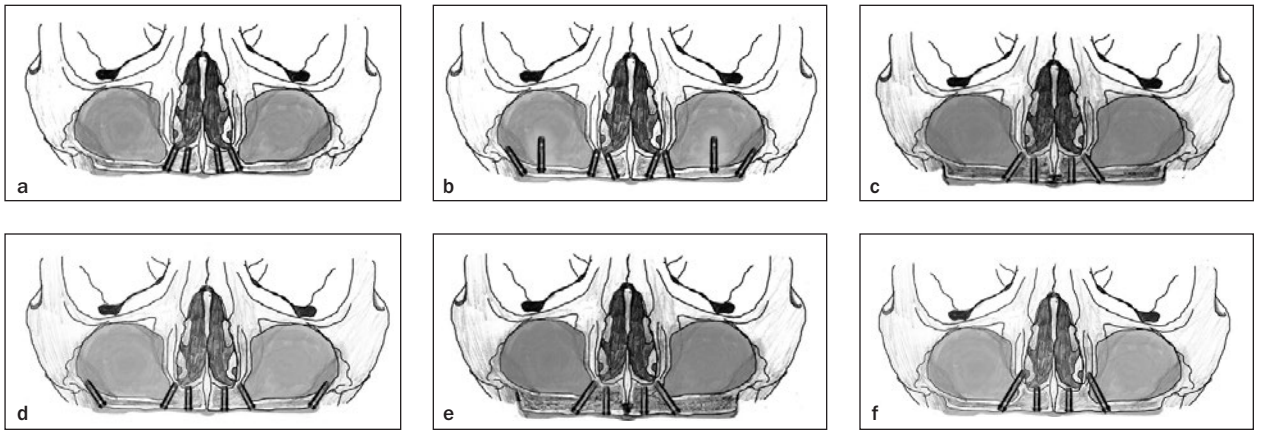


Fig 4 Examples of diversity of surgical approaches using tilted implants. Two left examples were alternatives to bone augmentation techniques in study participants with Cawood-Howell (C-H) bone class V/VI.[56, 57] *(a)* Four distally tilted Brånemark implants in a C-H V/VI maxilla[57]; *(b)* two axial and two 30- to 45-degree distally tilted Brånemark implants in C-H III/IV maxilla[55]; *(c)* two axial and two 30-degree distally tilted "externally hexed" implants in immediate extraction sockets (C-H II).[44] Note relative gain in tilted implant lengths vs axial as a function of increasing bone height. Bottom figures show alternatives to bone augmentation techniques in study participants with C-H V/VI bone; *(d)* two distally and four mesially 25- to 30-degree tilted and two Brånemark implants in palatal vault[56]; *(e)* two axial and four 25- to 30-degree mesially and distally tilted Brånemark implants[52]; *(f)* two axial and two distally tilted implants, but through the sinus to obtain fixation in four layers of cortical bone.[39]

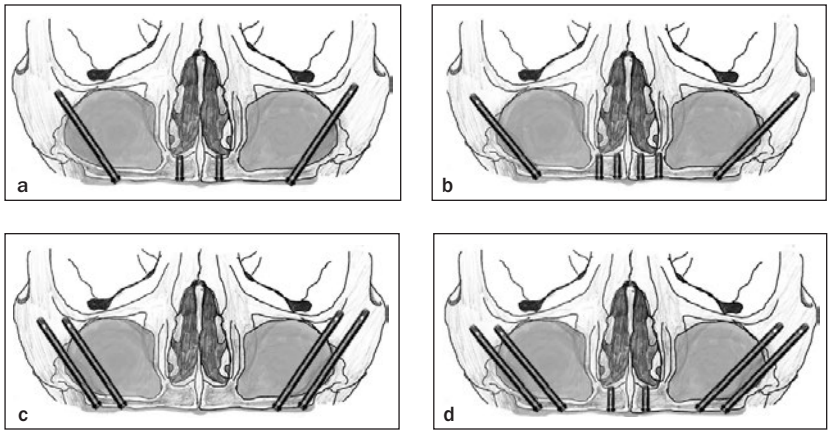


Fig 5 Examples of diversity of surgical approaches using zygomatic implants in study participants with Cawood-Howell bone class IV to VI. *(a)* Two trans-sinus zygomatic and two conventional implants[87]; *(b)* four trans-sinus zygomatic[86]; *(c)* two extrasinus zygomatic and four conventional implants[64]; *(d)* four extrasinus zygomatic implants and two conventional implants.[68]

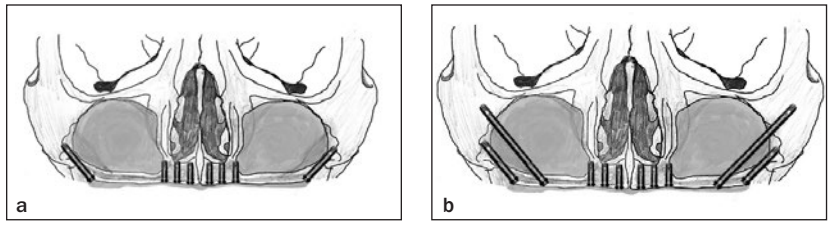


Fig 6 Examples of the use of pterygomaxillary implants in study participants with Cawood-Howell bone class IV to VI. *(a)* Two Brånemark pterygomaxillary and six conventional Brånemark implants[96]; *(b)* two Brånemark pterygomaxillary, six Brånemark conventional implants, and two zygomatic implants, also known as the "teeth-in-an-hour" concept.[95]

postextraction implants. In some reports, it was often difficult to judge whether they described outcomes of the same or different study cohorts.

Between 1990[85] and 2013,[60] 1,359 study participants received 6,394 conventional and zygoma implants. The study settings were single private (n = 15), university (n = 6), not reported (n = 4), public (n = 4), or multicenter (n = 1). The study cohorts ranged between 11 and 352[61] participants with 48 to 1,542[61] implants, followed up from 2 to 10 years. The implant system used was almost universally manufactured by Nobel Biocare (n = 30). Other systems were Defcon (n = 1), Phibo (n = 1), and one unreported implant manufacturer. Separate outcomes as a function of implant features, eg, turned vs oxidized implant surface, were not presented in any of the reports.

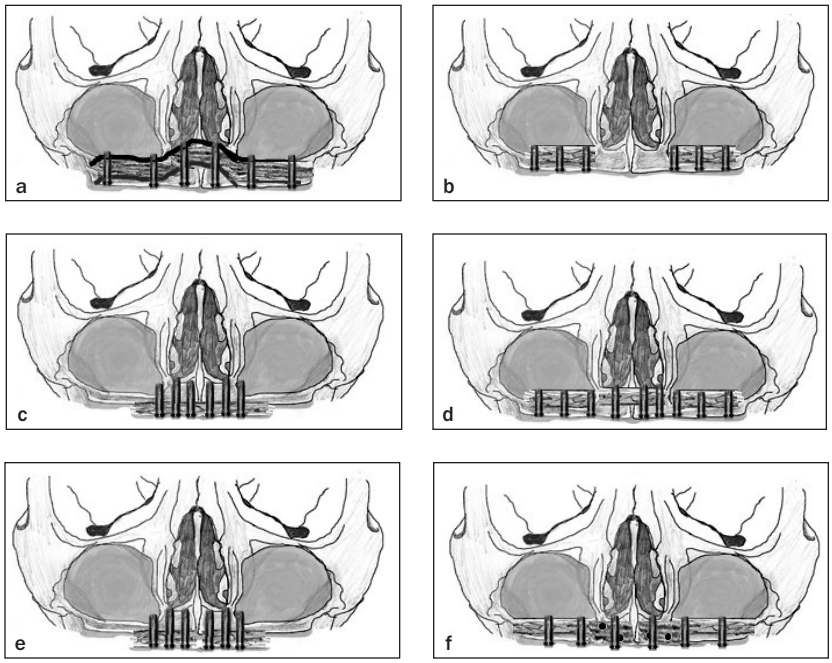


Fig 7 Examples of the diversity of surgical approaches for bone augmentation with simultaneous or delayed implant placement in study participants with Cawood-Howell bone class IV to VI. *(a)* Le Fort I fracture with interpositional fixation and immediate or delayed placement of six Brånemark implants.[109] *(b)* Full-arch onlay block with six immediate Brånemark implants.[104] *(c)* Segmental block onlay with delayed Brånemark implants. *(d)* Segmental inlay blocks in sinus with six immediate loading Brånemark implants.[112] *(e)* Right segmental inlay blocks in sinuses and nasally with nine immediate loading Brånemark implants.[106] *(f)* Segmental blocks in sinus and horizontal onlay anteriorly with Brånemark implants placed 4 to 7 months later.[102]

Studies Reporting the Effects of Implants Placed in Pterygoid Bone or Other Bony Buttresses With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 6). The literature search identified 13 reports, of which 9 were selected for data extraction, primarily with the intent to compare the outcome of the pterygomaxillary vs conventional implants (Table 9).[88–96]

The studies selected for data extraction were published between 1999[96] and 2013,[88] and included study participant cohorts that encompassed partially edentate or fully edentulous maxilla. Most studies reported that there was general or posterior atrophy. Two studies included participants with terminal teeth,[89,95] who received immediate postextraction implants. In some reports, it was often difficult to judge whether they described outcomes of the same or different study cohorts.

A total of 1,814 study participants received 6,808 implants between 1985[89,90] and 2010.[89,90] The study settings were a single private practice in the United States (n = 4), or from a single university in Spain (n = 4) and one private practice. The study cohorts had a range of 18 to 981[89] participants with 117 to 1,817[96] implants, followed up from 2 to 25 years.[89] The implant systems were manufactured by Nobel Biocare (n = 5), Defcon (n = 2), and one each by Astra Tech, Biomet 3i, Phibo, and Straumann. Four studies reported outcomes as a function of implant design.[89,90,95,96]

Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting An Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 7). The literature search identified 165 reports, of which 92 were not included because either the observation period was less than 2 years or the study population was less than 10. Fifty-five of the 57 excluded articles did not report outcomes as a function of implant design aspects specific to a rehabilitated edentulous maxilla. Sixteen reports remained for data extraction (Table 10).[97–112]

The studies selected for data extraction were published between 1994[112] and 2013,[97,98] and included cohorts that encompassed all categories of participant situations, or included only participants with a fully edentulous maxilla. Most articles described the study participants' atrophic maxilla according to the Cawood-Howell classification.[13] None of the studies included participants with terminal teeth, who received immediate postextraction implants. In some reports, it was often difficult to judge whether they described outcomes of the same or different study participant cohorts.

A total of 937 study participants received 5,667 implants between 1984[105,106,112] and 2009.[97] The study settings were public hospitals (n = 8), university (n = 5), or multicenter (n = 3). The study cohorts had a range of 10 to 224[97] participants with 60 to 1,120[102] implants, followed up for 2 to 14 years.[97] The implant systems were manufactured by Nobel Biocare (n = 11), Astra

Table 6 Characteristics of Studies Designed With an Objective to Assess Effects of Implant Design (/Feature) on Outcomes

Study	Patient Situation	Year Placed	Setting
Jungner et al (2014-2012e)[18]	Edentulous (31p, 148i) Partial edentate (39p, 103i), Single (33p, 36i), mandible, maxilla	2001–2002	Private practice, Umeå, Sweden
Vervaeke et al (2015-2013e)[19]	Terminal/edentulous mandible (52p, 269i), maxilla (39p,250i)	2002–2008	University clinic, Milano, Italy
Testori et al (2014-2013e)[20]	Edentulous(736i), partial dentate (419i), single (165i), mandible (563i), maxilla (757i)	2004–2007	Private practice
Ravald et al (2013)[21]	Edentulous mandible (32p, 165i), maxilla (34p, 206i)	1993–1995	Public health, Linköping, Sweden
Van Assche et al (2012-2011e)[22]	Edentulous maxilla	NR	University clinic, Leuven, Belgium
Cosyn et al (2012-2010e)[23]	All categories	2004–2007	University hospital, Ghent, Belgium
Kallus et al (2009-2008e)[24]	Edentulous mandible (358i), maxilla (222i)	NR	Private practice, Stockholm, Sweden
Li et al (2009)[25]	Terminal/edentulous mandible (63p, 371i), maxilla (48p, 319i)	2001–2007	Private practice, Hong Kong
Alsaadi et al (2008)[26]	All categories	NR	University clinic, Leuven, Belgium
Nelson et al (2008)[27]	Edentulous mandible/maxilla (418i), partial dentate mandible/maxilla (114i)	2000–2005	University clinic, Berlin, Germany
Maló et al (2007)[28]	Edentulous (54i), partial dentate (296i), single (58i), mandible (278i), maxilla (130i)	1996–2004	Private practice, Lisbon, Portugal
Hjalmarsson and Smedberg (2005)[29]	Edentulous mandible maxilla	1999–2000	Public health, Stockholm, Sweden
Degidi et al (2005)[30]	Terminal/edentulous maxilla	1995–1999	Private practice, Bologna, Italy
Schwartz-Arad et al (2004)[31]	Terminal/edentulous mandible (22p, 150i), maxilla (31p, 228i)	1989–1996	University clinic, Tel Aviv, Israel
Morris et al (2001)[32]	All categories	1991–NR	Multicenter (30): Veterans Affairs Medical Centers, USA
Friberg et al (1997)[33]	Edentulous mandible (69p, 363i), maxilla (33p, 200i)	1987–1990	Multicenter (3): public health, Sweden
Olsson et al (1995)[34]	Edentulous mandible (70p, 363i), maxilla (33p, 200i)	1987–1990	Multicenter (3): public health, Göteborg/Skövde/Umeå, Sweden

Ø = diameter; L = length; NR = not reported; TiU=TiUnite, HA= hydroxyapatite; p = patients; i = implants.

Tech (n = 2), Friatec/Friadent (n = 1), and Straumann (n = 1). One report did not specify the name of the implant manufacturer and another listed four systems with no further details about the performance of each.

Studies Designed With no A Priori Stated Objective to Assess a Particular Implant Design Feature.[113–123] The authors identified these reports amongst the remaining 522 reports, of which 253 were not included because either the observation period was less than 2 years or the study population was less than 10**.** Of the 259 excluded articles, 252 did not report outcomes as a function of implant design aspects specific to a rehabilitated edentulous maxilla. Ten reports remained for data extraction (Table 11).[113–123]

The studies selected for data extraction were published between 1994[123] and 2011,[113,114] and included study cohorts that encompassed participants with an edentulous maxilla. Two studies[113–115] included study participants with an atrophic maxilla described according to the Lekholm and Zarb bone classification system.[124] None of the studies included participants with terminal teeth, who received immediate postextraction implants. The articles by Jemt et al[113,114,116,122] described the same study cohort in combinations with other cohorts.

In total, 795 study participants received 4,382 implants between 1985[122,123] and 2004.[113,114,118] The study settings were public health clinic (n = 5), not

No. Patients	No. Implants	Time Range (Mean) (y)	Implant System(s)
103	287	5–8 (7)	Brånemark-Mk3-turned (133i)/-Mk3-TiU (154i)
80	519	4–9 (7)	3i, ø: 3.25/3.75/4/5 mm; L: 8.5/10/11.5/13/15 mm
376	1,320	0–6 (3)	Osseospeed, ø: 3.5/4.0/4.5/5.0 mm; L: 8–17 mm
66	371	12–15 (7)	Astra-TiO (184i), ø: 3.5 mm; L: 9–19 mm vs Brånemark-Mk2 (187i), ø: 3.75/4.0 mm; L: 10–18 mm
12	72	2	StraumannStdPlus-SLActive, ø: 3.3/4.1 mm; L: 6/10/12/14 mm
461	1,180	1–4 (2.5)	3i (125i), Astra (174i), NobelB (442i), Dentsply (183i), Straumann (266i), ø: 3–6.0 mm; L: 6–18 mm
60	580	5	Brånemark-Mk2 (290i) (Lifecore), Restore(359i), ø/L: NR
111	690	1–6 (2)	Brånemark-Mk3 (256i)/Mk4/NobelSpeedy(64i) Replace Select Taper/ NobelReplace(359i)/Straigtht(11i)
412	1,514	2	Brånemark-turned (1316i)/TiU (198i), ø: 3.3/3.75/4/5 mm; L: 10 mm (107/1514 < 10 mm)
117	532	2–5 (3.75)	Camlog-Rootline(410i)/Screwline(53i) vs Straumann-solidscrew(69i), ø: 3.3–6.0 mm; L: 8–16 mm
237	408	1–9 (5)	Brånemark-Mk2/Mk3/Mk4/NobelSpeedyShorty-Turned (272i)/TiU (136i), ø: 3.75/4.0 mm; L: 7/8.5 mm
46	276	3	Astra (135i), Brånemark (141i)
45	388	5	NR, ø: 3.8–5.5 mm; L: 10 mm
44	381	1–8.5 (3)	"HA-coated"/"cpTi,"ø: NR; L: 13 mm
829	2,955	4	BioVent (MdE:319i+MxP:172i+MdP:420i), CoreVent (MdE:291i+MdP:328i), MicroVent-HA (MxE:247i+MxP:249i), ScrewVent-HA (MxE:185i)/CPTi(MxE:199i /tiA(MdE:294i)
103	563	5	Brånemark-Std (275i)/Mk2(288i), ø: 3.75/4.0 mm; L: 7–20 mm
103	563	3	Brånemark-Std (275i)/Mk2 (288i), ø: 3.75/4.0 mm; L: 7–18 mm

reported (n = 3), private practice (n = 1), or multicenter (n = 1). The study cohorts had 25 to 165[113,114] participants with 59 to 1,120 implants,[113,114] followed up for 2 to 15 years.[116] The implant systems were manufactured by Nobel Biocare (n = 6), Calcitek (n = 1), Biomet 3i (n = 1), and Straumann (n = 1). One report listed six systems with no further details about the performance of each.

Risk of Bias Within Studies

The scientific quality as well as risk of potential bias of the studies included varied considerably. In this systematic review, the risk of bias was trichotomized roughly as high, medium, or low. The reader should consider these labels relative only within this review, and they are not comparable to stricter criteria used in other reviews, such as the Cochrane reviews.

Studies Designed With an Objective to Assess Effects of Implant Design (or Feature) on Outcomes (Fig 3).[18–34] Two studies were designed as randomized controlled trials (RCTs),[21,32] four as a prospective study with concurrent controls,[22,31,33,34] and 11 as retrospective case series, including one comparing the outcomes with a historical cohort (Table 12). Six of the 17 studies reported approval of an ethics committee.[19,20,23,27,30–32,34] Funding was declared in four reports.[21,22,30,32] The reported statistics were predominantly some form of time-to-event univariate statistical test, for example, Kaplan-Meier or

Table 7 Characteristics of Studies Reporting the Effects of Tilted Implants to Enable Placement of Longer Implants

Study	Patient Situation	Year Placed	Setting
Agliardi et al (2014-2012e)[35]	Terminal (44i)/edentulous maxilla posterior atrophy	2005–2008	NR
Agnini et al (2014-2012e)[36]	Terminal/edentulous mandible (16p), maxilla (20p)	2006–2010	University clinic, Foggia, Italy
Pera et al (2014)[37]	Terminal > edentulous maxilla	2005–2006	University clinic, Genova, Italy
Pozzi et al (2015–2013e)[38]	Edentulous mandible (61p), maxilla (34p)	2003–2012	University clinic, Milano, Italy
Maló et al (2013)[39]	Terminal/edentulous mandible (48p, 192i), maxilla (38p, 152i)	2008–2011	University clinic, Beijing, China
Testori et al (2013)[40]	Edentulous maxilla atrophy height < 5 mm-bone	2005–2010	Private practice, Lisbon, Portugal
Di et al (2013)[41]	Edentulous (32p)/partial dentate (3p), maxilla atrophy CH5	NR	NR
Maló et al (2012–2011e)[42]	Terminal/edentulous maxilla	2002–2006	Private practice, Lisbon, Portugal
Francetti et al (2012–2010e)[43]	Terminal/edentulous mandible (33p, 132i), maxilla (16p, 64i), LZ-A/B/C	2004–2008	Multicenter (2); NR
Mozzati et al (2012)[44]	Terminal/edentulous mandible (20p, 80i), maxilla (24p, 96i), posterior atrophy	2007–2007	University clinic, Milano, Italy
Crespi et al (2012)[45]	Terminal/edentulous maxilla	2001–2009	University clinic, Torino, Italy
Cavalli et al (2012)[46]	Terminal/edentulous maxilla, posterior atrophy	2007–2011	NR
Maló et al (2012)[47]	Terminal (18i)/edentulous mandible (94i), maxilla (133i)	2003-2009	Private practice, Lisbon, Portugal
Maló et al (2011)[48]	Terminal (31p, 45i)/edentulous maxilla posterior atrophy-levels 1–4	1998–2006	Private practice, Lisbon, Portugal
Agliardi et al (2010)[49]	Edentulous mandible (93p, 404i), maxilla (61p, 288i), atrophy	2004–2009	Private practice, Bollate, Italy
Degidi et al (2010)[50]	Edentulous maxilla	2005–2006	Private practice, Bologna, Italy
Pomares (2009)[51]	Terminal/edentulous mandible (9p, 36i), maxilla (19p, 91i)	2004–2006	Private practice, Alicante, Spain
Agliardi et al (2009)[52]	Terminal/edentulous maxilla	2005–2007	NR
Rosen and Gynther (2007)[53]	Edentulous maxilla atrophy CH5/6	1998–NR	University clinic, Stockholm, Sweden
Capelli et al (2007)[54]	Edentulous mandible (24p, 96i), maxilla (41p, 246i) atrophy	2002–2006	Multicenter (4); private practices, Italy
Fortin et al (2002)[55]	Edentulous maxilla	1991–1994	Private practice, Quebec, Canada
Krekmanov et al (2000)[56]	Edentulous/partial dentate mandible (25p, 78i), maxilla (22p, 138i)	NR	Public health, Västerås, Sweden
Mattsson et al (1999)[57]	Edentulous maxilla atrophy CH5/6	1998–NR	University clinic, Stockholm, Sweden

Ø = diameter; L = length; NR = not reported; CH = Cawood & Howell; LZ = Lekholm-Zarb classification.

actuarial life table, occasionally supplemented with a multivariate test, such as linear mixed models or Cox regression tests. The risk of bias varied from low (n = 1)[21] to medium (n = 9)[19,20,23,27,30–34] to high (n = 7).

Studies Reporting the Effects of Tilted Implants to Enable Placement of Longer Implants (Fig 4).[35–57] One study was designed as an RCT, but the comparison arms were not focused on implant design features. All other articles were prospective (n = 12) or retrospective (n = 10) case series (Table 13). Eight articles described an approval from an ethics committee, though only five included name and number.[36,39–42,44,48,52] Study funding was declared in three reports.[41,51,55] The reported statistics were predominantly simple parametric or nonparametric statistical hypothesis tests comparing the axial vs tilted implants (n = 7) with or without some additional form of time-to-event univariate statistical test, such as the Kaplan-Meier or actuarial life table. Two studies described the use of

No. Patients	No. Implants	Time Range (Mean) (y)	Implant System(s)
32	192	3–6.5 (4.5)	Brånemark-Mk4-TiU (30i), NobelSpeedyGroovy (162i), ø: 4.0 mm; L: 11.5/13/15 mm
30	272	1.5–5.5 (3.5)	(Zimmer) Spline(84i), ScrewVent-taper (188i)
37	164	6	Osseotite (108i)/NT(56i)+/Coronal etching, ø: 4.0 mm; L: > 13 mm
86	344	1–9 (5.5)	NR
69	344	1–4.5 (3)	Brånemark-Mk2-TiU (52i), NobelSpeedyGroovy (202i), ø: NR; L: 10–12 mm
70	280	3	NobelSpeedy, ø: 4 mm; L: 10/13/15/18 mm
35	190	0–10 (5)	NR, ø: 4 mm; L: 13/15 mm
242	968	5	Brånemark-Mk3 (21i)/Mk4-TiU (82i)U, NobelSpeedy (865i), ø: mm; L: 10–18 mm
47	196	2.5–5.5 (4)	Brånemark-Mk4-TiU (92i-all md.), NobelSpeedyReplace (104i), ø: 4.0 mm; L: 10–18 mm
36	176	3	(Sweden&Martina) PAD, ø: 3.75/4.0 mm; L: 13/15 mm
65	334	2	NR (“ext.hex”), ø: 4.0 mm; L: 11.5/13/15/18 mm
34	136	1–6 (3)	Brånemark-Mk4-TiU NobelSpeedyGroovy
142	227	1–3 (2)	Brånemark-Mk3-TiU /-Mk4-TiU NobelSpeedy, ø: 3.3/4.0 mm; L > 10 mm
221	995	5	Brånemark-Mk2 /-Mk3 /-Mk4 NobelSpeedy, ø: 3.3/4.0 mm; L:10–18 mm
173	616	1–5 (3.5)	Brånemark-Mk4-TiU(92i), NobelSpeedyGroovy (600i), ø: 4.0 mm; L: 8.5/10/11.5/13/15/18 mm
30	210	3	XiVEPlus, ø: 3.4/3.8 mm; L: 10–16 mm
20	127	2	NobelSpeedyMk3Groovy, ø: 4.0 mm; L ≥ 13 mm
20	120	1.5–3.5 (2)	Brånemark-Mk4-TiU (30i) NobelSpeedyGroovy (90i), ø: 4.0 mm; L: 11.5/13/15 mm
19	103	8–12 (10)	Brånemark-Mk2, ø: 3.75 mm; L: 7/10–18 mm
65	342	0–4.5 (2)	Osseotite-NT, NR
45	245	5	Brånemark, ø: 3.75 mm; L: 7/8.5/10/12/13/15/18 mm
47	206	3–5 (4)	Brånemark (NR)
15	68	3–4.5 (4)	Brånemark-Mk2, ø: 3.75 mm; L: 7/10–18 mm

a multivariate test.[37,48] The risk of bias was considered either medium (n = 5)[36,37,41,43,48] or high (n = 18).

Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 5).[58–87] All studies were prospective (n = 10) or retrospective (n = 22) case series (Table 14). The reported statistics were purely descriptive (n = 13), of which four reported 100% survival of the zygoma implants, using statistical hypothesis tests (n = 3) and/or some form of time-to-event univariate statistical test, such as the Kaplan-Meier or actuarial life table. No studies described the use of a multivariate test. Only 7 of the 30 articles described approval from an ethics committee,[59–64,74] and three studies specified the source of funding.[70,74,75,86] The risk of bias was considered either medium (n = 1)[59] or high (n = 29).

Table 8 Characteristics of Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of A Particular Implant Design Feature on One or more Treatment Outcomes

Study	Patient Situation	Year Placed	Setting
Yates et al (2014-2013e)[58]	Edentulous maxilla, atrophy, height < 6 mm-bone	2000–2006	NR
Aparicio et al (2014-2012e)[59]	Edentulous maxilla, atrophy	1998–2002	Private practice, Barcelona, Spain
Fernández et al (2014)[60]	Edentulous, partial dentate, maxilla	2009–2013	University Hospital, Bogotá, Colombia
Maló et al (2015-2013e)[61]	Edentulous maxilla, atrophy, CH5/6/>6	2006–2012	Private practice, Lisbon, Portugal
Davó et al (2013)[62]	Edentulous maxilla, atrophy CH4/5/6	2006–2009	Private practice, Alicante, Spain
Davó and Pons (2013)[63]	Edentulous (37p), partial dentate (5p), maxilla atrophy	2004–2006	Private practice, Alicante, Spain
Maló et al (2012)[64]	Edentulous maxilla, atrophy CH5/6	2006–2009	Private practice, Lisbon, Portugal
Miglioranca et al (2012)[65]	Edentulous maxilla, atrophy	2003–2006	Private practice, São Paulo, Brazil
Balshi et al (2012)[66]	Edentulous maxilla	NR	Private practice, Fort Washington, PA, USA
Aparicio et al (2010–2008e)[67]	Edentulous maxilla, atrophy	NR	Private practice, Barcelona, Spain
Aparicio et al (2010-2008e)[68]	Edentulous/partial dentate, maxilla atrophy	2004–2005	Private practice, Barcelona, Spain
Bedrossian (2010)[69]	Edentulous maxilla, atrophy	2003–2005	NR
Stiévenart & Malevez (2010)[70]	Edentulous maxilla, atrophy, LZ-D/E	NR	NR
Davó (2009)[71]	Edentulous maxilla, atrophy	1999–2003	Private practice, Alicante, Spain
Balshi et al (2009)[72]	Edentulous maxilla, atrophy	NR	Private practice, Fort Washington, PA, USA
Pi Urgell et al (2008)[73]	Edentulous/partial dentate, maxilla atrophy	2004–2006	Private practice, Alicante, Spain
Davó et al (2008)[74]	Edentulous maxilla, atrophy	NR	Private practice, Alicante, Spain
Davó et al (2008)[75]	Edentulous maxilla, atrophy CH4/5	1998–2004	Private practice, Barcelona, Spain
Kahnberg et al (2007)[76]	Edentulous maxilla, atrophy	NR	University Clinic, Bahia, Brazil
Duarte et al (2007)[77]	Edentulous/partial dentate, maxilla atrophy	1997–1999	Multicentre (18): Private/Public/ University International
Peñarrocha et al (2007)[78]	Edentulous maxilla, atrophy	2000–2005	University Clinic, Valencia, Spain
Peñarrocha et al (2007)[79]	Edentulous maxilla, atrophy	1998–2004	University Clinic, Valencia, Spain
Bedrossian et al (2006)[80]	Edentulous maxilla, atrophy	1999–2001	Public Health, Bergen, Norway
Farzad et al (2006)[81]	Edentulous maxilla, atrophy LZ-B/C	2003–2004	University Clinic, San Francisco, CA, USA
Ahlgren et al (2006)[82]	Edentulous maxilla, atrophy	2000–2002	Public Health, Västerås, Sweden
Aparicio et al (2006)[83]	Edentulous (66p), partial dentate (3p), maxilla atrophy	NR	Private practice, Barcelona, Spain
Becktor et al (2005)[84]	Edentulous maxilla_atrophy_CH5/6	1998–2002	Public Health, Halmstad, Sweden
Malevez et al (2004)[85]	Edentulous maxilla, atrophy	1990–1995	University Clinic, Göteborg, Sweden
Brånemark et al (2004)[86]	Edentulous maxilla, atrophy	1997–2001	University Clinic, Brussels, Belgium
Bedrossian et al (2002)[87]	Edentulous maxilla, atrophy	NR	NR

Ø = diameter; L = length; NR = not reported; LZ = Lekholm-Zarb classification; CH = Cawood & Howell; alv = alveolar; cor = coronal; TiU = TiUnite; ITI = International Team for Implantology.

No. Patients	No. Implants	Time Range (Mean) (y)	Implant System(s)
25	43	5–10 (6)	Brånemark-Zygomatic-turned, ø: 4–4.5 mm; L: 8 mm
22	172	10	Brånemark-Mk3/pter(29i), (131i), ø: 3.3–4 mm; L: 7–18 mm + Brånemark-zygomatic-turned (41i), L: 30–50 mm
80	244	0.5–4 (~2)	NR
352	1,542	0.5–7 (2.5)	NobelSpeedy(795i) + (NobelB) Zygoma-TiU
17	68	3	Brånemark-zygomatic, L: 30–52.5 mm
42	221	5	Brånemark-TiU (108i), Replace (32i), ø: 3.75/4/4.3/5 mm; L: 10–16 mm + Brånemark-Zygomatic turned (44i) /-TiU (37i), L: 40–52.5 mm
39	169	3	Nobel-TiU (77i) + (NobelB) Zygoma-TiU Prototype1/Prototype2 (92i), ø: 5 mm
25	114	8	NobelReplace-taper (74i) + Brånemark-Zygomatic (40i)
77	173	1–10	Brånemark-Mk3/pter (391i) + Zygoma-turned (76i)/-TiU (34i), ø: 4.0 mm; L: 30–52.5 mm
25	176	2–5	NobelB-TiU (129i), ø: 3.75/4.0 mm; L: 7–18 mm + (NobelB) Zygomatic-turned (47i), L: 35–52.5 mm
20	140	3–4 (3.5)	NobelB-TiU (104i), ø: 3.75/4.0 mm; L: 7–18 mm + Brånemark-Zygomatic-turned (36i), L: 35–52.5 mm
36	172	0.5–7	Brånemark-Mk4(54i), NobelSpeedy (44i), ø: 4.0 mm; L: 7–13 mm + Brånemark-Zygomatic-turned (74i), L: 30–-52.5 mm
20	80	0.5–3.5	Brånemark-Zygomatic, L: 30–52.5 mm
24	154	5	Brånemark-Mk3-turned (79i)/-TiU (30i), ø: 3.75/4.0 mm; L: 10–15 mm + Brånemark-Zygomatic-turned (45i), L: 40–50 mm
56	501	0.5–5	Brånemark-Mk3/pter(391i) + Zygoma-turned(76i)/-TiU(34i), ø: mm; L:30–52.5 mm
42	221	1–3.5 (2)	Brånemark-TiU (108i) Replace (32i), ø:3.75/4/4.3/5 mm; L:10–16 mm + Brånemark-Zygomatic-turned(44i)/TiU (37i), L:40–52 mm
36	196	1–3.5 (2)	Brånemark(125i) + Brånemark-Zygoma-turned (44i)/TiU (27i)
54	325	0–6 (3)	Brånemark-std(221i) + (NobelB)-Zygoma(101i), ø: 4 mm-apex/4.5 cor; L:30–52.5 mm
12	48	2.5 & 0.5 (NR)	Brånemark-Zygomatic-turned, ø: 4–5 mm
60	145	3	Brånemark/Zygomatic(103i), ø: 4.0 mm apex/5.0 mm alv; L: 35–50 mm
21	129	1–4 (2)	Defcon/(Straumann), ITI (89i) + Brånemark-Zygomatic (40i)
46	321	1–3.5 (2)	Defcon (122i) (Straumann), ITI (155i) + Brånemark-Zygomatic (44i); L: 30–42.5 mm
13	55	1–4 (~2)	Brånemark-Mk2/-Mk3/-TiU (30i) + Brånemark-Zygomatic (25i); L: 35–50 mm
14	83	1–3 (2)	Brånemark-Mk4-TiU(55i), ø: 4.0 mm; L: 7–13 mm + Brånemark-Zygomatic(28i); L: 35–52.5 mm
11	64	1.5–4 (3)	Brånemark(42i) + Brånemark-Zygomatic(22i)
69	435	0.5–5	Brånemark-Mk3/pter(84i) (304i), ø: 3.75/4.0 mm; L: 7–18 mm + Brånemark-Zygomatic(131i), ø: 4.0 mm apex/5.0 mm alv; L: 35–52.5 mm
16	105	0.9–5.5 (4)	Astra/Brånemark(74i) + Brånemark-Zygomatic(31i); L: 30–50 mm
28	158	5–10	Brånemark (106i) + Brånemark-BOC/Expro-Zygoma (52i), ø: 4.0 mm apex/4.5 mm (cor); L: 30–50 mm
55	297	0.5–4 (2.5)	Brånemark-Std(194i), ø: 3.75 mm + Brånemark-Zygomatic(103i), ø: 4.0 apex/5.0 mm alv; L:35–50 mm
22	124	3	Brånemark-Mk3 (80i), ø: 3.75 mm; L: 10/13 mm + Brånemark-Zygomatic(44i); L: 40–50 mm

Table 9 Characteristics of Studies Reporting the Effects of Implants Placed in Pterygoid Bone or Other Bony Buttresses With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Lead author	Patient Situation	Year Placed	Setting
Peñarrocha-Oltra et al (2013)[88]	Edentulous maxilla, atrophy CH5	2000–2004	University clinic, Valencia, Spain
Balshi et al (2013)[89]	Terminal/edentulous maxilla	1985–2011	Private practice, Fort Washington, PA, USA
Balshi et al (2013)[90]	Edentulous/partial dentate/single maxilla posterior	1985–2011	Private practice, Fort Washington, PA, USA
Rodriguez et al (2012)[91]	Edentulous partial dentate, maxilla < 8 mm bone-to-sinus	1997–2010	Private practice, Barcelona, Spain
Peñarrocha et al (2012)[92]	Edentulous maxilla atrophy CH4/5	2002–2010	University clinic, Valencia, Spain
Peñarrocha et al (2009)[93]	Edentulous maxilla, atrophy CH4/5	2000–2004	University clinic, Valencia, Spain
Peñarrocha et al (2009)[94]	Edentulous (23p), Partial dentate (22p), maxilla atrophy CH4/5	2000–2006	University clinic, Valencia, Spain
Balshi et al (2005)[95]	Terminal/edentulous maxilla	1999–2004	Private practice, Fort Washington, PA, USA
Balshi et al (1999)[96]	Edentulous maxilla	NR	Private practice, Fort Washington, PA, USA

Ø = diameter; L = length; CH = Cawood & Howell; NR = not reported; ITI = International Team for Implantology; TiU = TiUnite.

Table 10 Characteristics of Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Study	Patient Situation	Year Placed	Setting
Zinser et al (2013–2012e)[97]	Edentulous (278i), partial dentate (642i), single(124i) maxilla posterior atrophy CH2-6	1995–2009	Public health, Amstelveen, The Netherlands
Dasmah et al (2013–2012e)[98]	Edentulous maxilla, atrophy CH6	1999–2001	Public health, Stockholm, Sweden
Sjöström et al (2007)[99]	Edentulous maxilla, atrophy CH2-6	NR	University clinic, Umeå, Sweden
Chiapasco et al (2007)[100]	Edentulous maxilla, atrophy CH6	1995–2004	Multicenter (3): University, Milano, Italy
Hallman et al (2005)[101]	Edentulous maxilla atrophy CH6	Brånemark: 1993–1995; Astra: 1995–1997	Public health, Gävle, Sweden
Becktor et al (2004)[102]	Edentulous maxilla, atrophy CH3/4(22p), 5/6(41p)	1990–1996	Public health, Halmstad, Sweden
Pinholt (2003)[103]	Edentulous (11p) partial dentate (14p), maxilla atrophy; LZ-D/E	Brånemark: 1996–1998; Straumann: 1998–2000	Public health, Vejle, Denmark
Becktor et al (2002)[104]	Edentulous maxilla, atrophy CH3-6	1990–1996	Multicenter (2): Public health, Rochester, USA, & Halmstad, Sweden
Lekholm et al (1999)[105]	Edentulous (28p), partial dentate (4p), maxilla compromised	1984–1997	Public health, Rochester, MN, USA
Keller et al (1999)[106]	Edentulous partial dentate, maxilla	1984–1996	Public health, Rochester, MN, USA
Keller et al (1999)[107]	Edentulous maxilla, atrophy, LZ-D	1991–NR	Multicenter (23): Scandinavia
Watzek et al (1998)[108]	Edentulous maxilla, posterior atrophy CH6	1989–1995	University clinic, Wien, Austria

Ø = diameter, L = length; CH = Cawood & Howell; NR = not reported; ITI = International Team for Implantology; LZ = Lekholm-Zarb classification.

No. Patients	No. Implants	Time Range (Mean) (y)	Implant System(s)
33	222	5	(Phibo) TSA-Avantblast
981	1,608	1–25 (10+)	Astra(7i) Brånemark-std /-Mk2 /-Ebon /-Mk3 /-Mk4 /-turned /-TiU(1601i), ø: 3.75/4.0/5.0 mm; L: 7–18 mm
	992	1–10 (6)	Brånemark-pterygoid, ø: 4 mm; L:7-13/15–18 mm
392	454	0–14 (6)	Osseotite-pterygoid, ø: 3.75/4.0 mm; L: 15/18/20 mm
18	117	1–7 (3)	(Sentmenat)Phibo, ø:3.5/4.1/4.2/5.5; L:10/11.5/13 mm (NobelB) Zygoma(4i); L:35/45 mm
74	490	2–4 (3)	(Impladent) Defcon-Avantblast, ø: 3.6/4.2 mm; L: 10/11.5/13/14.5 mm (NobelB) Zygoma (36i)
45	268	1–5 (3)	(Impladent) Defcon-Avantblast(25p, 37i), (Straumann), ITI (20p, 31i), ø: 3.6/4.2 mm; L: 10/11.5/13/14.5 mm/pterygoid(68i)
82	840	0.5–4.5 (2.5)	Brånemark-Mk3-TiU (28p, 251i), ø: 3.75/4 mm; L: 7-15 mm /-Mk4-TiU (136p, 379i), ø: 4 mm; L: 7–18 mm /Zygoma-turned (46i); L: 30–50 mm
189	1,817	1.5–6(4.5)	Brånemark-std /selftap, ø: 3.75/(4.0/5.0) mm; L: (10/13)/15/(18) mm

No. Patients	No. Implants	Time Range (Mean) (y)	Implant System(s)
224	1,045	14	"Additive" & "ablative," ø: 3.3/3.8/4/4.4/4.5/5 mm; L: 11/12/13/14/15/16 mm
19	152	5	Astra-TiO, ø: 3.5 mm; L: 9/11/13/15/17 mm
29	222	3	Brånemark-Std (171i)/Mk2 (21i), ø: 3.75 mm; L: 10–18 mm
39	281	1–9 (4)	Brånemark, (Friadent) Frialit, IMZ, (Straumann) ITI
22	156	5	Astra-TiO (11p, 72i), ø: NR; L: 8/9/11/13/15 mm; Brånemark-Mk3-turned (11p, 84i), ø: NR; L: 7/10/13/15 mm
182	1,120	2–9 (6.5)	Brånemark, ø: 3.75/4/5 mm; L: 6/7/8/10/13/15/18 mm
25	158	2–5.5 (NR)	Brånemark-std/Mk2/Mk3-turned (12p, 78i), ø: NR; L: 8.5–18 mm and (Straumann) ITI-SLA (13p, 80i), ø: NR; L: 8–16 mm
90	643	2–9 (5)	Brånemark-Std /-Con /-Mk2, ø: 3.75/4.0/5.0 mm; L: 7/8/10/13/15/18/20 mm
32	204	1–11 (5)	Brånemark-Std /-Con /-Mk2, ø: 3.75/4.0 mm; L: 15/18 mm
54	248	1–11 (5)	Brånemark-Std /-Con /-Mk2, ø: 3.75/4.0 mm; L: 10/13/15/18/20 mm
150	781	3	Brånemark-Std /-Con /-Mk2, ø: 3.75/4.0 mm; L: 15/18 mm
20	155	1–6	(Friatec) Frialen(70i) (Friatec) IMZ(85i)

Table 10 ***Continued*** **Characteristics of Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes**

Study	Patient Situation	Year Placed	Setting
Nyström et al (1997)[109]	Edentulous maxilla, atrophy CH5/6	NR	University clinic, Umeå, Sweden
Köndell et al (1996)[110]	Edentulous maxilla, atrophy < 7 mm-bone-post	NR	University clinic, Stockholm, Sweden
Neukam (1996)[111]	Edentulous maxilla, atrophy, LZ-D/E	1987–1993	University clinic, Erlangen-Nurnburg, Germany
Keller et al (1994)[112]	Edentulous partial dentate, maxilla atrophy	1984–NR	Public health, Rochester, MN, USA

Ø = diameter, L = length; CH = Cawood & Howell; NR = not reported; ITI = International Team for Implantology; LZ = Lekholm-Zarb classification.

Table 11 Characteristics of Studies Designed With no A Priori Stated Objective to Assess a Particular Implant Design Feature

Study	Patient Situation	Year Placed	Setting
Jemt et al (2011)[113,114]	Edentulous maxilla LZ-B/C	Turned: 1986–1987; oxidized: 2001–2004	Public health, Göteborg, Sweden
Friberg and Jemt (2008-2007e)[115]	Edentulous maxilla wide (n = 33p, 226i) vs atrophy narrow LZ-C/D (n = 42p, 279i)	1993–1997	Public health, Göteborg, Sweden
Jemt and Johansson (2006)[116]	Edentulous maxilla	1986–1987	Public health, Göteborg, Sweden
Widbom et al (2005)[117]	Edentulous maxilla	1993–2002	Public health, Skövde, Sweden
Ibañez et al (2005)[118]	Edentulous mandible (126i) maxilla (217i)	1998–2004	Multicenter (3): University clinic & private practices, Cordoba, Spain
Degidi and Piattelli (2003)[119]	Edentulous mandible (39p) maxilla (14p), partial dentate, mandible post (23p), maxilla post (15p), single (58i)	1996–2001	Private practice, Bologna, Italy
Kiener et al (2001)[120]	Edentulous maxilla	1991–1998	NR
Watson et al (1998)[121]	Edentulous mandible (30p, 90i), maxilla (14p, 43i)	1990–1994	NR
Jemt and Lekholm (1995)[122]	Edentulous maxilla & maxilla, atrophy severe/intermediate	1985–1988	NR
Palmqvist et al (1994)[123]	Edentulous maxilla	1985–1992	Public health, Örebro, Sweden

LZ = Lekholm-Zarb classification; Ø = diameter; L = length; NR = not reported; ITI = International Team for Implantology.

Studies Reporting the Effects of Implants Placed in Pterygoid Bone or Other Bony Buttresses With or Without Additional Alveolar Implants Reporting An Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 6).[88–96] All studies were retrospective case series (n = 9) (Table 15). The reported statistics were descriptive (n = 5), statistical hypothesis tests (n = 2), and/or a time-to-event univariate statistical test (n = 4). No studies described the use of a multivariate test. One article reported approval from an ethics committee[88] and none specified the source of funding. The risk of bias was considered high for all the studies.

Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 7).[97–112] Three studies were designed as comparative prospective studies.[98,101,103] One of these focused on comparing block vs particulate bone augmentation, rather than implant design features.[98] The two other studies compared implant designs, but in succession, which risks introducing bias.[101,103] The remaining studies were prospective (n = 2) or retrospective (n = 9) case series (Table 16). The reported statistics were predominantly

No. Patients	No. Implants	Time Range (Mean) (y)	Implant System(s)
10	60	1–3	Brånemark-Mk2, ø: 3.75 mm; L: 13/15/18 mm
14	75	5	Brånemark-selftap, ø: 3.75 mm; L: 7–15 mm
43	284	3–6	Brånemark, ø: NR; L: 7/10/12/13/15/18 mm
20	83	1–6 (2)	Brånemark-Std /-Con /-Mk2, ø: 3.75/4.0 mm; L: 10/13/15/18/20 mm

No. Patients	No. Implants	Time Range (Mean) (y)	Implant System(s)
165	1,120	5	Brånemark-Std/-Mk2 /-Mk3 /-Mk4 (450i+360i)/-TiU(310i), ø: 3.75/4.0 mm; L: 7/8.5/10/11.5/13/15/18/20 mm
75	506	7	Brånemark-Std/-selftap/-Mk2/-Mk3-turned, ø: 3.75/4.0/5.0 mm; L: 6/7/8.5/10/11.5/13/15/18/20 mm (72 ≤ 8.5 mm)
76	450	15	Brånemark-Std, ø: 3.75 mm; L: 7–18 mm (106i/430 < 10 mm)
27	145	4–9 (5.5)	Brånemark-Mk2; L: 7–18 mm
41	343	0.5–6 (2.5)	Osseotite/-NT/-XP, ø: 3.75/4.0/≥ 5.0 mm; L: ≤ 10/> 10 mm (74 ≤ 10 mm)
152	646	0.5–5 (2)	Frialit2 (144i), Frialoc (37i), IMZ (51i), Brånemark (73i), Maestro (242i), Restore (97i)
41	173	1–5 (3)	(Straumann) ITI, ø: 3.3/4.1/4.8 mm; L: 6/8/10/12 mm
43	139	3–6 (4)	(Calcitek) Integral-HA, ø: 3.25/4.0 mm; L: 8/10/13/15 mm
150	801	5	Brånemark-Std/-selftap/-con, ø: 3.75 mm; L: 7/10/≥ 13 mm, (298/801 < 10 mm)
25	59	1–5 (3)	Brånemark, ø: 3.75 mm; L: 7/10/13/15/18/20 mm

descriptive (n = 7), statistical hypothesis tests (n = 4), and/or some form of time-to-event univariate statistical test, such as the Kaplan-Meier or actuarial life table (n = 6). Four reports applied a multivariate statistical test for data analysis.[97,99,104,111] Only one article described approval from an ethics committee, vaguely termed the "Local Research Ethics committee."[99] None of the reports described a source of funding for the study. The risk of bias was considered either medium (n = 3)[99,104,111] or high (n = 13).

Studies Designed With no A Priori Stated Objective to Assess a Particular Implant Design Feature.[113–123] The studies were prospective (n = 3) or retrospective (n = 7) case series (Table 17). The reported statistics were predominantly descriptive (n = 2), statistical hypothesis tests (n = 3), and/or some form of time-to-event univariate statistical test, such as the Kaplan-Meier or actuarial life table (n = 7). Three studies described the use of a multivariate test.[117,122,123] None of the studies described approval from an ethics committee. Three reports described a source of funding.[119,121,122] The risk of bias was considered high in all studies.

Table 12 Bias Assessment of Studies Designed to Assess Effects of Implant Design or Feature on Outcomes

Study	Study Objective
Jungner et al (2014–2012e)[18]	To compare the clinical performance of turned and oxidized implants after more than 5 years of loading
Vervaeke et al (2015–2013e)[19]	To identify predictors affecting implant treatment outcomes using multivariate tests that correct for confounding
Testori et al (2014–2013e)[20]	*(1)* To assess the reliability of immediate implant and immediate loading protocols in the edentulous jaws, and *(2)* to investigate the role of patient-related, implant-related, and surgery-related secondary variables in the occurrence of implant failure
Ravald et al (2013)[21]	To study the long-term outcome of implant survival rate, soft and hard tissue conditions, and prosthetic status in a group of individuals treated with either Astra Tech tioblast or Brånemark turned implants supporting a full-arch bridge
Van Assche et al (2012–2011e)[22]	To investigate the outcome of short implants additionally placed with longer implants to support a maxillary overdenture
Cosyn et al (2012–2010e)[23]	To explore factors associated with failure of surface-modified implants using data obtained in a university postgraduate training center
Kallus et al (2009–2008e)[24]	To compare survival rates and marginal bone resorption of the Lifecore Restore Implant System with the benchmark Nobel Biocare MK II Implant System
Li et al (2009)[25]	To describe immediate functional loading of completely edentulous maxillas and mandibles with fixed provisional prostheses and to compare cumulative survival rates between maxillas and mandibles
Alsaadi et al (2008)[26]	To evaluate the success rate of two different implant systems with sandblasted and acid-etched modified surfaces loaded after reduced healing times
Nelson et al (2008)[27]	To assess the influence of systemic and local bone and intraoral factors on the occurrence of implant loss from abutment connection up to 2 years
Maló et al (2007)[28]	To report on the placement of short Brånemark implants, testing the hypothesis that short implants in atrophied jaws might give similar long-term implant survival rates as longer implants used in larger bone volumes
Hjalmarsson and Smedberg (2005)[29]	To compare the prosthesis retention screw stability (ie, preload) and the clinical outcome after prosthesis connection in patients treated with traditional frameworks vs frameworks produced with the Cresco Ti Precision method
Degidi et al (2005)[30]	To evaluate the outcome of implants immediately loaded with a cross-arch fixed temporary restoration in the edentulous upper jaw in a consecutive study population
Schwartz-Arad et al (2004)[31]	To examine the cervical bone loss and its correlation with implant characteristics and anatomic factors, 1 to 8 years after implantation of immediate and delayed implants
Morris et al (2001)[32]	To separately examine a subset of data from the extensive DICRG database to determine what relationship, if any, exists between implant design and survival; six implant designs were randomized to five restorative applications and subsequently evaluated
Friberg et al (1997)[33]	To compare the clinical and radiographic evaluations of MK II self-tapping implants with standard implants of the Brånemark system after 5 years
Olsson et al (1995)[34]	To evaluate for over 3 years a modified self-tapping implant (Mk II) with improved cutting characteristics used in both maxillae and mandibles

REB = Research Ethics Board; ANOVA = analysis of variance; NR = not reported; ND = none declared; IRCCS = National Institute for Research and Treatment (Italy); RCT = randomized controlled trial; EC = Ethics committee; CCT = clinical controlled trial; DICRG = Dental Implant Clinical Research Group; HA = hydroxyapatite.

Study Design	Statistics	REB	Funding	Bias Risk
Retrospective case series	ANOVA	NR	ND	High
Retrospective case series	Mann-Whitney + log rank + Cox regression + linear mixed effect	Ghent University Hospital, Belgium	ND	Medium
Retrospective case series	Mann-Whitney + Kaplan-Meier + Cox Regression	IRCCS scientific review board	ND	Medium
RCT, two arms (Astra vs Brånemark)	Wilcoxon + life table	EC of Linköping University, Sweden	Astra Tech AB, Sweden & Research Council of Public Dental Services, Östergötland, Sweden	Low
CCT prospective study w/concurrent controls, split (short distally vs long anterior)	ANOVA + linear mixed models, including Dunnett-multiple tests	NR	Institut Straumann, Switzerland	High
Retrospective case series	Fisher exact + Kaplan-Meier + log rank + Cox regression + logistic regression	University Hospital Ghent, Belgium	ND	Medium
Retrospective case series (Lifecore) w/ historical controls (Nobel Biocare)	χ^2/Fisher exact + Kaplan-Meier	NR	ND	High
Retrospective case series	Fisher exact/*t* test	NR	ND	High
Retrospective case series	χ^2/*t* test + Kaplan-Meier	NR	ND	High
Retrospective case series	Logistic regression	NR	ND	Medium
Retrospective case series	χ^2 + life table	NR	ND	High
Retrospective case series	ANOVA/Fisher exact/ Kruskal Wallis	NR	ND	High
Retrospective case series	Kaplan-Meier + log rank + Cox regression	NR	Ministry of Education, Italy & National Research Council, Italy & Research Association for Dentistry, Italy	Medium
CCT prospective study w/ concurrent controls (Implant characteristics)	χ^2/*t* test + Kaplan-Meier + linear regression	NR	ND	Medium
RCT–split, 2 × 3 + 2 arms (edentulous max: HA-coated grooved vs HA-coated screw vs cpTi-screw/edentulous mandible: HA-coated cylinder vs Ti-alloy-basket vs Ti-alloy screw/partial edentulous; max. post HA-coated cylinder vs HA-coated grooved)	Kaplan-Meier + log rank + Breslow	NR	US Government	Medium (high dropout rate)
CCT prospective study w/ concurrent controls, split (with and without tapping)	Life table	NR	ND	Medium
CCT prospective study w/concurrent controls Split (Self-tapping vs pretapping implant)	Life table	NR	ND (one coauthor is NobelPharma employee)	Medium

Table 13 Bias Assessment of Studies Reporting the Effects of Tilted Implants to Enable Placement DICRG f Longer Implants

Study	Study Objective
Agliardi et al (2014-2012e)[35]	To prospectively evaluate the clinical and radiographic outcomes of immediate full-arch fixed maxillary prosthesis supported by two axial and four tilted implants after 3 years of loading
Agnini et al (2014-2012e)[36]	To evaluate full-arch fixed-dental restorations supported by immediate loaded axial and tilted implants in a single-cohort study; survival rate of axial and tilted implants was compared
Pera et al (2014)[37]	To report the 6-year outcomes for patients rehabilitated with an immediate loading protocol of the maxilla (Columbus Bridge Protocol)
Pozzi et al (2015-2013e)[38]	To retrospectively evaluate the implant and prosthetic survival and success rates of zirconia-based, implant-supported, screw-retained, cross-arch restorations up to 5 years after placement
Maló et al (2013)[39]	To report the outcome of trans-sinus tilted implants for the rehabilitation of the complete edentulous atrophic maxilla using the all-on-four concept with immediate loading
Testori et al (2013)[40]	To evaluate tilted trans-sinus implants for rehabilitation of the atrophic maxilla
Di et al (2013)[41]	To evaluate the outcome and special characteristics of immediate implant rehabilitation using the all-on-four treatment concept in completely or potentially completely edentulous Chinese patients
Maló et al (2012-2011e)[42]	To report on the medium- and long-term outcomes of a protocol for immediate function of four implants (all-on-four, Nobel Biocare) supporting a fixed prosthesis in the completely edentulous maxilla
Francetti et al (2012-2010e)[43]	To assess clinical outcomes and peri-implant bone level changes around tilted and axial implants supporting full-arch fixed immediate rehabilitations up to 60 months of loading
Mozzati et al (2012)[44]	To conduct an immediate postextraction implant placement with immediate loading in the maxilla
Crespi et al (2012)[45]	To compare definitive acrylic resin prostheses with or without a cast metal framework that were immediately loaded and supported by axial and tilted implants in completely edentulous patients after 3 years of function
Cavalli et al (2012)[46]	To assess the treatment outcome of immediately loaded full-arch fixed bridges anchored to both tilted and axially placed implants in the edentulous maxilla and to evaluate the incidence of biological and prosthetic complications
Maló et al (2012)[47]	To document complete rehabilitations in both jaws through the so-called all-on-four concept (ie, four implants with the posterior implants placed at an angle) using immediate function implants inserted in "nonideal" conditions (eg, implants inserted with dehiscences or fenestrations, in periodontally compromised sites, or in fresh extraction sockets)
Maló et al (2011)[48]	To report the long-term outcome of immediately loaded implants in the rehabilitations of completely edentulous maxillae with different classifications
Agliardi et al (2010)[49]	To evalute the clinical and radiographic outcomes of immediately loaded full-arch fixed prostheses supported by a combination of axially and nonaxially positioned implants in a large cohort of patients with completely edentulous jaws, up to 5 years of function
Degidi et al (2010)[50]	To evaluate the concept of intraoral welding as a suitable technique for the fabrication of a restoration for the edentulous atrophic maxilla on the day of placement of axial and tilted implants
Pomares (2009)[51]	To present clinical results of an implant placement protocol using 4 or 6 implants supporting immediately loaded fixed prostheses
Agliardi et al (2009)[52]	To report the preliminary results of a single cohort prospective study that sought to evaluate a new surgical protocol for the immediate rehabilitation of edentulous maxilla without using a bone grafting
Rosen and Gynther (2007)[53]	To evaluate retrospectively the surgical outcome of tilted implants in severely resorbed edentulous maxillas as an alternative to bone grafting and the prosthodontic outcome of posterior extension bridges on tilted implants
Capelli et al (2007)[54]	To assess the treatment outcome of immediately loaded full-arch fixed bridges anchored to both tilted and axially placed implants for the rehabilitation of fully edentulous maxillae and to compare the outcome of axial vs tilted implants
Fortin et al (2002)[55]	To develop a surgical and prosthetic implant treatment protocol for completely edentulous maxillae in which optimal lip support and phonetics is achieved in combination with substantial implant anchorage without bone grafting
Krekmanov et al (2000)[56]	To modify the method for implant placement in the posterior part of the jaws to extend fixed implant-connected prostheses further distally, and to reduce the length of cantilevers in complete-arch prostheses without transpositioning the mandibular nerve or performing bone grafting in the maxilla
Mattsson et al (1999)[57]	To describe the surgical technique for implant treatment in severely resorbed edentulous maxillae without any alveolar reconstruction before or combined with implant placement

REB = Research Ethics Board; ANOVA = analysis of variance; NR = not reported; ND = none declared; EC = Ethics committee; GEE = general estimation equation; RCT = randomized controlled trial; IRCCS = National Institute for Research and Treatment (Italy); IRB = institutional review board.

Study Design	Statistics	REB	Funding	Bias Risk
Prospective case series	ANOVA/Fisher exact/*t* test	NR	ND	High
Prospective case series	ANOVA/*t* test	Universita di Foggia EC	ND	Medium
Prospective case series	Friedman/Wilcoxon/ ANOVA + GEE	NR	ND	Medium
Retrospective case series	Fisher exact	NR	ND	High
Retrospective case series	Life table	Ethics Committee for Health, Lisboa, Portugal	ND	High
Retrospective case series	Life table	IRCCS ethics and scientific committee	ND	High
Prospective case series	Life table + log rank	Beijing Municipal Health Bureau 2008-99	National Program on Key Basic Research (973 Program) China	Medium
Retrospective case series	Kaplan-Meier	Independent ethical committee	ND	High
Prospective case series	ANOVA/paired *t*	NR	ND	Medium
Retrospective case series	Descriptive	Local ethics committee	ND	High
RCT, two arms (acrylic resin framework ± metal framework)	*t* test	NR	ND	High
Retrospective case series	Life table	NR	ND	High
Prospective case series	Kaplan-Meier	NR	ND	High
Retrospective case series	Kaplan-Meier + logistic regression	Ethics Committee for Health, Lisboa, Portugal	ND	Medium
Prospective case series	χ^2/*t* test + life table	NR	ND	High
Prospective case series	*t* test	NR	ND	High
Retrospective case series	No statistical tests	NR	Nobel Biocare research manager, Italy	High
Prospective case series	Life table	IRB	ND	High
Retrospective case series	Life table	NR	ND	High
Prospective case series	*t* test life table	NR	ND	High
Retrospective case series	Life table	NR	Nobel Biocare, Sweden	High
Prospective case series	Life table	NR	ND	High
Prospective case series	Descriptive	NR	ND	High

Table 14 Bias Assessment of Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Lead author	Study Objective
Yates et al (2014-2013e)[58]	To analyze and report the 5–10 year survival rates of endosseous zygomatic implants used in the rehabilitation of the atrophic maxilla
Aparicio et al (2014-2012e)[59]	To report on long-term outcomes in the rehabilitation of the atrophic maxilla using zygomatic and regular implants
Fernández et al (2014)[60]	To describe the surgical techniques, success rate, prosthetic rehabilitation, complications, and demographics of patients undergoing zygomatic implant surgery
Maló et al (2015-2013e)[61]	To report rehabilitation outcomes in 352 patients with complete edentulous atrophied maxillae using 747 zygomatic implants in immediate function inserted through the extramaxillary technique
Davó et al (2013)[62]	To assess the long-term outcome of immediately loaded zygomatic implants placed in atrophic maxillae
Davo and Pons (2013)[63]	To assess the clinical 3-year outcome of prostheses supported by four immediately loaded zygomatic implants
Maló et al (2012)[64]	To report retrospectively on the 3-year follow-up results in the rehabilitation of completely edentulous atrophied maxillae using extramaxillary zygomatic implants
Migliorança et al (2012)[65]	To evaluate the long-term success rate of immediate occlusal loading of extrasinus zygomatic implants after an 8-year follow-up
Balshi et al (2012)[66]	To view and measure the BIC of zygomatic implants in the zygomatic bone
Aparicio et al (2010-2008e)[67]	To report on the clinical outcomes of immediate early loading of zygomatic implants for prosthetic rehabilitation of edentulous and severely resorbed maxillary cases
Aparicio et al (2010-2008e)[68]	To report on the preliminary experiences with zygomatic implants placed with an extrasinus approach to have the implant head emerging at or near the top of the alveolar crest
Bedrossian (2010)[69]	To report on the 7-year follow-up of patients treated with zygomatic implants in conjunction with two to four anterior maxillary implants placed into immediate function and restored with a definitive fixed prosthesis
Stiévenart and Malevez (2010)[70]	To evaluate the results of a consecutive cohort of 20 patients (mean age, 56 years) with extremely resorbed maxillas provided with four zygomatic implants
Davó (2009)[71]	To evaluate the prosthetic rehabilitation success rate and the survival rates of machined surface zygomatic implants and conventional implants placed using a two-stage protocol
Balshi et al (2009)[72]	To determine the clinical effectiveness of the zygomatic implant in oral implant reconstruction under an immediate loading protocol
Pi Urgell et al (2008)[73]	To evaluate the survival of 101 zygomatic implants placed in upper maxilla presenting important bone reabsorption, with a follow-up of 1–72 months
Davó et al (2008)[74]	To evaluate the success rate of immediately loaded zygomatic implants placed in atrophic maxillae
Davó et al (2008)[75]	To evaluate the maxillary sinus in a cohort of patients by means of clinical criteria and CT performed before surgery and after zygomatic implant placement (immediate function protocol)
Kahnberg et al (2007)[76]	To evaluate the treatment outcome with zygoma implants with regard to implant survival, patient satisfaction, and function of prosthesis replacement after 3 years
Duarte et al (2007)[77]	To establish a new surgical/prosthetic protocol for the treatment of extremely atrophic maxillae using four zygomatic implants in an immediate loading system
Peñarrocha et al (2007)[78]	To describe the management of patients with extreme maxillary atrophy; their treatment consisted of maxillary fixed prostheses supported by conventional implants placed in residual anatomic structures in conjunction with zygomatic implants positioned using the sinus slot technique of Stella and Warner
Peñarrocha et al (2007)[79]	To evaluate the satisfaction of patients with maxillary fixed prostheses supported by conventional and/or zygomatic implants
Bedrossian et al (2006)[80]	To evaluate a protocol for immediate function (within 2 hours) of two zygomatic and four standard implants (Nobel Biocare) supporting a fixed prosthesis in the completely edentulous maxilla
Farzad et al (2006)[81]	To describe the experiences of 11 consecutively treated patients who received zygomatic implants

REB = Research Ethics Board; ANOVA = analysis of variance; NR = not reported; ND = none declared; BIC = bone-to-implant contact; CT = computed tomography.

Study Design	Statistics	REB	Funding	Risk of Bias
Retrospective case series	Fisher exact + Kaplan-Meier	NR	ND	High
Prospective case series	Life table	University of Barcelona EC	ND	Medium
Retrospective case series	Descriptive	"ERC guidelines of Universidad el Bosque"	ND	High
Retrospective case series	Kaplan-Meier	Ethics committee for health, Lisboa, 002/2012	ND	High
Prospective case series	Descriptive	Review board of the hospital	ND	High
Prospective case series	Descriptive	Medimar Int Hospital RB 3/2006	ND	High
Retrospective case series	Friedman/Wilcoxon + life table	Ethics committee for health, Lisboa, 003/2009	ND	High
Prospective case series	Descriptive	NR	ND	High
Retrospective case series	Life table	NR	ND	High
Retrospective case series	Life table	NR	ND	High
Retrospective case series	No statistical tests	NR	ND	High
Prospective case series	Life table	NR	ND	High
Retrospective case series	Life table	NR	Nobel Biocare	High
Retrospective case series	No statistical tests	NR	ND	High
Retrospective case series	Life table	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High
Retrospective case series	No statistical tests	Review board of the hospital	Nobel Biocare research manager, Italy	High
Prospective case series	No statistical tests	NR	Nobel Biocare research manager, Italy	High
Retrospective case series	Descriptive	NR	ND (one coauthor is employee of Nobel Biocare AB, Sweden)	High
Prospective case series	Descriptive	NR	ND	High
Retrospective case series	Descriptive (100% survival)	NR	ND	High
Retrospective case series	*t* test + Pearson correlation	NR	ND	High
Retrospective case series	Life table	NR	ND	High
Retrospective case series	Wilcoxon	NR	ND	High

Table 14 ***Continued*** **Bias Assessment of Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes**

Lead author	Study Objective
Ahlgren et al (2006)[82]	*(1)* To evaluate indications, surgical problems, complications, and treatment outcomes related to the placement of zygomatic implants, and *(2)* to determine any prosthetic difficulties and complications
Aparicio et al (2006)[83]	To report on the clinical outcome of using zygomatic and regular implants for prosthetic rehabilitation of the severely atrophic edentulous maxilla
Becktor et al (2005)[84]	To evaluate the clinical outcome of zygomatic implant treatment and consider if treatment with zygomatic implants could be an alternative to bone grafting and implant procedures in patients with edentulous maxillae
Malevez et al (2004)[85]	To evaluate retrospectively in consecutive patients, after a period of 6–48 months follow-up of prosthetic loading, the survival rate of 103 zygomatic implants inserted into 55 edentulous severely resorbed upper jaws
Brånemark et al (2004)[86]	To report the outcome of the first patients with a follow-up time of at least 5 years in whom zygoma fixtures were used in the treatment of the compromised edentulous maxilla and compared with bone grafting procedures
Bedrossian et al (2002)[87]	To present a preliminary report on 22 patients followed for 34 months who received the Brånemark Zygomaticus implant in conjunction with premaxillary standard implants for the reconstruction of resorbed edentulous maxillae

REB = Research Ethics Board; ANOVA = analysis of variance; NR = not reported; ND = none declared; BIC = bone-to-implant contact; CT = computed tomography.

Results of Individual Studies

Studies Designed With an Objective to Assess Effects of Implant Design (or Feature) on Outcomes (Fig 3).[18–34] Only 1 of the 17 papers reported patient-centered outcomes (Table 18). The prevailing reported outcome was incidence of adverse biological and technical events, clinical success or survival, and degree of bone loss. Radiographic techniques varied from standardized periapical radiographs to nonstandardized orthopantograms. Some studies also reported indices of periodontal tissues, secondary stability using resonance frequency analysis technology or periotest values. Based on the surrogate and clinical outcomes, it can be proposed that in the fully edentulous maxilla the choice of implant system does not appear to influence outcome (n = 8 reports). Moreover, the surface may influence outcome (n = 4 reports); the length appears not to influence outcome (n = 7 reports). Implants of wider diameter (n = 2 reports) may appear to perform not as well or similarly as implants of regular diameter (n = 4 reports). The healing period varied extensively after extraction and surgery procedures, as did the healing period before implant loading, the number of implants needed to support the supraconstruction, and the composition and design of the supraconstruction. We considered meta-analyses of the extracted data as inappropriate and therefore abandoned further statistical analyses of the extracted data.

Studies Reporting the Effects of Tilted Implants to Enable Placement of Longer Implants (Fig 4).[35–57] A relatively high proportion of the clinical studies (13 of 23) reported patient-centered outcomes, using a Likert-type scale, dichotomous or a visual analogue scale (Table 19), though these were about the treatment in general and none were pertinent to issues about implant length. The prevailing outcome reported was the incidence of adverse biological and technical events, clinical success or survival, and degree of bone loss. Radiographic techniques varied from standardized periapical radiographs to nonstandardized orthopantograms. Some studies also reported indices of periodontal tissues. Based on the surrogate and clinical outcomes, it can be proposed that the clinical performance of axial and tilted implants in the fully edentulous maxilla appear comparable. Moreover, different designs from the same manufacturer do not appear to influence outcome, or this was simply not reported when more than one implant design was used. There was extensive variation in the healing period after extraction and surgery, and before implant loading; number of implants needed to support the supraconstruction; and the composition and design of the supraconstruction. Formal meta-analyses can be performed for comparing tilted with axial implants, and have been published elsewhere (Table 2a).

Study Design	Statistics	REB	Funding	Risk of Bias
Retrospective case series	No statistical tests	NR	ND	High
Prospective case series	Descriptive (100% survival)	NR	ND	High
Retrospective case series	No statistical tests	NR	ND	High
Retrospective case series	Descriptive (100% survival)	NR	ND	High
Prospective case series	Descriptive	NR	Hilary Orton Memorial Foundation	High
Prospective case series	Descriptive (100% survival)	NR	ND	High

Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 5).[58–87] Two studies reported quality of life data using the Oral Health Impact Profile (OHIP)-14 scale,[59,63] and four studies described other patient-centered outcomes (Table 20).[76,79–81] Questions about study participant satisfaction did not pertain to implant design effects, but rather to the general treatment outcomes. The prevailing reported outcome was incidence of adverse biological events during or immediately after surgery and implant survival. The degree of bone loss is seldom reported, because there are no radiographic techniques that can adequately depict such loss. Nonstandardized orthopantograms, cone beam computer tomography scans, and conventional radiographs using Waters' projection have been attempted. Some studies also reported indices of periodontal tissues and secondary stability using resonance frequency analysis technology. A wide variation was observed in the healing period after extraction, surgery procedures, healing period before implant loading, number of implants to support the supraconstruction, and composition and design of the supraconstruction.

Appraising the potential effects of the implant design on outcomes related to zygoma implants is complex because of inadequate descriptions of the implant brand. The company Brånemark Integration manufactured a product named "Z-fixture" for a period, which many have confused with a product named "Brånemark system zygoma implant" manufactured by Nobel Biocare. One early generation of the zygoma implants included a cervical hole meant for the abutment screw that potentially could allow direct communication from the oral cavity to the sinus if the abutment screw did not completely obliterate the canal. The second generation of such implants contained no such holes. The third generation avoids threads in the coronal one third of the implant, whereas the fourth generation incorporates engaging threads and a narrow apical tip. So far, no studies have compared any of these designs one to one. A few studies that included both turned and oxidized zygoma implants did not report whether there were differences in outcomes between the two.[62,66,72,74,75,82]

When appraising the possible effects of zygoma implant design on outcomes it is important to be aware that at least four different surgical techniques have been described and an implant design used for one technique may not be optimal for another. The original protocol described a trans-sinus placement.[86] An alternative extrasinus approach could be used when large buccal concavity in the sinus area otherwise would displace the zygoma implant head very far palatinally.[68] A third approach named the sinus slot technique creates a different angulation of the zygoma implant, which places the implant head on the top of the alveolar crest while avoiding penetrating the sinus membrane.[73] The last alternative is to anchor the implant solely in the zygomatic bone, remaining mostly outside the maxilla.[64]

Table 15 Bias Assessment of Studies Reporting the Effects of Implants Placed in Pterygoid Bone or Other Bony Buttresses With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Study	Study Objective
Peñarrocha-Oltra et al (2013)[88]	To evaluate the 5-year outcome of a previously reported case series of patients with severely atrophic maxillae treated with palatally positioned implants and fixed full-arch rehabilitations
Balshi et al (2013)[89]	To determine if there is a statistically significant difference in the survival rates between different sized implants placed in the pterygomaxillary region
Balshi et al (2013)[90]	To determine if there is a significant difference in implant survival rates between implants in the pterygomaxillary region: implant placement with two-stage, single-stage, and guided surgery protocols
Rodríguez et al (2012)[91]	To review a series of 454 pterygoid implants placed more vertically than the previous standard angle (45 degrees) over a functional loading period ranging from 2 months to 14 years with a mean follow-up period of 6 years
Peñarrocha et al (2012)[92]	To assess the success and marginal bone loss, after 1 year of loading, of implants placed in anatomic buttresses of atrophic maxillae to rehabilitate patients with combination syndrome
Peñarrocha et al (2009)[93]	To evaluate implant-supported restorations supported by palatally positioned implants as an alternative treatment for rehabilitation of the atrophic maxilla and to assess the satisfaction of patients with the results
Peñarrocha et al (2009)[94]	To evaluate the success rate of implants placed in the pterygomaxillary region using drills and osteotomes with a minimum of 12 months' follow-up
Balshi et al (2005)[95]	To calculate the survival rate of Brånemark implants with ti-unite surfaces in edentulous maxillary sites, including the pterygomaxillary region, restored with complete fixed maxillary prostheses
Balshi et al (1999)[96]	To examine all patients whose dentition had been restored with a complete maxillary prosthesis supported by Brånemark implants in pterygomaxillary sites and to address the biomechanical aspects of implant size, position, and bone quality with patient age, gender, smoking habits, and medications

REB = Research Ethics Board; MANOVA = multivariate analysis of variance; NR = not reported; ND = none declared.

Table 16 Bias Assessment of Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Lead author	Study Objective
Zinser et al (2013-2012e)[97]	To assess the predictors of implant failure after grafted maxillary sinus
Dasmah et al (2013-2011e)[98]	To conduct a 5-year follow-up analysis with focus on bone-level alteration in block vs particulate onlay bone grafts
Sjöström et al (2007)[99]	To conduct a 3-year follow-up with respect to clinical, radiologic, and RFA parameters of implant stability in 29 patients with atrophic edentulous maxillae reconstructed with free autogenous iliac bone graft and titanium implants
Chiapasco et al (2007)[100]	To report the clinical outcome of osseointegrated implants placed in extremely atrophied edentulous maxillae after Le Fort I osteotomy and interpositional autogenous iliac bone grafts
Hallman et al (2005)[101]	To compare two different implant systems used after interpositional bone grafting of the severely resorbed maxilla with a modified augmentation technique using fibrin glue
Becktor et al (2004)[102]	To analyze and compare the survival rates of endosseous implants placed in the edentulous maxillae of patients in whom bone augmentation was undertaken prior to or in conjunction with implant placement with survival rates in patients who did not undergo bone augmentation
Pinholt (2003)[103]	To observe the clinical outcome of Brånemark machine-surfaced implants in a comparative evaluation with ITI SLA implants inserted into severely atrophied maxillae reconstructed with autogenous bone graft
Becktor et al (2002)[104]	To analyze the influence of the mandibular dentition on implant performance in the maxilla before definitive prosthesis attachment when reconstruction is possible only with the use of autogenous bone-grafting techniques

REB = Research Ethics Board; NR = not reported; ND = none declared; CCT = clinical controlled trial; REC = Regional Ethics committee; ISQ = implant stability quotient; GEE = general estimation equation; RFA = radiofrequency analysis; ANOVA = analysis of variance; ITI = International Team for Implantology.

Study Design	Statistics	REB	Funding	Risk of Bias
Retrospective case series	Descriptive	U Valencia Ethics Board H1330446292077	ND	High
Retrospective case series	Life table	NR	ND	High
Retrospective case series	Life table + MANOVA	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High
Retrospective case series	Kruskal Wallis/ Mann-Whitney *U*	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High
Retrospective case series	Life table	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High

Study Design	Statistics	REB	Funding	Risk of bias
Retrospective case series	Kaplan-Meier + Cox regression	NR	ND	High
CCT prospective study with concurrent controls, split	Wilcoxon	NR	ND	High
Prospective case series	Life table + logistic regression (ISQ: Mann-Whitney/ Spearman rho)	The local REC	ND	Medium
Prospective case series	Life table	NR	ND	High
CCT prospective study (Astra) with historical controls (Brånemark)	χ^2/Mann Whitney *U*	NR	ND	High
Retrospective case series	χ^2/Wilcoxon + life table	NR	ND	High
CCT prospective study (Straumann) with historical controls (Brånemark)	Descriptive	NR	ND	High
Retrospective study with concurrent controls	Logistic regression + GEE	NR	ND	Medium

Table 16 ***Continued*** **Bias Assessment of Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes**

Lead author	Study Objective
Lekholm et al (1999)[105]	*(1)* To study the extent to which different bone grafting procedures are performed, *(2)* to evaluate the treatment results obtained after 3 years of function, and *(3)* to assess possible complications occurring during treatment and follow-up
Keller et al (1999)[106]	To present a retrospective study of patients with advanced horizontal and vertical bone loss and complete or partial edentulism who were treated with an autogenous rigidly fixed block onlay bone graft
Keller et al (1999)[107]	To present a continuation of a study of medical, surgical, and prosthetic records of patients with advanced maxillary bone resorption in whom autogenous inlay bone grafts were placed in the maxillary antrum or nasal floor
Watzek et al (1998)[108]	To examine *(1)* whether the concept of sinus floor augmentation can also be recommended in the treatment of patients with extreme maxillary resorption, and *(2)* whether the concept of placing implants mainly in maxillary posterior regions is suitable for this group of patients
Nyström et al (1997)[109]	To present the results from 10 consecutive patients who, because of insufficient bone volume for conventional implant placement in the maxilla, were treated with an interpositional bone graft and Le Fort I osteotomy
Köndell et al (1996)[110]	To evaluate the treatment of patients with severely resorbed edentulous maxillae with immediate autogenous rib grafts and titanium implants in a one-stage procedure with the onlay technique
Neukam (1996)[111]	To report a retrospective study of 43 patients with extreme severe maxillary ridge resorption who had received onlay grafts from the iliac crest with simultaneous placement of osseointegrated implants
Keller et al (1994)[112]	To describe a one-stage antral and nasal inlay composite bone-grafting procedure and to present preliminary statistical data for 30 recipient sites in 20 patients

REB = Research Ethics Board; NR = not reported; ND = none declared; CCT = clinical controlled trial; REC = Regional Ethics committee; ISQ = implant stability quotient; GEE = general estimation equation; RFA = radiofrequency analysis; ANOVA = analysis of variance; ITI = International Team for Implantology.

Table 17 Bias Assessment of Studies Designed With no A Priori Stated Objective to Assess a Particular Implant Design Feature

Lead Author	Study Objective
Jemt et al (2011)[113,114]	To report and compare the treatment outcomes of two patient cohorts from the same clinic, rehabilitated with fixed implant prostheses in the edentulous maxilla from 1986 to 1987 (early) and 2001 to 2004 (late)
Friberg and Jemt (2008-2007e)[115]	To retrospectively evaluate and compare the outcome of implants placed in edentulous maxillae with either wide or narrow jaw shapes; the marginal bone loss and implant cumulative survival rates were calculated and analyzed with special reference to smoking habits
Jemt and Johansson (2006)[116]	To report 15-year patient-based data in relation to follow-up after treatment with fixed prostheses supported by implants in the edentulous upper jaw
Widbom et al (2005)[117]	To retroactively evaluate outcome in two groups of patients treated with implant-supported maxillary overdentures; various factors related to the treatment were compared among subjects in the two groups
Ibañez et al (2005)[118]	To determine whether, with proper care selection and adherence to established principles, immediate occlusal loading of double acid-etched surface implants could be considered for clinical use in both arches after strict evaluation and longer follow-up
Degidi and Piattelli (2003)[119]	To evaluate clinical implants subjected to immediate functional loading and to immediate nonfunctional loading in various anatomic configurations
Kiener et al (2001)[120]	To report on prosthetic complications and maintenance of maxillary overdentures supported by ITI implants
Watson et al (1998)[121]	*(1)* To evaluate the long-term effectiveness of Calcitek cylindrical HA-coated implants to support maxillary or mandibular overdentures; *(2)* to compare the maxillary and mandibular success and survival rates of implants and prostheses; and *(3)* to report on the maintenance requirements associated with overdenture treatment with this system
Jemt and Lekholm (1995)[122]	To compare the 5-year treatment result of the Brånemark implant technique, when used in different maxillary shape situations and when using various prosthetic solutions, to determine if the outcome is predictable based on the presurgical jaw shape assessment
Palmqvist et al (1994)[123]	To retrospectively compare the outcomes of implant-supported maxillary overdentures in planned and emergency cases

REB = Research Ethics Board; NR = not reported; ND = none declared; HA = hydroxyapatite; ITI = International Team for Implantology.

Study Design	Statistics	REB	Funding	Risk of bias
Retrospective case series	Descriptive	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High
Retrospective study with concurrent controls	ANOVA + Kaplan-Meier + log rank	NR	ND	High
Retrospective case series	Descriptive	NR	ND	High
Prospective case series	Descriptive	NR	ND	High
Retrospective case series	Kaplan-Meier + log rank +Cox regression	NR	ND	Medium
Prospective case series	Descriptive	NR	ND	High

Study Design	Statistics	REB	Funding	Risk of Bias
Retrospective study with historical controls	χ^2/t test + life table	NR	ND	High
Retrospective case series	χ^2/t test + Fisher permutation + life table	NR	ND	High
Prospective case series	χ^2/t test + life table	NR	ND	High
Retrospective case series	Life table + Cox regression	NR	ND	High
Prospective case series	Descriptive	NR	ND	High
Retrospective case series	Life table	NR	Apollonia, Italy; Biohorizons, USA; Friadent, Germany; Lifecore, USA; & Nobel Biocare, Sweden	High
Retrospective case series	Kaplan-Meier	NR	ND	High
Prospective case series	Life table	NR	Calcitek & Leeds General Infirmary Trust, UK	High
Retrospective case series	*t* test + life table + Cox regression	NR	Nobelpharma, Sweden	High
Prospective case series	Kaplan-Meier + logistic regression	NR	ND	High

Table 18 Results of Studies Designed to Assess Effects of Implant Design or Feature On Outcomes

Study	Presurgery	Surgery Details	Postsurgery
Jungner et al (2012e)[18]	Healed; no grafting	Two protocols: If stable, then 1-stage (32p, 59i), otherwise, 2-stage (57p, 174i)	Two protocols: *(1)* If stable ant mandible, then loading 13–32 days (14p, 54i); *(2)* healing 4–36 (av 17) weeks
Vervaeke et al (2015-2013e)[19]	No periodontitis	"According to manufacturers guidelines" 2 protocols: 1/2-stage	Two protocols: *(1)* If good stability, immediate impression, temp PMMA + metal < 24 h -> > 3 months perm; *(2)* healing
Testori et al (2014-2013e)[20]	Two protocols: *(1)* healed; *(2)* postextraction	AB, two protocols: 1/2-stage	Two protocols: *(1)* Stability > 32 Ncm, immediate impression, temp FDP < 48 h; otherwise, healing 2–6 months
Ravald et al (2013)[21]	Healed 3–6 months	2-stage	Healing mandible 4 months, maxilla 6.5 months
Van Assche et al (2012-2011e)[22]	Healed 6 months	AB, distal sites underprepared, 15+ NCm	Healing 6+ weeks, bar + denture -> 6 months, egg-shaped, bar new CoCr
Cosyn et al (2012-2010e)[23]	Three protocols: *(1)* postextraction (6%) or within 6 weeks (7%); *(2)* healed (87%), no periodontitis; *(3)* augmented-onlay/inlay (18%)	Two protocols: *(1)* (43%), *(2)* (57%)-stage	Two protocols: *(1)* Immediate
Kallus et al (2009-2008e)[24]	Healed 6 months	NR	Healing mandible 4 months, maxilla 6 months
Li et al (2009)[25]	Two protocols: *(1)* healed; *(2)* postextraction	AB, "standard protocol," 20–50 NCm	Immediate abutment, PMMA FDP -->
Alsaadi et al (2008)[26]	NR	NR	NR
Nelson et al (2008)[27]	Some augmented; some healed	Not AB, GA/La flap, 1-stage	Immediate reline –mandible > 6 weeks, maxilla 12 weeks; if > 35 Ncm then rehabilitation
Maló et al (2007)[28]	NR	AB, LA, Flap, Ø: undercontour, 0.8 mm supra, 32+ NCm	Immediate final abutment; two protocols: *(1)* immediate (16p/23i), *(2)* healing 4–6 months
Hjalmarsson and Smedberg (2005)[29]	NR	NR	NR
Degidi et al (2005)[30]	Two protocols: *(1)* postextract (23p, 175i); *(2)* healed (20p, 213i)	AB, LA, flap, Max ant/post Spread	Immediate PMMA FDP --> 4–6 months permanent
Schwartz-Arad et al (2004)[31]	Two protocols: *(1)* Postextract (144i); *(2)* healed (237i)	AB, maximal implant lengths, 2-stage	Immediate soft, reline --> healing time NR
Morris et al (2001)[32]	NR	AB	NR
Friberg et al (1997)[33]	Healed 3–4 months	2-stage	Healing 6 months
Olsson et al (1995)[34]	Healed 6 months	1 exp + 1 ctr implant in each contralateral quadrant, 2-stage	Healing mandible 4 months, maxilla 6 months

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; mc = Metal-Ceramic; OPGX = orthopantomogram; PMMA = polymethyl methacrylate; VAS = visual analogue scale; Adverse*: Adverse biological and technical outcomes.

Prosthesis	Outcome	Patient-Outcome	Findings
Crown (36i) pFDP (103i) fFDP (148i)	PAX bone, perioindex, implant removed	NR	Surface influence the outcome. Oxidized marginally better than turned
Crown pFDP fFDP	PAX/OPX bone SuccSurv	NR	Multivariate analyses indicated no effect of implant length, diameter, or design on survival or bone loss
4-8i FDP cement/ screw	Adverse* PAX bone SuccSurv	NR	The multivariate analyses indicated no effect of implant length, diameter, or design on survival or bone loss, contrasting the univariate estimates
5/6i-ga/TiA/mc-10/12u-FDP screw	Adverse* PAX bone Perioindices	NR	Implant system does not influence outcome; (corrects somewhat earlier data of same cohort by Engquist et al, 2002, & Åstrand et al, 1999 & 2004)
4i + 2 post short egg-shape bar CoCr overdenture	Adverse PAX bone Perioindices Stability-ptv/RFA SuccSurv	NR	Multivariate analyses indicated that implant length does not influence outcome; no differences were noted between the two short posterior implants vs the other implants supporting the FDP
Crown pFDP fFDP overdenture	PAX/OPX bone, SuccSurv	NR	Multivariate analyses indicated no effect of implant length or diameter on outcome. Surfaces/systems not compared
6i-FDP-ns	PAX bone, SuccSurv	NR	Implant system does not influence outcome
4/6i-FDP	OPX bone, SuccSurv	NR	No differences noted between designs lengths and diameter
Crown pFDP fFDP	PAX bone, stability-ptv SuccSurv	NR	Multivariate analyses indicated more bone loss around ø5mm than others. Trend for more loss with machined surfaces. No effect of length
FDP overdenture	Adverse OPGX bone, perioindices, SuccSurv	NR	Implant design does not influence outcome. (No implants were lost following the abutment connection)
Crown (58), pFDP (296i), total FDP (54i)	Adverse* PAX bone, SuccSurv	NR	Implant surface influence outcome; all the failed implants (n = 13) were turned and not microrough; possible learning curve effect; concurrent use of short and long implants to support FDP
4/8i-Au/Ti-FDP screw (24p) OR 4/8i-Au/Ti-FDP-cresco(26p)	Adverse* bone, perioindices, preload	Satisfaction VAS	No difference noted between two implant systems
6-12i-12u-mcFDP cement	PAX bone, SuccSurv	NR	Multivariate analyses indicated that implant diameter influenced outcome; implants with diameter more than 5.25 mm had a hazard rate of 3.1 compared to < 5.25 mm
mc-FDP	OPX bone	NR	Multivariate analyses indicated that implant length does not influence bone loss; implant coating may have a marginal effect on outcome
Crown/FDP 5-6i-ball/ bar-overdenture	PAX/OPX bone, perioindices, stability-ptv, SuccSurv	NR	Implant surface may influence outcome; cp titanium screw have worse outcomes compared to hydroxyapatite screw and cylinders
ga-FDP screw	PAX bone	NR	No difference between two designs, one with and one without tapping
4-6i FDP	*(1)* SurgComplic/Success 2; *(2)* adverse* PAX bone	NR	Implant design does not influence outcome

Table 19 Results of Studies Reporting the Effects of Tilted Implants to Enable Placement of Longer Implants

Study	Presurgery	Surgery Details	Postsurgery
Agliardi et al (2014-2012e)[35]	Two protocols: *(1)* postextraction-pal + autograft, *(2)* healed	AB, LA, flap, post tilt 30°– 45°, medial i, tilt 30°– 45°, axial, underprepared; 30+ Ncm	Immediate permanent abutment, suture, impression, PMMA-FDP 4–6 months > permanent
Agnini et al (2014-2012e)[36]	Two protocols: *(1)* postextraction autograft + allograft, no membrane, *(2)* healed	AB, LA, flap, two protocols: *(1)* if 9 mm bone then 6–8 axial imp, *(2)* If < 7 mm bone 2 tilted + 2 axial. If required, autograft + allograft/xenograft + Membrane	Immediate impression, healing abutment, suture, PMMA-FDP 6 months > permanent
Pera et al (2014)[37]	Postextraction	Underprepared, posterior angled if required, > 40 Ncm	Immediate abutment + impression > PMMA within 36 h > 4 months healing
Pozzi et al (2015-2013e)[38]	Two protocols: *(1)* postextraction (44i), *(2)* healed (126i)	NR, 30 Ncm, peri-implant autograft	Immediate prefabricated PMMA w/metal screws > 3–4 months > permanent
Maló et al (2012-2011e)[39]	Healed	AB, LA, flap, fenestration, trans-sinus, post tilt < 45°, 32+ Ncm	Immediate impression, PMMA screws 6 months > permanent
Testori et al (2013)[40]	NR	AB, LA, flap, fenestration, trans-sinus, post tilt < 30°, xenograft	Healing 6 months > permanent
Di et al (2013)[41]	Two protocols: *(1)* postextraction, *(2)* healed	AB, LA, flap, fenestration, post tilt < 45°, 35 Ncm	Immediate impression, PMMA screws 6 months > permanent
Maló et al (2012)[42]	Two protocols: *(1)* postextraction, *(2)* healed	AB, LA, flap, fenestration, post tilt 35°–45°, underprepared, 35+ Ncm	Immediate impression, PMMA screws 6 months > permanent
Francetti et al (2012-2010e)[43]	Two protocols: *(1)* postextraction, *(2)* healed	LA, flap, fenestration, post tilt 30°, 40–50 Ncm	Two protocols: *(1)* If > 40–50 Ncm then immediate abutment (straight/30° multiunit) + pickup pvs-impression, PMMA-FDP 4–6 months permanent
Mozzati et al (2012)[44]	Two protocols: *(1)* postextraction (210i), *(2)* healed (124i)	AB, LA, bone remodel, flap, post tilt 30°, "nanocrystalline paste" (35p, 108i), 40 Ncm	Immediate PMMA-screw > 6+ months healing > permanent
Crespi et al (2012)[45]	Two protocols: *(1)* postextraction, *(2)* healed	AB, LA, flap, post tilt 25°– 35° (4 mm–13/15 mm), axial (3.75/4–13 mm), underprepared	Two protocols: (1) If > 40 Ncm then immediate abutment (17/30°) + pickup preimpression + bite registration, prefab PMMA ± metal-FDP+ >
Cavalli et al (2012)[46]	Two protocols: *(1)* postextraction, *(2)* healed	AB, LA, flap, post tilt 30°, 40–50 Ncm	Immediate permanent abutment, suture, compression, PMMA-FDP 6 months > permanent
Maló et al (2012)[47]	Two protocols: *(1)* postextraction, *(2)* healed	AB LA, flap fenestration, post tilt 35°– 45°, underprepared 35+ Ncm	Immediate impression, PMMA screws 6 months > permanent
Maló et al (2011)[48]	Two protocols: *(1)* postextraction, *(2)* healed	AB LA, flap fenestration, post tilt 35°– 45°, underprepared 35+ Ncm	Immediate impression, PMMA screws 6 months > permanent
Agliardi et al (2010)[49]	Healed	AB, LA, flap post tilt 30°– 45°, underprepared 30+ Ncm	Immediate permanent abutment, suture, impression, PMMA-FDP 4–6 months > permanent
Degidi et al (2010)[50]	Healed	AB, LA, flap post tilt 30°– 45°, no bone grafting, minimum 25 Ncm/ISQ 60 for study inclusion	Immediate abutment, prefabricated PMMA FDP, welded framework, ø: 2 mm bar, removed & sandblasted, permanent
Pomares (2009)[51]	Two protocols: *(1)* postextraction, *(2)* healed	LA, MaloSurgGuide, if poor bone 6 implants, otherwise 4	Immediate abutment + impression > temp PMMA > 7 days > healing 5–15 months > permanent

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; ø = diameter; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; PMMA = polymethyl methacrylate; VAS = visual analogue scale; ZrO: Zirconium-oxide; CAD/CAM = computer-aided design/computer-assisted manufacture; Au/Ti: Gold alloy or Titanium.
*Adverse biological and technical outcomes.

Prosthesis	Outcome	Patient Outcome	Findings
4 tilt + 2i-CAD/CAM TiA-12u-FDP-Procera	Adverse* PAX bone, perioindices SuccSurv	Satisfaction-5-Likert	Tilted, axial implants performance comparable, effects of different implant systems were NR
2 tilt + 2i/6-8i-mc/ac/Tia-FDP/CAD-ZrO/TiO-FDP	Adverse* PAX bone	NR	Tilted, axial implants performance comparable for one system, but worse for tilted when alternative system described, could be an effect of unbalanced intraoral distribution/restorations
4-6-FDP screw	PAX bone	NR	Tilted, axial implants performance comparable, multivariate stats indicated that roughness of implant neck does not influence outcome
2 tilt + 2-8i-CAD-ZrOFDP	Adverse* OPGX bone, perioindices, SuccSurv	Satisfaction-VAS	Implant system does not influence outcome, no implants were lost, (however only 2 vs 10 patients had implants in the edentulous maxilla)
2 tilt + 2i-12u-FDP	Adverse* OPG/PAX bone, SuccSurv	"Complaints"	The axial implants performed slightly better than the tilted
2 tilt + 2/4i-12u-TiaFDP screw	Adverse* PAX bone, SuccSurv	Satisfaction-4-Likert	Tilted, axial implants performance comparable
2 tilt + 2i-12u-gaFDP	Adverse* OPGX bone, SuccSurv	Satisfaction-5-Likert	Tilted, axial implants performance comparable
2 tilt + 2i-TiC-FDP-Procera/TiA-FDP	Adverse* OPG/PAX bone, SuccSurv	"Complaints"	Tilted, axial implants performance comparable, implant design influence outcome, one implant system had higher failure rate than the others
2 tilt + 2i-12u-mcFDP-Procera-screw	Adverse* PAX bone, SuccSurv	NR	Tilted, axial implants performance comparable
2 tilt + 2/4i-mcFDP	Adverse* PAX bone, perioindices, SuccSurv	Satisfaction-Y/N	Tilted, axial implants performance comparable
2 tilt + 2i-10/12u-ga-FDP screw	Adverse* PAX bone, SuccSurv	NR	Axial implants performed slightly better than tilted
2 tilt + 2i-12u-CAD-TiA-FDP-Procera	Adverse* PAX bone, perioindex, SuccSurv	NR	Implant system does not influence outcome, no implants were lost
2 tilt + 2i-TiC-FDP-Procera/TiA-FDP	Adverse* OPG/PAX bone, SuccSurv	"Complaints"	Tilted, axial implants performance comparable, implant system does not influence outcome
2 tilt + 2i-TiC-FDP-Procera/TiA FDP	Adverse* OPG/PAX bone, SuccSurv	"Complaints"	Tilted, axial implants performance comparable, multivariate stats indicated that implant system does not influence outcome
2 tilt + 2i- CAD/CAM TiA-FDP-canti-Procera	Adverse* PAX bone, perioindices	NR	Tilted, axial implants performance comparable, effects of different implant systems were NR
4 tilt + 3i-10/12u-weld-bar-ga FDP screw	Adverse* PAX bone, perioindices, SuccSurv	NR	Tilted implants performed slightly better than axial
2 tilt + 2i- CAD/CAM TiA-FDP-canti-Procera	Adverse* OPG/PAX bone, SuccSurv	NR	Tilted, axial implants performance comparable

Table 19 ***Continued*** **Results of Studies Reporting the Effects of Tilted Implants to Enable Placement of Longer Implants**

Study	Presurgery	Surgery Details	Postsurgery
Agliardi et al (2009)[52]	Two protocols: *(1)* postextraction (40i), *(2)* healed (80i)	AB, LA, flap post tilt 30°–45°, medial. tilt 30°– 45°, axial, underprepared, 30+ Ncm	Immediate permanent abutment, suture, impression, PMMA-FDP 4–6 months > permanent
Rosen & Gynther (2007)[53]	NR	No AB, LA, fenestration, post tilt > 30°, if thin, palatal w/2-5 exposed threads, no graft, no membrane, 2-stage	Healing 6 months > permanent
Capelli et al (2007)[54]	Healed	AB, LA, flap fenestration, post tilt 25°– 35°, 1-stage crestal/subcrestal	Two protocols: *(1)* If > 30+ Ncm then immediate PMMA-FDP, 3 months permanent
Fortin et al (2002)[55]	Healed	30+ Ncm	Healing 3/6 months > permanent
Krekmanov et al (2000)[56]	Healed	AB, LA, flap fenestration, post tilt 30°–35°, anterior tilt varies	Healing 3/6 months > permanent
Mattsson et al (1999)[57]	NR	No AB, LA, fenestration, post tilt > 30°, if thin, palatal w/2-5 exposed threads, no graft, no membrane, 2-stage	Healing 6 months > permanent

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; ø = diameter; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; PMMA = polymethyl methacrylate; VAS = visual analogue scale; ZrO: Zirconium-oxide; CAD/CAM = computer-aided design/computer-assisted manufacture; Au/Ti: Gold alloy or Titanium.
*Adverse biological and technical outcomes.

Table 20 Results of Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Study	Presurgery	Surgery Details	Postsurgery
Yates et al (2014-2013e)[58]	Healed	GA, SinusSlot, suture, 2-stage	Healing 6 months
Aparicio et al (2014-2012e)[59]	Healed	AB, GA, flap vertical rectangular sinus window, trans-sinus implant, 2-stage	Healing 5–6 months
Fernández et al (2014)[60]	Healed	AB, GA, flap, two protocols: *(1)* vertical rectangular sinus window, trans-sinus implant (51p), *(2)* no window (29p) 2-stage	NR
Maló et al (2015-2013e)[61]	NR	AB, GA/LA, flap, three protocols? XtraMaxillary, ≥ 30 Ncm	Immediate impression, PMMA screws same day > 6 months > permanent
Davó et al (2013)[62]	Healed postextraction	AB, GA, flap, three protocols: *(1)* vertical rectangular sinus window, trans-sinus implant (66i), *(2)* SinusSlot (15i), *(3)* "minimal invasive" SinusSlot XtraSinus	Immediate impression, metal-reinforced PMMA 24–48 hours > healing 6 months
Davo and Pons (2013)[63]	Healed	AB, GA, flap, vertical rectangular sinus,window, trans-sinus implant, > 35 Ncm, suture	Immediate impression, metal-reinforced PMMA 24–48 hours > healing 6 months
Maló et al (2012)[64]	Healed	AB, GA (32p), LA (7p) flap XtraMaxillary ≥ 30 Ncm	Immediate PMMA temp same day > 6 months
Migliorança et al (2012)[65]	Healed	AB, GA + LA, flap XtraSinus, ≥ 35 Ncm, abutment, suture	Two protocols: *(1)* If > 40 Ncm then immediate impression, temp PMMA 6 months, *(2)* healing 6 months
Balshi et al (2012)[66]	Healed	AB, GA, flap, vertical rectangular sinus window, PrP-prep + trans-sinus implant	Immediate autopolymer PMMA in denture < 2 hours > 3 months
Aparicio et al (2010-2008e)[67]	Healed	AB, GA, flap, two protocols: *(1)* vertical rectangular sinus window, trans-sinus implant (7p), *(2)* XtraSinus (18p)	Two protocols: *(1)* immediate temp PMMA < 24 hours > 4–6 months, *(2)* immediate impression, suturing, denture relief, submerged healing 6 months, permanent FDP < 5 days

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; CAD/CAM = computer-aided design/computer-assisted manufacture; BIC = bone-to-implant contact; ptv = Periotest; zyg = zygomatic; pter = pterygoid; PMMA = polymethyl methacrylate; VAS = visual analogue scale; OHIP = Oral Health Impact Profile.
*Adverse biological and technical outcomes.

Prosthesis	Outcome	Patient Outcome	Findings
4 tilt + 2i-10/12u- CAD/CAM TiA-12u-FDP-Procera	Adverse* PAX bone, perioindices, SuccSurv	Satisfaction-5-Likert	Implant system does not influence outcome, no implants were lost
2 tilt + 4i-12u-CoCr/AgPd/ TiaFDP-canti-screw	Adverse* OPG/PAX bone, perioindices, SuccSurv	Satisfaction-Y/N	Tilted, axial implants performance comparable
2 tilt + 2/4i-12u-TiA-FDP screw	Adverse* PAX bone, SuccSurv	Satisfaction-Y/N	Tilted, axial implants performance comparable
2 tilt + 1-5i-bar-Marius bridge	Adverse* SuccSurv	Satisfaction-Y/N	Tilted, axial implants performance comparable
6 tilt-Ga/TiA-FDP	Adverse* bite force, SuccSurv	NR	Tilted implants performed slightly better than axial
2 tilt + 4i-12u-CoCr/AgPd/TiA FDP-canti screw	Adverse* SuccSurv	NR	Tilted, axial implants performance comparable

Prosthesis	Outcome	Patient Outcome	Findings
2-4i + 1/2 zyg-FDP screw, overdenture	SuccSurv	NR	
2-5i + 2 zyg-FDP, cement (3)/ screw (19)	Adverse* Stability-Ptv SuccSurv	Sinusitis-Y/N OHIP-Edent	
NR	Adverse* SuccSurv	NR	
1-4i + 2/4 zyg-FDP	Adverse* SuccSurv	NR	
2-6i + 2/4 zyg-FDP screw	Adverse* SuccSurv	NR	Performance of different conventional implants and turned vs oxidized zygoma implants NR
4 zyg-FDP screw (15p), overdenture (2p)	Adverse* SuccSurv	OHIP-14	
1-4i + 2/4 zyg-Tia/ga-FDP	Adverse* PAX bone, perioindices, SuccSurv	NR	Performance of different prototype zygoma implants NR
2-4i + 2 zyg-10u-FDP screw	Adverse* SuccSurv	NR	
2-4i + 2 zyg + 2p ter-ga/mcFDP	Adverse* BIC, SuccSurv	NR	Performance of turned vs oxidized zygoma implants NR
2-5i + 2 zyg-mcFDP	Adverse* SuccSurv	NR	

Table 20 ***Continued*** **Results of Studies Reporting the Effects of Implants Placed in Zygomatic Bone With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes**

Study	Presurgery	Surgery Details	Postsurgery
Aparicio et al (2010-2008e)[68]	Healed	AB, GA, flap, XtraSinus	Immediate impression, suturing, denture relief, two protocols: *(1)* immediate temp PMMA < 24 hours > 4–6 months, *(2)* permanent FDP < 5 days
Bedrossian (2010)[69]	Healed	AB, GA + LA, flap, vertical rectangular sinus window, trans-sinus implant	Immediate autopolymer PMMA in denture > 6 months permanent
Stiévenart and Malevez (2010)[70]	Healed	AB, GA + LA, flap, vertical rectangular sinus window, trans-sinus implant. 2 protocols: *(1)* 2-stage (10p), *(2)* 1-stage (10p) + immediate/early load	Two protocols: *(1)* healing 2–5 months, *(2)* immediate temp PMMA < 1–14 days
Davó (2009)[71]	Healed postextraction	AB, GA, flap, vertical rectangular sinus window, trans-sinus implant, 2-stage	Healing 6 months
Balshi et al (2009)[72]	Healed	AB, GA, flap, vertical rectangular sinus window, PrP-prep + trans-sinus implant	Immediate autopolymer PMMA in denture < 2 hours > 3 months
Pi Urgell et al (2008)[73]	Healed	AB, GA + LA, flap, SinusSlot. Suture. 2-stage	Healing 6–12 months
Davó et al (2008)[74]	Healed postextraction	AB, GA. flap, 3 protocols: *(1)* vertical rectangular sinus window, trans-sinus implant (66i), *(2)* SinusSlot (15i), *(3)* "minimal invasive" SinusSlot XtraSinus	Immediate impression, metal-reinforced PMMA 24–48 hours > healing 6 months
Davó et al (2008)[75]	Healed postextraction	AB, GA, flap, two protocols: *(1)* vertical rectangular sinus window, trans-sinus implant (61i), *(2)* SinusSlot (10i)	Immediate impression, metal-reinforced PMMA 24–48 hours > healing 6 months
Kahnberg et al (2007)[76]	Healed	AB, GA, flap, autograft + vertical rectangular sinus window, trans-sinus implant, 2-stage	Healing 6 months
Duarte et al (2007)[77]	Healed	AB, GA, flap, vertical rectangular sinus window, trans-sinus implant	Immediate abutment, autopolymer surgery guide, impression, permanent next day
Peñarrocha et al (2007)[78]	Healed	AB, GA + LA, flap, SinusSlot, suture, 2-stage	Healing 2 months
Peñarrocha et al (2007)[79]	Healed	AB, GA + LA, flap, two protocols: *(1)* conventional imp, 2-stage (23p), *(2)* conventional + SinusSlot (23p), 2-stage	Healing 2 months
Bedrossian et al (2006)[80]	Healed 12+ months	AB, GA + LA, flap, vertical rectangular sinus window, trans-sinus implant, 40 Ncm	Immediate autopolymer PMMA in denture > 6 months permanent
Farzad et al (2006)[81]	Healed	AB, GA, flap, vertical rectangular sinus window, trans-sinus implant, immediate impression, suturing, denture relief	Healing 6–11 months
Ahlgren et al (2006)[82]	Failed implant surgery, cleft palate, graft refusal	AB, GA, flap, onlay graft (2p), vertical rectangular sinus window, trans-sinus implant, 2-stage	Healing 5–6 months
Aparicio et al (2006)[83]	Healed	AB, GA, flap, vertical rectangular sinus window, trans-sinus implant, 2-stage	Healing 5–6 months
Becktor et al (2005)[84]	Healed	AB, GA, flap, vertical rectangular sinus window, trans-sinus implant, 2-stage	Healing 5–8 months
Malevez et al (2004)[85]	Healed graft (n = 7) > 4–6 months	AB, GA, flap, vertical rectangular sinus window, trans-sinus implant, 2-stage	Healing 6 months
Brånemark et al (2004)[86]	Healed	AB, GA, flap, autograft (17p), vertical rectangular sinus window, trans-sinus implant	Immediate impression, suturing, healing 6 months
Bedrossian et al (2002)[87]	Healed	AB, GA + LA, flap, vertical rectangular sinus window, trans-sinus implant	Immediate impression, suturing, denture relief, healing 6 months

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; CAD/CAM = computer-aided design/computer-assisted manufacture; BIC = bone-to-implant contact; ptv = Periotest; zyg = zygomatic; pter = pterygoid; PMMA = polymethyl methacrylate; VAS = visual analogue scale; OHIP = Oral Health Impact Profile.
*Adverse biological and technical outcomes.

Prosthesis	Outcome	Patient Outcome	Findings
3-4i + 2 zyg-FDP	Adverse* SuccSurv	NR	
2-4i + 2 zyg-FDP	Adverse* SuccSurv	NR	Performance of different conventional implants NR
4 zyg-Tia-FDP-Procera	Adverse* SuccSurv	NR	
3-6i + 2 zyg-ga-FDP screw (19p), overdenture (3p)	Adverse* SuccSurv	NR	Performance of turned vs oxidized conventional implants NR
2-6i + 2 zyg + 2 pter-ga/mcFDP	Adverse* SuccSurv	NR	Performance of turned vs oxidized zygoma implants NR
4i + 2 zyg-FDP/overdenture	Adverse* SuccSurv	NR	
2-6i + 2/4 zyg-FDP screw	Adverse* SuccSurv	NR	Performance of different conventional implants and turned vs oxidized zygoma implants NR
2-6i + 1/2/4 zyg-FDP screw	Adverse* SuccSurv	NR	Performance of turned vs oxidized zygoma implants NR
2-4i + 2 zyg-FDP/overdenture	Adverse* SuccSurv	Satisfaction	
4 zyg-ga-FDP screw	Adverse* SuccSurv	NR	
3-6i + 1/2 zyg-FDP screw/cem	Adverse* SuccSurv	NR	Performance of different conventional implants NR
3-6i + ½ zyg-FDP screw/cem	Adverse* SuccSurv	Satisfaction-VAS	Performance of different conventional implants NR
2-4i + 2 zyg-FDP	Adverse* SuccSurv	Satisfaction	
2-4i + 2 zyg-Tia-FDP-Procera	Adverse* Stability-RFA, SuccSurv	Satisfaction-VAS	
2-5i + 2 zyg-FDP/overdenture	Adverse* SuccSurv	NR	Performance of turned vs oxidized conventional implants NR
2-4i + 2/4 zyg-ga-FDP-cem	Adverse* Stability-Ptv SuccSurv	NR	
1-6i + 2 zyg-ga FDP	Adverse* SuccSurv	NR	Performance of different conventional implants NR
2-4i + 2 zyg-FDP	Adverse* Perioindices, SuccSurv	NR	
2-5i + 1-4 zyg-FDP screw	Adverse* SuccSurv	NR	
2-4i + 2 zyg-ma/ga-FDP	Adverse* SuccSurv	NR	

Table 21 Results of Studies Reporting the Effects of Implants Placed in Pterygoid Bone or Other Bony Buttresses With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Study	Presurgery	Surgery Details	Postsurgery
Peñarrocha-Oltra et al (2013)[88]	Healed	LA, flap, ≥ 4 imp placed tilted & palatal w/2–5 exposed threads covered w/autograft + xenograft, 2-stage	Healing 2 + 1–2 months
Balshi et al (2013b)[89]	NR	NR	NR
Balshi et al (2013)[90]	Two protocols: *(1)* postextraction, *(2)* healed	Three protocols: *(1)* 1-stage-freehand, *(2)* 1-stage-CAD guide, *(3)* 2-stage freehand	Two protocols, pending primary stability: *(1)* immediate abutment, suture, temp PMMA (since 2000)/CAD/CAM planned (since 2004), teeth in a day vs *(2)* healing 6–8 months
Rodríguez et al (2012)[91]	NR	AB, LA, flap, pter-med, 10°–15°/mes-dis 70°, 2-stage	Healing 4 months (2–7 months)
Peñarrocha et al (2012)[92]	Healed	GA + LA, drill/osteotome, palatal positions (35i), autograft-articles + xenograft-bovine covered, pterymax (10i), XtraSinus-zygomatic(4i)/frontomax buttress (30i), nasopalatal (6i); 2-stage	Healing 3 months
Peñarrocha et al (2009)[93]	Healed	GA + LA drill/osteotome, palatal positions, autograft-articles + xenograft-bovine covered, XtraSinus-zygomatic, 2-stage	Softlined denture, healing 2 + 1 months
Peñarrocha et al (2009)[94]	Healed	GA + LA, drill/osteotome, flap, 2-stage	Healing 3 months
Balshi et al (2005)[95]	Two protocols: *(1)* postextraction, *(2)* healed	NR	Two protocols, pending primary stability: *(1)* immediate abutment, suture, temp PMMA, teeth in a day (522i), healing 5–6 months > perm. FDP, *(2)* healing 4–6 months (318i)
Balshi et al (1999)[96]	NR	LA 2-stage	Healing 5–6 months

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; CAD/CAM = computer-aided design/computer-assisted manufacture; BIC = bone-to-implant contact; zyg = zygomatic; pter = pterygoid; PMMA = polymethyl methacrylate; VAS = visual analogue scale; OHIP = Oral Health Impact Profile; CAD/CAM = computer-aided design/computer-assisted manufacture.
*Adverse biological and technical outcomes.

Studies Reporting the Effects of Implants Placed in Pterygoid Bone or Other Bony Buttresses With or Without Additional Alveolar Implants Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 6).[88–96] One study reported quality-of-life data using the OHIP-14 scale,[88] while two more described other patient-centered outcomes (Table 21).[93,94] The prevailing reported outcome was incidence of adverse biological and technical events, clinical success or survival, and degree of bone loss, based on orthopantograms. Based on the surrogate and clinical outcomes, it appears that the clinical performance of implants placed in bony buttresses in the fully edentulous maxilla as well as in the pterygomaxillary bone, appear comparable. Several reports that describe implant placements in the pterygomaxillary bone combine these with zygoma implants (Table 20). One investigation center reported that different designs from the same manufacturer may not influence outcome (n = 2),[95,96] in contrast to influence of the surface (n = 1)[90] and the implant length (n = 1).[89] Extensive variation was seen in the healing period after extraction, surgery procedures, healing period before implant loading, number of implants needed to support the supraconstruction, and composition and design of the supraconstruction. We considered meta-analyses of the extracted data as inappropriate, and therefore abandoned further statistical analyses of the extracted data.

Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes (Fig 7).[97–112] Two of 16 clinical studies reported patient-centered outcomes (Table 22).[100,101] The prevailing reported outcome was the incidence of adverse biological events during or immediately after surgery, late adverse biological and technical events, clinical success or survival, and degree of bone loss. Some studies also reported indices of periodontal tissues. Based on the surrogate and clinical outcomes, it can be proposed that in the fully edentulous maxilla, the choice of implant system may not (n = 2) influence outcome.[97,108] Two studies

Prosthesis	Outcome	Patient-Outcome	Findings
6-8i-mcFDP-cement/ga-FDP screw/2 tilt + 2i-bar, overdenture	Adverse* OPGX bone, perioindices	OHIP-14 Satisfaction-VAS	(Long) tilted and palatally placed vs conventional implant comparable outcomes
NR	Adverse*	NR	The 7–13 mm long pter implants performed worse than the 15–18 mm
6i + 2 pter + 2zyg-12u-mcFDP screw	Osseointegration	NR	Titanium oxide surface performed better than machined Brånemark implants
6i + 2 pter-12u-mcFDP screw, part-FDP	*(1)* SurgSucc *(2)* adverse*	NR	Pterygoid and conventional implant comparable outcomes
tilt-10/12u-FDP/overdenture	Adverse* SuccSurv (Buser)	NR	Pterygoid & palatal and conventional implant comparable outcomes
6i + 2 pter ± zyg mc/ga-FDP screw	Adverse* OPX bone SuccSurv	Satisfaction-VAS	Palatal and conventional implant comparable outcomes
6i + 2 pter-FDP screw/cement	Adverse* OPX bone, SuccSurv	Satisfaction-VAS	Pterygoid and conventional implant comparable outcomes
6i + 2 pter + 2 zyg-12u-mcFDP screw	Osseointegration	NR	No difference between Mark III and Mark IV Brånemark implants
6-8i + 2 pter-12u-mcFDP screw	Adverse biol OPX bone	NR	No difference between standard and self-tapping Brånemark implants

reported differences between implant designs, but both compared implant system A during a learning curve vs design B afterwards.[101,103] Moreover, different designs from the same manufacturer may influence outcome (n = 1),[105] whereas the length may (n = 8) or may not (n = 3) influence outcome. Extensive variation was seen in the healing period after extraction, surgery procedures, healing period before implant loading, number of implants needed to support the supraconstruction, and the composition and design of the supraconstruction. We considered meta-analyses of the extracted data as inappropriate, and therefore abandoned further statistical analyses of the extracted data. The conclusions about the effect of implant length on outcome were all from studies applying a one-stage approach with extensive grafting and implants placed to stabilize the graft (n = 8).[102,104,106,107,109–112] The three studies found no such effect with a two-stage approach, with a 4- to 8-month healing period in between.[98–100]

Studies Designed With No A Priori Stated Objective to Assess a Particular Implant Design Feature.[113–123] None of the nine clinical studies reported patient-centered outcomes (Table 23). The prevailing reported outcome was incidence of adverse biological and technical events, clinical success or survival, and degree of bone loss, measured on periapical radiographs. Based on the surrogate and clinical outcomes, it can be proposed that in the fully edentulous maxilla the choice of implant system appears to influence outcome (n = 1).[119] Moreover, outcomes may or may not (n = 2)[117,118] be influenced by *(1)* different designs from the same manufacturer (n = 1); *(2)* the surface (n = 1)[113–114]; and (*3)* wide (n = 1)[121] and short implants (n = 5).[115,116,120,122,123] Extensive variation was noted in the healing period after extraction, surgery procedures, healing period before implant loading, number of implants to support the supraconstruction, and the composition and design of the supraconstruction. The authors considered meta-analyses of the extracted data as inappropriate and therefore abandoned further statistical analyses of the extracted data.

Table 22 Results of Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes

Lead author	Presurgery	Surgery Details	Postsurgery
Zinser et al (2013-2012e)[97]	Two protocols, 1 & 2 stage, AB, GA/LA, sinus later autograft-iliac/chin/ramus/ symphysis ± iliac-block-hor/vert onlay + membrane collagen > 3 months (autograft) 5 months (autograft + allograft)/6 months (allograft + xenograft)	AB, GA/LA, as for 2-stage procedure	3 months (autograft) 6 months (allograft + xenograft)/3–4 months if 2-stage
Dasmah et al (2013-2011e)[98]	AB, GA, LA flap, two protocols: (R) autograft_iliac_block-onlay vs (L) iliac particulate onlay + PrP + sinus lateral iliac particulate inlay (R) + PrP (L) – > 6 months	NR	Healing 6 months, stability-RFA
Sjöström et al (2007)[99]	AB, GA, two protocols: *(1)* Le Fort I fracture, autograft iliac interpositional (n = 5), *(2)* ant onlay + nasal floor inlay (24p) + sinus (6p)/post onlay (18p) > 6 months	AB, LA, 2-stage	Healing 6–8 months
Chiapasco et al (2007)[100]	AB, GA, Le Fort I fracture, autograft iliac block interposition > 4–8 months	NR	Healing 4–8 months
Hallman et al (2005)[101]	GA, Le Fort I fracture, autograft iliac block interposition midline + sinus iliac particulate > 6 months	AB, LA, 2-stage	Healing 6 months
Becktor et al (2004)[102]	AB, GA, three protocols (1990–94/1994–1996): *(1)* (1994–1996), autograft iliac block hor-vert onlay/sinus inlay (24p)-> 4–7 months	AB, GA, *(1,2)* (1990–1994). Autograft iliac block hor-vert onlay/inlay + 7–15 mm-i (40p, 260i) vs *(3)* nongrafted (118p/683i), 2-stage	Healing 5-12 months (av 9) graft group/5–14 months (av 7) nongraft group
Pinholt (2003)[103]	AB, GA + LA sinus lateral autograft-iliac (/symphysis/ramus) corttrab-block + particulate + edentulous: block secured to lateral crest > 4.5 months	AB, flap, 2-stage	Healing 8 months
Becktor et al (2002)[104]	GA, four protocols *(1)* 2-stage, *(2–4)* 1-stage, 1. Autograft iliac segment block + particulates onlay + sinus lateral inlay, resilient denture (24p) > 4–7 months	GA, three protocols: *(1)* segment block-inlay nasal floor + sinus lateral + 9 imp, *(2)* segment block onlay + 3 × 3 imp, *(3)* full block onlay + 8 imp, all autograft iliac block + particulates, 4(1): 2 × 3 implants, 2-stage, resilient denture (66p)	Healing 5–12 months
Lekholm et al (1999)[105]	Five protocols: *(1,2)* autograft onlay (general & local, *(3)* Autograft_sinus inlay, *(4)* onlay + sinus inlay, *(5)* Le Fort + autograft > 4–5 months (25p)	Same five protocols: *(1)* +2 × 3 imp (33p) (21p local), *(3)* +2 imp (55p), *(4)* +2 + 2 × 3 imp (13p), *(5)* 3 + 2 × 3 imp (23p) (125p, 624i) in grafted bone + 157 nongrafted	NR
Keller et al (1999)[106]	GA, Le Fort I fracture, autograft iliac block interposition midline + sinus Iliac particulate > 6 months (4p, 21i)	GA, Le Fort I fracture, autograft iliac block interposition midline + sinus iliac particulate, 2-stage, resilient denture (21p, 183i)	Healing 6 months
Keller et al (1999)[107]	GA, three protocols × 2/1-stage. *(1)* LeFort I fracture, autograft iliac block nasal floor + sinus iliac particulate (37p), *(2,3)* Le Fort I/crestal flap, autograft iliac corticocanc block + particulates nasal floor/sinus lat, resilient denture > 6 months (31p)	*(2,3)* As for 2-stage, 2 × 3 implants, 2-stage, resilient denture (87p)	Healing 6 months
Watzek et al (1998)[108]	GA, three protocols: *(1)* sinus graft lateral autograft iliac cancellous vs *(2)* iliac + allograft HA/xenograft bovine > 3–8 months (auto)/6 months (allo)	AB	Healing 6 months

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; R = right side; L = left side; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; CAD/CAM = computer-aided design/computer-assisted manufacture; BIC = bone-to-implant contact; PMMA = polymethyl methacrylate; VAS = visual analogue scale; HA = hydroxyapatite.
*Adverse biological and technical outcomes.

Prosthesis	Outcome	Patient Outcome	Findings
Crown (124), FDP (642i), overdenture (279i)	*(1)* SurgComplic/Success *(2)* PA/OPGX bone SuccSurv	NR	Multivariate analyses indicated that implant design or surface does not influence outcome
8i-mc-FDP screw	PAX bone SuccSurv	NR	Implant length does not influence outcome
6-8i-FDP	*(1)* SurgComplic/Success *(2)* adverse* PAX bone stability-RFA, SuccSurv	NR	Multivariate analyses indicated that implant length does not influence outcome within 10–13 mm vs 15–18 mm
4-10i-FDP/ overdenture (19p/20p)	*(1)* Surgery success (98) *(2)* PAX bone perioindex SuccSurv	Satisfaction-Likert-3p	Implant length does not influence outcome when chosen to engage the grafted bone; effects of different implant systems were NR
5-8i-mc-FDP screw	*(1)* SurgComplic/Success *(2)* PAX bone SuccSurv	Satisfaction-VAS	Implant system influences outcome; however, possible effect of learning curve since first patients received implant brand A and the following group brand B
ga-FDP bar overdenture	*(1)* Surgery success *(2)* PAX bone, perioindex, SuccSurv	NR	Implant length influences outcome. 15-mm implants perform better than 10-mm, which perform better than 6–8 mm; however, tables include implants placed both in grafted and in nongrafted cohort
10i-FDP/7-8i overdenture	*(1)* Surg Complic/Success *(2)* histology *(3)* adverse* PAX/OPGX bone	NR	Implant system influences outcome; however, possible effect of learning curve since first patients received implant brand A and the following group brand B; complex and incoherent data matrix
FDP (68p), overdenture (4p)	*(1)* SurgComplic/Success *(2)* "Failure"	NR	Multivariate analyses indicated that implant length influences outcome. 15/18/20-mm long implants perform better than 10/13 mm, which perform better than 7/8 mm
FDP overdenture	Adverse biol SurgSucc (NR)	NR	Implant design influences outcome; one design showed less success than other designs from same manufacturer
3-6i bar ball overdenture	*(1)* SurgComplic/Success *(2)* SuccSurv	NR	Implant length influences outcome; 18 & 20 mm implants performed better than 10/13/15 mm; however, potential influence by implant design
FDP (45p) fix remove (10p), overdenture (14p)	*(1)* SurgComplic/Success *(2)* SuccSurv	NR	Implant length may influence outcome, but no data presented to support statement; long implants preferred to stabilize graft
6-8i bar overdenture FDP	*(1)* SurgComplic/Success *(2)* adverse* OPGX bone	NR	Implant system does not influence outcome; two systems were comparable

Table 22 ***Continued*** **Results of Studies Designed to Report Effects of Bone Augmentation With Simultaneous or Delayed Implant Placement Reporting an Effect of a Particular Implant Design Feature on One or More Treatment Outcomes**

Lead author	Presurgery	Surgery Details	Postsurgery
Nyström et al (1997)[109]	GA, Le Fort I fracture, autograft iliac block-interposition midline + sinus iliac particulate > 6 months	LA, 6 implants, 2-stage	Healing 6 months
Köndell et al (1996)[110]	Healed 6–38 years, edentulous	GA, autograft rib 2 × 5 cm inlay nasal + sinus + 2 × 2–3 implants, 2-stage	Healing 6–11 months
Neukam (1996)[111]	NR	Autograft iliac onlay, 2-stage	Healing 2–16 months
Keller et al (1994)[112]	NR	GA, Le Fort I/crestal flap, nasal floor/ sinus lateral autograft iliac cortico-canc-block + particulates + 2 × 3 implants, 2-stage, resilient denture	Healing 6 months

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; R = right side; L = left side; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; CAD/CAM = computer-aided design/computer-assisted manufacture; BIC = bone-to-implant contact; PMMA = polymethyl methacrylate; VAS = visual analogue scale; HA = hydroxyapatite.
*Adverse biological and technical outcomes.

Table 23 **Results of Studies Designed With no A Priori Stated Objective to Assess a Particular Implant Design or Feature**

Study	Presurgery	Surgery Details	Postsurgery
Jemt et al (2011)[113,114]	Healed minimum 3 (Md) or 6–8 (Mx) months	Flap, 2-stage	Healing 5–8 months
Friberg and Jemt (2008-2007e)[115]	Healed 4 months–40 years	All narrow crests height reduced, no grafting	NR
Jemt and Johansson (2006)[116]	Healed 13.3 years	Flap, 2-stage	Healing 3–6 months
Widbom et al (2005)[117]	NR	NR	NR
Ibanez et al (2005)[118]	NR	AB, flap, flapless (10p)	Three protocols: : *(1)* immediate abutments + Prefab PMMA FDP-> healing 2–3 (Md) 6–12 (Mx) months, permanent, vs *(2)* immediate abutment metal-reinforced PMMA FDP 4–24 hours, vs *(3)* impression, permanent mc-FDP < 48 hours
Degidi and Piattelli (2003)[119]	Two protocols: *(1)* postextraction (187i) vs *(2)* healed (235i)	Flap, two protocols: 1-stage or 2-stage	Four protocols: *(1)* healing 8–10 weeks, *(2–4)* prefab FDP, exp *(1)* occluding same day (n = 422), exp *(2)* nonoccluding same day (n = 224), exp *(3)* permanent crown within 3 weeks
Kiener et al (2001)[120]	Healed	1-stage, membrane	NR
Watson et al (1998)[121]	Healed	AB, widest and longest i. as possible, 2-stage	Healing 3 (Md), 6 (Mx) months
Jemt and Lekholm (1995)[122]	Subgroup *(1)* autograft_ iliac block onlay (14p, 83i) > 6–18 months	Subgroups (3): *(1)* atrophic, no graft (33p, 127i), *(2)* intermediate atrophy (25p, 142i), *(3)* fixed P(76p, 449i)	Healing 5–14 months
Palmqvist et al (1994)[123]	NR	Two protocols: *(1)* “planned case” 2–4 implants, *(2)* lost implant + change of plan: 4–6 implants	NR

AB = antibiotics; GA = general anesthesia; LA = local anesthesia; NR = not reported; mc = metal ceramic; ac = all ceramic; ga = gold-acrylic; CoCr = cobolt-chrome; u = unit; PAX = periapical radiographs; OPX = panoramic radiographs; SuccSurv = clinical success or survival; ptv/RFA = periotest/radiofrequency analysis; pFDP = partial fixed dental prosthesis; fFDP = full fixed dental prosthesis; TiA = Titanium-Acrylic; OPGX = orthopantomogram; CAD/CAM = computer-aided design/computer-assisted manufacture; BIC = bone-to-implant contact; PMMA = polymethyl methacrylate; VAS = visual analogue scale.

Prosthesis	Outcome	Patient Outcome	Findings
6i-FDP	*(1)* SurgComplic/Success *(2)* SuccSurv	NR	Implant length may influence outcome, but no data presented to support statement; long implants preferred to stabilize graft
ga-FDP-canti Ceka-bar overdenture	*(1)* SurgComplic/Success *(2)* PA/OPGX bone SuccSurv	NR	Implant length influences outcome when placed in ribs; 10-mm implants performed better than 13-mm as well as 7-mm implants
FDP	*(1)* SurgComplic/Success *(2)* Adverse* PAX bone	NR	Multivariate analyses indicated that implant length influences outcome; 10+ mm implants performed better than 6–7-mm implants
NR	*(1)* SurgComplic/Success *(2)* SuccSurv	NR	Implant length may influence outcome, but no data presented to support statement; 18 mm preferred to stabilize graft

Prosthesis	Outcome	Patient Outcome	Findings
4-8i-10/12u-ga-FDP screw canti	Adverse* PAX bone SuccSurv	NR	Implant surface does not influence outcome; early failure less prevalent with oxidized surface, but turned perform as well as oxidized on longer term
NR	Adverse* PAX bone SuccSurv	NR	Implant length influences outcome; short implants performed worse than long in narrow jaws; however, this may be a secondary effect of crest height
4-8i-10/12u-ga-FDP screw canti	Adverse* PAX bone SuccSurv	NR	Implant length influences outcome; 7-mm turned implants in soft bone fail more than others
2-4i-bar overdenture	Adverse* SuccSurv	NR	Multivariate analyses indicated no effect of implant length on outcome
6-10i-mcFDP screw	Adverse* PAX bone Stability-RFA SuccSurv	NR	Implant design or length does not influence outcome
Crown-mix 8-11i-FDP mix bar overdenture	PAX bone SuccSurv	NR	Implant system may influence outcome; of 6 different implant systems used, all failures (n = 8) were one particular system; the data matrix is complex and incoherent; marg bone loss was only reported for 91/646 implants
4-6i-ball/dolder bar, overdenture	Adverse* maintenance	NR	Implant length influences outcome; ≤ 10 mm failed more than 12 mm
Ball/hader bar, overdenture	PAX bone maintenance, perioindices, stability-ptv, SuccSurv	NR	Implant length may influence outcome; highest failure rates were short and wide implants
4-8i-10/12u-ga-FDP screw-canti/4-6i-bar, overdenture	Adverse* PAX bone SuccSurv	NR	Implant length influences outcome; 7-mm turned implants in soft bone fail more than others and especially when there is severe height resorption
2-4i-ball/round-dolder bar, overdenture	Adverse* maintenance	NR	Multivariate analyses indicated that implant length influences outcome; 7-mm turned implants fail more than others

DISCUSSION

Summary of the Evidence

Arguably, the present authors identified far more clinical studies aimed at appraising possible effects of implant design on outcomes in the fully edentulous maxilla in comparison with other systematic reviews (Tables 2a and 2b). Unfortunately, the great majority of the primary reports aimed at appraising possible effects of implant design on outcomes lump their observed data, probably to obtain more statistical power. The consequence is that the readers cannot judge outcomes specifically related to the various clinical conditions, such as for the fully edentulous maxilla. Moreover, many reports present inadequate statistics generally associated with incorrect choice of statistical unit.[124–126] Multivariable linear or logistic regression models were occasionally applied in the reports, but often with clear violations of statistical assumptions generally associated with multiple within-subject factors.[127–129]

The general impression of the evidence available is that there is a lack of compelling data to state that one particular implant system or design feature stands out amidst others, when applied to restoring the fully edentulous maxilla with implant-retained prosthetics.

Limitations at the Study and Outcome Level

Characteristics of the Study Groups and Participant Inclusion and Exclusion Criteria. Although the term "edentulous maxilla" is easy to understand, it is more difficult to categorize into groups based on difficulties of rehabilitating facial form and oral functions. There are multiple variants and codification sets of the edentulous maxilla. The most well known is a classification system developed by the American College of Prosthodontics,[2] which emphasizes the restoration of form and function with conventional dentures in patients with increasing complexity depending on specific general and local elements. Several systems for describing jaw size and consistency have also been proposed in the implant literature.[13,124, 130–132] Further attempts to evaluate the risks associated with implant treatment have resulted in the Straightforward-Advanced-Complex (SAC) classification system developed by the International Team for Implantology (www.iti.org). The difficulties with the use of these classifications are to identify which of the many criteria used are prognostic factors for the treatment outcome, because these criteria are not necessarily risk factors.

Although not presented in this systematic review, a vast spectrum of study inclusion and exclusion criteria were identified. The most common inclusion and exclusion criteria were *(1)* participant level—maximum or minimum age, general health condition, past drug or alcohol abuse, extent of smoking, bruxism or clenching history, past radiation therapy, compliance, and commitment to follow-up; *(2)* intraoral condition—state of edentulousness, adequate bone height and width, bone quality, maxillomandibular discrepancy or lack of vertical space, no local pathology, no sinus inflammation, level of oral hygiene, healed alveolar ridge, augmentation or grafting; *(3)* surgical—minimum primary stability, minimum keratinized mucosa. Although most articles described a few or multiple criteria, it is likely that many reports have underreported the range of criteria. It is therefore uncertain how the potential effects of implant design on outcomes in the fully edentulous maxilla should be interpreted in light of the described or lack of described inclusion and exclusion criteria.

Description of the Intervention

The surgical protocols may significantly affect outcomes of studies comparing implant design aspects and therefore, protocols need to be appraised in the context of our data interpretation. Similarly, different settings and operators with different levels of skills and experience will probably influence outcomes of studies comparing implant design aspects. In particular, reports have shown that the level of surgical experience may influence the percentage of implants that fail.[133,134] Although some articles report these details, most do not.

In this regard, it is essential to consider the years when implants were placed and be reminded of the surgical principles at the time. Investigators designing studies in the 1980s followed the rather strict principle that implant parallelism was essential, which trumped implant angulation even in the presence of bone. Another argument was that costs would increase significantly, because angulated abutments would be required.[113,114] At the time, the clinician would strive to place a parallel, for instance, 7-mm implant, with a turned surface. Today, a clinician would angulate the implant to increase implant length beyond 7 mm in almost any direction. Comparing incidences of adverse outcomes in contemporary studies with historical data applying different standard operating procedures is therefore fraught with interpretational fallacies. It was not until around the turn of the century when data emerged that placing nonaxial loaded implants was not necessarily detrimental to the patient.[56,57] Subsequently, these concepts led to surgical protocols based on the use of two- or four-axial plus two tilted implant solutions. High-quality long-term studies of the concept are hopefully under way.

Studies that include grafting procedures in connection with implant placement may increase the risk of adverse outcomes irrespective of the implant design. The same applies to immediate placement after tooth extraction, and perhaps even the reason for extraction may have some bearing on the osseointegration process. Other clinical

variables that come into play are the time of loading of the implants, implant bed preparation protocol, and/or primary stability. In fact, most studies reviewed did not have a description about implant stability.

The number of implants needed to support a supraconstruction, as well as the material composition and design of the supraconstruction itself, probably influences the treatment outcomes in studies aimed at comparing implant design aspects. Currently, however, no published study findings can provide clinical guidance.

Some investigators and authors of systematic reviews have suggested that implant lengths and diameters influence outcomes. This may or may not be correct when applied to single implants and perhaps small fixed dental prostheses. However, unless planned a priori in a study protocol, it is more likely that a narrow, wide, and/or short implant placed among "standard" size implants to support a full jaw suprastructure is a reflection of an unfavorable site for osteotomy. It follows that the higher failure rates reported with these narrow or wide and/or short implants is not a reflection of the effect of the implant design on outcomes, but rather of the effect of unfavorable local anatomic conditions.[6]

With regard to the implant surface, we may be faced with a new dimension of scientific rationale and technological strategies based on novel approaches to enhance the biological process of osseointegration.[10] A focus of implant surface design and science has been its morphology or topography, as extensively documented in the studies comparing machined/turned surfaces and so-called rough surfaces. In fact, many studies reviewed herein compared implants from different manufacturers, presumably having different surface morphology. Recent studies have uncovered the significant role of physicochemical property of titanium surfaces in determining their biological capabilities.[135–137] Physicochemical properties include hydrophilicity or hydrophobicity, the degree of hydrocarbon contamination, and electrostatic status. More importantly, these properties change with time in an unfavorable way, as evidenced in the phenomenon that newly prepared titanium surfaces are hydrophilic, whereas the same titanium surfaces stored for a certain time are hydrophobic.[138] The degraded physicochemical properties may be restored by ultraviolet light treatment, for instance, immediately before use or by photofunctionalization.[135,139] Photofunctionalization is not categorized as either an additive or subtractive modification. It simply removes hydrocarbons from the implant surface and regenerates hydrophilicity. The process, termed surface conditioning, is theoretically universal for any titanium- and titanium alloy–based implant materials, which may affect how we think of the implant design and suggest the necessity to broaden our scope. These innovative implant surfaces have not yet been evaluated clinically in patients with a fully edentulous maxilla.

Reported outcomes after clinical studies should ideally be patient-centered. Most clinical studies, however, report implant survival data, and some also include peri-implant bone loss and advent of adverse biological events, but seldom patient-centered outcomes or other variables related to treatment morbidity.

Very few studies reported outcomes comparing different implant types or particular design features, at least pertaining to patients with a fully edentulous maxilla. One important issue in implant research is that most clinical studies are financed by industry. Hence, they are mostly case series or comparisons of implant systems from the same manufacturer. This possible bias related to the conflict of interest when reporting negative results may have prevented the publication of many completed investigations. Moreover, as stated earlier, very few studies reported patient-centered outcomes.

Limitations at the Review Level

The Academy of Osseointegration made an *a priori* determination of a very broad and general PICO question. As a consequence, it is likely that other investigators aiming to replicate this systematic review will possibly identify different studies and organize the extracted data in a different manner, perhaps even leading to different conclusions. The review of such a broad subject prevents the answer to a predefined null-hypothesis, and instead leads to a narrative description of a vast number of different studies, which prevent the appropriate data extraction and meta-analysis.

The online bibliographic searches identified fewer than half of the total number of relevant clinical studies (Fig 2). This moderate yield may appear surprising, but others have claimed that online searches identify only 20% to 40% of relevant studies, regardless of expert search algorithms.[140,141] Hence, hand searching of reference lists in identified reports is always required, and the process is greatly facilitated if further combined with the use of hyperlinked online references, for example, in the online Web of Science. Nevertheless, in this review, a substantial number of the identified reports were uncovered in a personal indexed database managed by the lead author since the mid-1990s and used in systematic reviews previously.[142]

CONCLUSIONS

This systematic review failed to identify compelling evidence to conclude that any particular implant or feature affects the outcome of the treatment of patients with fully edentulous maxillae. This conclusion is in line with the previous and recently updated Cochrane systematic review focused on the same

topic.[143] The difference between the current systematic review and the Cochrane review is that the latter reviewed only randomized clinical trials. On the other hand, the Cochrane review appraised effects in meta-analyses that merged data from a range of different clinical conditions, including single space and partially edentate situations in both jaws. In contrast, the current review appraises outcomes only in study participants with a fully edentulous maxilla.

ACKNOWLEDGMENTS

This systematic review was self-funded. No conflict of interest exists with any of the authors.

REFERENCES

1. Zarb G, Hobkirk JA, Eckert SE, Jacob RF. Prosthodontic Treatment for Edentulous Patients, ed 13. St Louis: Elsevier, 2012.
2. McGarry TJ, Nimmo A, Skiba JF, Ahlstrom RH, Smith CR, Koumjian JH. Classification system for complete edentulism. The American College of Prosthodontics. J Prosthodont 1999;8:27–39.
3. Brånemark PI, Hansson BO, Adell R, et al (eds). Osseointegrated Implants in the Treatment of the Edentulous Jaw. Experience From a 10-year Period. Stockholm: Almqvist & Wiksell, 1977.
4. English CE. Cylindrical implants. Parts I, II, III. California Dent Assoc J 1988;16:17–38.
5. Binon PP. Implants and components: Entering the new millennium. Int J Oral Maxillofac Implants 2000;15:76–94.
6. Jokstad A, Braegger U, Brunski JB, Carr AB, Naert I, Wennerberg A. Quality of dental implants. Int Dent J 2003;53(6, suppl):409–443.
7. Jokstad A. How many implant systems do we have and are they documented? In: Jokstad A. Osseointegration and Dental Implants. Ames, Iowa: Wiley, 2009:3–8.
8. Albrektsson T, Wennerberg A. Oral implant surfaces. Part 1. A review focusing on topographic and chemical properties of different surfaces and in vivo responses to them. Int J Prosthodont 2004;17:536–543.
9. Dohan Ehrenfest DM, Coelho PG, Kang BS, Sul YT, Albrektsson T. Classification of osseointegrated implant surfaces: Materials, chemistry and topography. Trends Biotechnol 2010;28:198–206.
10. Goriainov V, Cook R, Latham JM, Dunlop DG, Oreffo RO. Bone and metal: An orthopaedic perspective on osseointegration of metals. Acta Biomater 2014;10:4043–4057.
11. Swedish Council on Health Technology Assessment. Prosthetic rehabilitation of partially dentate or edentulous patient. ISBN: 978-91-85413-40-9. Report no: 204. 2010. URL: www.sbu.se/upload/Publikationer/Content0/1/Tandforluster/tandforluster_bilaga1.pdf Accessed Nov 11, 2014.
12. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6:e1000097.
13. Cawood JI, Howell RA. A classification of the edentulous jaws. Int J Oral Maxillofacial Surg 1988;17:232–236.
14. Den Hartog L, Slater JJ, Vissink A, Meijer HJ, Raghoebar GM. Treatment outcome of immediate, early and conventional single-tooth implants in the aesthetic zone: A systematic review to survival, bone level, soft-tissue, aesthetics and patient satisfaction. J Clin Periodontol 2008;35:1073–1086.
15. Chambrone L, Chambrone D, Lima LA, Chambrone LA. Predictors of tooth loss during long-term periodontal maintenance: A systematic review of observational studies. J Clin Periodontol 2010;37:675–684.
16. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomized Studies in Meta-Analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 11 November 2014.
17. Rosenfeld RM, Shiffman RN. Clinical practice guideline development manual: A quality-driven approach for translating evidence into action. Otolaryngol Head Neck Surg 2009;140(6, suppl):S1–S43.
18. Jungner M, Lundqvist P, Lundgren S. A retrospective comparison of oxidized and turned implants with respect to implant survival, marginal bone level and peri-implant soft tissue conditions after at least 5 years in function. Clin Implant Dent Relat Res 2014;16:230–237.
19. Vervaeke S, Collaert B, Cosyn J, Deschepper E, De Bruyn H. A multifactorial analysis to identify predictors of implant failure and peri-implant bone loss. Clin Implant Dent Relat Res 2015;17(1, suppl):e298–e307.
20. Testori T, Zuffetti F, Capelli M, Galli F, Weinstein RL, Del Fabbro M. Immediate versus conventional loading of post-extraction implants in the edentulous jaws. Clin Implant Dent Relat Res 2014;16:926–935.
21. Ravald N, Dahlgren S, Teiwik A, Gröndahl K. Long-term evaluation of Astra Tech and Brånemark implants in patients treated with full-arch bridges. Results after 12–15 years. Clin Oral Implants Res 2013;24:1144–1151.
22. Van Assche N, Michels S, Quirynen M, Naert I. Extra short dental implants supporting an overdenture in the edentulous maxilla: A proof of concept. Clin Oral Implants Res 2012;23:567–576.
23. Cosyn J, Vandenbulcke E, Browaeys H, Van Maele G, De Bruyn H. Factors associated with failure of surface-modified implants up to four years of function. Clin Implant Dent Relat Res 2012;14:347–358.
24. Kallus T, Bessing C, Homsi G, Eklund I. Five-year evaluation of Lifecore Restore implants: A retrospective comparison with Nobel Biocare MK II implants. Clin Implant Dent Relat Res 2009;11:167–177.
25. Li W, Chow J, Hui E, Lee PK, Chow R. Retrospective study on immediate functional loading of edentulous maxillas and mandibles with 690 implants, up to 71 months of follow-up. J Oral Maxillofac Surg 2009;67:2653–2662.
26. Alsaadi G, Quirynen M, Komárek A, van Steenberghe D. Impact of local and systemic factors on the incidence of late oral implant loss. Clin Oral Implants Res 2008;19:670–676.
27. Nelson K, Semper W, Hildebrand D, Ozyuvaci H. A retrospective analysis of sandblasted, acid-etched implants with reduced healing times with an observation period of up to 5 years. Int J Oral Maxillofac Implants 2008;23:726–732.
28. Maló P, de Araújo Nobre M, Rangert B. Short implants placed one-stage in maxillae and mandibles: A retrospective clinical study with 1 to 9 years of follow-up. Clin Implant Dent Relat Res 2007;9:15–21.
29. Hjalmarsson L, Smedberg JI. A 3-year retrospective study of Cresco frameworks: Preload and complications. Clin Implant Dent Relat Res 2005;7:189–199.
30. Degidi M, Piattelli A, Felice P, Carinci F. Immediate functional loading of edentulous maxilla: A 5-year retrospective study of 388 titanium implants. J Periodontol 2005;76:1016–1024.
31. Schwartz-Arad D, Yaniv Y, Levin L, Kaffe I. A radiographic evaluation of cervical bone loss associated with immediate and delayed implants placed for fixed restorations in edentulous jaws. J Periodontol 2004;75:652–657.
32. Morris HF, Winkler S, Ochi S. A 48-month multicentric clinical investigation: Implant design and survival. J Oral Implantol 2001;27:180–186.
33. Friberg B, Nilson H, Olsson M, Palmquist C. Mk II: The self-tapping Brånemark implant: 5-year results of a prospective 3-center study. Clin Oral Implants Res 1997;8:279–285.
34. Olsson M, Friberg B, Nilson H, Kultje C. MkII—a modified self-tapping Brånemark implant: 3-year results of a controlled prospective pilot study. Int J Oral Maxillofac Implants 1995;10:15–21.
35. Agliardi EL, Pozzi A, Stappert CF, Benzi R, Romeo D, Gherlone E. Immediate fixed rehabilitation of the edentulous maxilla: A prospective clinical and radiological study after 3 years of loading. Clin Implant Dent Relat Res 2014;16:292–302.
36. Agnini A, Agnini AM, Romeo D, Chiesi M, Pariente L, Stappert CF. Clinical investigation on axial versus tilted implants for immediate fixed rehabilitation of edentulous arches: Preliminary results of a single cohort study. Clin Implant Dent Relat Res 2014;16:527–539.

37. Pera P, Menini M, Bevilacqua M, et al. Factors affecting the outcome in the immediate loading rehabilitation of the maxilla: A 6-year prospective study. Int J Periodontics Restorative Dent 2014;34:657–665.
38. Pozzi A, Holst S, Fabbri G, Tallarico M. Clinical reliability of CAD/CAM cross-arch zirconia bridges on immediately loaded implants placed with computer-assisted/template-guided surgery: A retrospective study with a follow-up between 3 and 5 years. Clin Implant Dent Relat Res 2015;17(1, suppl):e86–e96.
39. Maló P, Nobre MD, Lopes A. Immediate loading of 'all-on-4' maxillary prostheses using trans-sinus tilted implants without sinus bone grafting: A retrospective study reporting the 3-year outcome. Eur J Oral Implantol 2013;6:273–283.
40. Testori T, Mandelli F, Mantovani M, Taschieri S, Weinstein RL, Del Fabbro M. Tilted trans-sinus implants for the treatment of maxillary atrophy: Case series of 35 consecutive patients. J Oral Maxillofac Surg 2013;71:1187–1194.
41. Di P, Lin Y, Li JH, et al. The all-on-four implant therapy protocol in the management of edentulous Chinese patients. Int J Prosthodont 2013;26:509–516.
42. Maló P, de Araújo Nobre M, Lopes A, Francischone C, Rigolizzo M. "All-on-4" immediate-function concept for completely edentulous maxillae: A clinical report on the medium (3 years) and long-term (5 years) outcomes. Clin Implant Dent Relat Res 2012;14(1, suppl):e139–e150.
43. Francetti L, Romeo D, Corbella S, Taschieri S, Del Fabbro M. Bone level changes around axial and tilted implants in full-arch fixed immediate restorations. Interim results of a prospective study. Clin Implant Dent Relat Res 2012;14:646–654.
44. Mozzati M, Arata V, Gallesio G, Mussano F, Carossa S. Immediate postextraction implant placement with immediate loading for maxillary full-arch rehabilitation: A two-year retrospective analysis. J Am Dent Assoc 2012;143:124–133.
45. Crespi R, Vinci R, Capparé P, Romanos GE, Gherlone E. A clinical study of edentulous patients rehabilitated according to the "all on four" immediate function protocol. Int J Oral Maxillofac Implants 2012;27:428–434.
46. Cavalli N, Barbaro B, Spasari D, Azzola F, Ciatti A, Francetti L. Tilted implants for full-arch rehabilitations in completely edentulous maxilla: A retrospective study. Int J Dent 2012;2012:1–6.
47. Maló P, de Araújo Nobre M, Lopes A. Immediate rehabilitation of completely edentulous arches with a four-implant prosthesis concept in difficult conditions: An open cohort study with a mean follow-up of 2 years. Int J Oral Maxillofac Implants 2012;27:1177–1190.
48. Maló P, de Araújo Nobre M, Lopes A. The rehabilitation of completely edentulous maxillae with different degrees of resorption with four or more immediately loaded implants: A 5-year retrospective study and a new classification. Eur J Oral Implantol 2011;4:227–243.
49. Agliardi EL, Panigatti S, Clerico M, Villa C, Maló P. Immediate rehabilitation of the edentulous jaws with full fixed prostheses supported by four implants: Interim results of a single cohort prospective study. Clin Oral Implants Res 2010;21:459–465.
50. Degidi M, Nardi D, Piattelli A. Immediate loading of the edentulous maxilla with a definitive restoration supported by an intraorally welded titanium bar and tilted implants. Int J Oral Maxillofac Implants 2010;25:1175–1182.
51. Pomares C. A retrospective clinical study of edentulous patients rehabilitated according to the 'all on four' or the 'all on six' immediate function concept. Eur J Oral Implantol 2009;2:55–60.
52. Agliardi EL, Francetti L, Romeo D, Del Fabbro M. Immediate rehabilitation of the edentulous maxilla: Preliminary results of a single-cohort prospective study. Int J Oral Maxillofac Implants 2009;24:887–895.
53. Rosen A, Gynther G. Implant treatment without bone grafting in edentulous severely resorbed maxillas: A long-term follow-up study. J Oral Maxillofac Surg 2007;65:1010–1016.
54. Capelli M, Zuffetti F, Del Fabbro M, Testori T. Immediate rehabilitation of the completely edentulous jaw with fixed prostheses supported by either upright or tilted implants: A multicenter clinical study. Int J Oral Maxillofac Implants 2007;22:639–644.
55. Fortin Y, Sullivan RM, Rangert BR. The Marius implant bridge: Surgical and prosthetic rehabilitation for the completely edentulous upper jaw with moderate to severe resorption: A 5-year retrospective clinical study. Clin Implant Dent Relat Res 2002;4:69–77.
56. Krekmanov L, Kahn M, Rangert B, Lindström H. Tilting of posterior mandibular and maxillary implants for improved prosthesis support. Int J Oral Maxillofac Implants 2000;15:405–414.
57. Mattsson T, Köndell PA, Gynther GW, Fredholm U, Bolin A. Implant treatment without bone grafting in severely resorbed edentulous maxillae. J Oral Maxillofac Surg 1999;57:281–287.
58. Yates JM, Brook IM, Patel RR, et al. Treatment of the edentulous atrophic maxilla using zygomatic implants: Evaluation of survival rates over 5–10 years. Int J Oral Maxillofac Surg 2014;43:237–242.
59. Aparicio C, Manresa C, Francisco K, et al. The long-term use of zygomatic implants: A 10-year clinical and radiographic report. Clin Implant Dent Relat Res 2014;16:447–459.
60. Fernández H, Gómez-Delgado A, Trujillo-Saldarriaga S, Varón-Cardona D, Castro-Núñez J. Zygomatic implants for the management of the severely atrophied maxilla: A retrospective analysis of 244 implants.
J Oral Maxillofac Surg 2014;72:887–891.
61. Maló P, de Araújo Nobre M, Lopes A, Ferro A, Moss S. Extramaxillary surgical technique: Clinical outcome of 352 patients rehabilitated with 747 zygomatic implants with a follow-up between 6 months and 7 years. Clin Implant Dent Relat Res 2015;17(1, suppl):e153–e162.
62. Davó R, Malevez C, Pons O. Immediately loaded zygomatic implants: A 5-year prospective study. Eur J Oral Implantol 2013;6:39–47.
63. Davó R, Pons O. Prostheses supported by four immediately loaded zygomatic implants: A 3-year prospective study. Eur J Oral Implantol 2013;6:263–269.
64. Maló P, de Araújo Nobre M, Lopes A, Francischone C, Rigolizzo M. Three-year outcome of a retrospective cohort study on the rehabilitation of completely edentulous atrophic maxillae with immediately loaded extra-maxillary zygomatic implants. Eur J Oral Implantol 2012;5:37–46.
65. Migliorança RM, Sotto-Maior BS, Senna PM, Francischone CE, Del Bel Cury AA. Immediate occlusal loading of extrasinus zygomatic implants: A prospective cohort study with a follow-up period of 8 years. Int J Oral Maxillofac Surg 2012;41:1072–1076.
66. Balshi TJ, Wolfinger GJ, Shuscavage NJ, Balshi SF. Zygomatic bone-to-implant contact in 77 patients with partially or completely edentulous maxillas. J Oral Maxillofac Surg 2012;70:2065–2069.
67. Aparicio C, Ouazzani W, Aparicio A, et al. Immediate/early loading of zygomatic implants: Clinical experiences after 2 to 5 years of follow-up. Clin Implant Dent Relat Res 2010;12(1, suppl):e77–e82.
68. Aparicio C, Ouazzani W, Aparicio A, et al. Extrasinus zygomatic implants: Three year experience from a new surgical approach for patients with pronounced buccal concavities in the edentulous maxilla. Clin Implant Dent Relat Res 2010;12:55–61.
69. Bedrossian E. Rehabilitation of the edentulous maxilla with the zygoma concept: A 7-year prospective study. Int J Oral Maxillofac Implants 2010;25:1213–1221.
70. Stiévenart M, Malevez C. Rehabilitation of totally atrophied maxilla by means of four zygomatic implants and fixed prosthesis: A 6–40-month follow-up. Int J Oral Maxillofac Surg 2010;39:358–363.
71. Davó R. Zygomatic implants placed with a two-stage procedure: A 5-year retrospective study. Eur J Oral Implantol 2009;2:115–124.
72. Balshi SF, Wolfinger GJ, Balshi TJ. A Retrospective analysis of 110 zygomatic implants in a single-stage immediate loading protocol. Int J Oral Maxillofac Implants 2009;24:335–341.
73. Pi Urgell J, Revilla Gutiérrez V, Gay Escoda C. Rehabilitation of atrophic maxilla: A review of 101 zygomatic implants. Med Oral Patol Oral Cir Bucal 2008;13:e363–e370.
74. Davó R, Malevez C, Rojas J, Rodríguez J, Regolf J. Clinical outcome of 42 patients treated with 81 immediately loaded zygomatic implants: A 12- to 42-month retrospective study. Eur J Oral Implantol 2008;1:141–150.
75. Davó R, Malevez C, López-Orellana C, Pastor-Beviá F, Rojas J. Sinus reactions to immediately loaded zygoma implants: A clinical and radiological study. Eur J Oral Implantol 2008;1:53–60.
76. Kahnberg KE, Henry PJ, Hirsch JM, et al. Clinical evaluation of the zygoma implant: 3-year follow-up at 16 clinics. J Oral Maxillofac Surg 2007;65:2033–2038.

77. Duarte LR, Filho HN, Francischone CE, Peredo LG, Brånemark PI. The establishment of a protocol for the total rehabilitation of atrophic maxillae employing four zygomatic fixtures in an immediate loading system—a 30-month clinical and radiographic follow-up. Clin Implant Dent Relat Res 2007;9:186–196.
78. Peñarrocha M, Garciía B, Martí E, Boronat A. Rehabilitation of severely atrophic maxillae with fixed implant-supported prostheses using zygomatic implants placed using the sinus slot technique: Clinical report on a series of 21 patients. Int J Oral Maxillofac Implants 2007;22:645–650.
79. Peñarrocha M, Carrillo C, Boronat A, Martí E. Level of satisfaction in patients with maxillary full-arch fixed prostheses: Zygomatic versus conventional implants. Int J Oral Maxillofac Implants 2007;22:769–773.
80. Bedrossian E, Rangert B, Stumpel L, Indresano T. Immediate function with the zygomatic implant: A graftless solution for the patient with mild to advanced atrophy of the maxilla. Int J Oral Maxillofac Implants 2006;21:937–942.
81. Farzad P, Andersson L, Gunnarsson S, Johansson B. Rehabilitation of severely resorbed maxillae with zygomatic implants: An evaluation of implant stability, tissue conditions, and patients' opinion before and after treatment. Int J Oral Maxillofac Implants 2006;21:399–404.
82. Ahlgren F, Størksen K, Tornes K. A study of 25 zygomatic dental implants with 11 to 49 months' follow-up after loading. Int J Oral Maxillofac Implants 2006;21:421–425.
83. Aparicio C, Ouazzani W, Garcia R, Arevalo X, Muela R, Fortes V. A prospective clinical study on titanium implants in the zygomatic arch for prosthetic rehabilitation of the atrophic edentulous maxilla with a follow-up of 6 months to 5 years. Clin Implant Dent Relat Res 2006;8:114–122.
84. Becktor JP, Isaksson S, Abrahamsson P, Sennerby L. Evaluation of 31 zygomatic implants and 74 regular dental implants used in 16 patients for prosthetic reconstruction of the atrophic maxilla with cross-arch fixed bridges. Clin Implant Dent Relat Res 2005;7:159–165.
85. Malevez C, Abarca M, Durdu F, Daelemans P. Clinical outcome of 103 consecutive zygomatic implants: A 6–48 months follow-up study. Clin Oral Implants Res 2004;15:18–22.
86. Brånemark PI, Gröndahl K, Ohrnell LO, et al. Zygoma fixture in the management of advanced atrophy of the maxilla: Technique and long-term results. Scand J Plast Reconstr Surg Hand Surg 2004;38:70–85.
87. Bedrossian E, Stumpel L 3rd, Beckely ML, Indresano T. The zygomatic implant: Preliminary data on treatment of severely resorbed maxillae. A clinical report. Int J Oral Maxillofac Implants 2002;17:861–865.
88. Peñarrocha-Oltra D, Candel-Martí E, Peñarrocha-Diago M, Martínez-González JM, Aragoneses JM, Peñarrocha-Diago M. Palatal positioning of implants in severely atrophic edentulous maxillae: Five-year cross-sectional retrospective follow-up study. Int J Oral Maxillofac Implants 2013;28:1140–1146.
89. Balshi TJ, Wolfinger GJ, Slauch RW, Balshi SF. Brånemark system implant lengths in the pterygomaxillary region: A retrospective comparison. Implant Dent 2013;22:610–612.
90. Balshi TJ, Wolfinger GJ, Slauch RW, Balshi SF. A retrospective comparison of implants in the pterygomaxillary region: Implant placement with two-stage, single-stage, and guided surgery protocols. Int J Oral Maxillofac Implants 2013;28:184–189.
91. Rodríguez X, Méndez V, Vela X, Segalá M. Modified surgical protocol for placing implants in the pterygomaxillary region: Clinical and radiologic study of 454 implants. Int J Oral Maxillofac Implants 2012;27:1547–1553.
92. Peñarrocha M, Viña JA, Carrillo C, Peñarrocha D, Peñarrocha M. Rehabilitation of reabsorbed maxillae with implants in buttresses in patients with combination syndrome. J Oral Maxillofac Surg 2012;70:e322–e330.
93. Peñarrocha M, Carrillo C, Boronat A, Balaguer J, Peñarrocha M. Palatal positioning of implants in severely resorbed edentulous maxillae. Int J Oral Maxillofac Implants 2009;24:527–533.
94. Peñarrocha M, Carrillo C, Boronat A, Peñarrocha M. Retrospective study of 68 implants placed in the pterygomaxillary region using drills and osteotomes. Int J Oral Maxillofac Implants 2009;24:720–726.
95. Balshi SF, Wolfinger GJ, Balshi TJ. Analysis of 164 titanium oxide-surface implants in completely edentulous arches for fixed prosthesis anchorage using the pterygomaxillary region. Int J Oral Maxillofac Implants 2005;20:946–952.
96. Balshi TJ, Wolfinger GJ, Balshi SF 2nd. Analysis of 356 pterygomaxillary implants in edentulous arches for fixed prosthesis anchorage. Int J Oral Maxillofac Implants 1999;14:398–406.
97. Zinser MJ, Randelzhofer P, Kuiper L, Zöller JE, De Lange GL. The predictors of implant failure after maxillary sinus floor augmentation and reconstruction: A retrospective study of 1045 consecutive implants. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;115:571–582.
98. Dasmah A, Thor A, Ekestubbe A, Sennerby L, Rasmusson L. Marginal bone-level alterations at implants installed in block versus particulate onlay bone grafts mixed with platelet-rich plasma in atrophic maxilla. A prospective 5-year follow-up study of 15 patients. Clin Implant Dent Relat Res 2013;15:7–14.
99. Sjöström M, Sennerby L, Nilson H, Lundgren S. Reconstruction of the atrophic edentulous maxilla with free iliac crest grafts and implants: A 3-year report of a prospective clinical study. Clin Implant Dent Relat Res 2007;9:46–59.
100. Chiapasco M, Brusati R, Ronchi P. Le Fort I osteotomy with interpositional bone grafts and delayed oral implants for the rehabilitation of extremely atrophied maxillae: A 1–9-year clinical follow-up study on humans. Clin Oral Implants Res 2007;18:74–85.
101. Hallman M, Mordenfeld A, Strandkvist T. A retrospective 5-year follow-up study of two different titanium implant surfaces used after interpositional bone grafting for reconstruction of the atrophic edentulous maxilla. Clin Implant Dent Relat Res 2005;7:121–126.
102. Becktor JP, Isaksson S, Sennerby L. Survival analysis of endosseous implants in grafted and nongrafted edentulous maxillae. Int J Oral Maxillofac Implants 2004;19:107–115.
103. Pinholt EM. Brånemark and ITI dental implants in the human bone-grafted maxilla: A comparative evaluation. Clin Oral Implants Res 2003;14:584–592.
104. Becktor JP, Eckert SE, Isaksson S, Keller EE. The influence of mandibular dentition on implant failures in bone-grafted edentulous maxillae. Int J Oral Maxillofac Implants 2002;17:69–77.
105. Lekholm U, Wannfors K, Isaksson S, Adielsson B. Oral implants in combination with bone grafts. A 3-year retrospective multicenter study using the Brånemark implant system. Int J Oral Maxillofac Surg 1999;28:181–187.
106. Keller EE, Tolman DE, Eckert SE. Surgical-prosthodontic reconstruction of advanced maxillary bone compromise with autogenous onlay block bone grafts and osseointegrated endosseous implants: A 12-year study of 32 consecutive patients. Int J Oral Maxillofac Implants 1999;14:197–209.
107. Keller EE, Tolman DE, Eckert SE. Maxillary antral-nasal inlay autogenous bone graft reconstruction of compromised maxilla: A 12-year retrospective study. Int J Oral Maxillofac Implants 1999;14:707–721.
108. Watzek G, Weber R, Bernhart T, Ulm C, Haas R. Treatment of patients with extreme maxillary atrophy using sinus floor augmentation and implants: Preliminary results. Int J Oral Maxillofac Surg 1998;27:428–434.
109. Nyström E, Lundgren S, Gunne J, Nilson H. Interpositional bone grafting and Le Fort I osteotomy for reconstruction of the atrophic edentulous maxilla. A two-stage technique. Int J Oral Maxillofac Surg 1997;26:423–427.
110. Köndell PA, Nordenram A, Moberg LE, Eliasson S, Nyberg B. Reconstruction of the resorbed edentulous maxilla using autogenous rib grafts and osseointegrated implants. Clin Oral Implants Res 1996;7:286–290.
111. Neukam FW. Klinische Erfahrungen zur Versorgung des atrophischen Oberkiefers in Kombination mit Knochentransplantaten und Implantaten. Dtsch Zahnarztl Z 1996;51:10–15.
112. Keller EE, Eckert SE, Tolman DE. Maxillary antral and nasal one-stage inlay composite bone graft: Preliminary report on 30 recipient sites. J Oral Maxillofac Surg 1994;52:438–447.

113. Jemt T, Stenport V, Friberg B. Implant treatment with fixed prostheses in the edentulous maxilla. Part 1: Implants and biologic response in two patient cohorts restored between 1986 and 1987 and 15 years later. Int J Prosthodont 2011;24:345–355.
114. Jemt T, Stenport V, Friberg B. Implant treatment with fixed prostheses in the endentulous maxilla. Part 2: Prosthetic technique and clinical maintenance in two patient cohorts restored between 1986 and 1987 and 15 years later. Int J Prosthodont 2011;24:356–362.
115. Friberg B, Jemt T. Turned Brånemark System implants in wide and narrow edentulous maxillae: A retrospective clinical study. Clin Implant Dent Relat Res 2008;10:78–85.
116. Jemt T, Johansson J. Implant treatment in the edentulous maxillae: A 15-year follow-up study on 76 consecutive patients provided with fixed prostheses. Clin Implant Dent Relat Res 2006;8:61–69.
117. Widbom C, Söderfeldt B, Kronström M. A retrospective evaluation of treatments with implant-supported maxillary overdentures. Clin Implant Dent Relat Res 2005;7:166–172.
118. Ibañez JC, Tahhan MJ, Zamar JA, et al. Immediate occlusal loading of double acid-etched surface titanium implants in 41 consecutive full-arch cases in the mandible and maxilla: 6- to 74-month results. J Periodontol 2005;76:1972–1981.
119. Degidi M, Piattelli A. Immediate functional and non-functional loading of dental implants: A 2- to 60-month follow-up study of 646 titanium implants. J Periodontol 2003;74:225–241.
120. Kiener P, Oetterli M, Mericske E, Mericske-Stern R. Effectiveness of maxillary overdentures supported by implants: Maintenance and prosthetic complications. Int J Prosthodont 2001;14:133–140.
121. Watson CJ, Ogden AR, Tinsley D, Russell JL, Davison EM. A 3- to 6-year study of overdentures supported by hydroxyapatite-coated endosseous dental implants. Int J Prosthodont 1998;11:610–619.
122. Jemt T, Lekholm U. Implant treatment in edentulous maxillae: A 5-year follow-up report on patients with different degrees of jaw resorption. Int J Oral Maxillofac Implants 1995;10:303–311.
123. Palmqvist S, Sondell K, Swartz B. Implant-supported maxillary overdentures: Outcome in planned and emergency cases. Int J Oral Maxillofac Implants 1994;9:184–190.
124. Cairo F, Sanz I, Matesanz P, Nieri M, Pagliaro U. Quality of reporting of randomized clinical trials in implant dentistry. A systematic review on critical aspects in design, outcome assessment and clinical relevance. J Clin Periodontol 2012;39(12, suppl):81–107.
125. Meijer HJ, Raghoebar GM. Quality of reporting of descriptive studies in implant dentistry. Critical aspects in design, outcome assessment and clinical relevance. J Clin Periodontol 2012;39(12, suppl):108–113.
126. Vere J, Joshi R. Quality assessment of randomised controlled trials of dental implant surgery and prosthodontics published from 2004 to 2008: A systematic review. Clin Oral Implants Res 2011;22:1338–1345.
127. Ottenbacher KJ, Ottenbacher HR, Tooth L, Ostir GV. A review of two journals found that articles using multivariable logistic regression frequently did not report commonly recommended assumptions. J Clin Epidemiol 2004;57:1147–1152.
128. Hannigan A, Lynch CD. Statistical methodology in oral and dental research: Pitfalls and recommendations. J Dent 2013;41:385–392.
129. Layton DM, Clarke M. Quality of reporting of dental survival analyses. J Oral Rehabil 2014;41:928–940.
130. Lekholm U, Zarb GA. Patient selection and preparation. In: Brånemark PI, Zarb GA, Albrektsson TA (eds). Tissue-Integrated Prostheses: Osseointegration in Clinical Dentistry. Chicago: Quintessence, 1985:199–210.
131. Chanavaz M, Donazzan M. Reconstitution maxillo-mendaibulaire et implantologie. In: Bio-Materiaux. Classification Francaise de l'os Disponible en Implantologie. Livre du XXXeme Congres de Stomatologie et de Chirugie Maxillo-Faciale;1986:189–204.
132. Misch CE. Density of bone: Effect on treatment planning, surgical approach, and healing. In: Misch CE (ed). Contemporary Implant Dentistry. St Louis: Mosby, 1993:469–485.
133. Lambert PM, Morris HF, Ochi S. Positive effect of surgical experience with implants on second-stage implant survival. J Oral Maxillofac Surg 1997;55:12–18.
134. Preiskel HW, Tsolka P. Treatment outcomes in implant therapy: The influence of surgical and prosthodontic experience. Int J Prosthodont 1995;8:273–279.
135. Att W, Ogawa T. Biological aging of implant surfaces and their restoration with ultraviolet light treatment: A novel understanding of osseointegration. Int J Oral Maxillofac Implants 2012;27:753–761.
136. Ogawa T. Ultraviolet photofunctionalization of titanium implants. Oral Craniofac Tissue Eng 2012;2:151–158.
137. Lee JH, Ogawa T. The biological aging of titanium implants. Implant Dent 2012;21:415–421.
138. Att W, Hori N, Takeuchi M, et al. Time-dependent degradation of titanium osteoconductivity: An implication of biological aging of implant materials. Biomaterials 2009;30:5352–5363.
139. Aita H, Hori N, Takeuchi M, et al. The effect of ultraviolet functionalization of titanium on integration with bone. Biomaterials 2009;30:1015–1025.
140. Whiting P, Westwood M, Burke M, Sterne J, Glanville J. Systematic reviews of test accuracy should search a range of databases to identify primary studies. J Clin Epidemiol 2008;61:357–364.
141. McKibbon KA, Wilczynski NL, Haynes RB, Hedges Team. Retrieving randomized controlled trials from medline: A comparison of 38 published search filters. Health Info Libr J 2009;26:187–202.
142. Esposito M, Coulthard P, Worthington HV, Jokstad A. Quality assessment of randomized controlled trials of oral implants. Int J Oral Maxillofac Implants 2001;16:783–792.
143. Esposito M, Ardebili Y, Worthington HV. Interventions for replacing missing teeth: Different types of dental implants. Cochrane Database Syst Rev 2014;7:CD003815.

Clinical Practice Guidelines: Role of Implant Design and Systems in Management of the Edentulous Maxilla

INTRODUCTION

The rehabilitation of the edentulous maxilla is a challenging topic in implant dentistry. Over the decades, a variety of surgical protocols and prosthetic rehabilitation modalities have been introduced. Along with changes in treatment protocols, dental implant design has dynamically changed to support novel surgical and prosthetic rehabilitation. These alterations in implant design include modifications in implant macrogeometry (shape, length, diameter, etc), implant-abutment connection, and surface morphology (at both micrometer and nanometer scale). These alterations in implant characteristics are intended to improve both surgical and prosthetic components of implant-based oral rehabilitation and are currently considered along with variables such as bone quality and quantity, clinician's experience, and the type of surgical and prosthetic protocol during treatment planning.

PURPOSE

The purpose of this report is to describe the evidence (based on systematic reviews [SR]) on specific implant designs and implant characteristics used in different clinical protocols for the rehabilitation of the edentulous maxilla. Anatomical constraints, patient characteristics, and level of experience, including clinician's skills for the selected protocol, were considered in order to develop the strategy for the selection of specific implant design. Such strategy allowed different clinical indications for specific implant designs using a patient-centered approach.

HEALTH CARE BURDEN

Predictable outcomes of surgical techniques with specific implant designs to improve and optimize the final clinical outcome without adverse events and negative financial impact have been evaluated based on SRs. Alternative solutions to prevent harm for the patient and serious disadvantages of decision-making were also considered. Since the patient preference for the specific type of treatment is a decisive factor in determining individual surgical approaches, a specific implant design may be favored relative to others.

METHODS

PICO questions were defined according to the degree of maxillary atrophy, sinus pneumatization, and interocclusal relationship. Studies designed based on the objective to use different implant designs and studies designed based on the different surgical approach were included.

A comprehensive search of the PubMed/MedLine, EMBASE, OVID, and Google Scholar databases using a combination of various MeSH terms and key words was performed. Case reports, letters to the editor, review studies, and unpublished data were excluded. A reference list of potentially relevant original and review studies was generated since search engines failed to retrieve a large number of manuscripts of interest. The present systematic review was customized to primarily summarize relevant information. The strength of the available evidence based on the SORT criteria determined by Ebell et al[1] (2004) was scored by a group of experts to define the Clinical Practice Guidelines (CPGs).

Implant survival, prosthesis survival, crestal bone loss, implant mobility, and adverse events were included in the assessment of the final outcome.

UMBRELLA KEY ACTION STATEMENT

Different implant designs may be used for rehabilitation of the edentulous maxilla and according to the patient preferences, financial challenges, need for bone augmentation procedures (with or without bone augmentation), and clinician's expertise in order to improve treatment outcome.

IMPLEMENTATION BARRIERS

The results from the SRs and the outcome assessment according to implant design and individual surgical approach were presented and discussed during the Academy of Osseointegration (AO) summit, and based on AO Summit discussion further crafted for submission shortly after the meeting. The variability of the results was classified in groups according to the anatomical constraints (primary decision-making factors), specific patient characteristics (secondary factors), and patient preferences (expenses/loading protocols). Hospital-based centers or institutional practices with different clinicians having various levels of expertise and with continuous interdisciplinary collaboration can implement some of these CPGs under the requirement of well-trained clinicians for specific approaches. This may include potential barriers for implementation of the CPGs in the private, traditional practice. Furthermore, "off-label" use of protocols and use of implant designs without regulatory approval (eg, FDA, CE) may be a challenge if their utilization is intended in different countries.

doi: 10.11607/jomi.16suppl.g2.cpg

PICO QUESTION

For patients with an edentulous maxilla who desire implant-supported prostheses, does the implant design and the type of surgical approach affect the following outcomes: *(1)* implant and prosthesis survival (technical adverse events), *(2)* crestal bone loss, *(3)* surgical complications, *(4)* implant failure, *(5)* economics, *(6)* patient satisfaction, and *(7)* maintenance?

CPG 1 (GREEN, G)

Patients with an edentulous maxilla receive implants to support fixed or removable prostheses. This includes a minimally invasive approach for patients with sufficient bone height (≥ 11 mm) and width (> 8 mm), with good bone quality (according to Lekholm and Zarb[2]) during osteotomy drilling (type I or II). The alveolar bone does not require any bone augmentation, and there is adequate prosthetic arch relationship (vertical and horizontal space) for the desired definitive restoration. Additional patient characteristics include lack of history of periodontal disease or previous implant failure, no bruxism, low smile line, and no smoking (or only socially) habit. Patient preferences are treatment with removable prostheses (eg, overdentures).

Recommendation G: Clinicians may use cylindrical or tapered implants, with or without surface texturing, at both micrometer and nanometer scales, varied thread design, and with a length and a diameter adapted to available bone volume.

Based on a comprehensive literature search evaluation, the clinical studies that have focused on a specific implant design or implant surface do not provide strong evidence for optimal clinical management for this kind of clinical scenario.

Evidence Level: 3

CPG 2 (YELLOW, Y)

Patients with an edentulous maxilla receive implants to support fixed or removable prostheses. This includes patients with sufficient bone height, 8 to 10 mm, and width, 4 to 8 mm, with poor bone quality (according to Lekholm and Zarb[2]) during osteotomy drilling (type III or IV). The alveolar bone does not require simultaneous bone augmentation, but a grafting procedure may have been performed at a previous stage. A vertical or horizontal unfavorable arch relationship may be present. Additional patient characteristics may include history of periodontal disease or previous implant failure, bruxism, low or moderate smile line, and no smoking (or only socially) habit. Patient preferences may be treatment with fixed or removable prostheses and various loading protocols.

Recommendation Y: Clinicians may use cylindrical or tapered implants, with or without surface texturing, at both micrometer and nanometer scales, varied thread design, and with a length and a diameter adapted to available bone volume, or tilted implants for better anchorage due to the possibility of using longer implants.

Based on a comprehensive literature search evaluation, the clinical studies that have focused on a specific implant design or implant surface do not provide strong evidence for optimal clinical management for this kind of clinical case.

Evidence Level: 3

CPG 3 (RED, R)

Patients with an edentulous maxilla receive implants to support fixed or removable prostheses. This includes patients with alveolar bone height < 8 mm and width < 4 mm, with poor bone quality (according to Lekholm and Zarb[2]) during osteotomy drilling (type IV). The alveolar bone requires simultaneous bone augmentation (fresh extraction sockets, vertical or horizontal). A vertical or horizontal unfavorable arch relationship may be included. Additional patient characteristics may include history of periodontal disease or previous implant failure, bruxism, high smile line, and heavy smoking. Patient preferences may be treatment with fixed or removable prostheses and immediate loading protocols.

Recommendation R: Clinicians may use cylindrical or tapered implants, with or without surface texturing, at both micrometer and nanometer scales, varied thread design and with a length and a diameter adapted to available bone volume in conjunction with bone grafting, with or without tilted implants in alveolar, pterygomaxilla, and zygomatic bone.

Based on a comprehensive literature search evaluation, the clinical studies that have focused on a specific implant design or implant surface do not provide strong evidence for optimal clinical management for this kind of clinical case.

Evidence Level: 3–2

ACKNOWLEDGMENTS

Funding was received from corporate sponsors through the Academy of Osseointegration. No conflict of interest exists with development of this CPG and the primary authors.

REFERENCES

1. Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): A patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548–556.
2. Lekholm U, Zarb GA. Patient selection and preparation. In: Brånemark PI, Zarb GA, Albrektsson T (eds). Tissue-Integrated Prostheses: Osseointegration in Clinical Dentistry. Chicago: Quintessence, 1985:199–209.

Role of Imaging to Guide Implant Placement

Group Co-Chairs

Veeratrishul Allareddy, BDS, MS
Kent Knoernschild, DMD, MS

Group Participants

Michael Bornstein, DMD, PhD
Lawrence Brecht, DDS
George Duello, DDS, MS
Scott Ganz, DMD
Rand Harlow, DDS
Reinhilde Jacobs, DDS, MSc, PhD
Isabelle Laleman, PhD
Ernest Lam, BSc, DMD, MSc, PhD
Sanjay Mallya, BDS, MDS, PhD
Michael Miloro, DMD, MD
Richard Nejat, DDS
Marc Quirynen, DDS
Robert Taft, DDS
Cristiano Tomasi, DDS, MSc, PhD
Johan Wolfaardt, BDS, MD, PhD
Mark Wong, DDS

Guided Implant Surgery in the Edentulous Maxilla: A Systematic Review

Isabelle Laleman, DDS, MSc[1]/Lauren Bernard, DDS, MSc[1]/
Marjolein Vercruyssen, DDS, MSc, PhD[1]/Reinhilde Jacobs, MSc, PhD, Dr hc[2]/
Michael M. Bornstein, Prof Dr Med Dent[2,3]/Marc Quirynen, DDS, MSc, PhD[1]

Purpose: *This systematic review verified the usefulness/limitations of static surgical guides during implant surgery in the edentulous maxilla. The PICO question was: "Does the use of digitally generated surgical guides vs conventional techniques affect the following outcomes: surgical complications, implant complications, prosthesis complications, implant survival, prosthesis survival, economics, patient satisfaction, and maintenance intervention?"* ***Materials and Methods:*** *The electronic searches retrieved 2,588 unique articles from which eventually 36 full-text articles were read for eligibility. Because no randomized controlled clinical trials could be found, the PICO question had to be reformulated, now only looking to the outcome of digitally generated surgical guides without comparison with conventional techniques.* ***Results:*** *Although long-term data are lacking, the outcome of implants placed with a static guide and of the prosthetic reconstruction seems similar to that expected from conventional techniques. The number of surgical complications with guided surgery is negligible. Guided flapless implant surgery offers slightly more comfort for the patient; however, the economic benefits are unclear.* ***Conclusion:*** *Implant therapy via static surgical guides in the maxilla is predictable, with slightly more comfort for the patient but with only minor economic advantages.* Int J Oral Maxillofac Implants 2016;31(suppl):s103–s117. doi: 10.11607/jomi.16suppl.g3

Keywords: *edentulous maxilla, guided surgery, computer planning, dental implant*

The rehabilitation of partially and fully edentulous patients by means of implant-supported prostheses is considered highly predictable and very successful.[1,2] In recent years, because of improved three-dimensional (3D)–imaging techniques, new treatment planning software, and advances in computer-aided design/computer-assisted manufacture techniques, computer-guided surgery has become possible.[3] Therefore implant positions can be virtually planned with the aid of cone-beam computed tomography (CBCT) images. Different methods are currently available to transfer the "planned" information to the "clinical" situation. To transfer the preoperative plan to the patient's mouth, static surgical guides are currently most often applied, more than dynamic methods.

Significant variations exist in the selection of static surgical guides. Most surgeons choose a flapless (mucosa-supported) approach with a small crestal incision or a punch before placement of the guide. The osteotomy preparation is then performed with minimal exposure of the bone. In case of a bone-supported guide, a full-thickness flap is reflected to position the guide directly onto the jawbone. Some guiding systems use different guides for one patient with sleeves with increasing diameter, whereas others apply one single guide but with different sleeve inserts. Some systems offer special drills or drill stops to allow depth control, whereas others only have depth indication on the drills. Some guides have to be removed at the moment of implant insertion, whereas others support guided placement of the implant (fully guided implant placement).

The introduction of guided surgery in implant dentistry facilitated an optimal 3D implant planning/placement with respect to both anatomic and prosthetic parameters. Taking critical anatomic structures (such as nerves,

[1]Department of Oral Health Sciences, Katholieke Universiteit Leuven, University Hospitals & Dentistry Leuven, Periodontology, Belgium.
[2]Department of Oral Imaging, Katholieke Universiteit Leuven, University Hospitals & Dentistry Leuven, Belgium.
[3]Section of Dental Radiology and Stomatology, Department of Oral Surgery and Stomatology, School of Dental Medicine, University of Bern, Bern, Switzerland.

Correspondence to: Dr Marc Quirynen, UZ St Raphael, Department of Periodontology, Kapucijnenvoer 33, B-3000 Leuven, Belgium. Email: Marc.quirynen@med.kuleuven.be.

arteries, sinuses) into account, implants also can be placed in an optimal prosthetic-driven position sometimes avoiding bone augmentation or sinus lift procedures. The final implant placement can be so accurate that it is possible to schedule an immediate loading protocol with a "prefabricated prosthesis."

A recent systematic review showed an acceptable level of accuracy of implants placed with static computer-assisted implant surgery. Mean overall global inaccuracies of 1.1 mm at the entry point and 1.4 mm at the apex were measured when the outcome of more than 1,400 implants was considered.[4] The average angular deviation was 3.9 degrees. It was also shown that implants placed with a guide had a good survival rate.[3–6] However, information on surgical peri-operative complications, subsequent implant and prosthetic complications, economics, and patient satisfaction is scarce. Moreover, none of the available systematic reviews made a distinction between dentate and edentulous patients, nor between the lower and upper jaws.

Therefore, the aim of this review was to systematically review the current literature regarding the perioperative complications and the implant- and patient-related outcomes of digitally generated static surgical guides for implant placement in the edentulous upper jaw.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the guidelines of Transparent Reporting of Systematic Reviews and Meta-Analyses (PRISMA).[7]

PICO Question

The PICO (population, intervention, comparison, outcome) was: "For patients with an 'edentulous maxilla' who desire implant-supported prostheses, does the use of digitally generated surgical guides vs conventional techniques affect the following outcomes: surgical complications, implant complications, prosthesis complications, implant survival, prosthesis survival, economics, patient satisfaction, and maintenance intervention?"

Search Strategy

A computerized literature search of PubMed Medline, Embase, and the Cochrane databases was conducted to identify studies concerning guided implant placement in the maxilla regardless of their publication status. These searches were restricted till January 2014. Additional hand searches were performed and included: *(1)* bibliographies of previous reviews on the subject,[3–6] and *(2)* bibliographies of all publications cited in the selected full-text articles. The search terms used were: (guided surgery OR computer-aided surgery) AND (dental implant* OR oral implant* OR tooth implantation OR implantology). The search strategy and terms were adapted according to the searched database.

Eligibility Criteria

The following criteria were used for inclusion: studies in English and conducted in humans, trials with at least 10 participants with guided implant placement, the use of a digitally generated static surgical guide, and availability of at least one of the following parameters:

- implant survival
- prosthesis survival
- surgical complications
- implant complications
- prosthesis complications
- economics
- patient satisfaction
- maintenance intervention

For implant and prosthesis survival data, follow-up of at least 12 months after implant placement had to be presented. A specific follow-up period was not defined for the other parameters. The review was specifically directed to the maxilla. Studies in which it was impossible to separate data between maxillae and mandibles were handled separately. Studies with a mix of partially and fully edentulous maxillae were excluded.

Exclusion Criteria

Studies that did not describe one of the stated outcome variables were excluded. In addition articles reporting on zygoma/pterygoid implants, mini-implants for orthodontic anchorage, and those restricted to radiographic evaluation of accuracy of implant positioning were excluded.

Data Extraction

Two reviewers (L.B., I.L.) independently screened the titles, and subsequently, the abstracts of all articles found. When there was disagreement or when an abstract contained insufficient information, the full text of the article was reviewed. The final inclusion of studies was made by discussion. Thereafter, both reviewers extracted the data separately from the selected articles. The data were collected for the studies reporting only guided implant placement in the upper jaw as well as for those treating both the upper and lower jaw and when it was not clear which jaw was treated. This information was transferred to a data extraction sheet. The following characteristics were abstracted from each study: study design, follow-up period, number of patients with guided surgery, sex, mean age, number of smokers, case type, the implant software and guide system used, implant system, number of implants, bone- or mucosa-supported guide, flapless or open flap approach, and immediate

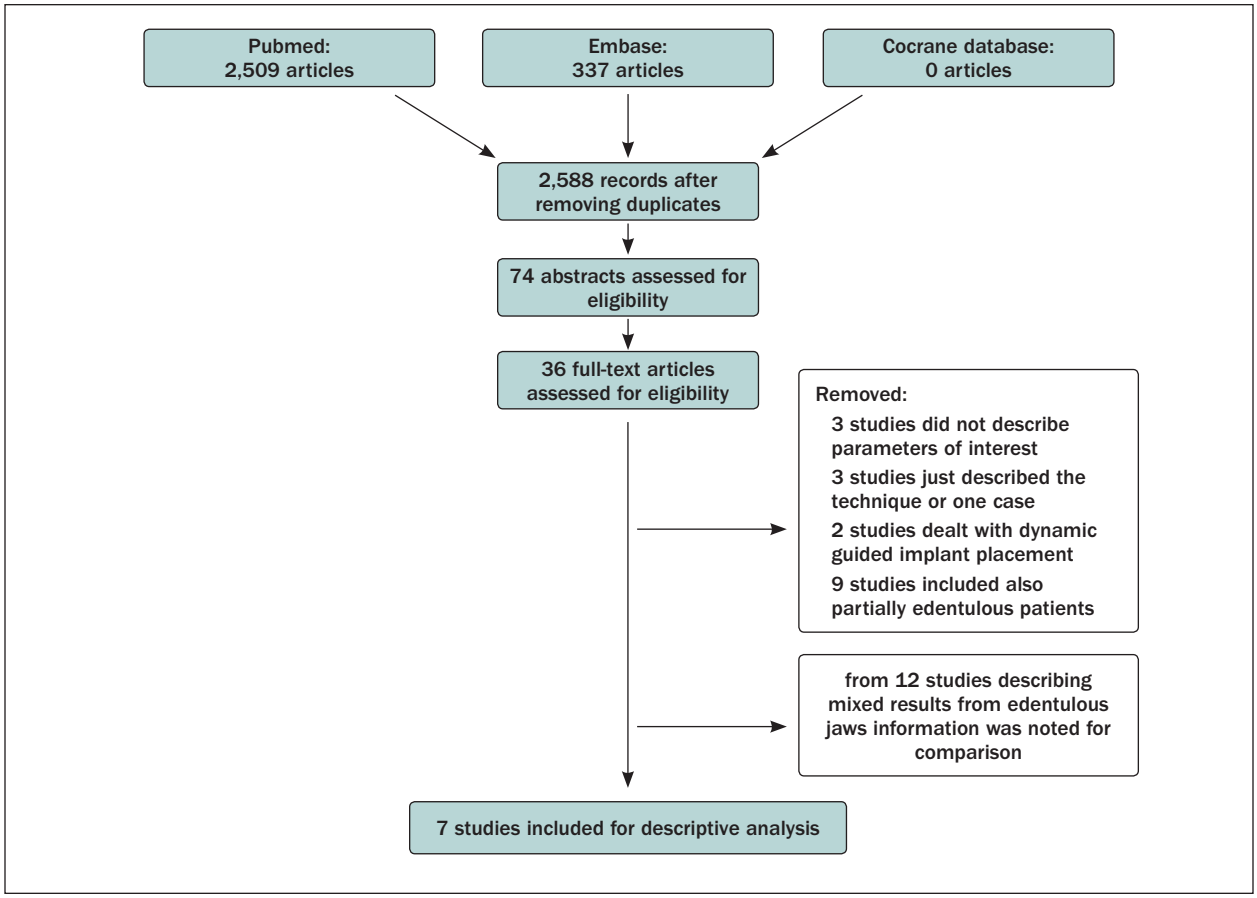


Fig 1 Flow chart of the search process.

or delayed loading. When early complications (defined as < 2 weeks after implant surgery) were reported, the number of surgical and prosthetic events and the reasons were noted in a table. The studies reporting implant and prosthesis survival (with a follow-up ≥ 12 months) were summarized in a table, together with the data on mean bone loss. Finally, for studies reporting patient-centered outcomes, the methods and outcome were noted.

RESULTS

Search and Selection

The electronic searches through the Medline, Cochrane, and ISI Web of Knowledge databases retrieved 2,588 unique articles (Fig 1). Of these, 2,514 were deleted after a first selection, and 74 abstracts were screened. Full texts of 36 articles were read for eligibility. Using hand searches, no additional articles were found.

No randomized controlled trials (RCTs) could be found that met the inclusion criteria and answered the PICO question; therefore, the authors reformulated their focused question as follows: *"For patients with an edentulous maxilla who desire implant-supported prostheses, what are the surgical complications, implant complications, prosthesis complications, implant survival, prosthesis survival, economics, patient satisfaction, and maintenance interventions when a digitally generated surgical guide is used during implant placement?"*

From the full-text articles read, three studies described only the technique or only one case.[8–10] Two studies dealt with dynamic guided implant placement.[11,12] Three studies did not describe the parameters of interest.[13–15] Nine studies included partially edentulous patients.[16–24] This resulted in the final inclusion of seven publications that met all criteria,[25–31] and another 12 studies that described results for both the upper and lower jaw without specifying where the implants were placed[32–43]; from these studies, information was gathered to compare with the seven articles included.

Study Demographics

Table 1 summarizes the study, patient, guide, and implant characteristics, as well as the techniques used. Of the seven studies included, only one was an RCT comparing flapless and flapped guided implant surgery.

Table 1 Demographics of Selected Studies*

Study	Study Characteristics		Patient Characteristics				
	Study Design	Follow-up Period (mo)	No. of Patients With Guided Surgery	No. of Treated Lower/Upper Jaws	Sex (F/M)	Mean age (range) (y)	No. of Smokers
Gillot et al (2010)*[25]	PO	12-51	33	0/33	21/12	61 (46–80)	0
Johansson et al (2009)*[26]	PO	12	52	0/52	21/31	72 (37–85)	7
Lindeboom and van Wijk (2010)*[27]	RCT	1	8	0/8	6/2	55	0
			8	0/8	7/1	59	0
Meloni et al (2010)*[28]	RO	18	15	0/15	10/5	52 (40–70)	5
Merli et al (2008)*[29]	PO	NR	13	0/13	9/4	62 (44–80)	6
Sanna et al (2007)*[30]	PO	60	30	0/30	12/18	56 (38–74)	13
van Steenberghe et al (2005)*[31]	PO	12	27	0/27	NR	63 (34–89)	5
Total/range	**–**	**1–60**	**186**	**0/186**	**–**	**34–89**	**36**
Arisan et al (2010)†[32]	PC	2–4	21	24/30	27/25	49 (28–63)	NR
			16				
			15				
Balshi et al (2008)‡[33]	PO	3–36	23	NR	NR	NR	NR
Di Giacomo et al (2012)‡[34]	PO	30	12	NR	8/4	60 (41–71)	0
Komiyama et al (2008)†[36]	PO	44	29	10/21	9/20	72	5
Komiyama et al (2012)‡[35]	PO	19	34	13/21	NR	72 (44–92)	3
Lal et al (2013)†[37]	RO	24–48	36	23/19	26/10	53 (35–71)	6
Malo et al (2007)†[38]	PO	12	23	5/18	NR	NR	NR
Marra et al (2013)†[39]	PO	36	30	30/30	18/12	NR	NR
Meloni et al (2013)†[40]	PO	24	12	1/11	8/4	57 (40–68)	NR
Pomares et al (2010)†[41]	RO	12	30	17/25	24/6	53 (35–84)	3
Pozzi et al (2013)†[42]	RO	36-60	22	14/12	11/11	68 (50–83)	NR
Tahmaseb et al (2012)†[43]	PO	12-36	35	15/25	18/17	NR	NR
Total/range	**–**	**2-60**	**338**	**152/212**	**–**	**35–92**	**17**

*Studies were restricted to full edentulous maxillae.
†These studies include both maxillae and mandibles (without clear data per jaw) or with unknown jaw allocation.
PO = prospective observational, RCT = randomized controlled trial, RO = retrospective observational, MS = mucosa-supported, BS = bone-supported, FL = flapless, OF = open flap, I = immediate loading, I† = immediate final prosthesis, D = delayed loading, NR = not reported, – = not applicable.

Patient Characteristics *Continued*	Guide and Implant Characteristics				Techniques	
Implant Software	Guide System	Implant System	No. of Implants	Bone-/mucosa-Supported	Flapless/Open Flap	Immediate/Delayed Loading
Procera	NobelGuide	Nobel Speedy, Nobel MkIII, Nobel MkIV	211	MS	FL	I†
Nobel Guide	NobelGuide	Bränemark System, MKIII TiUnite	312	MS	FL	I†
Procera	NobelGuide	Nobel Replace	48	MS	FL	D
			48	BS	OF	D
Procera	NobelGuide	Nobel Replace Tapered Groovy	90	MS	FL	I
Procera	NR	Nobel Speedy Groovy	89	MS	FL	I
Procera	NR	Bränemark System MKIII TiUnite	212	MS	FL	I†
NR	Oralim, Medicum	Bränemark System MKIII TiUnite	184	MS	FL	I
–	–	–	**1,194**	–	–	–
–	–	SPI-Element, Xive	141	–	–	D
3D StendCad	Aytasarim-classic system		101	BS	OF	D
Simplant Planner	Simplant-SAFE System		99	MS	FL	D
NR	NobelGuide	Bränemark System	168	MS	FL	I
Implantviewer 1.9 & Rhino 4.0	SLS-Guide	E-Fix	62	MS	FL	I†
Procera	NobelGuide	Bränemark System MKIII TiUnite	176	MS	FL	I†
Procera	NobelGuide	Bränemark System MKIII TiUnite	191	MS	FL	I†
Procera	NobelGuide	Bränemark System MKIII TiUnite	273	MS	FL	I/D
Procera	NobelGuide	NobelSpeedy	92	MS	FL	I
Procera	NobelGuide	Nobel Speedy, Bränemark Standard MKIII	312	MS	FL	I
Procera	NobelGuide	Nobel Replace Tapered Groovy	72	MS	FL	I
Procera	NobelGuide	NobelSpeedy, Bränemark MKIII	195	MS	FL	I
Procera	NobelGuide	Nobel Speedy, Nobel Active, Nobel Replace	170	MS	FL	I
Exeplan	NR	Straumann standard	240	MS	FL	I†
–	–	–	**2,292**	–	–	–

Table 2 Early (<2 weeks) Complications During Surgery, of the Implant and/or with Prosthesis

Study	Patient Groups	No. of Events	Reasons
Gillot et al (2010)[25]	33 MS, FL, I	3	Guide difficult to insert *(1)* and absence of primary stability of the implant in type IV bone *(2)*
Johansson et al (2009)[26]	52 MS, FL, I	9	Misfit of surgical silicone index *(3)*, misfit surgical guide *(2)*, and problems with installing implants *(4)*
Meloni et al (2010)[28]	15 MS, FL, I	1	Fracture of guide during surgery
Merli et al (2008)[29]	13 MS, FL, I	3	2 flaps had to be elevated to allow GBR; fracture of surgical guide *(1)*
van Steenberghe et al (2005)[31]	27 MS, FL, I	1	1 marginal fistula
Total	**140**	**17**	–
Arisan et al (2010)†[32]	21 - - D	2	Hematoma *(2)*
	16 BS, OF, D	3	Guides fractured during surgery *(2)*; hematoma *(1)*
	15 MS, FL, D	NR	NR
Balshi et al (2008)†[33]	23 MS, FL, I	NR	NR
Di Giacomo et al (2012)†[34]	12 MS, FL, I	11	Pulling of soft tissue *(4)*, insertion of wider implant than planned to improve implant stability *(4)*, implant instability in the tuber area *(2)*, prolonged pain because of proximity to nasopalatine nerve *(1)*
Komiyama et al (2008)†[36]	29 MS, FL, I	6	Surgical templates fractured *(3)*, bone defects led to a suspected infection *(3)*: in two patients around anchoring pins in the maxilla and in 1 patient around fixtures in the mandible
Pomares et al (2010)†[41]	30 MS, FL, I	7	Surgical template fractured *(3)*, a small flap had to be elevated in case of insufficient keratinized mucosa *(4)*
Tahmaseb et al (2012)†[43]	35 MS, FL, I	1	A flap had to be elevated to correct an extensive knife-edge ridge
Total	**181**	**30**	–

†These studies include both maxillae and mandibles (without clear data per jaw) or with unknown jaw allocation.
MS = mucosa-supported; BS = bone-supported; FL = flapless; OF = open flap; I = immediate loading; D = delayed loading; GBR = guided bone regeneration; NR = not reported; – = not applicable.

The remaining six were either prospective (n = 5) or retrospective observational (n = 1) studies.

A total of 186 patients with fully edentulous jaws could be included, representing a total of 1,194 implants. Patients ranged in age from 34 to 89 years. In five studies, smoking was not an exclusion criterion, so 36 smokers were included.

Most studies applied the NobelGuide system. All implants were from the Nobel Biocare Company (Nobel Speedy, Nobel Bränemark MKIII, Nobel Bränemark MKIV, and Nobel Replace). All studies, except one, used a flapless technique and a mucosa-supported guide. One RCT compared the flapless and open flap techniques; in the latter cases, a bone-supported guide was used.[27] This study by Lindeboom and van Wijk[27] was the only one applying a delayed loading protocol. In the remaining studies, an immediate loading protocol was followed. Three studies even directly placed an immediate "final" prosthesis in 101 cases (of 115 patients).[25,26,30] Five studies explicitly mentioned that the patients could eat only soft foods after the surgery.[26–30] The recommended period ranged from 1 week (in the study with the delayed loading protocol) to 2 months.

Of the 12 studies that evaluated both the upper and the lower jaws without clear separation, or when it was unclear which jaws were treated, all but one were of observational nature. Arisan et al[32] compared the surgical and postoperative outcomes of a standard technique, a bone- and a mucosa-supported guide.

No. of Prosthetic Events	Reasons
2	Major occlusal adjustment needed (1). Distal implant could not be connected to the prosthesis (1).
13	Not possibly to get prosthesis completely in place (10) and major occlusal adjustment necessary (3).
3	Prosthesis did not fit due to fracture of the template during surgery (2) and full acrylic resin complete denture fractured (1).
4	4 provisional prostheses did not fit.
NR	NR
22	–
NR	NR
NR	NR
NR	NR
2	All-acrylic bridges did not fit passively to all abutments (2)
1	Midline deviation of prosthesis (1)
8	Misfit of the abutment-bridge (5), extensive adjustment occlusion (3)
3	Bad fit of prosthesis (3)
1	Occlusal failure
15	–

Early Complications and Failures

Table 2 describes the early surgical and prosthetic failures. These were defined as events that occurred during surgery or during the subsequent 2-week period. Two studies did not report early complications or failures.[27,30] The total number of surgical complications at implant placement was 16 (out of 140 interventions). Most were related to problems with the guide and the surgical index: fracture of the guide during surgery (n = 2), guide difficult to insert (n = 3), and misfit of the silicone index (n = 3). In six patients, there were problems when installing the implants (such as absence of primary stability of an implant in type IV bone), and in two patients, flaps had to be elevated to allow guided bone regeneration. During the 2-week follow-up, a marginal fistula was detected in one patient.[31]

For the mixed study group, 28 complications were described for 181 interventions. During surgery, fracture of the guide was the most common complication, followed by problems when installing the implants (impossible to obtain primary stability). Furthermore, in five cases, a flap had to be raised, and four patients experienced pulling of the soft tissues. Various problems were described during the 2-week postoperative period. One patient experienced hematoma, three patients had infections, and one complained of prolonged pain. The reason for this was that an implant was placed in the proximity of the nasopalatine nerve.

Several studies evaluated the pain sensation after surgery. Meloni et al[28] reported that of 15 patients, five experienced mild pain and eight experienced mild swelling. Johansson and coworkers[26] reported that more than 90% of the patients had no pain during the 2-week postoperative interval, and that in general, only minor surgical-related complaints (swelling and minimal bleeding) occurred. In the study of van Steenberghe and coworkers,[31] 4 of 27 patients reported moderate pain. Gillot et al[25] concluded that the pain after the guided implant surgery was minimal, though one patient presented with a jugal hematoma and a slight genial tumefaction for 3 days.

With regard to the immediate connection of the prosthesis (n = 113), 22 unexpected events in 4 studies[25,26,28,29] are described; in almost all cases (n = 17), it was not possible to get the immediate prosthesis in position. Other possible problems were the fracturing of the full acrylic resin complete denture (n = 1) and the need for major occlusal adjustments (n = 4).

In the mixed study group, 15 complications (129 cases) of the immediate prosthesis placement were mentioned. In 10 cases, it was not possible to get the prosthesis into place. Other problems were midline deviation of the prosthesis (n = 1) and occlusal problems (n = 4).

Implant and Prosthesis Survival

The implant and prosthesis survival data are summarized in Table 3. Only studies with a follow-up of 12 months or longer were included in this evaluation. Of the seven studies included, four reported implant survival after 1 year,[26,28,30,31] of which three survived for an even longer period (1.5–3 years). Implant survival was defined as having the implant still in place.

Implant survival 1 year after placement ranged from 97.8% to 100%. Mean bone loss around these implants ranged from 0.8 to 1.7 mm. The studies with a longer follow-up reported implant survival of 97.8% after 18 months[28] or 98.1% and 91.5% (98.9% for

Table 3 Implant and Prosthesis Survival (Studies Reporting Outcomes ≥ 12 Months)

		1-Year Evaluation			
	Number of Implants at Baseline	Implant (cumulative) survival rate (%)	Mean (SD) Bone Loss in mm	Prosthesis Survival (%)	Evaluated/ Included Patients or Implants
Gillot et al (2010)[25]	Mx: 211	Mx: 99.1*	Mx: NR	Mx: NR	Mx: 33/33
Johansson et al (2009)[26]	Mx: 312	Mx: 99.4*†	Mx: 1.3 (1.3)	Mx: 96.2*	Mx: 48/52
Meloni et al (2010)[28]	Mx: 90	Mx: 97.8†	Mx: 1.4 (0.2)	Mx: NR	Mx: 15/15
Sanna et al (2007)[30]	Mx: 212	Mx: 100*†	Mx: S: 1.1 (1.4) Mx: NS: 0.8 (1.1)	Mx: NR	Mx: 28/30
van Steenberghe et al (2005)[31]	Mx: 184	Mx: 100†	Mx: M: 1.2 (1.1) Mx: D: 1.1 (1.0)	Mx: NR	Mx: 24/27
Total/range	**Mx: 1,009**	**Mx: 97.8–100**	**Mx: 0.8–1.4**	**Mx: 96.2**	**Mx: 148/15–48**
Balshi et al (2008)†[33]	168	97.6*	NR	100	I: 68/168
Di Giacomo et al (2012)†[34]	62	NR	NR	NR	NR
Komiyama et al (2008) †[36]	176	91.5† Mx: 92.7†	NR	NR	I: 168/176
Komiyama et al (2012)†[35]	191	NR	NR	NR	NR
Lal et al (2013)†[37]	273	NR	NR	NR	NR
Malo et al (2007) †[38]	92	97.8† Mx: 97.2†	1.5 (1.5) Mx: 2.0 (1.6)	NR	I: 55/92
Marra et al (2013)†[39]	312	NR	1.2 (0.7)	NR	30/30
Meloni et al (2013)†[40]	72	NR	1.2 (0.3)	NR	12/12
Pomares et al (2010) †[41]	195	98* Mx: 98.5*	NR	100*†	30/30
Pozzi et al (2013)†[42]	170	NR	NR	NR	NR
Tahmaseb et al (2012) †[43]	240	95.4† Mx: 93.6†	NR	NR	35/35
Total/range	**1,951**	**91.5–98**	**1.2–1.5**	**100**	**107/12–35**

*Cumulative survival rate.
†Survival rate.
‡These studies include both maxillae and mandibles (without clear data per jaw) or with unknown jaw allocation.
Mx = maxilla only; NR = not reported; NS = nonsmokers; S = smokers; M = mesial, D = distal
I = implants (when only reported on implant level and not on patient level; SD = standard deviation; – = not applicable.

nonsmokers, 81.2% for smokers after 48 months[25,30]). Meloni et al[28] reported a marginal bone loss of 1.6 mm after 18 months, and Sanna and coworkers[30] found a bone loss of 1.2 mm in nonsmokers and 2.6 mm in smokers after 48 months.

The mixed studies reported an implant survival ranging from 91.5% to 98% after 1 year, and 83.5% to 97.9% after 3 years of follow-up. Bone loss ranged from 1.2 to 1.5 mm after 1 year and 1.2 to 1.9 mm after 3 years.

Only two of the seven studies included reported on prosthesis survival. Johansson and coworkers[26] reported a 96.2% survival rate after 1 year, and Gillot and coworkers[25] 100% after 36 months. For the mixed study group, if reported, 100% survival rates were observed after a follow-up of 1 year or more.

Economics

Unfortunately, no study could be found reporting the exact cost or the cost-benefit ratio for the patient. Meloni and coworkers[28] and Merli and coworkers[29] mentioned that the treatment was worth the costs.

> 1-Year Evaluation				
Time Point (mo)	Implant Survival (%)	Mean (SD) Bone Loss (mm)	Prosthesis Survival (%)	Evaluated/Included Patients or Implants
36	Mx: 98.1*	Mx: NR	Mx: 100*†	Mx: 22/33
NR	Mx: NR	Mx: NR	Mx: NR	Mx: NR
18	Mx: 97.8†	Mx: 1.6	Mx: NR	Mx: 15/15
48	Mx: S: 81.2* Mx: NS: 98.9	Mx: S: 2.6 (1.6) Mx: NS: 1.3 (1.0)	Mx: NR	Mx: 6/30
NR	Mx: NR	Mx: NR	Mx: NR	Mx: NR
18–48	**Mx: 81.2–98.9**	**Mx: 1.3–2.6**	**Mx: 100**	**Mx: 43/6–22**
36	97.6*	NR	NR	I: 8/168
30	98.3*	NR	91.7*	12/12
36	88.4† Mx: 91.6†	NR	83*	I: 63/176
19	98.2†	1,2 (1,4) Mx: 1,2 (1,2)	100†	I: 165/191
36	83.5*	NR	100*†	34/36
NR	NR	NR	NR	NR
36	97.9† Mx: 96.6†	1.9 (1.3)	100*†	30/30
24	100*†	1.4 (0.3)	100*†	12/12
NR	NR	NR	NR	NR
36	100*†	NR	100*†	22/22
NR	NR	NR	NR	NR
19–36	**83.5–100**	**1.2–1.9**	**83–100**	**110/12–34**

Studies Reporting on Patient-Centered Outcomes

Table 4 summarizes the studies that explicitly investigated patient-centered outcomes and the way in which they were evaluated. Different research methods were used, and the timing of the evaluation varied largely (ranging from 1 month after implant placement[27] to 18 months after implant placement[28]). The RCT by Lindeboom and van Wijk[27] evaluated emotional impact, dental anxiety, the oral health-related quality of life (OHIP-14), and pain and anxiety (with a custom questionnaire). No differences could be observed with regard to pain (dental), anxiety, treatment invasiveness, treatment time, or differences in surgical difficulty between flapless and flap procedures. However, after dichotomizing pain during treatment, it was shown that the number of patients without any pain was higher in the flap group compared with the flapless group.

Four studies reported that the patients were really satisfied with the prosthesis.[25,28,29,31] Good scores for speech were also noted[31] and Meloni et al[28] reported that no patients experienced any phonetic problems during the provisional phase. When the

Table 4 Studies with Patient-Reported Outcomes

Study	Patient Groups	Methods	Outcome
Lindeboom and van Wijk (2010)[27]	8 MS, FL 8 BS, FL	IES-R, s-DAI, OHIP-14, Questionnaire (anxiety, pain)	No differences could be shown between conditions on dental anxiety, emotional impact, and anxiety. However, the flapless group did score consistently higher. The flap procedure group reported less impact on quality of life and included more patients who reported feeling no pain at all during placement.
Meloni et al (2010)[28]	15 MS, FL	Questionnaire	All patients but two reported that their quality of life and lifestyle improved with the implant-supported maxillary prosthesis. All patients answered that they would undergo the same therapy again and that the treatment was worthwhile.
Merli et al (2008)[29]	13 MS, FL	Questionnaire	Eleven patients (of 12) reported that their quality of life and lifestyle improved with the implant-supported maxillary prosthesis. All patients answered that the rehabilitation was worth the cost and that they would undergo the same therapy again.
van Steenberghe et al (2005)[31]	27 MS, FL	VAS	Most patients reported good scores for speech, oral function, esthetics, and tactile sensation. Less satisfaction with speech was reported by half of the patients at 3 months. Good satisfaction with other parameters.
Arisan et al (2010)†[32]	21, D 16 BS, OF, D 15 MS, FL, D	VAS	Flapless group reported a lower pain score than the bone-supported group and control group.
Marra et al (2013)†[39]	30 MS, FL, I	OHIP-EDENT	Patient's grade of satisfaction with this rehabilitation is very high, because it grants better stability and support, together with lower postoperative discomfort. Significant differences between base and 6-mo measurements: physical pain, self-consciousness, physiologic discomfort, psychological disability (embarrassment), and social disability.
Pozzi et al (2013)†[42]	22 MS, FL, I	VAS	All participants were functionally and esthetically satisfied with their prosthesis.

†These studies include both maxillae and mandibles (without clear data per jaw) or with unknown jaw allocation.
MS = mucosa-supported, BS = bone-supported, FL = flapless, OF = open flap, I = immediate loading, D = delayed loading, NR = not reported, IES-R = Impact of Event Scale-Revised, s-DAI = Short version of the Dental Anxiety Inventory, OHIP-14 = Oral Health Impact Profile (short form), VAS = visual analogue scale, OHIP-EDENT = Oral Health Impact Profile in Edentulous Adults; – = not applicable.

quality of life and lifestyle was questioned, 89% (24 out of 27 patients) reported clear improvements.

With regard to the mixed studies, it was also shown that the patients were satisfied with their rehabilitation. Arisan et al[32] concluded that the use of mucosa-supported guides for flapless implant placement may reduce the surgery duration, pain intensity, related analgesic drug use, and most other complications typical in the post–implant surgery period.

Treatment Duration and Maintenance

The reported duration of the surgery in the edentulous maxillae varied from 30 to 72 minutes (mean, 57 minutes[27,29]). Yet it is important to note the time spent by the clinician before surgery, for example, for manufacturing the scanning prosthesis and planning the guide. However, only one study included mentioned that the average time spent by the dentist and laboratory for preparing for and planning a case using the software was 145 minutes (range, 70–370 minutes).[29] Unfortunately, no comparison was made with nonguided surgery.

Various maintenance and follow-up protocols were described. However, most of the articles do not clearly describe what happened during these follow-up visits. Despite their heterogeneity, they have one thing in common: in each of these studies, the researchers continued to follow-up the patients regularly. Three articles on guided implant placement in the edentulous maxilla mention unexpected events during these follow-up visits.[28,29,31]: two fractures of the provisional prosthesis; fracturing of the porcelain material in three patients; and a loose retaining screw in two patients.

In the mixed studies chip-off fractures were also among the most commonly noted problems during follow-up (n = 13 patients).[34,39,42] In addition, peri-implant problems were detected in eight patients.[38,40,41]

Table 5 Specific Indications for the Use of Cone Beam Computed Tomography Imaging in the Upper Jaw*

Timing	Clinical Situation	Specific Indication(s)
Preoperative	All sites	Clinical doubt of alveolar bone height, width and/or shape Bone density evaluation
	Anterior maxilla	Nasal floor, nasopalatine canal, anterior superior alveolar canal
	Posterior maxilla	Maxillary sinus and related structures, posterior superior alveolar canal, maxillary tuberosity, pterygoid plates
	Anterior esthetic zone	Sinus augmentation Block or particulate bone grafting Ramus or symphysis grafting Pathology/impacted teeth in field of interest Prior traumatic injury
	Computer-assisted treatment planning, treatment options, optimal implant position	
Postoperative	Integration	Marginal peri-implant bone height Bone-implant interface Post augmentation assessment (eg, sinus, particulate/block)
	Postoperative complications	Altered sensation Infection/postoperative integration failure Implant mobility Rhinosinusitis

*Adapted from Bornstein et al (2014).[55]

DISCUSSION

Currently, a lot of research is available on guided implant placement. However, because this review focused solely on the upper jaw, few articles were found in which only those jaws were treated or where a distinction was made between the maxilla and mandible. Furthermore, no articles could be identified which answered the authors' original PICO question comparing surgical guides with conventional techniques, because there simply are no RCTs available on this topic. This led to the rephrasing of the focused question: "*For patients with an edentulous maxilla who desire implant-supported prostheses, what are the surgical complications, implant complications, prosthesis complications, implant survival, prosthesis survival, economics, patient satisfaction, and maintenance interventions when a digitally generated surgical guide is used for implant placement?*"

The current results point to the fact that, except for one study, all available studies describe results from mucosa-supported guides. In addition, it can be assumed that only normal jaws, not severely atrophied jaws were included, because only one study described a priori sinus augmentation techniques.

The present findings indicate that implants placed with a static guide have a good prognosis, with all studies reporting a survival rate of 97.8% or higher after 1 year. However, long-term follow-up data are not yet available. The studies with the longest follow-up period, 48 months, mention a survival of 91.5% and 98.1%. A longer follow-up period is of course necessary, but implants placed with a guide appear to have a comparable survival rate as those without a guide in the edentulous maxilla.[44] However, this comparison must be made with caution because there are no RCTs comparing both techniques and there are almost no long-term follow-up data on guided placed implants.

For future research, it is also important to distinguish between smokers and nonsmokers, taking into account the statistically significant lower implant survival rates

Table 6 Effective Doses (ICRP2007) for Specific CBCT, MSCT and Extraoral Two-Dimensional Images in Adults*

Imaging Type	Effective dose (μSv)
Panoramic imaging	10–50
Cephalometric imaging	4.5–10
MSCT	199–1,410
CBCT	
Small FOV (< 40 cm^2)	11–166
Medium FOV (40–100 cm^2)	28–674
Craniofacial (> 100 cm^2)	52–1,073

*Adapted from Bornstein et al (2014).[55]
CBCT = cone beam computed tomography; MSCT = multislice computed tomography; FOV = field of view.
ICRP = International Commission on Radiological Protection.

in smokers compared with nonsmokers.[45,46] Sanna and coworkers[30] distinguished between these groups and concluded that smoking may eventually compromise the outcome (implant survival and marginal bone loss) of guided implant placement in the edentulous maxilla.[30]

When the survival of implants placed via digitally generated static guides is compared between maxilla and mandible, an important heterogeneity was noticed. Two studies report a better implant survival in the maxilla,[35,41] with three studies reporting the opposite.[38,39,43] It is important to search for factors that could explain these differences. One of them could be the need for sinus lifting or bone regeneration. Tahmaseb and coworkers,[43] for example, showed a statistically significant lower survival rate for guided placed implants in the maxilla after sinus augmentation (90%) than when implants could be placed in the edentulous maxilla in a straightforward fashion (96.7%).[43]

In addition to good implant survival, high prosthesis survival was also demonstrated, ranging from 100% (36 months) to 96.2% (12 months).[25,26] However, these results are from studies in which an immediate "final" prosthesis was placed. In contrast to the good prosthesis survival, multiple early prosthesis complications were reported. A prosthetic problem was described in 12% of the patients.

Although guided implant placement means additional costs for the patient (manufacturing of the guide, anchoring screws) it is not clear how much this treatment costs compared with conventional implant treatment. Only two authors mention that their patients thought the guided implant placement was worth the costs,[28,29] the remaining authors did not include this in their analyses. In addition to the costs for the supplementary material, one must also consider the additional time invested by the clinician and the laboratory. The surgery time for a guided implant placement might be less than half compared with a conventional implant placement,[32] but on average, 145 minutes were spent on the preparation phase. It is therefore important that future research focuses on the costs (and time)–benefit ratio of guided implant placement vs conventional implant placement. In this calculation, the laboratory costs also should be included, because these costs might be less for guided cases, in which the implant placement is more prosthetically driven.

All patients appeared to be satisfied with the esthetics and function of their prostheses on guided placed implants, and said that they would undergo the same treatment again. However, given the differences in patient evaluation methods and time points chosen for evaluation, the studies are difficult to compare. It is important that future research uses standardized methods to describe patient-centered outcomes. Furthermore, the evaluation should take place at two distinct time points, just after implant placement (for evaluation of the implant placement and early/short-term problems) and a sufficient length of time later (for evaluation of the function of the prosthesis/long-term).

Almost all implants included in this review were placed without flaps. Theoretically, this could have several advantages: the procedure is less time consuming, bleeding is minimal, implant placement is expedited, and there is no need to place and remove sutures.[32,47–49] Thereby it was demonstrated that patients with flapless surgery reported less pain and for a shorter period compared with patients who underwent a classic, nonguided open flap approach with less postsurgical complications (swelling, hematoma, hemorrhage, trismus).[32,48,49] It was also shown that flapless implant placement reduces the incidence of surgery-related bacteremia.[14] However, the only study included in this review comparing flapless and open flap–guided implant placement in the edentulous maxilla did not find significant differences. It even exhibited a trend to the contrary: after dichotomizing pain felt during treatment, it was shown that more patients in the open flap group reported not feeling any pain at all compared with patients in the flapless group. However, it should be noted that in the open flap group, the mucosal flaps were repositioned before positioning of the guide, leaving the bone unexposed during implant placement.

These results are in line with recent observations from our own research group. Vercruyssen and coworkers[50–52] performed an RCT comparing accuracy and implant and patient-centered outcomes of guided implant surgery (bone or mucosa-supported) with conventional implant placement. Sixty patients (72 jaws, both mandibles and maxillae) were randomly assigned to one of the treatment groups (Materialise Universal/mucosa (Materialise Dental), Materialise Universal/bone, Facilitate/mucosa (Dentsply Implants), Facilitate/bone-supported, mental navigation, pilot drill template). The Materialise Universal system can be used to place oral implants of different manufacturers, but drilling is done without depth control and there is no guidance during implant placement. The Facilitate system is specially designed to place Astra Tech implants and drilling, and implant placement is performed both in a guided manner and with depth control (physical stops). In the mental navigation group, no guide was used, only images from the software planning as a reference were allowed. For the template group, a surgical stent was used to indicate the implant position with the pilot drill, the stent was then removed and further drilling was performed in the conventional way.

In this study,[50] the postoperative discomfort (Dutch version of the McGill Pain Questionnaire, the health-related quality of life instrument, visual analogue scales) was generally very low, with little difference between the different treatment groups. However, this finding is

in conflict with a recent systematic review,[6] but might be explained by the very low overall scores. There was a tendency for patients treated with conventional flapped implant placement to experience pain longer than those treated with the flapless guided approach. The mean marginal bone loss after the first year of loading was 0.04 mm (standard deviation [SD] = 0.34) for the guided surgery and 0.01 mm (SD = 0.38) for the control groups.[52] No significant difference in bone loss was observed between individual treatment groups, bone- and mucosa-supported guidance, or type of guidance. For all treatment groups, a significant improvement in quality of life (OHIP) was observed at 1-year follow-up ($P \leq .01$).

For this study, the authors performed a reanalysis comparing the data of the edentulous maxillae treated with guided surgery with the nonguided groups. A total of 208 implants were placed with a guide in 47 patients and 102 implants were placed in 24 patients with mental navigation or a pilot drill template. The mean marginal bone loss after the first year of loading in the maxilla was 0.06 mm for the guided surgery and –0.03 mm for the control group; in the mandible it was 0.03 for the guided group and 0.03 for the nonguided group. No differences were found between the guided and nonguided surgery in the maxilla with regard to the duration of the implant surgery, postoperative discomfort, and quality of life measurements.

Guided implant placement requires 3D imaging. In dental medicine, the latter is currently most often obtained using CBCT, because it is performed using a compact machine with a lower cost and lower radiation dose compared with multislice computed tomography (MSCT). The increased needs for 3D imaging when considering guided implant placement requires the proper justification of mechanisms. Table 5 summarizes guidelines and indications for cross-sectional imaging in the upper jaw, with CBCT being the preferred method for guided implant placement. If opting for CBCT on such occasions, it is obvious that the justification should meet the "as low as reasonably achievable" (ALARA) principle. Nowadays, CBCT may offer generally high-quality images at low radiation doses. Yet a wide variation in effective doses has been reported for different CBCT machines. Table 6 presents the published effective doses for panoramic and cephalometric imaging, MSCT, and CBCT, as measured in adults. Effective doses of CBCT may range from 11 to 1,073 μSv, depending on the machine used, the selected field of view and the parameter settings. This enormous dose range implies an equivalent dose of 1 to 107 panoramic radiographs. To obtain the lowest possible radiation exposure, it is important to reduce the field of view to the region of interest and to adjust the operating parameters (including exposure factors). At the same time, it should be realized that clinical MSCT may easily yield radiation doses up to 20 times higher than the lowest effective CBCT dose. In the vast majority of cases, CBCT is therefore preferred.

The justified use of CBCT for guided implant placement is not only related to the need for integrated 3D data, but also because of the crucial role of CBCT in visualizing critical anatomic structures. When implants are planned in the upper jaw, attention has to be paid to the maxillary sinus, the canalis sinuosus, and the nasopalatine canal. Through the canalis sinuosus, a clearly defined bony canal, palatal of the canine region, runs the anterior superior alveolar nerve supplying the incisors and the canines, as well as the adjacent soft tissues.[53,54] In a recent systematic review on the use of CBCT imaging in oral implantology, 24 articles were identified describing the critical anatomic structures on cross-sectional imaging in relation to implant placement, and 10 of these focused on the upper jaw.[52] Of these, six describe the maxillary sinus and four the nasopalatine canal.[55] Currently there are no articles describing the risks of canalis sinuosus involvement in relation to implant placement. Nevertheless, considering that all these nutrient canals have a clear neurovascular content, risks for neurovascular complications should always be taken into account.

Indeed, placement of dental implants is a relevant cause of iatrogenic nerve injuries. When analyzing data on neural injuries, the incidence of lingual nerve injury (mostly related to wisdom tooth surgery) appears to have remained stable over the last 30 years, while the incidence of inferior alveolar nerve injury (related to implant placement) has steadily increased.[56] To the best of the authors' knowledge, all articles up to date on neurosensory disturbances after implant placement relate to iatrogenic damage to the inferior alveolar nerve. For the maxillary nerve, no reports have been published on iatrogenic damage after implant placement. Renton and coworkers[57] described iatrogenic damage to the inferior alveolar nerve in 30 patients, of whom only 10% underwent preoperative CBCT.[57] All others had underwent 2D intraoral and panoramic imaging alone.[55,57] Interestingly, in three quarters of those patients with neurosensory disturbances caused by implant placement, nerve damage was of a permanent nature.[58] Thus the proportion of permanent nerve damage after implant placement seems to be much higher than in all other surgical procedures for iatrogenic injuries, with the majority being of a transient nature.[58] Only one article included in this systematic review pointed out a neurovascular problem. Di Giacomo and coworkers[34] mentioned that a patient complained of prolonged pain because of the proximity of the nasopalatine nerve. This implant was removed 1 week after installation.

Neurovascular complications of implant surgery can also result in severe intraoral hemorrhage. These are predominantly described after anterior mandibular implant placement (19 case reports available), but

significant bleeding may also be related to maxillary sinus augmentation (4 articles available).[59] Because of the location of different arterial structures in the lateral sinus wall, it is possible that bleeding complications occur during lateral window osteotomies. This concerns the anastomosis between the posterior superior alveolar artery and the infraorbital artery: the intraosseous artery and the extraosseous anastomosis.[60] Zijderveld and coworkers[61] revised 100 consecutive maxillary sinus floor elevation procedures and found a strong convexity of the lateral sinus wall in 6% of the patients. Hemorrhages were reported in 2% of cases, which were shown to be related to this anatomic constraint and to compromised visualization of the trapdoor preparation.[61]

CONCLUSIONS

Implants and prostheses placed in the edentulous maxilla with a static guide seem to have very good survival rates. Moreover, patients are satisfied with this treatment option. Most complications were found to be related to the surgery itself and the immediate loading protocol. Future research has to focus on comparing guided surgery with conventional nonguided open flap surgery, standardized protocols, the influence of smoking, and the cost-benefit ratio.

ACKNOWLEDGMENTS

All authors declare that they have no conflict of interest.

REFERENCES

1. Pjetursson BE, Brägger U, Lang NP, Zwahlen M. Comparison of survival and complication rates of tooth-supported fixed dental prostheses (FDPs) and implant-supported FDPs and single crowns (SCs). Clin Oral Implants Res 2007;18(3, suppl):97–113.
2. Jung RE, Pjetursson BE, Glauser R, Zembic A, Zwahlen M, Lang NP. A systematic review of the 5-year survival and complication rates of implant-supported single crowns. Clin Oral Implants Res 2008;19:119–130.
3. Jung RE, Schneider D, Ganeles J, et al. Computer technology applications in surgical implant dentistry: A systematic review. Int J Oral Maxillofac Implants 2009;24(suppl 1):92–109.
4. Tahmaseb A, Wismeijer D, Coucke W, Derksen W. Computer technology applications in surgical implant dentistry: A systematic review. Int J Oral Maxillofac Implants 2014;29(suppl 1):25–42.
5. Schneider D, Marquardt P, Zwahlen M, Jung RE. A systematic review on the accuracy and the clinical outcome of computer-guided template-based implant dentistry. Clin Oral Implants Res 2009;20(4, suppl):73–86.
6. Hultin M, Svensson KG, Trulsson M. Clinical advantages of computer-guided implant placement: A systematic review. Clin Oral Implants Res 2012;23(6, suppl):124–135.
7. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6(7):e1000097.
8. Randelzhofer P, de la Barrera JM, Spielberg M, Kurtz C, Strub JR. Three-dimensional navigation in oral implantology: A preliminary investigation. Int J Periodontics Restorative Dent 2001;21:617–626.
9. Katsoulis J, Pazera P, Mericske-Stern R. Prosthetically driven, computer-guided implant planning for the edentulous maxilla: A model study. Clin Implant Dent Relat Res 2009;11:238–245.
10. Nikzad S, Azari A. Computer-assisted implant surgery; a flapless surgical/immediate loaded approach with 1 year follow-up. Int J Med Robot Comput Assist Surg 2008;4:348–354.
11. Wittwer G, Adeyemo WL, Wagner A, Enislidis G. Computer-guided flapless placement and immediate loading of four conical screw-type implants in the edentulous mandible. Clin Oral Implants Res 2007;18:534–539.
12. Wittwer G, Adeyemo WL, Schicho K, Figl M, Enislidis G. Navigated flapless transmucosal implant placement in the mandible: A pilot study in 20 patients. Int J Oral Maxillofac Implants 2007;22:801–807.
13. Ersoy AE, Turkyilmaz I, Ozan O, McGlumphy EA. Reliability of implant placement with stereolithographic surgical guides generated from computed tomography: Clinical data from 94 implants. J Periodontol 2008;79:1339–1345.
14. Arısan V, Bölükbaşı N, Öksüz L. Computer-assisted flapless implant placement reduces the incidence of surgery-related bacteremia. Clin Oral Investig 2013;17:1985–1993.
15. Verhamme LM, Meijer GJ, Boumans T, de Haan AF, Bergé SJ, Maal TJ. A clinically relevant accuracy study of computer-planned implant placement in the edentulous maxilla using mucosa-supported surgical templates. Clin Implant Dent Relat Res 2013;17:343–352.
16. Nickenig HJ, Eitner S. Reliability of implant placement after virtual planning of implant positions using cone beam CT data and surgical (guide) templates. J Craniomaxillofac Surg 2007;35:207–211.
17. Berdougo M, Fortin T, Blanchet E, Isidori M, Bosson JL. Flapless implant surgery using an image-guided system. A 1- to 4-year retrospective multicenter comparative clinical study. Clin Implant Dent Relat Res 2010;12:142–152.
18. Danza M, Zollino I, Carinci F. Comparison between implants inserted with and without computer planning and custom model coordination. J Craniofac Surg 2009;20:1086–1092.
19. Danza M, Carinci F. Flapless surgery and immediately loaded implants: A retrospective comparison between implantation with and without computer-assisted planned surgical stent. Stomatologija 2010;12(2):35–41.
20. Vasak C, Watzak G, Gahleitner A, Strbac G, Schemper M, Zechner W. Computed tomography-based evaluation of template (NobelGuideTM)-guided implant positions: A prospective radiological study. Clin Oral Implants Res 2011;22:1157–1163.
21. Cassetta M, Stefanelli LV, Giansanti M, Di Mambro A, Calasso S. Depth deviation and occurrence of early surgical complications or unexpected events using a single stereolithographic surgi-guide. Int J Oral Maxillofac Surg 2011;40:1377–1387.
22. Landázuri-Del Barrio RA, Cosyn J, De Paula WN, De Bruyn H, Marcantonio E Jr. A prospective study on implants installed with flapless-guided surgery using the all-on-four concept in the mandible. Clin Oral Implants Res 2013;24:428–433.
23. Lee JH, Park JM, Kim SM, Kim MJ, Lee JH, Kim MJ. An assessment of template-guided implant surgery in terms of accuracy and related factors. J Adv Prosthodont 2013;5:440–447.
24. D'haese J, Vervaeke S, Verbanck N, De Bruyn H. Clinical and radiographic outcome of implants placed using stereolithographic guided surgery: A prospective monocenter study. Int J Oral Maxillofac Implants 2013;28:205–215.
25. Gillot L, Noharet R, Cannas B. Guided surgery and presurgical prosthesis: Preliminary results of 33 fully edentulous maxillae treated in accordance with the NobelGuide protocol. Clin Implant Dent Relat Res 2010;12(1, suppl):e104–e113.
26. Johansson B, Friberg B, Nilson H. Digitally planned, immediately loaded dental implants with prefabricated prostheses in the reconstruction of edentulous maxillae: A 1-year prospective, multicenter study. Clin Implant Dent Relat Res 2009;11:194–200.

27. Lindeboom JA, van Wijk AJ. A comparison of two implant techniques on patient-based outcome measures: A report of flapless vs. conventional flapped implant placement. Clin Oral Implants Res 2010;21:366–370.
28. Meloni SM, De Riu G, Pisano M, Cattina G, Tullio A. Implant treatment software planning and guided flapless surgery with immediate provisional prosthesis delivery in the fully edentulous maxilla. A retrospective analysis of 15 consecutively treated patients. Eur J Oral Implantol 2010;3:245–251.
29. Merli M, Bernardelli F, Esposito M. Computer-guided flapless placement of immediately loaded dental implants in the edentulous maxilla: A pilot prospective case series. Eur J Oral Implantol 2008;1:61–69.
30. Sanna AM, Molly L, van Steenberghe D. Immediately loaded CAD-CAM manufactured fixed complete dentures using flapless implant placement procedures: A cohort study of consecutive patients. J Prosthet Dent 2007;97:331–339.
31. Van Steenberghe D, Glauser R, Blombäck U, et al. A computed tomographic scan-derived customized surgical template and fixed prosthesis for flapless surgery and immediate loading of implants in fully edentulous maxillae: A prospective multicenter study. Clin Implant Dent Relat Res 2005;7(1, suppl):S111–S120.
32. Arisan V, Karabuda CZ, Ozdemir T. Implant surgery using bone- and mucosa-supported stereolithographic guides in totally edentulous jaws: Surgical and post-operative outcomes of computer-aided vs. standard techniques. Clin Oral Implants Res 2010;21:980–988.
33. Balshi SF, Wolfinger GJ, Balshi TJ. Guided implant placement and immediate prosthesis delivery using traditional Brånemark System abutments: A pilot study of 23 patients. Implant Dent 2008;17:128–135.
34. Di Giacomo GA, da Silva JV, da Silva AM, Paschoal GH, Cury PR, Szarf G. Accuracy and complications of computer-designed selective laser sintering surgical guides for flapless dental implant placement and immediate definitive prosthesis installation. J Periodontol 2012;83:410–419.
35. Komiyama A, Hultin M, Näsström K, Benchimol D, Klinge B. Soft tissue conditions and marginal bone changes around immediately loaded implants inserted in edentate jaws following computer guided treatment planning and flapless surgery: A ≥1-year clinical follow-up study. Clin Implant Dent Relat Res 2012;14:157–169.
36. Komiyama A, Klinge B, Hultin M. Treatment outcome of immediately loaded implants installed in edentulous jaws following computer-assisted virtual treatment planning and flapless surgery. Clin Oral Implants Res 2008;19:677–685.
37. Lal K, Eisig SB, Fine JB, Papaspyridakos P. Prosthetic outcomes and survival rates of implants placed with guided flapless surgery using stereolithographic templates: A retrospective study. Int J Periodontics Restorative Dent 2013;33:661–667.
38. Malo P, de Araujo Nobre M, Lopes A. The use of computer-guided flapless implant surgery and four implants placed in immediate function to support a fixed denture: Preliminary results after a mean follow-up period of thirteen months. J Prosthet Dent 2007;97(6, suppl):S26–S34.
39. Marra R, Acocella A, Rispoli A, Sacco R, Ganz SD, Blasi A. Full-mouth rehabilitation with immediate loading of implants inserted with computer-guided flap-less surgery: A 3-year multicenter clinical evaluation with oral health impact profile. Implant Dent 2013;22:444–452.
40. Meloni SM, De Riu G, Pisano M, Tullio A. Full arch restoration with computer-assisted implant surgery and immediate loading in edentulous ridges with dental fresh extraction sockets. One year results of 10 consecutively treated patients: Guided implant surgery and extraction sockets. J Maxillofac Oral Surg 2013;12:321–325.
41. Pomares C, Pomares Puig C. A retrospective study of edentulous patients rehabilitated according to the "all-on-four" or the "all-on-six" immediate function concept using flapless computer-guided implant surgery. Eur J Oral Implantol 2010;3:155–163.
42. Pozzi A, Holst S, Fabbri G, Tallarico M. Clinical reliability of CAD/CAM cross-arch zirconia bridges on immediately loaded implants placed with computer-assisted/template-guided surgery: A retrospective study with a follow-up between 3 and 5 years. Clin Implant Dent Relat Res 2013;17(1, suppl):e86–e96.
43. Tahmaseb A, De Clerck R, Aartman I, Wismeijer D. Digital protocol for reference-based guided surgery and immediate loading: A prospective clinical study. Int J Oral Maxillofac Implants 2012;27:1258–1270.
44. Lambert FE, Weber HP, Susarla SM, Belser UC, Gallucci GO. Descriptive analysis of implant and prosthodontic survival rates with fixed implant-supported rehabilitations in the edentulous maxilla. J Periodontol 2009;80:1220–1230.
45. Heitz-Mayfield LJ, Huynh-Ba G. History of treated periodontitis and smoking as risks for implant therapy. Int J Oral Maxillofac Implants 2009;24(suppl 1):39–68.
46. Klokkevold PR, Han TJ. How do smoking, diabetes, and periodontitis affect outcomes of implant treatment? Int J Oral Maxillofac Implants 2007;22(suppl 1):173–202.
47. Campelo LD, Camara JR. Flapless implant surgery: A 10-year clinical retrospective analysis. Int J Oral Maxillofac Implants 2002;17:271–276.
48. Fortin T, Bosson JL, Isidori M, Blanchet E. Effect of flapless surgery on pain experienced in implant placement using an image-guided system. Int J Oral Maxillofac Implants 2006;21:298–304.
49. Nkenke E, Eitner S, Radespiel-Tröger M, Vairaktaris E, Neukam FW, Fenner M. Patient-centred outcomes comparing transmucosal implant placement with an open approach in the maxilla: A prospective, non-randomized pilot study. Clin Oral Implants Res 2007;18:197–203.
50. Vercruyssen M, De Laat A, Coucke W, Quirynen M. An RCT comparing patient-centred outcome variables of guided surgery (bone or mucosa supported) with conventional implant placement. J Clin Periodontol 2014;41:724–732.
51. Vercruyssen M, Cox C, Coucke W, Naert I, Jacobs R, Quirynen M. A randomized clinical trial comparing guided implant surgery (bone- or mucosa-supported) with mental navigation or the use of a pilot-drill template. J Clin Periodontol 2014;41:717–723.
52. Vercruyssen M, van de Wiele G, Teughels W, Naert I, Jacobs R, Quirynen M. Implant and patient-centered outcome of guided surgery, a 1-year follow-up. An RCT comparing guided surgery with conventional implant placement. J Clin Periodontol 2014;41:1154–1160.
53. De Oliveira-Santos C, Rubira-Bullen IRF, Monteiro SA, León JE, Jacobs R. Neurovascular anatomical variations in the anterior palate observed on CBCT images. Clin Oral Implants Res 2013;24:1044–1048.
54. Von Arx T, Lozanoff S, Sendi P, Bornstein MM. Assessment of bone channels other than the nasopalatine canal in the anterior maxilla using limited cone beam computed tomography. Surg Radiol Anat 2013;35:783–790.
55. Bornstein MM, Scarfe WC, Vaughn VM, Jacobs R. Cone beam computed tomography in implant dentistry: A systematic review focusing on guidelines, indications, and radiation dose risks. Int J Oral Maxillofac Implants 2014;29(l, suppl 1):55–77.
56. Renton T, Yilmaz Z. Profiling of patients presenting with post-traumatic neuropathy of the trigeminal nerve. J Orofac Pain 2011;25:333–344.
57. Renton T, Dawood A, Shah A, Searson L, Yilmaz Z. Post-implant neuropathy of the trigeminal nerve. A case series. Br Dent J 2012;212:E17.
58. Libersa P, Savignat M, Tonnel A. Neurosensory disturbances of the inferior alveolar nerve: A retrospective study of complaints in a 10-year period. J Oral Maxillofac Surg 2007;65:1486–1489.
59. Jacobs R, Quirynen M, Bornstein MM. Neurovascular disturbances after implant surgery. Periodontol 2000 2014;66:188–202.
60. Solar P, Geyerhofer U, Traxler H, Windisch A, Ulm C, Watzek G. Blood supply to the maxillary sinus relevant to sinus floor elevation procedures. Clin Oral Implants Res 1999;10:34–44.
61. Zijderveld SA, van den Bergh JPA, Schulten EA, ten Bruggenkate CM. Anatomical and surgical findings and complications in 100 consecutive maxillary sinus floor elevation procedures. J Oral Maxillofac Surg 2008;66:1426–1438.
62. Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): A patient-centered approach to grading evidence in the medical literature. J Am Board Fam Pract 2004;17:59–67.

Clinical Practice Guidelines: Role of Imaging to Guide Implant Placement in the Edentulous Maxilla

INTRODUCTION

Patients with an edentulous maxilla receive implants to support fixed or removable prostheses. Accurate implant positioning and distribution of forces may affect implant survival, implant complications, and prosthetic complications in straightforward and more complex situations. Use of computer-generated, static guides with an advanced method of diagnosis, planning, and guided implant placement may be used to improve care logistics, placement accuracy, and predict definitive implant position[1–4] for implant and prosthetic outcomes and patient satisfaction.

PURPOSE

Based upon maxillary edentulous patient presentation, prosthetic design, and desired implant position, clinicians prescribe the radiographic assessment that supports the selection of surgical guide design. A systematic review (Laleman et al) was developed to report the outcomes of computer-assisted guided surgery using static guides for maxillary edentulous patients.

HEALTH CARE BURDEN

Definitive therapy with implants for the edentulous maxilla has incidence of failure and complications at implant and prosthesis levels. Depending on patient presentation and prosthesis design, a significant proportion of patients develop complications during therapy and following prosthesis insertion.[5–7] The use of computer-generated guided surgery with static guides may decrease this burden.

METHODS

Search of primary references was conducted through PubMed MEDLINE, EMBASE, and Cochrane databases using pertinent search terms. Hand search of these selected papers and previous systematic reviews was completed. SORT criteria determined strength of the available evidence relating to the CPGs.

doi: 10.11607/jomi.16suppl.g3.cpg

KEY ACTION STATEMENT

When considering static guided surgery for the edentulous maxilla, advanced imaging (cross-sectional imaging, computed tomography [CT], cone beam computed tomography [CBCT]) is performed following pertinent guidelines[8–12] and ALARA principles.

1. All acquired radiographic volumetric datasets must be evaluated for pathosis and anatomical constraints. Referral to a person who is trained in advanced interpretation techniques in radiology may be necessary.
2. Computer-generated static guides may enhance the communication within the clinical team.
3. Competent clinical application of guided surgery should depend upon the design and fabrication of computer-generated static guides based on effective clinician diagnosis, and clinical prosthetic planning with a scanning template when appropriate. For implant placement accuracy, clinicians must have competence in guide workflow with understanding of sources of error.
4. A computer-generated static surgical guide (bone supported or soft tissue supported) may lead to prosthetic and implant survival and success, and patient satisfaction (Laleman et al).

IMPLEMENTATION BARRIERS

Three-dimensional printed guides could contribute to improved clinical outcomes. Outcomes from selection of such guides are clinician decision–dependent. Guide use is dependent upon the confidence in related technology as applied by the clinician. Market penetration for the computer-generated, guided surgery approach is limited.

ACKNOWLEDGMENTS

Funding was received from corporate sponsors through the Academy of Osseointegration. Group members have associations with computer-assisted static surgical guide manufacturers.

REFERENCES

1. Hämmerle CH, Cordaro L, van Assche N, et al. Digital technologies to support planning, treatment, and fabrication processes and outcome assessments in implant dentistry. Summary and consensus statements. The 4th EAO consensus conference 2015. Clin Oral Implants Res 2015;26(suppl 11):97–101.
2. Vercruyssen M, Cox C, Coucke W, Naert I, Jacobs R, Quirynen M. An RCT comparing guided implant surgery (bone or mucosa supported) with mental navigation or the use of pilot-drill template. J Clin Periodontol 2014;41:717–723.
3. Vercruyssen M, De Laat A, Coucke W, Quirynen M. An RCT comparing patient centered outcome variables of guided surgery (bone or mucosa supported) with conventional implant placement. J Clin Periodontol 2014;41:724–732.
4. Vercruyssen M, Coucke W, Naert I, Jacobs R, Quirynen M. Depth and lateral deviations in guided implant surgery: An RCT comparing guided surgery with mental navigation or the use of a pilot-drill template. Clin Oral Implants Res 2015;26:1315–1320. 8.
5. Bryant SR, MacDonald-Jankowski D, Kim K. Does the type of implant prosthesis affect outcomes for the completely edentulous arch? Int J Oral Maxillofac Implants 2007;22(suppl):117–139.
6. Papaspyridakos P, Chen C, Chuang S, Weber HP. Implant loading protocols for edentulous Patients with Fixed Prostheses: A systematic review and meta-analysis. Int J Oral Maxillofac Implants 2014;29(suppl):256–270.
7. Raghoebar GM, Meijer HJ, Slot W, Slater JJ, Vissink A. A systematic review of implant-supported overdentures in the edentulous maxilla, compared to the mandible: How many implants? Eur J Oral Implantol 2014;7(suppl 2):S191–S201.
8. Academy of Osseointegration. 2010 Guidelines of the Academy of Osseointegration for the Provision of Dental Implants and Associated Patient Care. Int J Oral Maxillofac Implants 2010;25:620–627.
9. Bornstein MM, Al-Nawas B, Kuchler U, Tahmaseb A. Consensus statements and recommended clinical procedures regarding contemporary surgical and radiographic techniques in implant dentistry. Int J Oral Maxillofac Implants 2014;29(suppl):78–82.
10. Bornstein M, Scarfe WC, Vaughn VM, Jacobs R. Cone beam computed tomography in implant dentistry. A systematic review focusing on guidelines, indications and radiation dose risks. Int J Oral Maxillofac Implants 2014;29(suppl):55–77.
11. Harris D, Horner K, Grondahl K, Jacobs R, et al. E.A.O. guidelines for the use of diagnostic imaging in implant dentistry 2011. A consensus workshop organized by the European Association for Osseointegration at the Medical University of Warsaw Clin Oral Implants Res 2012;23:1243–1253.
12. Tyndall DA, Price JB, Teradis S, Ganz SD, Hildebolt C, Scarfe W. Position statement of the American Academy of Oral and Maxillofacial Radiology on selection criteria for the use of radiology in dental implantology with emphasis on cone beam computed tomography. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113:817–826.

Role of Biologics to Assist in Ridge Development

Group Co-Chairs

Gustavo Avila-Ortiz, DDS, MS, PhD
Daniel Spagnoli, DDS, PhD

Group Participants

P. Mark Bartold, DDS, PhD
Rolf Ewers, MD, DMD, PhD
William Giannobile, DDS, MS, DMSc
Alan Herford, DDS, MD
Wataru Katagiri, DDS, PhD
Salvador Nares, DDS
Marc Nevins, DMD, MMSc
Hector Rios, DDS
Anton Sculean, DMD, MS, PhD
Gilbert Triplett, DDS, PhD
Ulf Wikesjö, DDS, DMD, PhD
Mark Wong, DDS
Yuval Zubery, DMD

Biologics and Cell Therapy Tissue Engineering Approaches for the Management of the Edentulous Maxilla: A Systematic Review

Gustavo Avila-Ortiz, DDS, MS, PhD[1]/P. Mark Bartold, DDS, PhD[2]/
William Giannobile, DDS, MS, DMSc[3]/Wataru Katagiri, DDS[4]/Salvador Nares, DDS, PhD[5]/
Hector Rios, DDS, PhD[6]/Daniel Spagnoli, DDS, MS, PhD[7]/Ulf M.E. Wikesjö, DDS, DMD, PhD[8]

Purpose: *The aim of this systematic review was to evaluate current and emerging regenerative approaches for implant site development in the edentulous atrophic maxilla using tissue engineering and regenerative medicine (TERM) principles and to identify priorities for future research.* ***Materials and Methods:*** *Two independent examiners conducted a comprehensive search using specific keywords to identify original clinical studies using TERM for implant site development in the edentulous atrophic maxilla including indications for alveolar ridge preservation, horizontal alveolar augmentation, maxillary sinus augmentation, and augmentation of severe vertical or combined defects. Endpoints included clinical, radiographic, histologic, and patient-centered outcomes.* ***Results:*** *The initial search identified 3,061 articles. The final selection included 89 articles, of which 12 evaluated alveolar ridge preservation, 6 horizontal defects, 61 maxillary sinus augmentation, and 11 management of severe vertical or combined defects. A summary of the main findings relative to the effect of TERM-based approaches applied for implant site development in the atrophic maxillary segments is presented. Marked heterogeneity among included studies prevented meaningful quantitative analysis. The following relevant effects of TERM-based therapies for site development in the edentulous atrophic maxilla were observed:* (1) *recombinant human bone morphogenetic protein-2 in an absorbable collagen sponge carrier increased bone augmentation;* (2) *recombinant human platelet-derived growth factor BB in combination with freeze-dried bone allograft or beta tricalcium phosphate accelerated bone formation through accelerated remodeling of carrier biomaterials;* (3) *autologous cell therapy enhanced clinical and radiographic outcomes;* (4) *autologous cell therapy in alveolar ridge preservation provided superior histomorphometric outcomes (vital bone formation) at 6 weeks; and* (5) *platelet-rich plasma formulations combined with autologous bone grafts for maxillary sinus augmentation increased radiographic density and accelerated bone mineralization at 6 months.* ***Conclusion:*** *Clinical success has been demonstrated with the application of different TERM modalities for implant site development in the edentulous atrophic maxilla. However, indications are narrow and further study is needed. Clinical trials assessing meaningful outcomes, involving larger populations, and with longer follow-up are warranted to discern the effectiveness of the achieved results compared with a valid control.* Int J Oral Maxillofac Implants 2016;31(suppl):s121–s164. doi: 10.11607/jomi.16suppl.g4

Keywords: *atrophic maxillae, biological agents, cell- and tissue-based therapy, dental implants, implant-supported dental prosthesis, tissue engineering*

Prosthetic rehabilitation of the completely or partially edentulous atrophic maxilla often meets considerable clinical, technical, and biologic challenges. Alveolar ridge aberrations as a sequel to bone loss/remodeling after tooth extractions, periodontal disease, resective surgery, trauma, and/or congenital conditions commonly require augmentation to allow implant-supported prosthetic rehabilitation. Thus, access flap

[1]Associate Professor, Department of Periodontics, University of Iowa, Iowa City, Iowa, USA.
[2]Director, Colgate Dental Research Centre, University of Adelaide, Adelaide, Australia.
[3]Professor and Chair, Department of Periodontics, University of Michigan, Ann Arbor, Michigan, USA.
[4]Assistant Professor, Maxillofacial Surgery and Sensory Organ Medicine, Graduate School of Medicine, Nagoya University, Nagoya, Japan.
[5]Associate Professor and Chair, Department of Periodontics, University of Illinois at Chicago, Chicago, Illinois, USA.

[6]Assistant Professor, Department of Periodontics and Oral Medicine, University of Michigan, Ann Arbor, Michigan, USA.
[7]Associate Professor, Department of Oral and Maxillofacial Surgery, Louisiana State University, New Orleans, Louisiana, USA.
[8]Interim Associate Dean for Research and Enterprise, Professor, Department of Periodontics, Georgia Regents University, Augusta, Georgia, USA.

Correspondence to: Dr Gustavo Avila-Ortiz, Assistant Professor, Department of Periodontics, The University of Iowa, 801 Newton Rd, Iowa City, IA 52242.
Email: gustavo-avila@uiowa.edu.

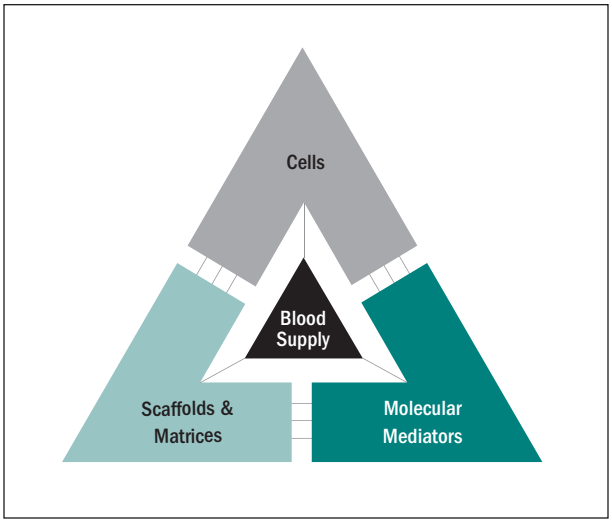


Fig 1 Four essential requirements for successful tissue engineering are a suitable source of cells, a biologically acceptable scaffold, appropriate molecular mediators, and the induction of an adequate blood supply.

procedures for horizontal and/or vertical alveolar ridge augmentation,[1,2] as well as modified Caldwell-Luc and transalveolar osteotomy protocols to augment the subantral space,[3,4] combined with implantable autogenous bone preparations, cadaver-sourced (allogeneic or xenogeneic) or synthetic (alloplastic) biomaterials, and devices for guided tissue/bone regeneration (GBR), have been used as stand-alone therapies or in combination protocols. The immediate past decades have witnessed the beginnings of a paradigm shift in implant dentistry, adopting concepts from regenerative medicine for bioengineering with the expectation of a more predictable, strategic, and idealized soft and hard tissue reconstruction. Thus, after rigorous preclinical and clinical evaluation, tissue engineering has become an emerging reality in clinical dentistry. Nevertheless, in spite of the expected therapeutic potential, questions and concerns regarding efficacy and effectiveness remain unanswered. This review focuses on presenting and analyzing the evidence on the effect of current and emerging strategies for maxillary ridge reconstruction to facilitate dental implant placement.

There are several potential tissue engineering approaches for repair or regeneration of alveolar bone to enable implant placement.[5,6] These essentially include the use of scaffolding matrices, cell therapies, and biologics/growth factors, to prevent alveolar bone resorption and/or to augment alveolar bone and/or soft tissues (Fig 1). The largest body of evidence concerns the use of bone biomaterials including cadaver-sourced, xenogeneic, and synthetic biomaterials for localized bone augmentation. These biomaterials generally serve as biologically inactive matrices allowing cell ingrowth from adjoining tissue resources; thus, they mostly express the osteogenic potential of the site (Table 1). There is a significant body of biologic evidence documenting the limited effectiveness of these biomaterials as stand-alone therapeutics and when combined with guided tissue regeneration and GBR.

The use of cell therapy has been recently explored for the potential of enhancing bone regeneration in a more robust manner over the relatively inactive bone biomaterials.[7] Cell-rich bone autografts or cells harvested from extraoral and intraoral locations have demonstrated potential to enrich constructs that may more effectively regenerate the alveolar bone using several modes of application.[8,9] Cell procurement methods are heterogeneous and range from simple cell harvests and delivery to enrichment of adult mesenchymal stem cell populations constituting a potentially highly regenerative milieu.

Another emerging area of bone regenerative agents under intense investigation includes biologically active agents. The most well-documented biologics/growth factors applied in maxillofacial settings include bone morphogenetic proteins (BMP-2 and -7),[10–12] platelet-derived growth factor (PDGF),[13] fibroblast growth factor-2 (FGF-2),[14] and growth and differentiation factor-5 (GDF-5).[15] These growth factors have been carefully evaluated in preclinical and clinical studies for various indications including extraction sockets, horizontal/vertical alveolar ridge augmentation, and sinus floor augmentation[16,17] or delivered from implant surfaces.[18] These agents work through various mechanisms to promote tissue regeneration, including the promotion of cell differentiation, mitogenesis, and matrix biosynthesis via specific induction of cell-receptor–mediated signal transduction pathways. The use of autologous blood–derived products, such as platelet-rich gels or platelet-rich plasma (PRP), is conceptually of interest for the enrichment of constructs with naturally derived platelet contents including PDGF and transforming growth factor beta (TGF-β) and epidermal growth factor (EGF). In spite of reported equivocal results for bone regeneration in association with PRP,[19] the literature pertinent to its application in the clinical settings contemplated in this review will be evaluated.

The aim of this systematic review was to identify and analyze the available evidence on current and emerging regenerative approaches based on tissue engineering for implant site development in atrophic maxillary segments, with special emphasis on the outcomes of these therapies. This systematic review served as a conduit to develop specific clinical practice guidelines in the context of the Academy of Osseointegration (AO) 2014 Summit on "Current Best Evidence for Management of the Edentulous Maxilla."

MATERIALS AND METHODS

This systematic review follows the guidelines of the Preferred Reporting of Systematic Reviews and Meta-analyses (PRISMA) statement.[20]

PICO Question (Population, Intervention, Comparison, Outcome/s)

"In human subjects who desire an implant-supported prosthesis and are in need of bone and/or soft tissue augmentation because of maxillary atrophy, what is the effect of tissue engineering–based therapies compared with conventional site development approaches considering clinical, radiographic, histologic, and patient-centered outcomes?"

Clinical Scenarios and Consideration of Treatment Options

In this review, the clinical scenarios of interest were: horizontal, vertical, or combined hard or soft tissue defects that require implant site development before implant placement, including alveolar ridge preservation at the time of tooth extraction (ie, socket defect). The proposed continuum of clinical complexity and commonly indicated therapies for the treatment of these scenarios are displayed in Fig 2.

Outcomes of Interest

Various outcomes of interest were considered in the context of this review, including (but not limited to):

1. Clinical: Incidence of complications, dimensional changes of the ridge, implant primary stability, need for additional grafting at the time of implant placement, implant survival, and success rate
2. Radiographic: Marginal bone loss around implants and dimensional (linear or volumetric) and densitometry changes of the grafted area
3. Histologic: Evidence of bone formation, characteristics of the tissues, and proportion of different tissue compartments
4. Patient-centered: Safety, perceived benefit, and changes in quality of life

Literature Search Protocol

Six electronic databases were searched for relevant articles in the context of this systematic review: National Library of Medicine (MEDLINE–PubMed), Web of Knowledge, Scopus, Embase, Cochran Library/Wiley, and ProQuest Dissertations and Theses (in an attempt to capture gray literature). No limits were set on the language of the article, publication date, or status to conduct as comprehensive a search as possible. The last search was conducted on March 17, 2014. The terms and strategy used to search each individual database are displayed in Tables 2 through 7. To complement the database search, cited references were also searched.

Table 1 Scaffolds and Matrices Used for Tissue Engineering Applications to Treat Craniofacial Defects*

Scaffold Origin	Biomaterial	Components
Naturally derived	Allografts	FDBA/DFDBA
	Xenografts	Bovine mineral matrix, bovine-derived HA, bovine inorganic bone material
	Collagen	Sponge
		Membrane
		Gel/gelatin
Synthetic/ alloplasts	Polymers	PLLA
		PGA
		PLGA (copolymer of PLLA and PGA)
	CaP-based ceramics	βTCP/CaP cement
	Hydroxyapatite-based scaffolds	Dense HA, porous HA, absorbable HA, nonporous nonabsorbable granular HA
	Hydrogels	HA ester
		Methylcellulose
		Coralline calcium carbonate ester

*Adapted from Rios et al (2011). Reproduced with permission from the American Academy of Periodontology
FDBA = freeze-dried bone allograft; DFDBA = demineralized freeze-dried bone allograft; HA = hydroxyapatite; PLLA = polylactic acid; βTCP = beta tricalcium phosphate; CaP= calcium phosphate.

Article Eligibility Criteria

Articles reporting original studies (ie, randomized controlled trials [RCTs], clinical trials, cohort studies, case series, and case reports) that recruited human adult patients who received implant site development in atrophic maxillae (fully or partially edentulous) via tissue engineering approaches were eligible. Tissue engineering approaches were defined as "therapies that involve the application of at least one of the following elements: cell therapy and molecular mediators (eg, growth factors, bone morphogenetic proteins, biomimetic peptides, etc…), with or without scaffolds or matrices."

Descriptive reviews and editorials were not included. In addition, included studies must have reported at least one outcome of interest (ie, clinical, radiographic, histologic, or patient-centered outcomes). With the ultimate purpose of being inclusive and to perform a comprehensive review, no minimum follow-up time was established because of the heterogeneity of therapeutic approaches and protocols historically reported in this field. Specifically for clinical trials, studies must have at least one surgical

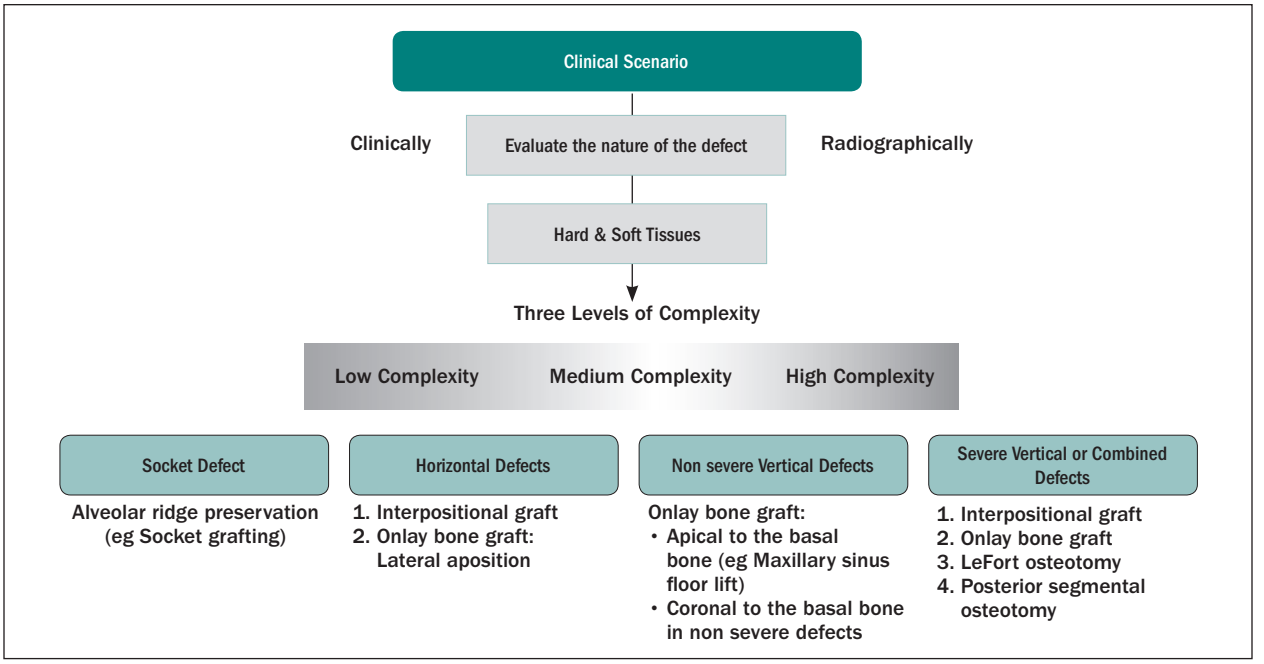


Fig 2 Diagram representing the clinical scenarios and commonly associated therapies considered in this systematic review.

Table 2 Terms and Strategy Used to Search PubMed

Search No.	Search Parameters	Results
1	"tissue engineering" OR "regenerative medicine" OR Bone Tissue Engineering OR Tissue engineering OR Tissue culture OR Regenerative medicine OR Tissue Engineering Constructs OR Microencapsulation OR "bone transplantation" OR Bone Grafting OR Bone Augmentation OR bone transplantation	365,570
2	Search Intracellular Signaling Peptides and Proteins OR TGF-beta Superfamily Proteins OR Transforming growth factors OR Transforming growth factor beta OR Transforming growth factor beta1 OR Transforming growth factor beta2 OR Transforming growth factor beta3 OR Bone Morphogenetic Proteins OR Bone Morphogenetic Protein 1 OR Bone Morphogenetic Protein 15 OR Bone Morphogenetic Protein 2 OR Bone Morphogenetic Protein 3 OR Bone Morphogenetic Protein 4 OR Bone Morphogenetic Protein 5 OR Bone Morphogenetic Protein 6 OR Bone Morphogenetic Protein 7 OR Growth Differentiation Factor 10 OR Growth Differentiation Factor 2 OR Growth Differentiation Factors OR Bone Morphogenetic Protein 15 OR Growth Differentiation Factor 1 OR Growth Differentiation Factor 10 OR Growth Differentiation Factor 15 OR Growth Differentiation Factor 2 OR Growth Differentiation Factor 3 OR Growth Differentiation Factor 5 OR Growth Differentiation Factor 6 OR Growth Differentiation Factor 9 OR Myostatin OR Platelet-Derived Growth Factor OR Growth Substances OR Vascular Endothelial Growth Factors OR Vascular Endothelial Growth Factor A OR Vascular Endothelial Growth Factor B OR Vascular Endothelial Growth Factor C OR Vascular Endothelial Growth Factor D OR Vascular Endothelial Growth Factor, Endocrine-Gland-Derived OR Paracrine Peptide Factors OR Growth Factors OR TGF beta Superfamily Proteins OR Transforming Growth Factor beta Superfamily Proteins OR TGF B OR Transforming growth factors OR Transforming growth factor beta OR BMP OR Bone Morphogenetic Protein OR rhBMP-2 OR recombinant human bone morphogenetic protein-2 OR RhBMP-7 OR RHOP-1 OR rhoptry associated protein OR Growth Differentiation Factor OR GDF OR Platelet-Derived Growth Factor OR PDGF-A protein OR PDGF OR PDGFA protein OR PDGF1 protein OR DGF A-chain protein OR platelet-derived growth factor alpha polypeptide OR Platelet-Derived Growth Factor OR Growth Substances OR Endogenous Mitogens OR VEGF* OR Vascular Endothelial Growth Factor* OR Stem Cells OR Adult Stem Cells OR Induced Pluripotent Stem Cells OR Stem Cell* OR Adult Stem Cell* OR Induced Pluripotent Stem Cell* OR iPSC OR IPS Cells OR IPS Cell OR Fibroblast-Derived Induced Pluripotent Stem Cells OR Fibroblast Derived Induced Pluripotent Stem Cells OR Fibroblast-Derived IPS Cells OR Fibroblast Derived IPS Cells OR Fibroblast-Derived IPS Cell OR Novel Scaffolds OR Autologous Osteoblasts OR Polymeric Scaffolds OR Mechanotransduction, Cellular OR Mechanical Signal Transduction OR Mechanosensory Transduction OR Cellular Mechanotransduction OR SOSTDC1 protein OR USAG-1 protein OR sclerostin domain containing 1 protein OR sclerostin OR ectodin protein OR hect protein OR Platelet-Rich Plasma OR Platelet Rich Plasma	2,176,123
3	"osseointegration" OR "dental implantation, endosseous" OR Endosseous Dental Implantation OR Endosseous Implantation OR Osseointegrated Dental Implantation OR Osseointegrated Implantation OR Endosseous Implants OR Osseointegrated Implants OR Osseointegrated Dental Implants OR Endosseous Dental Implants	20,311

Table 2 *Continued* **Terms and Strategy Used to Search PubMed**

Search No.	Search Parameters	Results
4	(Jaw, Edentulous AND Maxilla) OR Edentulous Maxilla OR ((Edentulous Ridge OR Edentulous Jaw OR Alveolar Bone Loss OR Alveolar Bone Loss OR Alveolar Ridge Augmentation OR Alveolar Ridge Augmentation) AND (Maxillae OR Maxilla OR Maxillary))	5,531
5	#1 AND #2 AND #3 AND #4 ((((“tissue engineering” OR “regenerative medicine” OR Bone Tissue Engineering OR Tissue engineering OR Tissue culture OR Regenerative medicine OR Tissue Engineering Constructs OR Microencapsulation OR “bone transplantation” OR Bone Grafting OR Bone Augmentation OR bone transplantation)) AND (Intracellular Signaling Peptides and Proteins OR TGF-beta Superfamily Proteins OR Transforming growth factors OR Transforming growth factor beta OR Transforming growth factor beta1 OR Transforming growth factor beta2 OR Transforming growth factor beta3 OR Bone Morphogenetic Proteins OR Bone Morphogenetic Protein 1 OR Bone Morphogenetic Protein 15 OR Bone Morphogenetic Protein 2 OR Bone Morphogenetic Protein 3 OR Bone Morphogenetic Protein 4 OR Bone Morphogenetic Protein 5 OR Bone Morphogenetic Protein 6 OR Bone Morphogenetic Protein 7 OR Growth Differentiation Factor 10 OR Growth Differentiation Factor 2 OR Growth Differentiation Factors OR Bone Morphogenetic Protein 15 OR Growth Differentiation Factor 1 OR Growth Differentiation Factor 10 OR Growth Differentiation Factor 15 OR Growth Differentiation Factor 2 OR Growth Differentiation Factor 3 OR Growth Differentiation Factor 5 OR Growth Differentiation Factor 6 OR Growth Differentiation Factor 9 OR Myostatin OR Platelet-Derived Growth Factor OR Growth Substances OR Vascular Endothelial Growth Factors OR Vascular Endothelial Growth Factor A OR Vascular Endothelial Growth Factor B OR Vascular Endothelial Growth Factor C OR Vascular Endothelial Growth Factor D OR Vascular Endothelial Growth Factor, Endocrine-Gland-Derived OR Paracrine Peptide Factors OR Growth Factors OR TGF beta Superfamily Proteins OR Transforming Growth Factor beta Superfamily Proteins OR TGF B OR Transforming growth factors OR Transforming growth factor beta OR BMP OR Bone Morphogenetic Protein OR rhBMP-2 OR recombinant human bone morphogenetic protein-2 OR RhBMP-7 OR RHOP-1 OR rhoptry associated protein OR Growth Differentiation Factor OR GDF OR Platelet-Derived Growth Factor OR PDGF-A protein OR PDGF OR PDGFA protein OR PDGF1 protein OR DGF A-chain protein OR platelet-derived growth factor alpha polypeptide OR Platelet-Derived Growth Factor OR Growth Substances OR Endogenous Mitogens OR VEGF* OR Vascular Endothelial Growth Factor* OR Stem Cells OR Adult Stem Cells OR Induced Pluripotent Stem Cells OR Stem Cell* OR Adult Stem Cell* OR Induced Pluripotent Stem Cell* OR iPSC OR IPS Cells OR IPS Cell OR Fibroblast-Derived Induced Pluripotent Stem Cells OR Fibroblast Derived Induced Pluripotent Stem Cells OR Fibroblast-Derived IPS Cells OR Fibroblast Derived IPS Cells OR Fibroblast-Derived IPS Cell OR Novel Scaffolds OR Autologous Osteoblasts OR Polymeric Scaffolds OR Mechanotransduction, Cellular OR Mechanical Signal Transduction OR Mechanosensory Transduction OR Cellular Mechanotransduction OR SOSTDC1 protein OR USAG-1 protein OR sclerostin domain containing 1 protein OR sclerostin OR ectodin protein OR hect protein OR Platelet-Rich Plasma OR Platelet Rich Plasma)) AND (“osseointegration” OR “dental implantation, endosseous” OR Endosseous Dental Implantation OR Endosseous Implantation OR Osseointegrated Dental Implantation OR Osseointegrated Implantation OR Endosseous Implants OR Osseointegrated Implants OR Osseointegrated Dental Implants OR Endosseous Dental Implants)) AND ((Jaw, Edentulous AND Maxilla) OR Edentulous Maxilla OR ((Edentulous Ridge OR Edentulous Jaw OR Alveolar Bone Loss OR Alveolar Bone Loss OR Alveolar Ridge Augmentation OR Alveolar Ridge Augmentation) AND (Maxillae OR Maxilla OR Maxillary)))	98

control group and one surgical experimental group that involved the application of a tissue engineering regenerative approach. For study series that used the same population, only the study with the longest follow-up was included. Finally, articles for which full-text versions could not be found by the library services of Louisiana State University or the University of Iowa were excluded.

Article Selection and Data Extraction

Two reviewers (G.A. and H.R.) independently read the title and abstract of the entries yielded by the initial electronic database search. After this initial assessment, both reviewers separately read the full-text versions of the studies that could be potentially included in this review. A final selection of articles was made on the basis of the aforementioned eligibility criteria. Any disagreement in the final selection was resolved by open discussion between reviewers. In case no agreement could be reached, another coauthor (D.S.) was designated as the arbiter. One reviewer (G.A.) extracted the data of the studies in the final selection, including: year of publication and first author, tissue engineering approach(es) used, study design, description of a priori eligibility criteria, number of patients enrolled and sites treated, type of maxillary edentulism (ie, complete or partial), number of groups and interventions in each group (if applicable), description of randomization (only for clinical trials), blind/masked assessment of outcomes, outcome measures (ie, clinical, radiographic, histologic, and/or patient-centered), healing period before reopening, whether implants were placed or not and their number (if reported), total study follow-up time, number of dropouts (if applicable), summary of the main findings, and level of evidence for each individual study.

Table 3 Terms and Strategy Used to Search Web of Knowledge

Search No.	Search Parameters	Results
1	(tissue engineering OR regenerative medicine OR bone tissue engineering OR tissue engineering OR tissue culture OR regenerative medicine OR tissue engineering constructs OR microencapsulation OR bone transplantation OR bone grafting OR bone augmentation OR bone transplantation)	267,276
2	(gdf OR Platelet Derived Growth Factor OR pdgf OR PDGFA protein OR DGF A chain protein OR platelet derived growth factor alpha polypeptide OR Growth Substance OR Endogenous Mitogen OR vegf OR Vascular Endothelial Growth Factor OR Stem Cell OR Adult Stem Cell OR Induced Pluripotent Stem Cell OR psc OR IPS Cell OR Fibroblast Derived Induced Pluripotent Stem Cell OR Fibroblast Derived IPS Cell OR Novel Scaffold OR Autologous Osteoblast OR Polymeric Scaffold OR Mechanical Signal Transduction OR Mechanosensory Transduction OR Cellular Mechanotransduction OR SOSTDC1 protein OR USAG 1 protein OR sclerostin OR ectodin protein OR hect protein OR Platelet Rich Plasma OR Intercellular Signaling Peptides Proteins OR TGF beta Superfamily Proteins OR Transforming growth factor OR Bone Morphogenetic Protein OR Growth Differentiation Factor OR myostatin OR Platelet Derived Growth Factor OR Growth Substances OR Vascular Endothelial Growth Factor OR Paracrine Peptide Factor OR Growth Factor OR TGF beta Superfamily Protein OR bmp OR rhbmp OR recombinant human bone morphogenetic protein OR rhoptry associated protein)	859,621
3	(osseointegration OR Endosseous Dental Implantation OR Endosseous Implantation OR Osseointegrated Dental Implantation OR Osseointegrated Implantation OR Endosseous Implant OR Osseointegrated Implant OR Osseointegrated Dental Implant OR Endosseous Dental Implant)	8,591
4	((Edentulous Jaw AND maxilla) OR Edentulous Maxilla OR ((Edentulous Ridge OR Edentulous Jaw OR Alveolar Bone Loss OR Alveolar Ridge Augmentation) AND (maxillae OR maxilla OR maxillary)))	2,056
5	Nos. 4 and 3 AND Nos. 2 and 1	34

Table 4 Terms and Strategy Used To Search Scopus

Search No.	Search Parameters	Results
1	("tissue engineering" OR "regenerative medicine" OR bone tissue engineering OR tissue engineering OR tissue culture OR regenerative medicine OR tissue engineering constructs OR microencapsulation OR "bone transplantation" OR bone grafting OR bone augmentation OR bone transplantation)	27,572
2	((gdf OR "Platelet Derived Growth Factor" OR pdgf OR "PDGFA protein" OR "DGF A chain protein" OR "platelet derived growth factor alpha polypeptide" OR "Growth Substance" OR "Endogenous Mitogen" OR vegf OR "Vascular Endothelial Growth Factor" OR "Stem Cell" OR "Adult Stem Cell" OR "Induced Pluripotent Stem Cell" OR psc OR "IPS Cell" OR "Fibroblast Derived Induced Pluripotent Stem Cell" OR "Fibroblast Derived IPS Cell" OR "Novel Scaffold" OR "Autologous Osteoblast" OR "Polymeric Scaffold" OR "Mechanical Signal Transduction" OR "Mechanosensory Transduction" OR "Cellular Mechanotransduction" OR "SOSTDC1 protein" OR "USAG 1 protein" OR sclerostin OR "ectodin protein" OR "hect protein" OR "Platelet Rich Plasma") OR ("Intercellular Signaling Peptides Proteins" OR "TGF beta Superfamily Proteins" OR "Transforming growth factor" OR "Bone Morphogenetic Protein" OR "Growth Differentiation Factor" OR myostatin OR "Platelet Derived Growth Factor" OR "Growth Substances" OR "Vascular Endothelial Growth Factor" OR "Paracrine Peptide Factor" OR "Growth Factor" OR "TGF beta Superfamily Protein" OR bmp OR rhbmp OR "recombinant human bone morphogenetic protein" OR "rhoptry associated protein"))	1,578,233
3	(osseointegration OR "Endosseous Dental Implantation" OR "Endosseous Implantation" OR "Osseointegrated Dental Implantation" OR "Osseointegrated Implantation" OR "Endosseous Implant" OR "Osseointegrated Implant" OR "Osseointegrated Dental Implant" OR "Endosseous Dental Implant")	29,690
4	(("Edentulous Jaw" AND maxilla) OR "Edentulous Maxilla" OR (("Edentulous Ridge" OR "Edentulous Jaw" OR "Alveolar Bone Loss" OR "Alveolar Ridge Augmentation") AND (maxillae OR maxilla OR maxillary)))	8,770
5	Nos. 1 and 2 AND Nos. 3 and 4	102

Assessment of the Level of Evidence

To assess and report in a standardized manner the level of evidence of each one of the individual studies selected in this systematic review, the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence scale was applied.[21] For the assessment of the body of evidence, the "SORT" grading and scoring system was followed at the 2014 AO Summit.[22]

RESULTS

Results of Literature Selection Process

The initial search yielded a total of 3,061 entries, of which 98 were found in PubMed, 34 in Web of Knowledge, 102 in Scopus, 2,114 in Embase, 114 in the Cochrane Library/Wiley, 496 in ProQuest, and 103 through cited reference searching. Excluding all duplicate studies, the

Table 5 Terms and Strategy Used to Search Embase

Search No.	Search Parameters	Results
1	'bone regeneration'/exp OR 'bone regeneration' OR 'tooth implantation'/exp OR 'tooth implantation'	
2	'tissue engineering'/exp OR 'tissue engineering' OR 'tissue culture'/exp OR 'tissue culture' OR 'regenerative medicine'/exp OR 'regenerative medicine' OR 'cell, tissue or organ culture'/exp OR 'cell, tissue or organ culture' OR 'bone transplantation'/exp OR 'bone transplantation' OR 'transforming growth factor'/exp OR 'transforming growth factor' OR 'bone morphogenetic protein'/exp OR 'bone morphogenetic protein' OR 'growth differentiation factor'/exp OR 'growth differentiation factor' OR 'myostatin'/exp OR 'myostatin' OR 'platelet derived growth factor'/exp OR 'platelet derived growth factor' OR 'signal peptides'/exp OR 'signal peptides' OR 'growth promoter'/exp OR 'growth promoter' OR 'vasculotropin'/exp OR 'vasculotropin' OR 'growth factor'/exp OR 'growth factor' OR 'stem cell'/exp OR 'stem cell' OR 'adult stem cell'/exp OR 'adult stem cell' OR 'pluripotent stem cell'/exp OR 'pluripotent stem cell' OR 'mechanotransduction'/exp OR 'mechanotransduction' OR 'platelet rich plasma'/exp OR 'platelet rich plasma'	
3	'maxilla'/exp OR 'maxilla' AND ('edentulousness'/exp OR 'edentulousness') OR 'alveolar bone loss'/exp OR 'alveolar bone loss' OR 'alveolar ridge augmentation'/exp OR 'alveolar ridge augmentation'	
4	Nos. 1 and 2 AND No. 3	2,114

Table 6 Terms and Strategy Used To Search Cochrane Library/Wiley

Search No.	Search Parameters	Results
1	tissue engineering or tissue culture or regenerative medicine or bone transplantation or transforming growth factor* or bone morphogenetic protein* or growth differentiation factor* or myostatin* or platelet-derived growth factor* or growth substances* or vascular endothelial growth factor* or stem cell* or adult stem cell* or induced pluripotent stem cells or cellular mechanotransduction or platelet-rich plasma:ti,ab,kw	486
2	edentulous maxilla or alveolar bone loss or alveolar ridge augmentation	78
3	osseointegration or dental implantation, endosseous or endosseous dental implantation	85
4	Nos. 5 and 6 And No. 7 (in Cochrane Reviews (Reviews and Protocols) and Other Reviews)	114

Table 7 Terms and Strategy Used to Search Proquest

Search No.	Search Parameters	Results
1	(tissue engineering OR tissue culture OR regenerative medicine OR bone transplantation OR transforming growth factor* OR bone morphogenetic protein* OR growth differentiation factor* OR nystatin* OR platelet-derived growth factor* OR growth substances* OR vascular endothelial growth factor* OR stem cell* OR adult stem cell* OR induced plenipotent stem cells OR cellular mechanotransduction OR platelet-rich plasma) AND (edentalous maxilla or alveolar bone loss or alveolar ridge augmentation) AND (osseointegration or dental implantation, endosseous or endosseous dental implantation)	469

total number of articles selected after reviewing the titles and abstracts was 2,753. A total of 2,633 articles were excluded after reading the title and abstract. Of the 120 remaining articles, a total of 31 were excluded after full-text review.[23–53] The list of excluded articles and the reasons for exclusion are shown in Table 8. The final selection consisted of 89 articles, of which 12 were on the application of tissue engineering therapies for the treatment of socket defects to prevent alveolar ridge remodeling,[9,11,54–63] 6 articles were on horizontal defects,[64–69] 61 were related to maxillary sinus augmentation[10,12,70–128] and 11 were on the treatment of severe vertical or combined defects.[62,129–138] The flow diagram illustrating this process of literature selection is shown in Fig 3. Noteworthy, one case series reported on the application of a tissue engineering approach on both socket and combined defects.[62] That particularity explains the apparent discrepancy in the final count of articles included in Fig 3 (numbers are marked with an asterisk).

Available Evidence on Specific Clinical Scenarios

Alveolar Ridge Preservation: Socket Defect. A total of 12 articles were identified in this clinical scenario. Of these 12 articles, five were RCTs, all with a parallel arm design,[11,54,58,60,63] six were case series studies,[9,55–57,59,62] and one was a case report.[61]

RCTs (Table 9). Of the five RCTs selected, two studies evaluated the effect of PRP alone or in combination with scaffolds (ie, freeze-dried bone allograft [FDBA] and beta

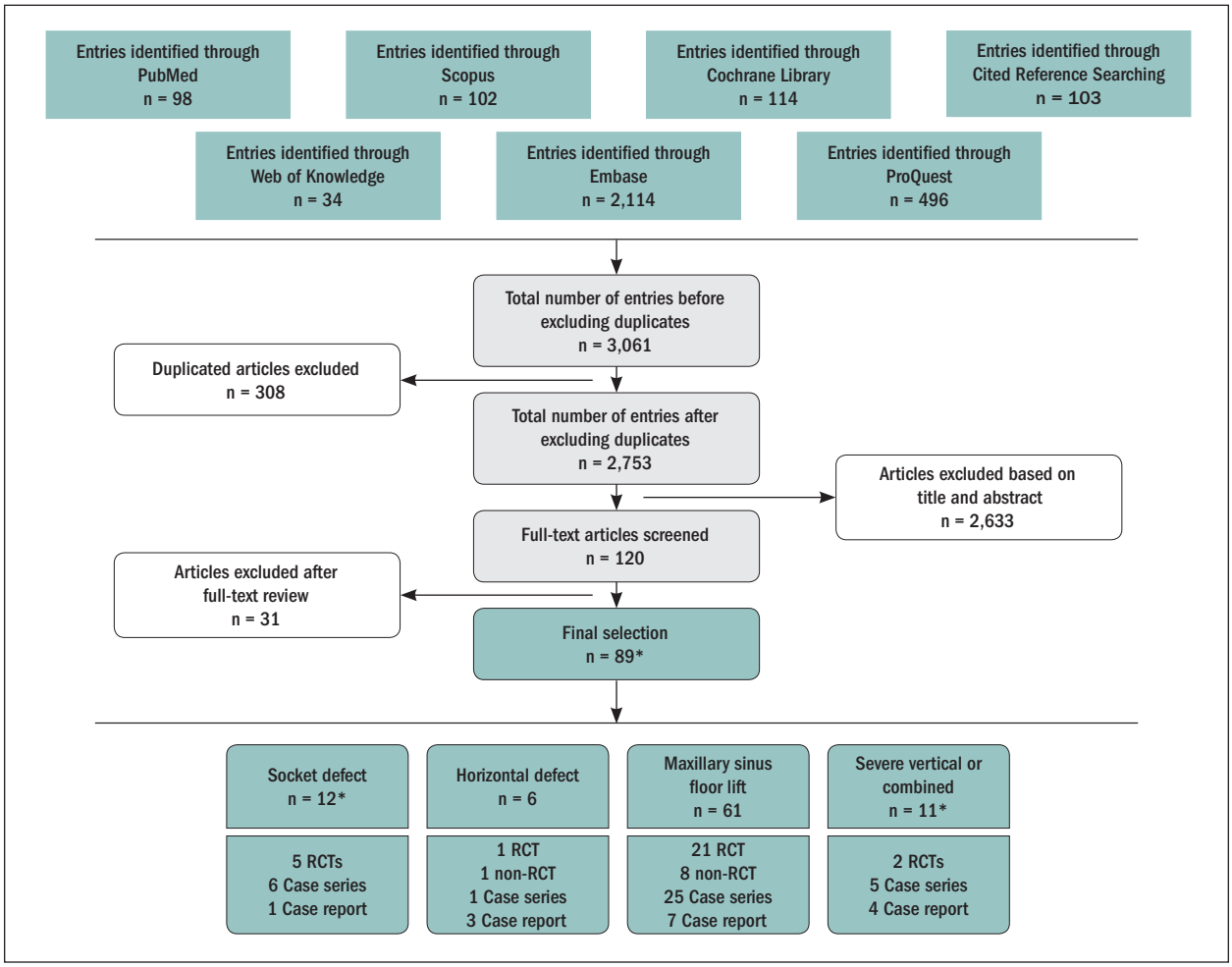


Fig 3 Flowchart displaying the search process and article selection.

tricalcium phosphate [βTCP]),[54,60] one study evaluated the effect of recombinant human platelet–derived growth factor BB (rhPDGF-BB),[54] two studies aimed at assessing the effect of autologous pluripotential cell therapy,[58,63] and in another study the patients in the experimental groups (a total of two) received a therapy consisting of recombinant human bone morphogenetic protein 2 (rhBMP-2) in an absorbable collagen sponge (ACS) carrier, using two different dosages.[11] The numeric discrepancy is explained by the fact that the most recent RCT included four arms,[54] two of which involved the use of a different tissue engineering–based approach. The total follow-up time ranged from 8 weeks from grafting to 12 months after initial grafting[63] (Table 9). Three studies assessed clinical outcomes.[58,60,63]

In a study that evaluated the effect of PRP,[60] it was observed that the sites treated with this autologous product exhibited significantly better soft tissue healing index at 1 week, by a magnitude of 1 point in a scale of 5 (average values were 4.1 in the experimental and 3.1 in the control group). Kaigler et al[63] observed that the control sites (ie, GBR with collagen membrane) exhibited a sixfold increased need of additional grafting at the time of implant placement compared with the test sites, which received pluripotential mesenchymal cells. Similarly, Pelegrine and collaborators[58] found that the test group (bone marrow aspirate concentrate) showed statistically significantly better results in preserving alveolar ridge facial height and cortical thickness. Five control sites required additional grafting at the time of implant placement, which did not occur in any of the experimental sites. Three studies reported radiographic outcomes.[11,60,63] Kaigler et al[63] observed that the cell-based therapy outperformed the control therapy in terms of radiographic linear gain in standardized radiographs. In the study that involved the application of PRP,[60] it was observed that trabecular density assessed on standardized radiographs by a masked examiner was significantly better in the experimental group. Fiorellini and coworkers[11] assessed the effect of rh-BMP2 in terms of ridge height and width changes, volume available for implant placement, and bone density in cone beam computed tomography (CBCT)

Table 8 Articles Excluded Based on Content After Full-Text Review and Reason For Exclusion

Study	Reason for Exclusion
Dasmah et al (2013)[26]	A control group that did not receive a tissue engineering–based therapy was not included in this randomized controlled trial
Montanari et al (2013)[25]	Clinical scenario reported was not contemplated in this systematic review/ experimental therapy used was not a tissue engineering–based approach on the basis of the predefined criteria
Tajima et al (2013)[24]	Experimental therapy used was not a tissue engineering–based approach on the basis of the predefined criteria
Yamada et al (2013)[23]	Case report on the treatment of a combined mandibular defect
Chang et al (2012)[31]	Animal study
Chung et al (2012)[30]	Animal study
Heberer et al (2012)[29]	No outcomes of interest were reported
Snyder (2012)[28]	Case report on the treatment of a mandibular defect
Tatullo et al (2012)[27]	Applied therapy did not qualify as a tissue engineering approach
Nam et al (2011)33	Data from maxillary and mandibular sites were pooled
Rickert et al (2011)[32]	Same population included in a later publication (Rickert et al [2014][70])
Badr et al (2010)39	Data from maxillary and mandibular sites were pooled
Davies & Ochs (2010)[38]	Review including the description of cases, but no outcomes of interest were reported
Herford & Cicciu (2010)[37]	Clinical scenario reported was not contemplated in this systematic review
Koch et al (2010)[36]	Same population included in a later publication (Stavropoulos et al [2011][83])
Luaces-Rey et al (2010)[35]	Clinical scenario reported was not contemplated in this systematic review
Torres et al (2010).[34]	Application of the described tissue engineering–based therapy is outside of the scope of this review
Jung et al (2009)[41]	Data from maxillary and mandibular sites were pooled
Lee at al (2009)[40]	Clinical scenario reported was not contemplated in this systematic review
Byun et al (2008)[43]	Clinical scenario reported was not contemplated in this systematic review
Lee et al (2008)[42]	Clinical scenario reported was not contemplated in this systematic review
Simion et al (2007)[44]	Reported cases from mandibular sites
Klongnoi et al (2006)[46]	Animal study
Klongnoi et al (2006)[47]	Animal study
Mannai (2006)[45]	Outcomes after applying different therapies in various clinical scenarios were pooled
Bianchi et al (2004)[48]	Same population included in a later publication (Fiorellini et al [2005][11])
Shanaman et al (2001)[49]	Reported cases from mandibular sites
Kassolis et al (2000)[50]	Data from two different clinical scenarios (horizontal guided bone regeneration and maxillary sinus augmentation) were pooled
Marx et al (1998)[51]	Review including the description of cases out of the scope of this review
Howell et al (1997)[52]	Clinical trial focused on periodontal regeneration (out of the scope of this review)
Howell et al (1997)[53]	Same population included in a later publication (Cochran et al [2000][62])

scans, and found that patients treated with the higher dose of morphogenetic protein exhibited significantly greater bone augmentation compared with controls.

Histologic outcomes were reported in four RCTs.[11,54,58,63] In one study, the histologic assessment was merely descriptive and no differences between native and newly formed bone were observed in all groups.[11] The microCT and histomorphometric analyses conducted in the study by Kaigler et al[63] showed that bone volume fraction, bone mineral density, and bone/tissue ratio were more favorable for the experimental therapy at the 6-week mark. Interestingly, no significant differences between treatments were observed at 12 weeks. The other two studies conducted histomorphometric analyses. Although the study that involved the use of cell therapy[58] found no significant differences between groups in terms of new bone formation, another RCT[54] observed that the application of both PRP and rhPDGF-BB produced less residual bone graft material, possibly indicating more rapid turnover of the bone graft (ie, combination of βTCP and FDBA). This beneficial effect was more marked when rhPDGF-BB was used. Two RTCs recorded patient-centered outcomes.[11,60] In the study by Alissa et al,[60] differences in patients' responses in a health-related quality-of-life questionnaire were statistically significant in favor of the experimental therapy (ie, PRP) only for the presence of bad taste/bad smell in the mouth and food stagnation in the surgical area.

Table 9 RCTs (n = 5) on the Application of Tissue Engineering–Based Therapies for Alveolar Ridge Preservation After Socket Grafting

Study	Objective(s)	Tissue Engineering Approach (Biologics, Scaffolds, Cell-based, Gene Therapy)	Study Design	A Priori Eligibility Criteria Described	Number of Patients and Sites	Type of Maxillary Edentulism	Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
Geurs et al (2014)[54]	To evaluate healing of grafted and nongrafted sockets and the effect of PRP and rhPDGF-BB on early remodeling	Biologic agents (PRP/rhPDGF-BB) + scaffolds (FDBA/βTCP)	RCT (parallel arms)	Yes	41	Partial	Four groups - Group 1: collagen plug (control); group 2: FDBA + βTCP + collagen plug ; group 3: FDBA + βTCP + PRP + collagen plug; group 4: FDBA + βTCP + rhPDGF-BB + collagen plug	Yes
Kaigler et al (2013)[63]	To evaluate the efficacy of a novel cell-based therapy in terms of bone formation in an alveolar ridge preservation model as compared to a control	Cell therapy (autologous bone marrow pluripotential cells) in a carrier (absorbable gelatin sponge)	RCT (parallel arms)	Yes	24 patients for 24 sockets (n = 6 per group)	Partial	Four groups - Control 1 (reentry at 6 weeks): extraction + gelatin carrier + collagen membrane barrier; control 2 (reentry at 12 weeks): extraction + gelatin carrier + collagen membrane barrier; experimental 1 (reentry at 6 weeks): extraction + autologous mesenchymal pluripotential cells in gelatin carrier; experimental 2 (reentry at 12 weeks: extraction + autologous mesenchymal pluripotential cells in gelatin carrier	Yes
Alissa et al (2010)[60]	To investigate the effect of PRP on the healing of hard and soft tissues of extraction sockets	Biologic agent (PRP)	RCT (parallel arms)	Yes	23 patients (12 controls for 15 sockets and 11 experimental for a total of 14 sockets)	Partial	Two groups - Control: extraction alone; experimental: extraction + PRP in the socket	Yes
Pelegrine et al (2010)[58]	To evaluate the potential of an autologous bone marrow graft in preserving the alveolar ridge following tooth extraction	Cell-based therapy (autologous bone marrow)	RCT (parallel arms)	Yes	13 patients for a total of 30 maxillary anterior sockets (15 control and 15 experimental)	Partial	Two groups - Control: extraction alone; experimental: extraction + autologous bone marrow graft	Yes
Fiorellini et al (2005)[11]	To evaluate the efficacy of bone induction for the placement of dental implants by two concentrations of rhBMP-2 in a carrier (ACS) compared to placebo (ACS alone) and control (no treatment) in a human buccal wall defect model after tooth extraction	Biologic agent (rhBMP-2)	RCT (parallel arms)	Yes	80 patients for 80 sockets (21 in experimental group 1, 22 in experimental group 2, 17 in placebo group, and 20 in control group)	Partial	Four groups - Experimental group 1: 1.50 mg/mL + ACS; experimental group 2: 0.75 mg/mL + ACS; placebo: ACS alone; control: no treatment (extraction alone)	Yes

The difference between groups was not statistically significant for patient satisfaction with the treatment. In the study by Fiorellini et al,[11] safety of the therapy was assessed by monitoring the occurrence of adverse events and determining serum antibody response. Interestingly, a higher percentage of adverse events was observed in the experimental groups than in the placebo and control groups. Compared with the control and placebo groups, increased postoperative edema and pain were reported in approximately two thirds of the patients in both experimental groups.

Case Series (Table 10). Of the six case series selected, the therapeutic agent applied was rhBMP-2 in an ACS carrier in four studies,[9,55,59,62] the sole application of platelet-rich fibrin in one study,[56] and a combination of FDBA and rhPDGF-BB to graft the sockets in another

Tooth Extraction (Socket Defect)

Socket Grafting

Masking (Only for clinical trials)	Outcomes Measures	Healing Period Prior to Reopening	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If Applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Yes (histologic assessments only)	Histologic: Quantification of tissue compartments %	8 weeks	No	8 weeks	Not specified, but apparently not	Inclusion of bone replacement graft suppressed new bone formation during early healing. Inclusion of PRP and rhPDGF-BB produced less residual bone graft material, indicating more rapid turnover of bone graft.	2
Yes (All assessments: radiographic, histologic, and biochemical)	Clinical: Incidence of complications, tactile bone density, and need for additional grafting at the time of implant placement; radiographic: bone height changes using standardized radiographs; histologic: histomorphometric and biochemical analyses of bone core biopsies using light microscopy and microCT (ie, bone volume fraction, bone mineral density, and bone/tissue area ratio)	6–12 weeks	Yes	1 year after initial grafting	One subject from the control group missed the last two visits	All sites healed in absence of significant complications independent of the reentry time and the therapy applied. Bone density at the time of implant placement was comparable. Control sites exhibited a sixfold increased need for additional grafting at the time of implant placement. The experimental therapy outperformed the control one in terms of radiographic linear bone height, bone volume fraction, bone mineral density, and bone/tissue ratio at the 6-week mark. Interestingly, no significant differences were observed at 12 weeks.	2
Yes (radiographic assessments only)	Clinical: Incidence of complications and soft tissue healing index; radiographic: densitometry and trabecular pattern on standardized radiographs; patient-centered outcomes: QoL index	12 weeks	No	12 weeks	Two at baseline (both from the control group) and five at the 3-month radiographic assessment (1 control and 4 experimental)	All recorded complications occurred in subjects from the control group. More pain was reported in the control group up to the 4th day. Soft tissue healing index and trabecular density was significantly better in the experimental group. Differences in patients' responses in the health-related QoL questionnaire were statistically significant in favour of PRP treatment only for the presence of bad taste or bad smell in the mouth, and food stagnation in the operation area. The difference between groups was not statistically significant for patient satisfaction with the treatment.	2
Not reported	Clinical: Ridge width and height changes; histologic: quantification of tissue compartments %	6 months	Yes	6 months (implants were not followed up)	No	The test group showed statistically significant better results in preserving alveolar ridge facial height and cortical thickness. In five control sites additional grafting was required at the time of implant placement. No significant differences between groups were observed in terms of new bone formation.	2
Yes	Radiographic: Height and width changes at three different vertical levels, volume available for implant placement and bone density, all of them assessed in CBCT scans; histologic: descriptive (67 bone cores); patient-centered outcomes: safety of therapy (adverse events and serum antibody response)	4 months	Yes	4 months (implants were not followed up)	No	Patients treated with 1.50 mg/mL rh-BMP-2/ACS had significantly greater bone augmentation compared with controls. Patients in the experimental groups required less additional bone augmentation at the time of implant placement. Histologic analyses revealed no differences between native and newly formed bone in the experimental groups. There was a higher percentage of adverse events reported in the experimental groups than in the placebo and control groups. Edema and pain were reported in 75% and 68% of the cases, respectively.	2

study.[57] The follow-up time in these studies ranged from 3 to 6 months. All studies reported clinical outcomes, four reported radiographic outcomes,[9,57,59,62] and three reported histologic outcomes.[55,57,62] Only one study reported patient-centered outcomes.[62] Independent of the therapy applied, all studies reported positive clinical, radiographic, and histologic outcomes, but the absence of controls prevents any inferential interpretation of the data on effectiveness and efficacy. Nevertheless, the observations on safety in the study by Cochran et al[62] published in 2000 are of particular significance because they observed that rhBMP-2 + ACS can be safely used as a socket grafting therapy in humans, which was critical information for the development of this therapy at the time.

Table 10 Case Series (n = 6) on the Application of Tissue Engineering–Based Therapies for Alveolar Ridge Preservation

			Socket Grafting					
Study	Objective(s)	Tissue Engineering Approach (Biologics, Scaffolds, Cell-based, Gene Therapy)	Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites	Type of Maxillary Edentulism	Groups/ Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
Spagnoli et al (2013)[9]	To discuss the indications of ridge preservation therapy employing rhBMP-2 in a carrier (ACS) and present several cases illustrating these applications	Biologic agent (rhBMP-2)	Case series	No	7 patients for a total of 13 sockets (two of them were mandibular sockets)	Partial	N/A	N/A
Levin et al (2012)[55]	To present a case series of consecutively treated patients who received socket grafting with rhBMP-2 in a carrier (ACS) at the time of molar extraction	Biologic agent (rhBMP-2)	Case series	No	6 patients for 6 sockets (two maxillary, four mandibular)	Partial	N/A	N/A
Nevins et al (2011)[57]	To report on clinical experiences using rhPDGF-BB with bone allografts for socket grafting	Biologic agent (rhPDGF-BB) + scaffold (FDBA)	Case series	N/A	3 patients for 3 sockets (one intervention was in an intact alveolus and the other two in sites presenting severe facial dehiscence)	Partial	N/A	N/A
Simon et al (2011)[56]	To quantify the dimensional alveolar ridge changes that occur when using PRF alone as a graft material in extraction sockets for ridge preservation procedures	Biologic agent (PRF)	Case series	Yes	21	Partial	N/A	N/A
Misch (2010)[59]	To evaluate the use of rhBMP-2 in a carrier (ACS) for the repair of significant bone defects following tooth removal	Biologic agent (rhBMP-2)	Case series	No	10 patients for 10 sockets (all were maxillary central incisors)	Partial	N/A	N/A
Cochran et al (2000)[62]	To monitor the long-term safety of patients treated with rhBMP-2 for socket grafting and to evaluate the implants placed in the grafted sites	Biologic agent (rhBMP-2)	Case series	No	6 patients for 6 sockets	Partial	N/A	N/A

Table 11 Case Report on the Application of Tissue Engineering–Based Therapies for Alveolar Ridge Preservation

			Socket Grafting					
Study	Objective(s)	Tissue Engineering Approach (Biologics, Scaffolds, Cell-based, Gene Therapy)	Study Design	A Priori Eligibility Criteria Described	Number of Patients and Sites	Type of Maxillary Edentulism	Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
Hahn et al (2003)[61]	To report 1 case in which an alloplastic particulate material containing a surface cell-binding peptide was applied for alveolar ridge preservation via socket grafting	Scaffold (bone graft presenting cell-binding peptide on the surface)	Case report	N/A	1 patient for 2 maxillary sockets: 1 socket received the graft in a particulate form, while the other socket was grafted with the same material vehiculized in a hydrogel	Partial	N/A	N/A

N/A = Not applicable.

Case Reports (Table 11). Only one case report was selected in this clinical scenario after applying the pre-established eligibility criteria. In this study,[61] one patient received two different forms of a xenograft (ie, particles or gel) presenting a surface biomimetic peptide (ie, P-15). Clinical (ie, perception of bone density at implant placement), radiographic (ie, bone density in non-

After Tooth Extraction (Socket Defect)

Socket Grafting

Masking (Only for clinical trials)	Outcomes Measures	Healing Period Prior to Reopening	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Incidence of complications and available volume at the time of implant placement; radiographic: bone gain and density changes	4–6 months	Yes	8 weeks to 2 years from implant placement	N/A	The use of rhBMP-2/ACS for ridge preservation was associated with satisfactory outcomes.	4
Not reported	Clinical: Perception of primary stability and need for additional bone grafting at implant placement; histologic: description of one bone core at low magnification	3–6 months	Yes	Up to 8 months from grafting (implants were loaded at that time)	N/A	The use of rhBMP-2 for socket grafting is a safe and effective therapy that resulted in adequate bone formation, implant primary stability, and no need for additional grafting in all reported cases.	4
Not reported	Clinical: Incidence of complications and perception of bone density at implant placement; radiographic: bone density; histologic: description of a bone core at 5× and 10× magnification (only from one case)	5 months	Yes	Up to 10 months from grafting (implants were loaded at that time)	N/A	The application of rhPDGF-BB in combination with allograft particles was associated with favorable clinical, radiographic, and histologic outcomes.	4
Not reported	Clinical: Ridge width and height changes at 3 points (midpoint of the socket, 3 mm distal to the midpoint and 3 mm mesial to the midpoint) using custom stents	4 months	Yes	4 months (implants were not followed up)	No	Average height and width loss was minimal, below 1 mm. Sites grafted with PRF alone displayed rapid clinical healing, minimal flap reopening, and excellent bone density.	4
Not reported	Clinical: Perception of bone density at implant placement; radiographic: ridge width assessed on CBCT scans to determine if there is enough bone substrate for implant placement	4–6 months	Yes	Up to 10 months from grafting	N/A	Alveolar ridge width changes, from pre-extraction to healed graft, ranged from a gain of 0.63 mm to a loss of 2.18 mm. All implants were stable at the time of placement. Additional CTG were required in 50% of the sites.	4
Yes (radiographic assessments only)	Clinical: Buccolingual, apicocoronal, and mesiodistal linear changes of the ridge; radiographic: bone height and density changes, and incidence of radiographic pathology; histologic: description of representative bone cores; patient-centered outcomes: incidence of adverse experiences	16 weeks	Yes	532 weeks	No	In this long-term case series with a limited number of subjects (n = 6), clinical, radiographic, histologic, and patient-centered outcomes indicate that rhBMP-2 + ACS can be safely used as a socket grafting therapy in humans.	4

After Tooth Extraction (Socket Defect)

Socket Grafting

Masking (Only for clinical trials)	Outcomes Measures	Healing Period Prior to Reopening	Implants Placed	Total Follow-up time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Perception of bone density at implant placement; radiographic: bone density in nonstandardized periapical radiographs; histologic: quantification of tissue compartments %	13 weeks	Yes	13 weeks (implants were not followed up)	N/A	In this case report with a split-mouth design, it was shown that more favorable clinical, radiographic, and histologic outcomes were achieved in the site that received the bone graft in a flowable form.	4

standardized periapical radiographs), and histologic (ie, percentage of quantification of tissue compartments) outcomes were assessed 13 weeks after grafting. The results indicated that the gel form achieved more favorable outcomes for all the parameters analyzed. Although worth noting, this case report is of limited value in the context of this systematic review.

Table 12 Nonrandomized Clinical Trial on the Application of Tissue Engineering–Based Therapies for the Treatment of

Study Year of publication + Author(s)	Objective(s)	Tissue Engineering Approach (Biologic agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Horizontal Defects				Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility (Criteria Described)	No. of Patients and Sites	Type of Maxillary Edentulism		
de Freitas et al (2013)[69]	To compare the effect of recombinant human bone morphogenetic protein-2 (rhBMP-2) in an absorbable collagen sponge carrier (ACS) with autogenous bone graft for augmentation of the edentulous atrophic anterior maxilla	Biologic agent (rhBMP-2)	RCT (parallel arms)	Yes	24 patients for 24 edentulous ridges (12 patients per group)	Partial	Control: Autogenous bone particles; experimental: rhBMP-2/ACS	Yes
Nevins et al (2009)[68]	To evaluate a minimally invasive ridge augmentation procedure (tunneling technique) that used rhPDGF-BB in combination with three particulate scaffolds, namely FDBA (cortical), xenograft (bovine), and mineralized collagen xenograft (bovine) substitute	Biologic agent (rhPDGF-BB) + scaffolds (FDBA/bovine xenograft)	Nonrandomized clinical trial	Yes	12 patients for 12 edentulous ridges (4 patients per group)	Partial	Group A: rhPDGF-BB + FDBA; group B: rhPDGF-BB + bovine xenograft; group C: rhPDGF-BB + mineralized collagen xenograft (bovine) substitute	No

rhBMP-2 = recombinant human bone morphogenetic protein type 2; ACS = absorbable collagen sponge; RCT = randomized clinical trial; CBCT = cone beam computed tomography; FDBA = freeze-dried bone allograft; rhPDGF-BB = recombinant human platelet derived growth factor type BB.

Table 13 Case Series on the Application of Tissue Engineering–Based Therapies for the Treatment of Horizontal Defects

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Horizontal Defects			Type of Maxillary Edentulism	Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility (Criteria Described)	No. of Patients and Sites			
Anitua et al (2013)[65]	To evaluate the clinical outcomes of a split-crest technique using PRGF for implant site development in humans	Biologic agent (PRGF)	Case series	Yes	15 patients for 15 edentulous ridges	Partial	N/A	N/A

PRGF = plasma rich in growth factors; N/A = not applicable; CBCT = cone beam computed tomography.

Horizontal Defects

Six articles were identified in this clinical scenario. Of these six studies, one was an RCT,[69] one was a nonrandomized clinical trial,[68] one was a case series,[65] and three were case reports.[64,66,67] Surgical techniques described in this body of evidence included onlay bone grafting and interpositional grafts (ie, split ridge technique).

RCTs and Nonrandomized Clinical Trials (Table 12). Only one RCT was identified in this category.[69] This was a two-arm study that enrolled 24 patients (12 per group), in which the control group received autologous bone particulate alone and the experimental group received rhBMP-2/ACS. In both groups, a titanium mesh and fixation screws were applied for space-holding purposes. Clinical and radiographic horizontal gain was evaluated. Interestingly, no statistically significant differences were observed between groups for any of the parameters evaluated, except for increased bone width 2 mm below the bone crest in favor of the experimental group (magnitude of the difference = 1 mm). The authors concluded that the use of rhBMP-2/ACS may be considered a reliable alternative to autogenous bone grafts. One three-arm nonrandomized clinical trial[68] published in 2009 aimed at evaluating a minimally invasive ridge augmentation procedure that used rhPDGF-BB in combination with three different scaffolds: cortical FDBA particles (group A), bovine xenograft particles (group B), and a mineralized collagen bovine xenograft block (group C). A total of 12 patients were enrolled (four per group). There was no control group. All sites healed uneventfully after bone grafting. CBCT scans and surgical reopening revealed insufficient volume for implant placement in two patients from group C. Histologic assessments revealed normal and consistent bone formation in all specimens of groups A and B, while group C had variable results with some areas of fibrous encapsulation and limited evidence of new bone formation. Three implants from group A failed before the final

Horizontal Defects

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Yes (radiographic assessments)	Clinical: Rate of complications, horizontal bone gain upon surgical reentry using a stent and implant survival rate at 6 months; radiographic: horizontal linear gain assessed on CBCT scans	6 months	Yes (n = 62)	6 months from implant placement	No	No statistically significant differences were observed between groups for any of the parameters evaluated, except for increased bone width at 2 mm below the bone crest in favor of the experimental group (magnitude of the difference = 1 mm). Authors concluded that the use of rhBMP-2/ACS can be considered a reliable alternative to autogenous bone grafts.	2
Yes (radiographic assessments)	Clinical: Incidence of complications, implant failure rate and available volume for implant placement upon reopening; radiographic: ridge width gain assessed on CBCT scans; histologic: microCT analysis and quantification of tissue compartments % in bone core biopsies	14 weeks	Yes (n = 20)	12 months from implant placement	No	All sites healed uneventfully after grafting. CBCT scans and surgical reopening revealed insufficient volume for implant placement in two patients from Group C. Histologic assessments revealed normal and consistent bone formation in all specimens of Groups A and B, while Group C had variable results with some areas of fibrous encapsulation and limited evidence of new bone formation. Three implants from Group A failed prior to the final 12-month assessment.	3

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Implant success, plaque index, bleeding index, suppuration and probing depth around implants; radiographic: bone gain assessed using CBCT scans	6 months	Yes, simultaneously with horizontal augmentation (n = 37)	6 to 25 months from implant loading	No	The average horizontal gain at the time of final follow-up was 3.35 mm from baseline. No implants failed during the study period and all of them met the success criteria defined. Peri-implant soft tissue conditions were deemed as optimal, in general.	4

12-month assessment. The absence of a control group (ie, where rhPDGF-BB was not applied) and the nonrandomized nature of this study limit its significance in the context of this systematic review.

Case Series (Table 13). One case series study was selected in this clinical scenario.[65] A total of 15 patients in need of horizontal ridge augmentation in the maxilla were enrolled. The therapeutic approach consisted of a split ridge technique in combination with plasma rich in growth factors (PRGF). A total of 37 implants were simultaneously placed. Clinical (ie, implant success, plaque index, bleeding index, suppuration, and probing depth around implants) and radiographic (ie, bone gain assessed using CBCT scans) outcomes were reported. The total follow-up time ranged from 6 to 25 months after implant loading. Average horizontal gain upon study completion was 3.35 mm from baseline. No implants failed during the study period, and all met the predefined success criteria. Peri-implant soft tissue conditions were generally deemed as optimal. In spite of the positive results reported, it should be taken into account that the absence of a control limits the significance of this study to address the PICO question of this systematic review.

Case Reports (Table 14). Three case reports on the treatment of horizontal defects with tissue engineering therapies were included.[64,66,67] The remaining case report demonstrated the application of a cell-based therapy consisting of a living cell construct (ie, heterologous fibroblasts and keratinocytes in an absorbable bovine type I collagen matrix) in combination with a scaffold (ie, FDBA particles) to horizontally augment both soft and hard tissues in deficient ridges.[67] The maximum follow-up time among these case reports was 36 months after implant loading.[64] Two case reports looked at clinical outcomes (ie, horizontal augmentation[58] and incidence of complications[67]), two others included radiographic outcomes (ie, marginal

Table 14 Case Reports (n = 3) on the Application of Tissue Engineering–Based Therapies for the Treatment of Horizontal Defects

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Horizontal Defects			Type of Maxillary Edentulism	Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Urban et al (2013)[64]	To present the successful use of rhPDGF-BB in conjunction with autogenous bone and anorganic bovine-derived bone mineral and a barrier membrane to reconstruct a severe alveolar posterior maxillary bone defect	Biologic agent (rhPDGF-BB) + scaffold (xenograft and autogenous bone)	Case report	N/A	1	Partial	N/A	N/A
De Angelis et al (2011)[66]	To demonstrate the use of rhPDGF-BB in combination with a xenograft block in a bone augmentation procedure	Biologic agent (rhPDGF-BB) + scaffold (xenograft)	Case report	N/A	1	Partial	N/A	N/A
Block (2010)[67]	To demonstrate the successful reconstruction of an anterior mandibular ridge using a living cell construct in a patient with severe bone loss secondary to multiple dental procedures for long-term treatment of amelogenesis imperfecta	Cell-based therapy via a living cell construct (living heterologous fibroblasts and keratinocytes in a bovine type I collagen matrix) + Scaffold (FDBA)	Case report	N/A	1	Partial	N/A	N/A

rhPDGF-BB = recombinant human platelet derived growth factor type BB; N/A = not applicable; CBCT = cone beam computed tomography; FDBA = freeze-dried bone allograft.

bone level around implants[64] and bone gain at 3 months in a CBCT scan[66]), and only one reported histologic outcomes (ie, descriptive histology of one bone core obtained at 3 months).[66] Although the reported results were generally positive in these three studies, these data are of very limited significance to assess efficacy or effectiveness given the absence of a control group and the low sample size.

Maxillary Sinus Floor Lift

A total of 60 articles were identified in this clinical scenario. A total of 21 RCTs,[10,12,70,71,74,75,78,80,83,86,91,98,102,106,108,110,111,113,117,121,128] 8 nonrandomized clinical trials,[76,77,79,81,96,107,116,122] 25 case series,[72,73,82,84,85,87–89,93–95,97,99–101,104,112,114,115,118–120,124–126] and 7 case reports[90,92,103,105,109,123,127] were selected. As expected, all surgical techniques described in this body of evidence included onlay bone graft apical to the basal bone. Only one study reported maxillary sinus augmentation via a transcrestal approach,[72] and in the other studies the intervention was performed using a lateral approach.

RCTs (Table 15). Of the 21 RCTs that met the eligibility criteria for this clinical scenario, 12 evaluated the effect of autologous blood-derived products (PRP or PRGF) alone or in combination with a scaffold (ie, bovine xenograft, allografts, or alloplastic materials) and/or autologous bone,[71,74,91,98,102,106,108,110,111,113,117,121] three studies evaluated the use of cell therapy,[70,80,86] four clinical trials evaluated the effect of rhBMP-2/ACS,[10,12,78,128] one study assessed the effect of rhBMP-7/ACS,[75] and one study evaluated different outcomes after the application of βTCP coated with GDF-5 in maxillary sinus augmentation.[83] The total follow-up time in these studies ranged from 4 months after grafting[75] to 36 months after implant loading.[10] All the included RCTs had an adequate control group, and 13 studies reported masking for radiographic and/or histologic assessments.[10,12,70,71,80,83,86,98,108,111,113,121,128]

Of the 12 clinical trials on autologous blood-derived products, 6 reported clinical outcomes (ie, incidence of complications, implant survival rate),[74,91,102,108,111,117] 10 included radiographic outcomes (ie, density of the grafted volume and bone height gain),[71,74,91,98,102,108,110,111,113,117] and 11 included histologic outcomes (ie, descriptive histology, bone-to-implant contact, and histomorphometric analyses of bone core biopsies).[71,74,91,98,102,106,108,110,111,117,121] No study reported patient-centered outcomes. When analyzed from a general perspective and giving special emphasis to the studies with the largest populations and the longest follow-up times,[91,102,117] the results presented in these RCTs indicate that the use of blood-derived products did not suppose a significant benefit compared with the diverse control therapies for all the parameters analyzed, with the exception of improved short-term bone formation[108] and increased radiographic density.[74]

Of the three RCTs that assessed the effect of cell therapy, two studies reported clinical outcomes (ie, incidence of complications, implant survival rate, and several peri-implant parameters, such as probing depth and bleeding on probing),[70,80] two included

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Horizontal ridge augmentation; radiographic: marginal bone level around implants	9 months	Yes, in a delayed approach (n = 3)	36 months after implant loading	N/A	Significant (although not quantified) horizontal bone augmentation was achieved using the reported therapeutic approach. This allowed for the placement of 3 implants that served as support for a fixed partial prosthesis. Stable crestal bone after 36 months of loading was shown radiographically.	4
Not reported	Radiographic: Bone gain at 3 months assessed using CBCT scan; histologic: description of one bone core	3 months	Yes, in a delayed approach (n = 3)	6 months (3 months from implant placement)	N/A	The findings reported in this case report support the use of rhPDGF-BB in combination with allograft blocks for the treatment of horizontal defects.	4
Not reported	Clinical: Incidence of complications	4 months	Yes	4 months (implants were not followed up)	N/A	The grafted edentulous segment healed uneventfully and implants were placed without the need of additional grafting.	4

radiographic outcomes (ie, bone volume obtained for implant placement[86] and marginal bone loss around implants[70]), two reported histologic outcomes (ie, histomorphometric analyses of bone core biopsies),[80,86] and only one evaluated patient-centered outcomes (ie, overall satisfaction using a 10-point scale).[70] The results of these three RCTs consistently indicate that the experimental and control therapies performed similarly for all the parameters analyzed.

Of the four studies that evaluated the effect of rhBMP-2/ACS alone or in combination with a scaffold (ie, bovine xenograft), two reported clinical outcomes (ie, incidence of complications, implant survival, and success rate)[10,12] and radiographic outcomes (ie, density and height gain in grafted sites and marginal bone loss around implants)[10,12]; all reported histologic outcomes (ie, qualitative assessment of bone formation using a 5-point scale[10,12] or histomorphometric analyses[78,128]); and one reported patient-centered outcomes (ie, functional use of implant-supported prostheses for up to 24 months).[12] The findings from the RCTs that reported only histologic data were diverging. Kao et al[78] found that the percentage of vital bone in the test sites (ie, bovine xenograft + rhBMP-2/ACS) was significantly lower than that in the control sites (ie, bovine xenograft alone). However, Froum et al[128] observed no statistically significant differences in vital bone formation between the two experimental groups that received two different doses of rhBMP-2/ACS with an allograft compared with the control group that was treated with allograft particles alone. It must be mentioned that the other two RCTs included a substantially larger population, a longer follow-up time, and a more complete set of outcomes.[10,12] In these studies, no significant differences in terms of clinical, radiographic, histologic, and patient-centered outcomes were observed, except for increased edema in the experimental group, which indicates that the test therapy (ie, rhBMP-2/ACS) performed similarly to the control treatment (ie, autologous bone alone) in maxillary sinus augmentation. However, it is worth noting that the implant survival rates in both groups were remarkably low compared with current clinical standards (Table 15).

The RCT that tested the effect of rhBMP-7 in maxillary sinus augmentation reported clinical (ie, incidence of complications or adverse events), radiographic (ie, height gain in grafted sites), and histologic outcomes (ie, histomorphometric analyses of bone core biopsies).[75] The authors observed that the test and control groups exhibited similar results in terms of clinical and radiographic parameters, but the control group performed better in terms of vital bone formation (control: 19.8% vs test: 6.5%).

The study that evaluated the effect of βTCP coated with GDF-5 reported clinical outcomes (ie, implant survival rate) and histologic outcomes (ie, histomorphometric analyses of bone core biopsies to determine tissue compartments and cell counts).[83] Implant survival rate was only reported for the test group (ie, 90.5%, follow-up time not specified). No significant differences in histologic outcomes were found between groups for any of the parameters analyzed.

Table 15 RCTs (n = 21) on the Application of Tissue Engineering–Based Therapies for Maxillary Sinus Augmentation

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/ Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Rickert et al (2014)[70]	To assess implant survival and 1-year clinical performance of implants placed in maxillary sinuses grafted with a particulated xenograft mixed with MSCs or a particulated xenograft mixed with autogenous bone	Cell-based therapy + scaffold (xenograft)	RCT (split mouth)	Yes	12 patients for 24 maxillary sinuses	Complete	Control: Particulated xenograft (bovine) with particulated autologous bone; experimental: particulated xenograft (bovine) with MSCs obtained from autologous bone marrow aspirations	Yes
Corinaldesi et al (2013)[75]	To evaluate the efficacy of 2 different therapies for maxillary sinus lift in terms of bone formation	Biologic agent (rhOP-1/ BMP-7) + scaffold (xenograft)	RCT (split mouth)	Yes	9 patients for 18 maxillary sinuses	Not specified	Control: Particulated xenograft (bovine); experimental: particulated xenograft (bovine) with rhOP-1	Yes
Froum et al (2013)[128]	To determine the amount of vital bone formed 6–9 months after grafting the maxillary sinus with 2 different doses of rhBMP-2/ ACS in combination with an allograft as compared to an allograft alone.	Biologic agent (rhBMP-2) + scaffold (allograft)	RCT (split mouth)	Yes	18 patients for 36 maxillary sinuses	Not specified	Control: Allograft particles (n = 12); experimental 1: allograft particles + rhBMP-2/ ACS containing 8.4 mg of rhBMP-2 (n = 12); experimental 2: allograft particles + rhBMP-2/ ACS containing 4.2 mg of rhBMP-2 (n = 12)	Yes
Khairy et al (2013)[74]	To evaluate the potential benefit of adding PRP to autogenous bone in maxillary sinus augmentation	Biologic agent (PRP) + autologous bone	RCT (parallel arms)	Yes	15 patients for 15 maxillary sinuses	Partial	Control: Autologous bone and delayed implants at 6 months (n = 5); experimental 1 autologous bone + PRP and delayed implants at 4 months (n = 5); experimental 2: autologous bone + PRP and delayed implants at 6 months (n = 5)	Yes
Yilmaz et al (2013)[71]	To evaluate the effect on sinus floor augmentation of PRP with bovine xenograft as compared to bovine xenograft alone in terms of radiographical and histologic outcomes	Biologic agent (PRP) + scaffold (bovine xenograft)	RCT (split mouth)	Yes	20 patients for 40 maxillary sinuses	Complete and partial	Control: Particulated xenograft (bovine); experimental: particulated xenograft (bovine) with PRP	Yes
Hermund et al (2012)[80]	To evaluate histologically whether the addition of cultivated, autogenous bone cells to a composite graft of bovine xenograft and autogenous bone for sinus floor augmentation enhance bone formation compared to the bovine xenograft and autogenous bone mixture alone.	Cell-based therapy + scaffold (xenograft) + autologous bone	RCT (parallel arms)	Yes	20 patients for 20 maxillary sinuses	Partial	Control: Particulated xenograft (bovine) with autologous bone; experimental: particulated xenograft (bovine) and autologous bone with autologous, intraoral MSCs	Yes
Kao et al (2012)[78]	To evaluate the effect of rhBMP-2/ACS combined with bovine bone particles to the bovine bone alone for sinus elevation procedures in terms of histologic bone formation	Biologic agent (rhBMP-2) + scaffold (xenograft)	RCT (parallel arms)	Yes	22 patients for 22 sinuses (11 in each group)	Not specified	Control: Particulated xenograft (bovine); experimental: particulated xenograft (bovine) combined with rhBMP-2/ ACS	Yes
Sauerbier et al (2011)[86]	To evaluate the therapeutic potential of BMAC compared with autogenous bone in maxillary sinus augmentation	Cell-based therapy + scaffold (xenograft)	RCT (parallel arms)	Yes	26 patients for 45 maxillary sinuses, of which 7 were unilateral (11 control and 34 experimental)	Not specified	Control: bovine xenograft + autologous bone; experimental: bovine xenograft + BMAC	Yes
Stavropoulos et al (2011)[83]	To evaluate histologically the outcomes of maxillary sinus augmentation with rhGDF-5-coated βTCP as compared to a βTCP and autogenous bone composite	Biologic agent (rhGDF-5)	RCT (parallel arms)	Yes	31 patients for 31 maxillary sinuses	Not specified	Control: βTCP and autogenous bone; experimental: βTCP coated with rhGDF-5	Yes

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Yes	Clinical: Plaque index, gingival index, bleeding index, probing depth, and incidence of complications; radiographic: peri-implant marginal bone loss after 1 year of function; patient-centered: overall satifaction with therapy using a 1–10 scale	13–16 weeks	Yes (n = 66)	Up to 16 months (12 months from implant placement)	No	All clinical parameters and marginal bone loss changes were within normal limits and no differences were observed between groups. Three implants were lost prior to functional loading (no group specified), after that no implant was lost. The overall patient satisfaction was high (8.4/10).	2
Not reported	Clinical: Incidence of complications or adverse events; radiographic: height gain assessed on CT scans; histologic: quantification of tissue compartments % in bone core biopsies	4 months	Yes, but total number not specified	4 months (implants were not followed up)	No	No complications were observed. Radiographic height gain was adequate for implant placement and comparable between both groups. However, histologic and histomorphometric analyses showed unfavorable results on the test side evidenced by significantly less bone formation (test: 6.55% vs control: 19.88%).	2
Yes (histologic assessments)	Histologic: Quantification of tissue compartments % in bone core biopsies	6–9 months	Yes, but total number not specified	Not specified	Yes, 2 patients, but they were replaced	The results showed no statistically significant differences in vital bone formation between the 2 experimental groups compared to the control group. However, there was a statistically significant difference in terms of residual graft particles between experimental group A (10.5%) and the control group (23.2%) ($P = .003$).	2
Not reported	Clinical: Incidence of complications or adverse events; radiographic: densitometry assessed on panoramic radiographs; histologic: quantification of tissue compartments % in bone core biopsies	4–6 months	Yes	Up to 12 months (6 months after implant placement)	Not reported	No significant postoperative complications occurred during the study. The addition of PRP did not significantly improve bone density or histomorphometric values at 4 months after grafting. PRP-enriched bone grafts were associated with more bone density at 6 months postgrafting.	2
Yes (radiographic and histologic assessments)	Radiographic: Bone height gain assessed on CT scans; histologic: description of bone cores	8 months	Yes	8 months (implants were not followed up)	No	Both therapies lead to satisfactory and comparable radiographic and histologic outcomes.	2
Yes (histologic assessments)	Clinical: Incidence of complications and implant survival; histologic: quantification of tissue compartments % in bone core biopsies	4 months	Yes	4 months from implant placement	No	Clinical and histologic outcomes were satisfactory and comparable between both groups. This study failed to demonstrate any significant effect of cultivated autogenous bone cells in combination with a composite bone graft regarding the amount of new bone formation in maxillary sinus augmentation.	2
Not reported	Histologic: Quantification of tissue compartments % in bone core biopsies	Not specified	Yes	Not specified	No	Histologic analyses showed that the % of newly formed bone was less in those sinuses that received rhBMP-2/ACS + xenograft than those with xenograft alone.	2
Yes	Radiographic: Assessment of bone volume obtained using CT scans; histologic: quantification of tissue compartments % in bone core biopsies	3–4 months	Yes	Up to 4 months (implants were not followed up)	Yes, number and distribution not specified	Radiologic gain and stability of augmented bone height was statistically higher in the test group, but the average volumetric difference was 0.4 mL. New bone formation was similar in both groups, though the control group was slightly higher (14.3% vs 12.6%).	2
Yes (histologic assessments)	Clinical: Implant survival rate; histologic: quantification of tissue compartments % in bone core biopsies	3–4 months	Yes (n = 66)	Not specified	Yes, 1 patient	Implant survival rate in the experimental group was 91.5%. Sinus augmentation with rhGDF-5/b-TCP resulted in comparable amounts of new bone and of similar quality as those obtained with a βTCP/AB composite graft.	2

Table 15 *Continued* **RCTs (n = 21) on the Application of Tissue Engineering–Based Therapies for Maxillary Sinus Augmentation**

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/ Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Bettega et al (2009)[98]	To evaluate the osteogenic potential of PRP mixed with autologus bone in maxillary sinus augmentation as compared to autologous bone alone in terms of clinical, radiographic, and histologic outcomes	Biologic agent (PRP) + autologous bone	RCT (split mouth)	Yes	18 patients for 36 maxillary sinuses	Not specified	Control: Autologous bone; experimental: autologous bone + PRP	Yes
Torres et al (2009)[91]	To evaluate whether or not PRP improves the efficacy of bovine xenograft particles in sinus floor augmentation	Biologic agent (PRP) + scaffold (bovine xenograft)	RCT (parallel arms)	Yes	87 patients for 144 maxillary sinuses	Not specified	Control: particulated xenograft (bovine); experimental: particulated xenograft (bovine) with PRP	Yes
Triplett et al (2009)[12]	To evaluate the safety and effectiveness of rhBMP-2/ACS compared with an autogenous bone graft when used for 2-stage maxillary sinus floor augmentation	Biologic agent (rhBMP-2)	RCT (parallel arms)	Yes	160 patients	Both patients exhibiting complete and partial edentulism were recruited	Control: Autologous bone; experimental: rhBMP-2 + ACS	Yes
Aimetti et al (2008)[106]	To evaluate the histologic outcomes after using autogenous bone or autogenous bone combined with PRP in maxillary sinus augmentation	Biologic agent (PRP) + autologous bone	RCT (split mouth)	Yes	4 patients for 8 maxillary sinuses	Partial	Control: Autologous bone; experimental: autologous bone + PRP	Yes
Schaaf et al (2008)[102]	To examine the effect of PRP in addition to autologous bone in sinus floor augmentation	Biologic agent (PRP) + autologous bone	RCT (split mouth)	Yes	34 patients for 68 maxillary sinuses	Not specified	Control: Autologous bone; experimental: autologous bone + PRP	Yes
Consolo et al (2007)[108]	To evaluate the influence of PRP in addition to autologous bone in the process of osteogenesis after sinus floor augmentation	Biologic agent (PRP) + autologous bone	RCT (split mouth)	Yes	16 patients for 32 maxillary sinuses	Not specified	Control: Autologous bone; experimental: autologous bone + PRP	Yes
Boyne et al (2005)[10]	To evaluate two different concentrations of rhBMP-2 for safety and efficacy in terms of osteogenesis when applied for maxillary sinus floor augmentation	Biologic agent (rhBMP-2)	RCT (parallel arms)	Yes	48 patients for 89 maxillary sinuses	Both patients exhibiting complete and partial edentulism were recruited	Control: Autologous bone; experimental 1: rhBMP-2 0.75 mg/mL + ACS; experimental 2: rhBMP-2 1.50 mg/mL + ACS	Yes

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Yes (radiographic and histologic assessments)	Radiographic: assessment of bone density gains in CT scans; histologic: quantification of tissue compartments % in bone core biopsies	6 months	Yes (n = 111)	1 year after implant placement	No	The bone obtained in the experimental group had the same radiographic, histologic, and mechanical characteristics as the bone obtained by traditional graft.	2
Yes	Clinical: Incidence of complications and implant survival; radiographic: assessment of dimensional and density changes of the grafted volume using CT scans and panoramic radiographs taken at 6 months postgrafting; histologic: quantification of tissue compartments % in 10 bone core biopsies obtained from 5 patients that received bilateral sinus grafting	6 months	Yes (n = 286), some were placed simultaneously at the time of grafting, while others were placed in a delayed approach	24 months after implant placement	Not reported	Sinus membrane perforation was 5.7%. All sites healed uneventfully. Implant survival rate at 24 months was 98.6% and 96.2% in the experimental and control groups, respectively. Radiographic height gains and density were similar between groups. Histomorphometric analyses revealed that the area occupied by newly formed bone was higher in the experimental sites, while the average areas occupied by remaining xenograft particles were comparable between groups.	2
Yes (radiographic and histologic assessments)	Clinical: Safety, incidence of complications and implant survival and success; radiographic: assessment of density and height gain in CT scans + marginal bone loss around implants at 9 months after placement; histologic: qualitative assessment of bone formation using a scale (1–5) and cell counts; patient-centered outcomes: functional use of implant-supported prostheses up to 24 months	6 months	Yes (n = 492, of which 251 were placed in the control group and 241 in the experimental group)	24 months after implant loading	Yes, 33 patients	No abnormal adverse events were observed, however facial edema was more common in the experimental group. Mean height gain was 7.8 mm and 9.4 mm in the experimental and control sites, respectively. Radiographic bone density was higher in the experimental group. No marked differences were found in the histologic parameters evaluated between groups. Implant survival at 24 months was 82.5% in the experimental group and 80% in the control group.	2
Not reported	Histologic: BIC on mini-implants retrieved at 12 months after bone grafting	6 months	Yes, in each sinus one mini-implant that was retrieved after 6 months of healing was placed	6 months after implant placement	No	All sites healed in absence of complications. The average BIC was 46.7% in the experimental group and 20.5% in the control group.	2
Not reported	Clinical: Implant survival rate; radiographic: density and height changes; histologic: newly formed bone area % assessed in core biopsies	4 months	Yes (n = 245)	6 months after implant placement	No	Sinusitis incidence was 5.8%. Average implant failure rate was 3.6%, with no significant differences between groups. Bone density and newly formed bone area was not different between groups, either.	2
Yes (radiographic and clinical assessments)	Clinical: Incidence of complications; radiographic: densitometry of the grafted sites assessed on CT scans; histologic: quantification of tissue compartments % in bone core biopsies	Four biopsy harvesting times: 4, 5, 6, and 7 months	Yes	Up to 7 months (implants were not followed up)	No	Clinical and radiographic outcomes showed no significant differences between control and experimental sites. However, histologic analyses revealed that sites treated with PRP exhibited better short-term results in terms of earlier bone formation.	2
Yes (Radiographic assessments)	Clinical: Safety, incidence of complications and implant survival and success; radiographic: assessment of alveolar ridge height, width and density in CT scans + marginal bone loss around implants; Histologic: qualitative assessment of bone formation using a scale (1 to 5) and cell counts	4 months	Yes (n=219)	36 months after implant loading	Yes, 5 patients, all from the experimental groups	All of the patients that participated in the study experienced adverse events, but the majority of events (94%) were of transient and of mild or moderate nature. Edema was more common in the control group. At 4 months, mean height gain was 11.2 mm in experimental group 1, 9.4 mm in experimental group 2, and 10.1 mm in control sites. Radiographic bone density was higher in the control group. No significant differences were found in the histologic parameters evaluated between groups. Implant survival at 36 months was 88% in the experimental group 1, 79% in the experimental group 2, and 81% in the control group.	2

Table 15 *Continued* **RCTs (n = 21) on the Application of Tissue Engineering–Based Therapies for Maxillary Sinus Augmentation**

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/ Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Kassolis et al (2005)[113]	To compare bone formation after subantral maxillary sinus augmentation with FDBA plus PRP versus FDBA plus resorbable membrane	Biologic agent (PRP) + Scaffold (allograft)	RCT (split mouth)	No	10 patients for 20 maxillary sinuses	Not specified	Control: FDBA; experimental: FDBA + PRP	Yes
Raghoebar (2005)[111]	To evaluate the effect of PRP on remodeling of autologous bone grafts used for augmentation of the floor of the maxillary sinus	Biologic agent (PRP) + autologous bone	RCT (split mouth)	Yes	5 patients for 10 maxillary sinuses	Complete	Control: Autologous bone; experimental: autologous bone + PRP	Yes
Steigmann et al (2005)[110]	To compare the alveolar bone growth after using PRP alone versus βTCP alone in maxillary sinus augmentation with simultaneous implant placement	Biologic agent (PRP)	RCT (split mouth)	No	20 patients for 40 maxillary sinuses	Not specified	Control: βTCP; experimental: PRP	Yes
Wiltfang et al (2003)[117]	To investigate whether the addition of PRP to βTCP enhances bony regeneration and resorption of the alloplastic material in a sinus augmentation model	Biologic agent (PRP) + scaffolds (βTCP)	RCT (parallel arms)	No	39 patients for 45 maxillary sinuses	Not specified	Control: βTCP (n = 23); experimental: PRP + βTCP (n = 22)	Yes
Froum et al (2002)[121]	To test the efficacy of PRP with grafts of anorganic bovine bone that contained minimal or no autogenous bone in maxillary sinus grafting	Biologic agent (PRP) + scaffold (bovine xenograft)	RCT (split mouth)	Yes	3 patients for 6 maxillary sinuses	Not specified	Control: Particulated xenograft (bovine); experimental: particulated xenograft (bovine) with PRP	Yes

Nonrandomized Clinical Trials (Table 16). Eight nonrandomized clinical trials were identified for this clinical scenario after the search and selection protocol was applied. Three of them evaluated the use of autologous blood-derived products (PRP or PRGF) in combination with a scaffold (ie, bovine xenograft or alloplastic materials) and/or autologous bone,[76,79,81] two assessed the use of a bovine xenograft with a surface biomimetic peptide,[77,116] two clinical trials evaluated the application of cell therapy approaches,[96,107] and one study tested the effect of rhBMP-7/ACS in maxillary sinus augmentation.[122] The total follow-up time ranged from 5 months from the time of implant placement[81] to 24 months after implant loading. All the clinical trials had an adequate control group, but the absence of randomization and, in some instances, blinding of the examiners makes these data less significant for the assessment of efficacy and effectiveness of tissue engineering therapies for maxillary sinus augmentation.

The therapy associated with the largest patient population was autologous blood-derived products. In only one of the three selected studies, clinical (ie, incidence of complications and subjective visual perception of healing)[81] and radiographic (ie, marginal bone loss around implants)[79] outcomes were assessed, while histologic outcomes (ie, histomorphometric analyses of bone core biopsies) were reported in two of them.[76,81] Unfortunately, the results reported in these studies were either poorly presented or lacked significance to extract valid conclusions regarding the efficacy and effectiveness of this therapy.

Histologic outcomes (ie, histomorphometric analyses of bone core biopsies) were reported in the two studies that compared the effect of bovine xenograft with a surface biomimetic peptide compared with conventional grafting therapies,[77,116] while only one looked at clinical outcomes (ie, incidence of complications).[116] The results reported in these two studies indicate that the experimental therapy performed similarly to the control.

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Yes (histologic assessments)	Radiographic: Assessment of bone height gain in CT scans; histologic: quantification of tissue compartments % in bone core biopsies	4.5–6 months	Yes	8 weeks after implant placement	No	Average height gain was comparable between both groups (~8 mm). All biopsy specimens demonstrated histologic findings consistent with bone formation. A significantly greater percentage of vital tissue (bone and connective tissue) was found in subantral spaces grafted with FDBA and PRP (78.8%) than with FDBA alone (63.0%).	2
Yes (histologic and clinical assessments)	Clinical: Incidence of complications and implant failure rate; radiographic: microradiographic density assessments of core biopsies; histologic: quantification of tissue compartments % in bone core biopsies using light microscopy	3 months	Yes (n = 30)	Average of 20 months after implant loading	Not reported	No significant differences in terms of microradiographic density, wound healing, complications, and implant failure rate were observed between groups. Only one implant failed (from the experimental group). Similarly, histologic analyses revealed no remarkable differences between biopsies from both groups: average mineralized tissue area was 41.1% in the test group and 38.4% in the control group.	2
Not reported	Radiographic: Subjective perception of bone density on panoramic radiographs	6 months	Yes	Not specified	No	Radiographic density was compatible with new bone formation on both groups, with slightly higher density on the control side, probably because of the presence of remaining graft particles.	2
Not reported	Clinical: Incidence of complications; radiographic: bone height achieved assessed on panoramic radiographs; histologic: quantification of tissue compartments % in bone core biopsies using light microscopy	6 months	Yes, but total number not specified	Not specified	Not reported	All sites healed in absence of complications. Radiographic bone height achieved at 6 months was comparable between groups and sufficient for regular implant placement. In control sites bone area ranged from 25%–37%, while in the experimental group it ranged from 32%–43%. A faster degradation of the alloplastic material was not observed in the experimental group.	2
Yes (histologic assessments)	Histologic: BIC on mini-implants retrived at 11 months after bone grafting and quantification of tissue compartments % in bone core biopsies using light microscopy	7–11 months	Yes	Up to 11 months (implants were not followed-up)	No	Histomorphometric analysis indicated that the addition of PRP did not make a significant difference either in vital bone formation or in BIC. Vital bone formation was 21.3% and 23.3% in the control and experimental sites, respectively.	2

In the studies that involved the use of cell therapy, clinical (ie, incidence of complications), radiographic (ie, dimensional linear and density changes of the grafted volume), and histologic (ie, histomorphometric analysis of 10 bone core biopsies) outcomes were assessed only in one of them,[96] whereas the other clinical trial reported only radiographic outcomes (ie, density and volumetric changes of the graft).[107] Interestingly, the results of both clinical trials indicate that the control therapy outperformed the experimental therapy for all the parameters analyzed.

A study comparing the effect of rhBMP-7/ACS with that of autologous bone reported clinical (ie, incidence of complications and adverse events), radiographic (ie, height gain at 6 months), and histologic (ie, histomorphometric analysis of bone core biopsies) outcomes.[122] The results were very unfavorable for the test therapy because successful clinical, radiographic, and histologic outcomes were observed only in one of four sinuses treated with rhBMP-7/ACS. Hence, the application of osteogenic protein 1 for maxillary sinus augmentation was found to be unpredictable, compared with the use of autologous bone as the sole grafting material.

Case Series (Table 17). A total of 25 case series on maxillary sinus augmentation performed using a tissue engineering–based approach were selected. The follow-up time in these case studies ranged from 4 months from the time of grafting[95] to up to 6 years after implant loading.[85,100] Ten studies reported the use of autologous blood-derived products (PRP, platelet-rich fibrin, or PRGF) alone or in combination with a scaffold (ie, bovine xenograft or alloplastic materials) and/or autologous bone. Of these 10 studies, 9 reported clinical outcomes (ie, incidence of complications, implant survival, and success rate),[72,73,84,85,93,99,115,119,126] 8 included radiographic outcomes (ie, bone height gain, density of the graft and dimensional changes of the grafted volume),[72,73,84,85,93,114,119,126] and 5 assessed histologic parameters (ie, descriptive histology and histomorphometric analyses of bone core biopsies).[84,93,99,119,126]

Table 16 Nonrandomized Clinical Trials (n = 8) on the Application of Tissue Engineering–Based Therapies for Maxillary Sinus Augmentation

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/ Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Anitua et al (2012)[81]	To evaluate the effect of PRGF with bovine xenograft compared with bovine xenograft alone in the clinical and histologic outcomes of maxillary sinus augmentation	Biologic agent (PRGF) + scaffold (bovine xenograft)	Nonrandomized clinical trial (split mouth)	Yes	5 patients for 10 maxillary sinuses	Partial	Control: Particulated xenograft (bovine); experimental: particulated xenograft (bovine) with PRGF	Not reported
Inchingolo et al (2012)[79]	To show the effectiveness of a protocol involving the use of PRP as a grafting material in maxillary sinus augmentation	Biologic agent (PRP) + autologous bone	Nonrandomized clinical trial (parallel arms)	No	127 patients for 127 maxillary sinuses (64 control and 63 experimental)	Not specified	Control: Autologous bone with simultaneous implant placement; experimental: autologous bone + PRP with simultaneous implant placement	Not reported
Pettinicchio et al (2012)[77]	To compare the histologic behavior of three bone grafting materials (synthetic hydroxyapatite, bovine xenograft, and bovine xenograft with a biomimetic peptide [P-15])	Scaffold with biomimetic peptide (xenograft + peptide P-15)	Nonrandomized clinical trial (parallel arms)	No	15 patients for 15 maxillary sinuses (5 per group)	Not specified	Group 1 (control): synthetic hydroxyapatite; group 2 (control): bovine xenograft; group 3: bovine xenograft with biomimetic peptide	No
Poeschl et al (2012)[76]	To evaluate the effect of PRP on new bone formation and remodeling after grafting of the maxillary sinus with an algae-derived hydroxyapatite	Biologic agent (PRP) + scaffold (algae-derived hydroxyapatite) + autologous bone	Nonrandomized clinical trial	Yes	25 patients for 32 sinuses, some patients underwent bilateral augmentation (14 control and 18 experimental)	Not specified	Control: Alloplast (algae-derived) + autologous bone; experimental: alloplast (algae-derived) + autologous + PRP	No
Mangano et al (2009)[96]	To evaluate the outcomes of maxillary sinus augmenation performed with engineered bone tissue, obtained through a culture of autogenous osteoblasts seeded on PLGA as compared to calcium phosphate	Cell-based therapy + sLGA	Nonrandomized clinical trial (split mouth)	Yes	5 patients for 10 maxillary sinuses	Not specified	Control: Calcium phosphate; experimental: autologous osteoblasts + PLGA matrix	Not reported
Zizelmann et al (2007)[107]	To quantify the resorption rate of tissue-engineered bone grafts in the maxillary sinus using volume measurements	Cell-based therapy + scaffold (PLGA)	Nonrandomized clinical trial	Yes	20 patients for 31 maxillary sinuses	Not specified	Control: Autologous bone; experimental: autologous osteoblasts + PLGA matrix	Not reported
Degidi et al (2004)[116]	To evaluate the outcomes after maxillary sinus augmentation procedures using a xenograft covered with a biomimetic peptide or xenograft in combination with autologous bone	Scaffold with biomimetic peptide (xenograft with peptide P-15)	Nonrandomized clinical trial	Yes	7 patients for 11 maxillary sinuses	Partial	Control: Xenograft particles with autologous bone; experimental 1: xenograft + xenograft with peptide P-15; experimental 2: autologous bone + xenograft with peptide P-15	Not reported
van den Bergh et al (2000)[122]	To determine the osteogenic response after using OP-1 in a collagen carrier for maxillary sinus augmentation	Biologic agent (rhOP-1/BMP-7)	Nonrandomized clinical trial	Yes	6 patients for 7 maxillary sinuses	Partial	Control: Autologous bone (n = 3 sinuses); experimental: OP-1 in a collagen carrier (n = 4 sinuses)	Not reported

PRGF = plasma rich in growth factors; RCT = randomized clinical trial; PRP = platelet-rich plasma; SEM = scanning electronic microscopy; PLGA = polylactic-co-glycolic acid; CT = computed tomography; HU = Hounsfield unit(s); OP-1 = osteogenic protein 1 (also known as recombinant human bone morphogenetic protein type 7); BMP = bone morphogenetic protein.

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Incidence of complications and visual perception of healing; histologic: quantification of new bone formation in bone core biopsies (only two biopsy specimens were analyzed)	5 months	Yes	5 months (implants were not followed-up)	1	The findings of this low-powered RCT revealed that the addition of PRGF to xenograft particles may enhance maxillary sinus floor augmentation histologic outcomes.	3
Not reported	Radiographic: Changes in peri-implant bone levels expressed in mm ranges	6 months	Yes	6 months (implants were placed simultaneously)	No	The results are poorly reported and displayed, however it seems that both therapies achieved comparable outcomes.	3
No	Histologic: Quantification of tissue compartments % in bone core biopsies using light microscopy and SEM	6 months	Yes	6 months (implants were not followed-up)	No	All the tested materials exhibited a close integration with the surrounding bone. None of the materials was completely absorbed. The observed outcomes were comparable for both the xenograft and the xenograft with a biomimetic peptide.	3
No	Histologic: Quantification of tissue compartments % in bone core biopsies	6 months	Yes	Not specified	No	Significantly better overall resorption of algae-derived hydroxyapatite and increased new bone formation, particularly in the apical region, was observed in the samples harvested from the experimental group.	3
Not reported	Clinical: Incidence of complications; radiographic: assessment of dimensional and density changes of the grafted volume using CT scans taken at 2 different time points; histologic: quantification of tissue compartments % in 10 bone core biopsies	6 months	Yes	Up to 5 months after implant placement	No	No complications were observed during the healing period. Mean vertical bone gain was 6.47 mm and 9.14 mm in test and control sites, respectively. Mean bone tissue in the grafted area was 37.3% and 54.6% in the test and control groups, respectively. Hence, the experimental therapy does not seem to offer an additional benefit.	3
Not reported	Radiographic: Density and volumetric changes of the grafted area	3 months	Yes, some were placed simultaneously at the time of grafting, while others were placed in a delayed approach	3 months (implants were not followed-up)	Not reported	The total resorption rate for the control group at 3 months was 29%, while the experimental group showed a resorption rate of 90%. Similarly, bone density ranged from 266–551 HU, while the experimental group showed very poor densitometry results with only one case exhibiting sufficient density compatible with mineralization (152 HU).	3
Not reported	Clinical: Incidence of complications; histologic: quantification of tissue compartments % in bone core biopsies using light microscopy	6 months	Yes (n = 33)	24 months after implant loading	Not reported	All sites healed uneventfully, except for minor localized inflammation. No implants were lost during the study period. Average newly formed bone area was 38.8% in the control group, 36.7% in experimental group 1, and 32.2% in experimental group 2. Residual graft particles areas were 14.4% in the control group, 19.6% in experimental group 1, and 28.8% in experimental group 2.	3
Not reported	Clinical: Incidence of complications or adverse events; radiographic: height gain assessed on panoramic radiographs; histologic: quantification of tissue compartments % and cell counts in bone core biopsies	6 months	Yes	6 months (implants were not followed-up)	No	Only in 1 of 4 sinuses treated with OP-1 was a successful set of clinical, radiographic, and histologic outcomes observed. Hence, the application of OP-1 for maxillary sinus augmentation was found to be not predictable, compared with the use of autologous bone as the sole grafting material.	3

Table 17 Case Series (n = 25) on the Application of Tissue Engineering–Based Therapies for Maxillary Sinus Augmentation

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/ interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Mendonça-Caridad et al (2013)[73]	To assess the long-term outcomes of implants placed simultaneously with maxillary sinus floor elevation using a combined scaffold of laminated calvarial bone, PRP, and βTCP	Biologic agent (PRP) + scaffolds (βTCP) + autologous bone	Case series	Yes	30 patients for 52 maxillary sinuses (22 bilateral and 8 unilateral sinus grafting)	Not specified	N/A	N/A
Yamada et al (2013)[72]	To evaluate the effects of tissue-engineered bone (autologous bone marrow stem cells and PRP) used as a grafting material for sinus grafting via an osteotome technique with simultaneous implant placement	Cell-based therapy + biologic agent (PRP)	Case series	Yes	23 patients for 23 maxillary sinuses	Partial	N/A	N/A
Butz et al (2011)[88]	To investigate the time-dependent efficacy of bovine xenograft with a biomimetic peptide (P-15) for maxillary sinus augmentation	Scaffold with biomimetic peptide (xenograft + peptide P-15)	Case series	Yes	24 patients for 48 maxillary sinuses	Complete	Patients were randomly assigned to 4 different groups depending on the time of biopsy harvesting, but all participants received the same therapy	N/A
Montesani et al (2011)[87]	To report 2 cases in which a maxillary sinus augmentation technique was applied using tissue-engineered bone	Cell-based therapy + autologous bone	Case series	No	2 patients for 3 maxillary sinuses	Partial	N/A	N/A
Simonpieri et al (2011)[85]	To describe the use of PRF clots as the sole filling material during lateral sinus lift with simultaneous implant placement	Biologic agent (PRF)	Case series	No	20 patients for 23 maxillary sinuses	Not specified	N/A	N/A
Sohn et al (2011)[84]	To evaluate the predictability of new bone formation in the maxillary sinus using autologous fibrin-rich blocks with concentrated growth factors alone	Biologic agent (PRP)	Case series	Yes	53 patients for 61 maxillary sinuses	Not specified	N/A	N/A
Trautvetter et al (2011)[82]	To evaluate the long-term effect of autologous tissue-engineered periosteal bone grafts on atrophic maxillary bone	Cell-based therapy	Case series	No	10 patients for 13 maxillary sinuses	Not specified	N/A	N/A
Tarnow et al (2010)[89]	To determine an appropriate method of incorporating a mineralized bone replacement graft into the Infuse bone graft and to compare 2 different doses of this combination	Biologic agent (rhBMP-2) + scaffold (xenograft)	Case series	No	3 patients for 6 maxillary sinuses	Not specified	N/A	N/A
Anitua et al (2009)[99]	To report the clinical and histologic outcomes of maxillary sinus augmentation using PRGF	Biologic agent (PRGF) + scaffold (bovine xenograft)	Case series	Yes	18 patients, number of maxillary sinuses was not specified	Not specified	N/A	N/A
Fuerst et al (2009)[97]	To examine the healing process after maxillary sinus augmentation with culture-expanded autogenous bone-derived cells	Cell-based therapy + scaffold (xenograft)	Case series	Yes	12 patients for 22 maxillary sinuses	Not specified	N/A	N/A

PRP = platelet-rich plasma; βTCP = beta-tricalcium phosphate; N/A = not applicable; CT = computed tomography; PRF = platelet-rich fibrin; PRGF = plasma rich in growth factors; rhBMP-2 = recombinant human bone morphogenetic protein type 2; CBCT = cone beam computed tomography; rhPDGF-BB = recombinant human platelet derived growth factor type BB; PLA = polylactic acid; rhTF = human recombinant tissue factor; ACS = absorbable collagen sponge.

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Incidence of complications, implant survival and success rate; radiographic: bone height gain	4–6 months	Yes (n = 86)	Average: 12.8 months (range: 3.1–34.2 months)	No	Sinus floor elevation and implant placement via the described technique is compatible with satisfactory clinical outcomes, including high long-term implant survival and success rates.	4
Not reported	Clinical: Incidence of complications; radiographic: bone height gain assessed on CT scans	6 months	Yes (n = 23)	1 year (implants were placed simultaneously)	No	The technique presented in this case series study was not associated with any significant complications. Bone height gains appeared stable over the observational period. Implant survival rate was 100% 1 year after placement.	4
Not reported	Clinical: Incidence of complications; histologic: quantification of tissue compartments % in bone core biopsies using microCT and light microscopy	2, 4, 6, or 9 months	Yes (n = 127)	Not specified	No	The use of bovine xenograft with a biomimetic peptide is a viable option for maxillary sinus augmentation. Bone core biopsies harvested at different time points revealed that sufficient bone healing for implant placement could be achieved at 2 months postgrafting.	4
Not reported	Clinical: Incidence of complications	4 months	Yes	12 months	No	The reported augmentation technique was not associated with complications. During a 12-month follow-up period, no implant failure was observed.	4
Not reported	Clinical: Implant failure rate; radiographic: bone height gain and stability of the grafted area assessed on panoramic radiographs and CT scans	6 months	Yes (n = 52)	2–6 years	Not reported	No implant was lost during the observational period. Radiographic height gain ranged from 8.5–12 mm, and remained generally stable in all grafted sites.	4
Not reported	Clinical: Incidence of complications; radiographic: bone height achieved assessed on panoramic radiographs or CT scans; histologic: quantification of tissue compartments % in bone core biopsies	Average of 5 months	Yes (n = 113)	Average of 10 months after implant loading	No	No significant complications occurred. Implant survival rate was 98.2%. Observed outcomes indicate that the use of PRP as a sole grafting material may be an alternative in maxillary sinus augmentation; however, it is important to note that bone height gains ranged from 6–10 mm.	4
Not reported	Clinical: Incidence of complications; radiographic: bone height achieved assessed on panoramic radiographs; histologic: description of 2 bone core biopsies	6 months	Yes (n = 21)	5 years	No	No significant complications occurred during the observation period. Median radiographic bone height was 6.9 and 14.2 mm at baseline and at 5 years, respectively. Histologic features of the 2 bone biopsies harvested at 6 months were compatible with normal osseous tissue.	4
Not reported	Clinical: Incidence of complications; radiographic: dimensional changes of the grafted volume using CBCT; histologic: description of bone core biopsies obtained from 2 patients	6 months	Yes	6 months (implants were not followed up)	No	The grafted sites healed uneventfully in all cases. Radiographic bone density tended to increase over time during the 6-month observational period. Histology revealed robust new woven bone formation with only minimal traces of residual allograft, which appeared to have undergone accelerated remodeling or rhBMP-2–mediated resorption.	4
Not reported	Clinical: Incidence of complications; histologic: description and quantification of tissue compartments % in 8 bone core biopsies	5–6 months	Yes (n = 43)	Average: 33 months (range: 24–44 months)	No	On the basis of the reported outcomes, the described clinical protocol can be considered a viable approach for maxillary sinus augmentation.	4
Not reported	Clinical: Incidence of complications and implant survival; radiographic: assessment of dimensional changes of the grafted volume using CT scans taken at 3 different time points; histologic: quantification of tissue compartments % in bone core biopsies	6 months	Yes	6 months after implant placement	No	All graft sites healed uneventfully. Average newly formed bone was 17.9%. The average graft volume was 2,218.4 mL at the time of CT 1, 1,694 mL at the time of CT 2, and 1,347.9 mL at the time of CT 3. Three implants were lost at implant uncovery.	4

Table 17 *Continued* **Case Series (n = 25) on the Application of Tissue Engineering–Based Therapies for Maxillary Sinus Augmentation**

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/ interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
McAllister et al (2009)[95]	To evaluate the bone formation following sinus augmentation procedures using an allograft cellular bone matrix containing native mesenchymal stem cells	Cell-based therapy + scaffold (allograft)	Case series	Yes	5 patients, number of maxillary sinuses was not specified	Not specified	N/A	N/A
Nevins et al (2009)[94]	To examine the potential of enhanced osteogenesis in maxillary sinus augmentation procedures when rhPDGF-BB is combined with particulate bovine xenograft	Biologic agent (rhPDGF-BB) + scaffold (xenograft)	Case series	Yes	10 patients for 13 maxillary sinuses	Not specified	N/A	N/A
Papa et al (2009)[93]	To evaluate clinical, radiographic, and histologic outcomes of 47 sinus lifts with lateral approach using a mixture of aragonitic calcium carbonate and PRP	Biologic agent (PRP) + scaffold (aragonitic calcium carbonate)	Case series	Yes	34 patients for 47 maxillary sinuses	Not specified	N/A	N/A
Beaumont et al (2008)[104]	To report the clinical, radiographic, and histologic outcomes after employing a tissue-engineered bone for maxillary sinus augmentation	Cell-based therapy + scaffolds (primary carrier: PLA matrix; adjuvant scaffold: bovine xenograft particles)	Case series	Yes	3 patients for 6 maxillary sinuses	Not specified	N/A	N/A
Shayesteh et al (2008)[101]	To evaluate the effect of the addition of mesenchymal stem cells to βTCP for maxillary sinus grafting	Cell-based therapy + scaffold (alloplast: βTCP)	Case series	Yes	30 patients for 34 maxillary sinuses	Not specified	N/A	N/A
Yamada et al (2008)[100]	To clinically evaluate injectable tissue-engineered bone (autologous bone marrow stem cells and PRP) for maxillary sinus floor augmentation and simultaneous implant placement	Cell-based therapy + biologic agent (PRP)	Case series	Yes	12 patients for 16 maxillary sinuses	Both patients exhibiting complete and partial edentulism were recruited	N/A	N/A
Graziani et al (2005)[114]	To evaluate the clinical efficacy of PRP, autologous bone, and autologous fibrinogen as cryoprecipitate in maxillary sinus augmentation procedures	Biologic agent (PRP) + autologous bone	Case series	No	6 patients for 6 maxillary sinuses	Not specified	N/A	N/A
Philippart et al (2005)[112]	To evaluate the effect of a combination bone graft consisting of autologous bone, xenograft with a biomimetic peptide, PRP, and rhTF in the histologic outcomes of maxillary sinus augmentation	Biologic agents (PRP and rhTF) + biomimetic peptide in a scaffold (xenograft with peptide P-15) + autologous bone	Case series	No	3 patients for 4 maxillary sinuses	Both patients exhibiting complete and partial edentulism were recruited	N/A	N/A
Ueda et al (2005)[125]	To evaluate the use of tissue-engineered bone consisting of a combination of mesenchymal stem cells, PRP, and βTCP as a grafting material for maxillary sinus augmentation	Cell-based therapy + biologic agent (PRP) + scaffold (βTCP)	Case series	Yes	6 patients for 7 maxillary sinuses	Partial	N/A	N/A

PRP = platelet-rich plasma; βTCP = beta-tricalcium phosphate; N/A = not applicable; CT = computed tomography; PRF = platelet-rich fibrin; PRGF = plasma rich in growth factors; rhBMP-2 = recombinant human bone morphogenetic protein type 2; CBCT = cone beam computed tomography; rhPDGF-BB = recombinant human platelet derived growth factor type BB; PLA = polylactic acid; rhTF = human recombinant tissue factor; ACS = absorbable collagen sponge.

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Histologic: Quantification of tissue compartments % in bone core biopsies	4 months	Yes	4 months (implants were not followed up)	No	Histologic analyses revealed an average vital bone content of 33% (range: 22%–40%) and a residual allograft content of 6% (range: 3%–7%). Hence, this case series shows that the described therapeutic approach may be a valid option for maxillary sinus augmentation.	4
Not reported	Histologic: Quantification of tissue compartments % in bone core biopsies using light microscopy and microCT	6–8 months	Yes	Up to 8 months (implants were not followed up)	No	Histologic analysis showed strong osteogenic response when rhPDGF was combined with bovine xenograft particles, evidenced by the observation of large areas of dense, well-formed lamellar bone and abundant numbers of osteoblasts in concert with significant osteoids in all sites, which may be indicative of ongoing osteogenesis.	4
Not reported	Clinical: Incidence of complications; radiographic: assessment of height gain in CT scans and x-ray microanalysis; histologic: quantification of tissue compartments % in bone core biopsies	Maximum of 12 months	Yes, some were placed simultaneously at the time of grafting, while others were placed in a delayed approach	Up to 18 months from the time of grafting	Yes, 4 patients for a total of 7 maxillary sinuses	Observed complications were essentially sinus membrane perforation (51%), premature wound dehiscence (27.6%), and excessive graft resorption and/or infection (38.5%). Average radiographic height gain was adequate (> 12 mm) in both simultaneous and delayed implant placement sites. A slight decrease of radiographic bone height was observed over time up to the 12-month follow-up. Histologically, new bone formation and microhardness were compatible with a successful osteogenic response.	4
Not reported	Clinical: Incidence of complications and implant primary stability; radiographic: assessment of height and density changes using periapical radiographs and CT scans; histologic: description of bone core biopsies using light microscopy	6 months	Yes (n = 19 total, but 10 in maxillary sinus areas)	12 months after implant placement	No	No significant complications were observed. All implants achieved primary stability. Radiographic bone height in augmented areas at 18 months was significantly greater than at baseline, as expected. Histologic analyses demonstrated that the biopsies were constituted by normal osseus tissue in absence of inflammation or other signs of pathology.	4
Not reported	Clinical: Implant failure rate; radiographic: bone height gain assessed on panoramic radiographs; histologic: quantification of tissue compartments % in bone core biopsies	3 months	Yes (n = 30)	9 months after implant placement	Not reported	Two implants failed at the time of uncovery, hence failure rate was 6.6%. Average radiographic height gain was 10.8 mm. Histologic analysis showed that newly formed bone area was 41.3%.	4
Not reported	Clinical: Incidence of complications; radiographic: bone height gain assessed on panoramic radiographs and CT scans; histologic: description of bone core biopsies under light microscopy	5–9 months	Yes (n = 41)	Range of 2–6 years after implant placement	Not reported	No significant complications occurred during the observation period. Average radiographic height gain was 8.8 mm at 24 months. Histologic description of biopsies is compatible with normal bone.	4
Not reported	Radiographic: Assessment of bone height and density gain in CT scans	6 months	Yes	6 months (implants were not followed up)	No	The technique appeared to be safe and effective on the basis of the observed outcomes. Average radiographic height gain was 6.2 mm and the Hounsfield-Misch density was D2 in 5 cases and D3 in 1 case.	4
Not reported	Histology: Description of bone core biopsies using light microscopy	Two biopsy harvesting times: 6 and 10 months	Yes	Up to 10 months from the time of grafting (implants were not followed up)	No	Histologic analysis showed a high degree of xenograft integration and new bone formation. The proportion of remaining xenograft particles decreased from 6 to 10 months.	4
Not reported	Clinical: Incidence of complications; radiographic: bone height gain assessed on CT scans	4–6 months	Yes (n = 20, all simultaneously placed with grafting)	12 months after implant loading	No	No significant complications occurred during the observation period. All implants were stable at implant uncovery surgery. Average radiographic height gain was 7.3 mm at 6 months.	4

Table 17 *Continued* **Case Series (n = 25) on the Application of Tissue Engineering–Based Therapies for Maxillary Sinus Augmentation**

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/ interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Mazor et al (2004)[115]	To report clinical and radiographic outcomes after the use of PRP in combination with autologous bone and xenograft particles for maxillary sinus augmentation	Biologic agent (PRP) + scaffold (bovine xenograft) + autologous bone	Case series	No	105 patients for 105 maxillary sinuses	Partial	N/A	N/A
Maiorana et al (2003)[126]	To present preliminary clinical and histologic results after using PRP in combination with bovine xenograft particles for maxillary sinus augmentation	Biologic agent (PRP) + scaffold (bovine xenograft)	Case series	Yes	10 patients for 11 maxillary sinuses	Not specified	N/A	N/A
Philippart et al (2003)[120]	To evaluate the effect of a combination bone graft consisting of autologous bone, PRP, and rhTF in the histologic outcomes of maxillary sinus augmentation	Biologic agents (PRP and rhTF) + biomimetic peptide in a scaffold (xenograft with peptide P-15) + autologous bone	Case series	No	18 patients for 25 maxillary sinuses	Both patients exhibiting complete and partial edentulism were recruited	N/A	N/A
Rodriguez et al (2003)[119]	To evaluate the use of PRP in combination with particulated bovine xenograft as a grafting material for maxillary sinus floor lift	Biologic agent (PRP) + scaffold (bovine xenograft)	Case series	No	15 patients for 24 maxillary sinuses	Not specified	N/A	N/A
Schmelzeisen et al (2003)[118]	To report the clinical and histologic outcomes of a grafting technique consisting on the application of periosteal-derived autologous cells in a polymer carrier for maxillary sinus augmentation	Cell-based therapy + scaffold (polymer-specific composition not specified)	Case series	No	2 patients for 2 maxillary sinuses	Partial	N/A	N/A
Boyne et al (1997)[124]	To test the technical feasibiiity and safety of using rhBMP-2/ ACS for inducing osteogenesis in patients requiring maxiilary sinus augmentation	Biologic agent (rhBMP-2)	Case series	Yes	12 patients for 12 maxillary sinuses	Not specified	N/A	N/A

PRP = platelet-rich plasma; βTCP = beta-tricalcium phosphate; N/A = not applicable; CT = computed tomography; PRF = platelet-rich fibrin; PRGF = plasma rich in growth factors; rhBMP-2 = recombinant human bone morphogenetic protein type 2; CBCT = cone beam computed tomography; rhPDGF-BB = recombinant human platelet derived growth factor type BB; PLA = polylactic acid; rhTF = human recombinant tissue factor; ACS = absorbable collagen sponge.

Eight case series were on the application of cell therapy alone or in combination with a scaffold. Of these eight studies, seven reported clinical outcomes (ie, incidence of complications, implant primary stability, and implant survival or failure rate),[72,82,87,97,101,104,118] five included radiographic outcomes (ie, bone height gain and density of the grafted volume),[72,82,97,101,104] and six reported histologic parameters (ie, descriptive histology and histomorphometric analyses of bone core biopsies).[82,95,97,101,104,118] Two studies assessed the effect of rhBMP-2/ACS alone or in combination with a scaffold (ie, bovine xenograft),[89,124] both reported clinical (ie, incidence of complications and implant survival and success rate), radiographic (ie, height gain and density of the grafted volume), and histologic outcomes (ie, descriptive and qualitative assessment of bone formation in bone core biopsies). Two studies evaluated a combination of βTCP, PRP, and expanded pluripotential bone marrow cells.[100,125] Both studies reported clinical (ie, incidence of complications) and radiographic (ie, bone height gain) outcomes, and only one of them presented histologic results (ie, descriptive histology of bone

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Incidence of complications and perception of healing	6 months	Yes, all were placed simultaneously with grafting	Not specified	Not reported	The impression of the authors was that the soft tissue healing was faster than in cases where PRP was not used. Three patients had postoperative sinus infections. Two implants were lost at second-stage surgery, but implant failure rate was not reported.	4
Not reported	Clinical: Subjective perception of bone healing; radiographic: apparent density and grafted volume stability assessed on 2 CT scans obtained at 3 and 6 months postgrafting; histologic: quantification of tissue compartments % in 2 bone core biopsies using light microscopy	6–7 months	Yes (n = 30)	Up to 7 months (implants were not followed up)	No	All grafting procedures were considered successful because of the absence of significant complications and the ability to place implants of at least 13 mm in length in the planned prosthetic position. Grafted volumes appeared to be stable between 3 and 6 months postgrafting. In the 2 bone core biopsies analyzed, the proportion of newly formed bone plus remaining xenograft particles was approximately 40%.	4
Not reported	Clinical: Incidence of complications and implant failure rate; histologic: description of bone core biopsies using light microscopy	5–6 months	Yes (n = 58)	48 months after implant loading	Only 1 patient was evaluated at the 48-month follow-up visit	All sites healed uneventfully. Five implants failed during the observational period (Implant failure rate was 8.6%). Histologic analyses revealed indicated a well-reconstructed bone with living osteocytes and osteoblasts. The connective tissue was highly vascularized, and inflammatory cells were infrequent.	4
Not reported	Clinical: Incidence of complications and implant failure rate; radiographic: density of the grafted volume assessed on CT scans obtained at 4 months postgrafting; histologic: description of 1 bone core biopsy using light microscopy at low magnification	4 months	Yes (n = 70, all simultaneously placed with grafting)	Up to 6 months after implant loading	Not reported	A total of 5 implants were lost (failure rate: 7.1%). Radiographic density of the grafted area was comparable to the surrounding native bone. Histologic analysis of the core biopsy showed evidence of new bone formation in contact with the xenograft particles.	4
Not reported	Clinical: Incidence of complications; histologic: description of bone core biopsies using light microscopy	4 months	Yes (n = 6)	4 months (implants were not followed up)	No	Both techniques were successful given the absence of complications and the successful placement of a total of 6 implants at 4 months postgrafting. Histologic analyses showed that bone biopsies were constituted by normal osseous tissue with remnants of polymer material.	4
Yes (radiographic and histologic assessments)	Clinical: Safety, incidence of complications and implant survival and success; radiographic: assessment of alveolar ridge height and density in periapical radiographs and CT scans; histologic: qualitative assessment of bone formation	4 months	Yes	Not specified	Not reported	"There were no serious or unexpected immunologic or adverse effects and no clinically significant changes in complete blood counts, blood chemistries, or urine analyses results. Radiographic and histologic efficacy assessments revealed that the use of rhBMP-2/ACS is a viable therapeutic alternative for maxillary sinus augmentation."	4

core biopsies).[100] Two other studies used a combination therapy consisting of PRP, a biologic agent (rhTF), a bovine xenograft with a surface biomimetic peptide (P-15), and autologous bone.[112,120] Both studies reported histologic outcomes (ie, descriptive histology of bone core biopsies), whereas only one of these case series reported clinical outcomes (ie, incidence of complications and implant failure rate).[120] One case series on the application of a bovine xenograft with a surface biomimetic peptide (P-15) was included, which reported clinical (ie, incidence of complications) and histologic (ie, histomorphometric analyses via light microscopy and microCT) outcomes.[88] The remaining case series evaluated histologic outcomes (ie, histomorphometric analyses via light microscopy and microCT) at 8 months after the application of rhPDGF-BB in combination with bovine xenograft particles.[94] Generally, the analysis of all these case series studies indicates that favorable results were obtained, independent of the therapeutic approach, with the exception of a relatively high implant failure rate of 7.1% at 6 months,[119] 6.6% at 9 months,[101] and 8.6% at 48 months[120] after implant

Table 18 Case Reports (n = 7) on the Application of Tissue Engineering–Based Therapies for the Treatment of Horizontal Defects

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Mangano et al (2010)[90]	To evaluate the histologic behavior of engineered bone tissue, obtained through a culture of autogenous osteoblasts seeded on PLGA in maxillary sinus augmentation	Cell-based therapy + scaffold (PLGA)	Case report	N/A	1 patient for 1 maxillary sinus	Partial	N/A	N/A
Smith et al (2009)[92]	To clinically test the healing potential of PRP with a higher concentration of platelets as a sole-grafting material in a case study involving augmentation of the maxillary sinus floor	Biologic agent (PRP)	Case report	N/A	1 patient for 1 maxillary sinus	Partial	N/A	N/A
Antoun et al (2008)[105]	To report clinical, radiographic, and histologic outcomes of a grafting technique consisting on the application of PRP in combination with 2 different grafting materials for maxillary sinus augmentation	Biologic agent (PRP) + scaffold (bovine xenograft or alloplast: βTCP)	Case report	N/A	1 patient for 2 maxillary sinuses	Partial	Right sinus: Xenograft + PRP; left sinus: βTCP + PRP	N/A
Nikolidakis et al (2008)[103]	To present the clinical, radiographic and histologic results after using a combination of βTCP with PRP for maxillary sinus augmentation	Biologic agent (PRP) + scaffold (alloplast: bβTCP)	Case report	N/A	1 patient for 1 maxillary sinus	Partial	N/A	N/A
Whitesides et al (2006)[109]	To report on the use of a combination of rhBMP-2 and allograft for maxillary sinus augmentation in one case	Biologic agent (rhBMP-2) + scaffold (allograft)	Case report	N/A	1 patient for 2 maxillary sinuses	Complete	N/A	N/A
Krauser et al (2000)[127]	To compare the efficacy, in terms of bone formation, of a xenograft with a biomimetic peptide and xenograft combined with autologous bone in maxillary sinus grafting	Biomimetic peptide in a scaffold (xenograft with peptide P-15)	Case report	N/A	1 patient for 2 maxillary sinuses	Complete	Right sinus: Xenograft and autologous bone; left sinus: xenograft with peptide P-15	N/A
Rosenberg et al (2000)[123]	To describe the use of PRP in combination with other grafting materials for maxillary sinus augmentation and to report one case	Biologic agent (PRGF) + scaffold (non-specified alloplastic material)	Case report	N/A	1 patient for 1 maxillary sinus	Partial	N/A	N/A

PLGA = polylactic-co-glycolic acid; N/A = not applicable; PRP = platelet-rich plasma; HU = Hounsfield unit(s); CT = computed tomography; βTCP = beta-tricalcium phosphate; rhBMP-2 = recombinant human bone morphogenetic protein type 2; PRGF = plasma rich in growth factors.

loading. However, it should be noted again that given the nature of case series studies, they are not valid to assess the efficacy and effectiveness of the aforementioned tissue engineering–based therapeutic approaches in the maxillary sinus augmentation scenario.

Case Reports (Table 18). Seven case reports were selected for this clinical scenario, of which four studies described the use of autologous blood-derived products (PRP or PRGF) alone[92] or in combination with a scaffold (ie, bovine xenograft or βTCP),[103,105,123] one study presented the application of cell therapy with a polylactic-co-glycolic acid scaffold,[90] another described the application of rhBMP-2/ACS in combination with allograft particles,[109] and the remaining study reported the application of bovine xenograft particles with a surface biomimetic peptide (P-15) for maxillary sinus augmentation.[127] The total follow-up time ranged from 6 months from the time of grafting[90,92] to 4 years after implant loading.[105] Five studies reported clinical outcomes (ie, incidence of complications and implant

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time Specific or range	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
N/A	Clinical: Incidence of complications; histologic: description of 2 bone core biopsies	6 months	Yes (n = 2)	6 months (implants were not followed up)	N/A	This case report shows proof-of-principle that the newly formed bone provided by engineered bone tissue allowed proper initial stability for dental implant placement.	4
N/A	Clinical: Incidence of complications; radiographic: density (HU units) of grafted area, assessed in a CT scan; histologic: description of 2 bone core biopsies	6 months	Yes	6 months (implants were not followed up)	N/A	Healing was uneventful. Radiographic outcomes demonstrated that the grafted area exhibited higher density than surrounding natural bone. Histomorphometric analyses showed that the percentage of mineralized tissue in the two bone cores was 34% and 39%, respectively.	4
Not reported	Clinical: Incidence of complications and implant survival rate; radiographic: assessment of height gain using CT scans; histologic: quantification of tissue compartments % in 2 bone core biopsies, 1 from each side	6 months	Yes (n = 4, two on each side)	4 years after implant loading	N/A	No complications were observed. All implants were stable and surrounded by bone up to the first thread at the 4-year visit. Radiographic bone height assessment revealed enough bone substrate for regular implant placement. Histologic analyses revealed that vital bone was 19.9% and 13.9% on the βTCP and xenograft sides, respectively. On the other hand, remaining graft area was 60.3% on the βTCP side and 45.5% on the xenograft side.	4
N/A	Clinical: Incidence of complications; radiographic: assessment of height gain periapical radiographs; histologic: description of one bone core biopsy and newly formed bone % using light microscopy	6 months	Yes (n = 1)	12 months after implant loading	N/A	No complications occurred during the healing period. Sufficient bone height gain to place a regular implant was demonstrated radiographically. Histologic analyses revealed that the sections were composed of trabecular bone, marrow spaces with fat cells, and particles of the βTCP bone substitute. Newly formed bone area was approximately 14%.	4
N/A	Radiographic: Assessment of bone height and density gain in CT scans; histologic: quantification of tissue compartments % in bone core biopsies	8 months	Yes (n = 7)	8 months (implants were not followed up)	N/A	Radiographic assessments inidicate that adequate bone height to place implants was obtained after grafting. Density gains compatible with new bone formation were observed on both sinuses. Histologic analyses revealed that new bone area was 28.6% and 53.5% in the left and right maxillary sinus, respectively.	4
N/A	Histologic: Quantification of tissue compartments % in bone core biopsies	8 months for the right sinus and 4 months for the left sinus	Yes (n = 6, a total of 3 per side)	6 months after implant placement	N/A	Average vital bone formation was 16% on the right side and 14% on the left side (P-15 side), while remaining xenograft particles area was 22% and 28%, respectively. The authors speculated that given the healing time difference the biomimetic peptide enhanced the healing response after grafting.	4
N/A	Clinical: Incidence of complications	3 months	Yes (n = 3)	Not specified	N/A	The site healed uneventfully and the implants could be placed as prosthetically planned.	4

survival rate),[90,92,103,105,123] of which four reported radiographic data (ie, height gain and density of the grafted volume).[92,103,105,109] Interestingly, six studies reported histologic outcomes (ie, descriptive histology and histomorphometric analyses of bone core biopsies).[90,92,103,105,109,127] As reflected in Table 18, favorable outcomes were observed in all cases reports for all the parameters analyzed irrespective of the therapeutic approach. These data are useful as proof-of-principle demonstrations of the application of diverse tissue engineering–based therapies for maxillary sinus augmentation; however, it should be noted that it is not valid to assess therapeutic efficacy or effectiveness.

Severe Vertical and Combined Defects

Two RCTs,[135,137] five case series,[62,129–131,136] and four case reports[132–134,138] constituted the 11 studies selected, which focused on the treatment of severe vertical and combined defects. Surgical techniques described in this body of evidence included onlay

Table 19 RCTs (n = 2) on the Application of Tissue Engineering-Based Therapies for the Treatment of Severe Vertical or Combined Defects

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Maxillary Sinus Lift			Type of Maxillary Edentulism	Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Schaaf et al (2008)[102]	To test the hypothesis that PRP has an influence on bone formation in the maxilla after lateral augmentation and sinus floor elevation in combination with autologous cancellous bone from the iliac crest	Biologic agent (PRP) + Autologous bone	RCT (split mouth)	Yes	53 patients for a total of 87 atrophic posterior maxillary segments	Both complete and partial, not specified how many subjects were in each category	Control group: Autologous bone from the iliac crest alone; experimental group: autologous bone from the iliac crest in combination with PRP	Yes
Thor et al (2005)[137]	(1) To evaluate whether PRP in conjunction with particulated autogenous bone for implant site development in atrophic maxillae could improve the integration and clinical function of dental implants; (2) to compare block bone grafts without PRP with PRP-treated particulated bone	Biologic agent (PRP) + autologous bone	RCT (split mouth)	Yes	19 patients for a total of 76 edentulous segments (19 anterior controls and 19 anterior experimentals that underwent horizontal and vertical augmentation/19 posterior controls and 19 posterior experimentals that underwent maxillary sinus floor lift)	Complete	Anterior controls: Autologous bone blocks; anterior experimentals: particulated autologous bone with PRP; posterior controls: particulated autologous bone; posterior experimentals: particulated autologous bone with PRP	Yes

RCT = randomized clinical trial; PRP = platelet-rich plasma; RFA = resonance frequency analysis.

bone graft (lateral and/or coronal to the basal bone) and posterior segmental osteotomy; no selected studies reported on interpositional graft or Le Fort osteotomy.

RCTs (Table 19). Interestingly, the two RCTs selected had a split-mouth design, and both evaluated the effect of PRP in combination with autologous bone to treat severely resorbed maxillae compared with autologous bone graft alone.[135,137] A total of 53 patients were treated in one study,[135] whereas the other RCT enrolled a total of 19 patients.[137] The total follow-up time in the study by Thor et al[137] was 1 year after functional loading, whereas the other study did not specify that information. These RCTs complement each other in terms of reported measures of interest, because one study reported only histologic outcomes (ie, quantification of the percentage of tissue compartments in bone core biopsies obtained at 4 months)[135] and the other one looked at clinical (ie, resonance frequency analysis and implant survival rate) and radiographic (ie, peri-implant bone loss on nonstandardized radiographs) outcomes.[137] Interestingly, other than a slightly increased failure rate in favor of the experimental group (2 of 76 implants failed at the time of implant uncovering) in the study by Thor and collaborators,[137] no significant differences were observed between groups for any of the other evaluated parameters.

Case Series (Table 20). Of the five case series, four were focused on bone augmentation[62,129,130,136] and one study evaluated soft tissue augmentation exclusively.[131] In three studies on hard tissue augmentation, the treatment involved the application of rhBMP-2/ACS: in one article, it was applied in combination with either allograft particles or autologous bone,[129] and in the other two, it was used as the sole grafting material.[62,130] The tissue engineering–based therapy applied in the remaining article was a combination of PRP, cell therapy (bone marrow aspirate concentrate), and allograft particles.[136] The follow-up time ranged from 4 to 9 months from the time of grafting in the studies that used rhBMP-2[62,129,130] up to 4 years after implant placement in the study by Filho-Cerruti et al.[136]

All the studies on hard tissue augmentation reported clinical (ie, incidence of complications, available volume at the time of implant placement, dimensional changes after the healing period, and implant survival rate) and radiographic (ie, bone height and volume gain, density changes, and presence of radiographic pathology) outcomes.[62,129,130,136] Two studies reported histologic outcomes (ie, descriptive histology of selected bone core biopsies)[62,136] and only one reported patient-centered outcomes (ie, incidence of adverse experiences).[62] In the three studies that used rhBMP-2, consistent outcomes were observed in terms of favorable safety, and there was no incidence of significant complications (other than local transient mucosal swelling), and sufficient available volume for implant placement. The results in the study that involved PRP and cell therapy[136] revealed that 30 of 32 grafting procedures healed in the absence of complications (those two patients were excluded from the study); all implants in the remaining 30 patients were stable and functioning 4 years after placement (survival rate: 100%) and had

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Histologic: Quantification of tissue compartments % of bone core biopsies	4 months	Yes	Not specified	17 patients (7 from the bilateral group and 10 from the unilateral treatment group)	Both groups obtained similar results in terms of new bone formation, assessed histologically.	2
Not reported	Clinical: Implant survival rate and RFA analysis after one year of functional loading; radiographic: peri-implant marginal bone height changes	6 months	Yes (n = 152, of which 76 were in control sites and 76 in experimental sites)	1 year after functional loading	No	Two implants in control sites were found to be failed at the time of abutment connection. The overall 1-year survival rate was 98.7%. RFA measurements at 1 year after loading revealed significantly better stability for implants at the test site. Average marginal bone level changes were comparable in both groups (0.2 mm of difference). Hence, no obvious positive effects of PRP on bone graft healing were observed.	2

radiographically enough bone substrate for implant placement.

Histologic analyses showed lines of bone formation and the presence of osteoblasts around the bone trabecula in all biopsy specimens. In the study focused on soft tissue augmentation of severe combined defects, the outcomes of interest were clinical (ie, changes in soft tissue thickness at different locations) and histologic (ie, descriptive histology of soft tissue biopsies).[131] It was found that the application of rhPDGF-BB in combination with a bovine collagen matrix carrier led to an average gain in mucosal thickness over the 4-month healing period in all sites. The mean soft tissue thickness gain on the apical location at 3.5 years was approximately 1 mm. Histologic analyses revealed the formation of well-organized mucosal tissue with isolated remnants of bovine matrix that were encapsulated by fibrous connective tissue. As mentioned for other clinical scenarios, independent of the positive results reported in these case series, it should be noted that the absence of a control group prevents the extraction of conclusions on the effectiveness and efficacy of the applied therapies. However, this information is of great value to demonstrate the safety and predictability of these approaches.

Case Reports (Table 21). Two of the four selected case reports (one patient per study) described the use of rh-PDGF-BB in combination with bovine xenograft particles and autologous bone[133,134]; one reported the application of a combination of rhBMP-2/ACS, rhPDGF-BB, and βTCP blocks[132]; and the remaining study presented a case in which PRP with autologous bone[138] was used for the treatment of severe vertical and/or combined defects. The total follow-up time in three case reports ranged from 8 months to 3 years from the time of implant placement.[132,134,138] In one case report, the study duration was not specified.[133] All case reports considered clinical outcomes (ie, incidence of complications, sufficient available bone for implant placement, horizontal and vertical gain, and survival rate),[132–134,138] three reported radiographic outcomes (ie, marginal bone level around implants and gain in bone height and width),[132–134] and only one study included histologic data (ie, descriptive histology of bone core biopsies).[132] In all case reports, favorable clinical, radiographic, and histologic outcomes were consistently observed, regardless of the therapy applied and the particularities of the maxillary defect. Once again, it must be mentioned that, although valid as proof-of-principle information, the information contained in these case reports is not valid to assess therapeutic efficacy or effectiveness given the absence of a control group and the low sample size (n = 1).

Effect of Tissue Engineering Therapies Observed on Specific Clinical Scenarios

As reflected in the PICO question, this review was primarily focused on presenting and discussing the evidence available on the effect of current and emerging regenerative approaches based on tissue engineering principles for implant site development in atrophic maxillary segments compared with conventional augmentation techniques. Hence, only the data from the RCTs and nonrandomized

Table 20 Case Series (n = 5) on the Application of Tissue Engineering-Based Therapies for the Treatment of Severe Vertical or Combined Defects

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Severe Vertical and Combined Defects			Type of Maxillary Edentulism	Groups/Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Jensen et al (2013)[129]	To demonstrate the use of rhBMP-2 in an ACS carrier alone or in combination with other bone grafts for the treatment of severely resorbed maxillae	Biologic agent (rhBMP-2) + Different scaffolds (Allografts) or autologous bone in some cases	Case series	No	6	Complete	All 6 cases received Le-Fort I advancement with interpositional rhBMP-2/ACS. Allograft particles were used in combination with the biologic agent in 3 of the 6 cases. In one case autologous bone was used concomitantly with the biologic agent. Hence, in two cases the sole grafting material was rhBMP-2/ACS	N/A
Jensen (2013)[130]	To report on the early results of the clinical use of rhBMP-2/ACS placed into dental extraction sites after simultaneous segmental alveolar split (through the extraction sites) and osteotome sinus floor intrusion	Biologic agent (rhBMP-2)	Case series	No	3	Partial	N/A	N/A
Simion et al (2012)[131]	To present a case series on the use of an absorbable collagen matrix (bovine) as a carrier for rhPDGF-BB to increase the peri-implant soft tissue volume (horizontal and vertical) in the anterior maxilla	Biologic agent (rhPDGF-BB)	Case series	No	6	Partial	N/A	N/A
Filho Cerruti et al (2007)[136]	To describe a tissue regeneration technique using an allograft in combination with autologous bone marrow cells and PRP and to report its clinical results	Biologic agent (PRP) + cell-based therapy (BMAC) + scaffold (allograft)	Case series	No	32 patients for 32 atrophic posterior and anterior maxillary segments	Not specified	N/A	N/A
Cochran et al (2000)[62]	To monitor the long-term safety of patients treated with rhBMP-2 for the reconstruction of combined defects in the posterior maxilla and to evaluate the implants placed in the grafted sites	Biologic agent (rhBMP-2)	Case series	No	6 patients for 6 edentulous segments	Partial	N/A	N/A

rhBMP-2 = recombinant human bone morphogenetic protein type 2; ACS = absorbable collagen sponge; N/A = not applicable; rhPDGF-BB = recombinant human platelet derived growth factor type BB; GBR = guided bone regeneration; PRP = platelet-rich plasma; BMAC = bone marrow aspirate concentrate.

clinical trials included were considered for this purpose. Observed beneficial effects of tissue engineering–based therapies for the treatment of maxillary defects compared with a control can be summarized as: *(1)* alveolar ridge preservation using PRP appears to accelerate soft tissue healing in early postsurgical stages and yielded to superior patient-centered outcomes (ie, food stagnation and halitosis)[60]; *(2)* alveolar ridge preservation in buccal wall socket defects using rhBMP-2/ACS led to increased bone augmentation[11]; *(3)* alveolar ridge preservation using rhPDGF-BB in combination with an allograft (ie, FDBA) or an alloplast (βTCP) led to accelerated remodeling of carrier biomaterials[54]; *(4)* autologous cell therapy in alveolar ridge preservation provided enhanced clinical and radiographic outcomes[58,63]; *(5)* autologous cell therapy in alveolar ridge preservation provided superior histomorphometric outcomes at 6 weeks[63]; and *(6)* PRP combined with autologous bone grafts for maxillary sinus augmentation led to increased radiographic density and accelerated bone mineralization at 6 months.[74,108]

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
Not reported	Clinical: Incidence of complications and available volume at the time of implant placement / Radiographic: Bone height gain	6 to 9 months	Yes	Not specified for each case	No	All 6 patients were treated successfully, in absence of major complications. Combination grafts produced a better result than full down-fracture interpositional grafts using rhBMP-2/ACS alone	4
Not reported	Clinical: Incidence of complications and available volume at the time of implant placement; radiographic: bone height gain	4 months	Yes (n = 8)	Up to 3 years in one of the cases reported	No	No complications were observed during the healing phase. Sufficient bone volume for implant placement was available upon the 4-month reopening surgery. No implants or implant-supported restorations failed during the observation period.	4
Not reported	Clinical: Changes in soft tissue thickness at different ridge locations; histologic: description of soft tissue biopsies	4 months	Yes, simultaneously in 2 cases and previously (at the time of GBR) in 4 cases	Up to 3.5 years from grafting	No	All sites healed uneventfully after soft tissue grafting. An average gain in mucosal thickness over the 4-month healing period was observed in all sites. The mean soft tissue thickness gain on the apical location at 3.5 years was approximately 1 mm. Histologic analyses revealed the formation of well-organized mucosal tissue with isolated remnants of bovine matrix that were encapsulated by fibrous connective tissue.	4
Not reported	Clinical: Incidence of complications and implant survival; radiographic: assessment of available bone in CT scans at 8 months; histologic: description of bone core biopsies	8 months	Yes	Up to 4 years after implant placement	Yes, 2 patients had to be excluded due to postop complications	Thirty bone grafting procedures healed in absence of complications (success rate: 94.7%). All implants were stable and functioning 4 years after placement. Radiographic assessment revealed enough bone substrate in all the 30 cases that did not exhibit early postop complications. Histologic analyses showed lines of bone formation and the presence of osteoblasts around the bone trabecula in all biopsies.	4
Not reported	Clinical: Buccolingual, apicocoronal, and mesiodistal linear changes of the ridge; radiographic: bone height and density changes, and incidence of radiographic pathology; histologic: description of representative bone cores from 2 sites; patient-centered outcomes: incidence of adverse experiences	16–28 weeks	Yes (n = 7 implants in 4 patients)	528 weeks	No	In this long-term case series with a limited number of subjects (n = 6), clinical, radiographic, histologic, and patient-centered outcomes indicate that rhBMP-2 + ACS can be safely used as an alveolar ridge augmentation therapy in humans.	4

DISCUSSION

This review is focused on the use of biologic agents, scaffolding matrices, and cell-based therapies that have shown clinical applicability for tissue engineering applications in the treatment of the edentulous maxilla with implant-supported prostheses. The concepts of tissue engineering approaches for regeneration of dental and oral tissues first began to appear in the literature in the early 1990s.[139] By the latter part of that decade, preliminary concepts of tissue engineering for periodontal and peri-implant bone regeneration, via the use of selected growth factors, were emerging.[140] These early concepts focused principally on the use of polypeptide growth and differentiation factors such as PDGF, TGF-β, insulinlike growth factor 1, and basic fibroblast growth factors. However, at this time it was also recognized that tissue engineering was a far more complex process than merely supplying exogenous growth factors to diseased/damaged sites with the expectation of tissue

Table 21 Case Reports (n = 4) on the Application of Tissue Engineering–Based Therapies for the Treatment of Severe Vertical or Combined Defects

Study	Objective(s)	Tissue Engineering Approach (Biologic Agents, Scaffolds, Cell-based Therapy, Gene Therapy)	Severe Vertical and Combined Defect			Type of Maxillary Edentulism	Groups/ Interventions (Describe interventions, if applies)	Randomization (Only for clinical trials)
			Study Design	A Priori Eligibility Criteria Described	No. of Patients and Sites			
Schuckert et al (2010)[132]	To discuss the advantages, disadvantages and indications of both rhBMP-2 and rhPDGF-BB, and present one case demonstrating a combined application for the treatment of a severely resorbed maxilla	Biologic agents (rhBMP-2 and rhPDGF-BB) + scaffold (βTCP blocks)	Case report	N/A	1	Complete	N/A	N/A
Urban et al (2009)[133]	To demonstrate the use of rhPDGF-BB in conjunction with autogenous bone, xenograft particles (bovine), and collagen barrier membranes to reconstruct severe alveolar bone defects	Biologic agent (rhPDGF-BB) + scaffold (xenograft and autologous bone)	Case report	N/A	1	Partial	N/A	N/A
Simion et al (2008)[134]	To present a case illustrating the use of rhPDGF-BB in combination with autologous bone and a xenograft to treat a severe combined defect in the anterior maxilla	Biologic agent (rhPDGF-BB) + scaffold (xenograft and autologous bone)	Case report	N/A	1	Partial	N/A	N/A
Thor (2002)[138]	To describe the combined use of particulated corticocancellous autologous bone, PRP, and a titanium mesh for implant site development in one case of severe anterior maxillary atrophy	Biologic agent (PRP) + autologous bone	Case report	N/A	1	Partial	N/A	N/A

rhBMP-2 = recombinant human bone morphogenetic protein type 2; rhPDGF-BB = recombinant human platelet derived growth factor type BB; βTCP = beta-tricalcium phosphate; N/A = not applicable; PRP = platelet-rich plasma.

regeneration. Thus, a more concise paradigm for tissue engineering began to emerge, which was based on the concept that regenerative treatments with an agent or procedure would require that each functional stage of reconstruction is grounded in a biologically directed process.[141] As a result, tissue engineering became an evolving branch of biomedical and biomechanical science focused on developing materials and procedures for the regeneration of damaged tissues based on fundamental principles of cell biology, developmental biology, and biomaterials science.[141,142] These insights in regenerative healing biology triggered the coupling of an emerging science and technology, in order to respond to challenging clinical demands, and made the concept of tissue engineering a clinical reality.

Today, tissue engineering is no longer considered an emerging field of experimental endeavor, but is recognized as an established contemporary area of biomedical research attracting the attention of scientists, clinicians, biotechnology industries, and government agencies, because of its considerable therapeutic potential.[143] Tissue engineering is now defined as the science of combining cells, prefabricated biomaterials, and specific biological signaling agents with the expectation of tissue regeneration. The vision for tissue engineering is that suitable cells (stem, progenitor, fully differentiated, or even genetically modified cells), produced in large enough quantities through cell culture methods, can be implanted into tissues and organs in a suitable carrier vehicle capable of undergoing timed biodegradation leading to the production of fully functional and architecturally correct regenerated tissues. Other essential requirements for successfully engineered tissues are the efficient delivery of regulatory signals at appropriate levels, a temporal sequence, and a biocompatible/biodegradable carrier construct. Importantly, the establishment of a viable blood supply to the construct is central to the biological and clinical success of these procedures (Fig 1). Recent advances in growth factor biology, stem cell technology, and biodegradable polymer constructs have led to successful tissue engineering of cartilage, bone, and many other tissues. For the purposes of this review, tissue engineering in the context of osseous augmentation in the edentulous maxilla was considered.

The original topic assigned to this group was "Tissue Engineering Approaches for the Management of the Edentulous Maxilla." However, in light of the discussion herein, it became apparent that the field has not yet fully embraced all the concepts of tissue engineering, with most clinical studies to date focusing mainly on

Masking (Only for clinical trials)	Outcomes Measures	Healing Period	Implants Placed	Total Follow-up Time (Specific or range)	Dropouts (If applies)	Summary of Main Findings	Level of Evidence (Oxford Scale)
N/A	Clinical: Incidence of complications; radiographic: bone height and width gain; histologic: description of bone core biopsies	4 months	Yes (n = 6)	12 months from implant placement	N/A	The observations from this case report illustrate that the combined application of rhPDGF-BB and rhBMP-2 with alloplastic blocks for the treatment of severe completely edentulous maxillae is a viable treatment option.	4
N/A	Clinical: Horizontal and vertical ridge augmentation; radiographic: marginal bone level around implants	9 months	Yes (n = 3)	Not specified	N/A	Significant horizontal and vertical bone gain was achieved using the reported therapy. However, this gain was not quantified and reported. This tissue engineering–based procedure allowed for the placement of 3 implants that served as support for a fixed partial prosthesis.	4
N/A	Clinical: Incidence of complications and bone availability for implant placement upon surgical reopening; radiographic: bone height gain	6 months	Yes (n = 2)	8 months from the time of implant placement, which is when the final prosthesis was delivered	N/A	This case report shows that the combined application of rhPDGF-BB with autologous bone and xenograft particles is an effective therapy for the reconstruction of localized severe combined maxillary bone defects.	4
N/A	Clinical: Bone volume gain at the time of implant placement and implant survival rate after 3 years of functional loading	18 weeks	Yes (n = 10)	3 years after functional loading	N/A	Alveolar ridge reconstruction (in height and width) was accomplished with the described surgical technique. All implants were placed without needing additional bone grafting. All implants survived after 3 years of functional loading, with minimal alveolar bone changes.	4

delivery of growth factors or the use of biocompatible/biological scaffolds either alone or in various combinations, but definitely not within the aforementioned definitions of tissue engineering. To date, only a few studies have embraced an integral tissue-engineering approach, as defined herein, for such reconstructive purposes.[32,63,72,96,100,101,136,144] Accordingly, the title of this review was changed to "Biologics and Cell Therapy Tissue Engineering Approaches For The Management of the Edentulous Maxilla," to reflect an assessment of the current state of the art in this field.

The 87 articles selected illustrate the dynamic principle that constitutes this evolving field. Its application for the management of the partially edentulous maxilla brings a plethora of viable clinical protocols that range from the application of autologous concentrated factors and emerging recombinant biologic agents to the utilization of optimized scaffold technology as well as cell-based graft alternatives. Significant literature attrition occurred during the selection process given the tremendous heterogeneity in the field, along with the lack of standardized reporting protocols in this emerging area. In all four clinical scenarios considered in this review, most studies were either case series or case reports, which are not valid to determine efficacy or effectiveness of a given therapy. In addition, a marked heterogeneity of study designs, therapies applied, and outcome measures was encountered. This made the analysis of the data substantially challenging and the performance of a quantitative analysis impractical. However, it is important to highlight that despite these burdens, the selected literature showcases clear applications and tissue engineering strategies to overcome common clinical scenarios, and offers viable alternatives for contemporary practitioners. The sinus elevation and alveolar socket grafting are clinical scenarios that have systematically and comprehensively captured most of the scope of different tissue engineering strategies as a regenerative therapy for maxillary edentulous areas. These common clinical scenarios have served, without doubt, as clinical models to validate the safety and predictability, as well as the therapeutic potential, of tissue engineering approaches to achieve optimal treatment outcomes.

In lieu of offering the evidence to position these innovative alternatives as clinically superior therapies, the studies collectively challenge the dogma of autogenous bone as the "gold standard." These studies discuss comparable clinical regenerative outcomes without the increased morbidity associated with traditional approaches. It is clear that the modest numbers of studies that fulfill the

scope of this review may be perceived as a misrepresentation to some extent of the significant impact that bioengineering-driven therapies have in today's surgical practice, particularly in the case of horizontal deficiencies and severe vertical or combined defects. However, it is important to emphasize that the indications for many of these approaches are still fairly narrow. This is especially so given the paucity of robust evidence supporting the superiority of tissue engineering approaches over conventional augmentation therapies in certain clinical applications, the inherent cost of some of these treatments, and the strict safety regulatory processes. However, the off-label use has become a common and appealing practice. Nevertheless, it is not within the scope of this review to discuss the indications and validity of on-label and off-label applications.

It was the consensus of the present group that, before tissue engineering for the edentulous maxilla is adopted as a gold standard or desirable alternative, a number of issues still need to be resolved, mostly related to the success of tissue engineering in general. Successful tissue engineering relies on two fundamental principles: *(1)* the biomechanical properties of the scaffold, architectural geometry, and space-maintaining properties, and *(2)* the biological functions of the engineered matrix, including cell recruitment, permission of neovascularization, and delivery of the requisite morphogenetic, regulatory, and growth factors for tissue regeneration. The major challenge that remains is to establish control of the exact sequence of events required for cell recruitment, differentiation, and maturation to effectively promote healing and regeneration without compromising normal cell function. New materials and signaling molecules delivered by gene therapy are therefore of great interest. More evidence and practice standardization are needed to successfully meet the regulatory requirements to apply these technologies to the clinical scenario. Differences between chronic pathology and other defects, such as implant sites or extraction sockets, must be taken into consideration, because their regenerative processes are different. Therefore, the application of tissue engineering also requires a detailed understanding of the homeostasis and pathogenesis of different defects. Identification of genetic and epigenetic variants and their impact in alveolar wound healing dynamics is also fundamental to discover novel determinants of alveolar stability. Currently, the lack of a biology-based classification system distracts the scientific community from establishing more homogeneous diagnostic categories and more predictable treatment outcomes. A biology-driven, as well as anatomic and topographic, assessment of the clinical scenarios and the systemic factors of each patient would provide an important insight that could assist in tailoring treatment to enhance regenerative outcomes while providing more predictable and personalized care.

CONCLUSIONS

On the basis of the evidence reviewed, it can be concluded that although good early-stage clinical success has been demonstrated with these modalities, the indications for tissue engineering approaches for the treatment of the edentulous maxilla with implant-supported prostheses are still fairly narrow and further studies are needed. Clinical trials assessing meaningful outcomes, involving larger populations, and with longer follow-up periods are warranted to discern the effectiveness of the achieved results compared with a valid control therapy. In addition, optimization of currently available tissue engineering approaches and the study of emerging approaches including three-dimensional printing,[145] refined cell therapies,[63] gene therapy, and biomatrix designs[146] are warranted to improve the predictability and ease of use of reconstructive approaches for the repair of maxillary defects of different nature and complexity.

Without doubt, the future of regeneration stems from constantly evolving tissue-engineering strategies despite today's limited clinical evidence. Even though the cell-based, scaffold, and gene therapies interface and complement each other, some are still at the preclinical level. In the near future, the outcomes of regeneration will undoubtedly be enhanced by the ability to correctly identify clinical situations in which these techniques can be successfully applied with predictable results considering inherent local and systemic factors.

ACKNOWLEDGMENTS

The authors received no financial support to conduct this systematic review. They would like to thank Julie Schiavo and Chris White, specialist librarians at the Lousiana State University School of Dentistry and at the University of Iowa College of Dentistry, respectively, for their valuable assistance in conducting the search and finding full-text versions of multiple articles. G.A. and H.R. would like to acknowledge the American Academy of Periodontology Foundation (AAPF) for the support provided to pursue a career in academia.

Drs Gustavo Avila-Ortiz, Mark Bartold, Wataru Katagiri, Salvador Nares, and Hector Rios declare no conflict of interest with regard to this systematic review. Dr William Giannobile has been a consultant for Osteohealth, Medtronic Spine & Biologics, Geistlich Pharma, and Straumann. Dr Daniel Spagnoli has been a consultant for, done clinical research with, and received lecture support from Medtronic Spine & Biologics. Dr Ulf ME Wikesjö was part of the team at Genetics Institute/Wyeth Research that provided the evidence and background for the development and registration of recombinant human bone morphogenetic protein-2 (Infuse). He directed the preclinical/clinical development of recombinant human growth/differentiation factor-5 for periodontal indications as a consultant to Scil Technology. He has also conducted research studies for/provided consultation services to WL Gore & Associates, Genetics Institute/Wyeth Research, Nobel Biocare, Medtronic Spine & Biologics, Osstem, Scil Technology, Daewoong Pharmaceuticals, OraPharma, and Dentsply International in corporate and academic settings.

REFERENCES

1. Simion M, Fontana F, Rasperini G, Maiorana C. Vertical ridge augmentation by expanded-polytetrafluoroethylene membrane and a combination of intraoral autogenous bone graft and deproteinized anorganic bovine bone (Bio Oss). Clin Oral Implants Res 2007;18:620–629.
2. Buser D, Dula K, Belser U, Hirt HP, Berthold H. Localized ridge augmentation using guided bone regeneration. 1. Surgical procedure in the maxilla. Int J Periodontics Restorative Dent 1993;13:29–45.
3. Boyne PJ, James RA. Grafting of the maxillary sinus floor with autogenous marrow and bone. J Oral Surg 1980;38:613–616.
4. Summers RB. A new concept in maxillary implant surgery: The osteotome technique. Compendium 1994;15:152;154–156.
5. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? Int J Oral Maxillofac Implants 2007;22(suppl 1):49–70.
6. Lang NP, Pun L, Lau KY, Li KY, Wong MC. A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. Clin Oral Implants Res 2012;23(5, suppl):39–66.
7. Pagni G, Kaigler D, Rasperini G, Avila-Ortiz G, Bartel R, Giannobile WV. Bone repair cells for craniofacial regeneration. Adv Drug Deliv Rev 2012;64:1310–1319.
8. Avila-Ortiz G, Elangovan S, Kramer KW, Blanchette D, Dawson DV. Effect of alveolar ridge preservation after tooth extraction: A systematic review and meta-analysis. J Dent Res 2014;93:950–958.
9. Spagnoli D, Choi C. Extraction socket grafting and buccal wall regeneration with recombinant human bone morphogenetic protein-2 and acellular collagen sponge. Atlas Oral Maxillofac Surg Clin North Am 2013;21:175–183.
10. Boyne PJ, Lilly LC, Marx RE, et al. De novo bone induction by recombinant human bone morphogenetic protein-2 (rhBMP-2) in maxillary sinus floor augmentation. J Oral Maxillofac Surg 2005;63:1693–1707.
11. Fiorellini JP, Howell TH, Cochran D, et al. Randomized study evaluating recombinant human bone morphogenetic protein-2 for extraction socket augmentation. J Periodontol 2005;76:605–613.
12. Triplett RG, Nevins M, Marx RE, et al. Pivotal, randomized, parallel evaluation of recombinant human bone morphogenetic protein-2/absorbable collagen sponge and autogenous bone graft for maxillary sinus floor augmentation. J Oral Maxillofac Surg 2009;67:1947–1960.
13. Kaigler D, Avila G, Wisner-Lynch L, et al. Platelet-derived growth factor applications in periodontal and peri-implant bone regeneration. Expert Opin Biol Ther 2011;11:375–385.
14. Kitamura M, Akamatsu M, Machigashira M, et al. FGF-2 stimulates periodontal regeneration: Results of a multi-center randomized clinical trial. J Dent Res 2011;90:35–40.
15. Lee J, Wikesjo UM. Growth/differentiation factor-5: Pre-clinical and clinical evaluations of periodontal regeneration and alveolar augmentation—review. J Clin Periodontol 2014;41:797–805.
16. Simion M, Nevins M, Rocchietta I, et al. Vertical ridge augmentation using an equine block infused with recombinant human platelet-derived growth factor-BB: A histologic study in a canine model. Int J Periodontics Restorative Dent 2009;29:245–255.
17. Simion M, Rocchietta I, Kim D, Nevins M, Fiorellini J. Vertical ridge augmentation by means of deproteinized bovine bone block and recombinant human platelet-derived growth factor-BB: A histologic study in a dog model. Int J Periodontics Restorative Dent 2006;26:415–423.
18. Wikesjö UM, Huang YH, Xiropaidis AV, et al. Bone formation at recombinant human bone morphogenetic protein-2-coated titanium implants in the posterior maxilla (Type IV bone) in non-human primates. J Clin Periodontol 2008;35:992–1000.
19. Schilephake H. Bone growth factors in maxillofacial skeletal reconstruction. Int J Oral Maxillofac Surg 2002;31:469–484.
20. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Ann Intern Med 2009;151:264–269; W64.
21. Oxford Center for Evidence-Based Medicine 2011 Levels of Evidence. http://www.cebm.net/index.aspx?o=5653. Accessed 24 April 2002.
22. Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): A patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548–556.
23. Yamada Y, Hara K, Nakamura S, Ueda M, Ito K, Nagasaka T. Minimally invasive approach with tissue engineering for severe alveolar bone atrophy case. Int J Oral Maxillofac Surg 2013;42:260–263.
24. Tajima N, Ohba S, Sawase T, Asahina I. Evaluation of sinus floor augmentation with simultaneous implant placement using platelet-rich fibrin as sole grafting material. Int J Oral Maxillofac Implants 2013;28:77–83.
25. Montanari M, Callea M, Yavuz I, Maglione M. A new biological approach to guided bone and tissue regeneration. BMJ Case Rep 2013;2013.
26. Dasmah A, Thor A, Ekestubbe A, Sennerby L, Rasmusson L. Marginal bone-level alterations at implants installed in block versus particulate onlay bone grafts mixed with platelet-rich plasma in atrophic maxilla. A prospective 5-year follow-up study of 15 patients. Clin Implant Dent Relat Res 2013;15:7–14.
27. Tatullo M, Marrelli M, Cassetta M, et al. Platelet Rich Fibrin (P.R.F.) in reconstructive surgery of atrophied maxillary bones: Clinical and histological evaluations. Int J Med Sci 2012;9:872–880.
28. Snyder MB. Treatment of a large postextraction buccal wall defect with mineralized allograft, β-TCP, and rhPDGF-BB: A growth factor-mediated bone regenerative approach. Int J Periodontics Restorative Dent 2012;32:705–711.
29. Heberer S, Wustlich A, Lage H, Nelson JJ, Nelson K. Osteogenic potential of mesenchymal cells embedded in the provisional matrix after a 6-week healing period in augmented and non-augmented extraction sockets: An immunohistochemical prospective pilot study in humans. Clin Oral Implants Res 2012;23:19–27.
30. Chung VH, Chen AY, Jeng LB, Kwan CC, Cheng SH, Chang SC. Engineered autologous bone marrow mesenchymal stem cells: Alternative to cleft alveolar bone graft surgery. J Craniofac Surg 2012;23:1558–1563.
31. Chang PC, Lim LP, Chong LY, et al. PDGF-simvastatin delivery stimulates osteogenesis in heat-induced osteonecrosis. J Dent Res 2012;91:618–624.
32. Rickert D, Sauerbier S, Nagursky H, Menne D, Vissink A, Raghoebar GM. Maxillary sinus floor elevation with bovine bone mineral combined with either autogenous bone or autogenous stem cells: A prospective randomized clinical trial. Clin Oral Implants Res 2011;22:251–258.
33. Nam HW, Park JB, Lee JY, et al. Enhanced ridge preservation by bone mineral bound with collagen-binding synthetic oligopeptide: A clinical and histologic study in humans. J Periodontol 2011;82:471–480.
34. Torres J, Tamimi F, Alkhraisat MH, et al. Platelet-rich plasma may prevent titanium-mesh exposure in alveolar ridge augmentation with anorganic bovine bone. J Clin Periodontol 2010;37:943–951.
35. Luaces-Rey R, Arenaz-Búa J, Lopez-Cedrún-Cembranos JL, et al. Is PRP useful in alveolar cleft reconstruction? Platelet-rich plasma in secondary alveoloplasty. Med Oral Patol Oral Cir Bucal 2010;15:e619–e623.
36. Koch FP, Becker J, Terheyden H, Capsius B, Wagner W. A prospective, randomized pilot study on the safety and efficacy of recombinant human growth and differentiation factor-5 coated onto β-tricalcium phosphate for sinus lift augmentation. Clin Oral Implants Res 2010;21:1301–1308.
37. Herford AS, Cicciú M. Recombinant human bone morphogenetic protein type 2 jaw reconstruction in patients affected by giant cell tumor. J Craniofac Surg 2010;21:1970–1975.
38. Davies SD, Ochs MW. Bone morphogenetic proteins in craniomaxillofacial surgery. Oral Maxillofac Surg Clin North Am 2010;22:17–31.
39. Badr M, Coulthard P, Alissa R, Oliver R. The efficacy of platelet-rich plasma in grafted maxillae. A randomised clinical trial. Eur J Oral Implantol 2010;3:233–244.
40. Lee C, Nishihara K, Okawachi T, Iwashita Y, Majima HJ, Nakamura N. A quantitative radiological assessment of outcomes of autogenous bone graft combined with platelet-rich plasma in the alveolar cleft. Int J Oral Maxillofac Surg 2009;38:117–125.

41. Jung RE, Windisch SI, Eggenschwiler AM, Thoma DS, Weber FE, Hämmerle CH. A randomized-controlled clinical trial evaluating clinical and radiological outcomes after 3 and 5 years of dental implants placed in bone regenerated by means of GBR techniques with or without the addition of BMP-2. Clin Oral Implants Res 2009;20:660–666.
42. Lee CY, Rohrer MD, Prasad HS. Immediate loading of the grafted maxillary sinus using platelet rich plasma and autogenous bone: A preliminary study with histologic and histomorphometric analysis. Implant Dent 2008;17:59–73.
43. Byun HY, Wang HL. Sandwich bone augmentation using recombinant human platelet-derived growth factor and β-tricalcium phosphate alloplast: Case report. Int J Periodontics Restorative Dent 2008;28:83–87.
44. Simion M, Rocchietta I, Dellavia C. Three-dimensional ridge augmentation with xenograft and recombinant human platelet-derived growth factor-BB in humans: Report of two cases. Int J Periodontics Restorative Dent 2007;27:109–115.
45. Mannai C. Early implant loading in severely resorbed maxilla using xenograft, autograft, and platelet-rich plasma in 97 patients. J Oral Maxillofac Surg 2006;64:1420–1426.
46. Klongnoi B, Rupprecht S, Kessler P, et al. Lack of beneficial effects of platelet-rich plasma on sinus augmentation using a fluorohydroxyapatite or autogenous bone: An explorative study. J Clin Periodontol 2006;33:500–509.
47. Klongnoi B, Rupprecht S, Kessler P, Thorwarth M, Wiltfang J, Schlegel KA. Influence of platelet-rich plasma on a bioglass and autogenous bone in sinus augmentation. An explorative study. Clin Oral Implants Res 2006;17:312–320.
48. Bianchi J, Fiorellini JP, Howell TH, et al. Measuring the efficacy of rhBMP-2 to regenerate bone: A radiographic study using a commercially available software program. Int J Periodontics Restorative Dent 2004;24:579–587.
49. Shanaman R, Filstein MR, Danesh-Meyer MJ. Localized ridge augmentation using GBR and platelet-rich plasma: Case reports. Int J Periodontics Restorative Dent 2001;21:345–355.
50. Kassolis JD, Rosen PS, Reynolds MA. Alveolar ridge and sinus augmentation utilizing platelet-rich plasma in combination with freeze-dried bone allograft: Case series. J Periodontol 2000;71:1654–1661.
51. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85:638–646.
52. Howell TH, Fiorellini JP, Paquette DW, Offenbacher S, Giannobile WV, Lynch SE. A phase I/II clinical trial to evaluate a combination of recombinant human platelet-derived growth factor-BB and recombinant human insulin-like growth factor-I in patients with periodontal disease. J Periodontol 1997;68:1186–1193.
53. Howell TH, Fiorellini J, Jones A, et al. A feasibility study evaluating rhBMP-2/absorbable collagen sponge device for local alveolar ridge preservation or augmentation. Int J Periodontics Restorative Dent 1997;17:124–139.
54. Geurs N, Ntounis A, Vassilopoulos P, Van der Velden U, Loos BG, Reddy M. Using growth factors in human extraction sockets: A histologic and histomorphometric evaluation of short-term healing. Int J Oral Maxillofac Implants 2014;29:485–496.
55. Levin BP, Tawil P. Posterior tooth replacement with dental implants in sites augmented with rhBMP-2 at time of extraction—a case series. Compend Contin Educ Dent 2012;33:104–108;110.
56. Simon BI, Gupta P, Tajbakhsh S. Quantitative evaluation of extraction socket healing following the use of autologous platelet-rich fibrin matrix in humans. Int J Periodontics Restorative Dent 2011;31:285–295.
57. Nevins ML, Reynolds MA. Tissue engineering with recombinant human platelet-derived growth factor BB for implant site development. Compend Contin Educ Dent 2011;32:18;20–27.
58. Pelegrine AA, da Costa CE, Correa ME, Marques JF Jr. Clinical and histomorphometric evaluation of extraction sockets treated with an autologous bone marrow graft. Clin Oral Implants Res 2010;21:535–542.
59. Misch CM. The use of recombinant human bone morphogenetic protein-2 for the repair of extraction socket defects: A technical modification and case series report. Int J Oral Maxillofac Implants 2010;25:1246–1252.
60. Alissa R, Esposito M, Horner K, Oliver R. The influence of platelet-rich plasma on the healing of extraction sockets: An explorative randomised clinical trial. Eur J Oral Implantol 2010;3:121–134.
61. Hahn J, Rohrer MD, Tofe AJ. Clinical, radiographic, histologic, and histomorphometric comparison of PepGen P-15 particulate and PepGen P-15 flow in extraction sockets: A same-mouth case study. Implant Dent 2003;12:170–174.
62. Cochran DL, Jones AA, Lilly LC, Fiorellini JP, Howell H. Evaluation of recombinant human bone morphogenetic protein-2 in oral applications including the use of endosseous implants: 3-year results of a pilot study in humans. J Periodontol 2000;71:1241–1257.
63. Kaigler D, Pagni G, Park CH, et al. Stem cell therapy for craniofacial bone regeneration: A randomized, controlled feasibility trial. Cell Transplant 2013;22:767–777.
64. Urban IA, Lozada JL, Jovanovic SA, Nagy K. Horizontal guided bone regeneration in the posterior maxilla using recombinant human platelet-derived growth factor: A case report. Int J Periodontics Restorative Dent 2013;33:421–425.
65. Anitua E, Begona L, Orive G. Clinical evaluation of split-crest technique with ultrasonic bone surgery for narrow ridge expansion: Status of soft and hard tissues and implant success. Clin Implant Dent Relat Res 2013;15:176–187.
66. De Angelis N, Scivetti M. Lateral ridge augmentation using an equine flex bone block infused with recombinant human platelet-derived growth factor BB: A clinical and histologic study. Int J Periodontics Restorative Dent 2011;31:383–388.
67. Block MS. Use of living cell construct to enhance bone reconstruction: Preliminary results. J Oral Maxillofac Surg 2010;68:2914–2919.
68. Nevins ML, Camelo M, Nevins M, et al. Minimally invasive alveolar ridge augmentation procedure (tunneling technique) using rhPDGF-BB in combination with three matrices: A case series. Int J Periodontics Restorative Dent 2009;29:371–383.
69. de Freitas RM, Susin C, Spin-Neto R, et al. Horizontal ridge augmentation of the atrophic anterior maxilla using rhBMP-2/ACS or autogenous bone grafts: A proof-of-concept randomized clinical trial. J Clin Periodontol 2013;40:968–975.
70. Rickert D, Vissink A, Slot WJ, Sauerbier S, Meijer HJ, Raghoebar GM. Maxillary sinus floor elevation surgery with BioOss® mixed with a bone marrow concentrate or autogenous bone: Test of principle on implant survival and clinical performance. Int J Oral Maxillofac Surg 2014;43:243–247.
71. Yilmaz S, Karaca EO, Ipci SD, et al. Radiographic and histologic evaluation of platelet-rich plasma and bovine-derived xenograft combination in bilateral sinus augmentation procedure. Platelets 2013;24:308–315.
72. Yamada Y, Nakamura S, Ueda M, Ito K. Osteotome technique with injectable tissue-engineered bone and simultaneous implant placement by cell therapy. Clin Oral Implants Res 2013;24:468–474.
73. Mendonça-Caridad JJ, Nunez M, Juiz-Lopez P, Pita-Fernandez S, Seoane J. Sinus floor elevation using a composite graft: Clinical outcome of immediate implant placement. Int J Oral Maxillofac Implants 2013;28:252–260.
74. Khairy NM, Shendy EE, Askar NA, El-Rouby DH. Effect of platelet rich plasma on bone regeneration in maxillary sinus augmentation (randomized clinical trial). Int J Oral Maxillofac Surg 2013;42:249–255.
75. Corinaldesi G, Piersanti L, Piattelli A, Iezzi G, Pieri F, Marchetti C. Augmentation of the floor of the maxillary sinus with recombinant human bone morphogenetic protein-7: A pilot radiological and histological study in humans. Br J Oral Maxillofac Surg 2013;51:247–252.
76. Poeschl PW, Ziya-Ghazvini F, Schicho K, et al. Application of platelet-rich plasma for enhanced bone regeneration in grafted sinus. J Oral Maxillofac Surg 2012;70:657–664.
77. Pettinicchio M, Traini T, Murmura G, et al. Histologic and histomorphometric results of three bone graft substitutes after sinus augmentation in humans. Clin Oral Investig 2012;16:45–53.

78. Kao DW, Kubota A, Nevins M, Fiorellini JP. The negative effect of combining rhBMP-2 and Bio-Oss on bone formation for maxillary sinus augmentation. Int J Periodontics Restorative Dent 2012;32:61–67.
79. Inchingolo F, Tatullo M, Marrelli M, et al. Regenerative surgery performed with platelet-rich plasma used in sinus lift elevation before dental implant surgery: An useful aid in healing and regeneration of bone tissue. Eur Rev Med Pharmacol Sci 2012;16:1222–1226.
80. Hermund NU, Stavropoulos A, Donatsky O, et al. Reimplantation of cultivated human bone cells from the posterior maxilla for sinus floor augmentation. Histological results from a randomized controlled clinical trial. Clin Oral Implants Res 2012;23:1031–1037.
81. Anitua E, Prado R, Orive G. Bilateral sinus elevation evaluating plasma rich in growth factors technology: A report of five cases. Clin Implant Dent Relat Res 2012;14:51–60.
82. Trautvetter W, Kaps C, Schmelzeisen R, Sauerbier S, Sittinger M. Tissue-engineered polymer-based periosteal bone grafts for maxillary sinus augmentation: Five-year clinical results. J Oral Maxillofac Surg 2011;69:2753–2762.
83. Stavropoulos A, Becker J, Capsius B, Acil Y, Wagner W, Terheyden H. Histological evaluation of maxillary sinus floor augmentation with recombinant human growth and differentiation factor-5-coated β-tricalcium phosphate: Results of a multicenter randomized clinical trial. J Clin Periodontol 2011;38:966–974.
84. Sohn DS, Heo JU, Kwak DH, et al. Bone regeneration in the maxillary sinus using an autologous fibrin-rich block with concentrated growth factors alone. Implant Dent 2011;20:389–395.
85. Simonpieri A, Choukroun J, Del Corso M, Sammartino G, Dohan Ehrenfest DM. Simultaneous sinus-lift and implantation using microthreaded implants and leukocyte- and platelet-rich fibrin as sole grafting material: A six-year experience. Implant Dent 2011;20:2–12.
86. Sauerbier S, Rickert D, Gutwald R, et al. Bone marrow concentrate and bovine bone mineral for sinus floor augmentation: A controlled, randomized, single-blinded clinical and histological trial—per-protocol analysis. Tissue Eng Part A 2011;17:2187–2197.
87. Montesani L, Schulze-Späte U, Dibart S. Sinus augmentation in two patients with severe posterior maxillary height atrophy using tissue-engineered bone derived from autologous bone cells: A case report. Int J Periodontics Restorative Dent 2011;31:391–399.
88. Butz F, Bächle M, Ofer M, Marquardt K, Kohal RJ. Sinus augmentation with bovine hydroxyapatite/synthetic peptide in a sodium hyaluronate carrier (PepGen P-15 Putty): A clinical investigation of different healing times. Int J Oral Maxillofac Implants 2011;26:1317–1323.
89. Tarnow DP, Wallace SS, Testori T, Froum SJ, Motroni A, Prasad HS. Maxillary sinus augmentation using recombinant bone morphogenetic protein-2/acellular collagen sponge in combination with a mineralized bone replacement graft: A report of three cases. Int J Periodontics Restorative Dent 2010;30:139–149.
90. Mangano C, Piattelli A, Tettamanti L, et al. Engineered bone by autologous osteoblasts on polymeric scaffolds in maxillary sinus augmentation: Histologic report. J Oral Implantol 2010;36:491–496.
91. Torres J, Tamimi F, Martinez PP, et al. Effect of platelet-rich plasma on sinus lifting: A randomized-controlled clinical trial. J Clin Periodontol 2009;36:677–687.
92. Smith AE, Prasad HS, Rohrer MD. Bone regeneration with autologous biomaterial; rapid induction of vital new bone in maxillary sinus floor by platelet concentrate alone at 23x baseline (PRP23x): A case report. Implant Dent 2009;18:210–219.
93. Papa F, Cortese A, Sagliocco R, et al. Outcome of 47 consecutive sinus lift operations using aragonitic calcium carbonate associated with autologous platelet-rich plasma: Clinical, histologic, and histomorphometrical evaluations. J Craniofac Surg 2009;20:2067–2074.
94. Nevins M, Garber D, Hanratty JJ, et al. Human histologic evaluation of anorganic bovine bone mineral combined with recombinant human platelet-derived growth factor BB in maxillary sinus augmentation: Case series study. Int J Periodontics Restorative Dent 2009;29:583–591.
95. McAllister BS, Haghighat K, Gonshor A. Histologic evaluation of a stem cell-based sinus-augmentation procedure. J Periodontol 2009;80:679–686.
96. Mangano C, Piattelli A, Mangano A, et al. Combining scaffolds and osteogenic cells in regenerative bone surgery: A preliminary histological report in human maxillary sinus augmentation. Clin Implant Dent Relat Res 2009;11(1, suppl):e92–e102.
97. Fuerst G, Strbac GD, Vasak C, et al. Are culture-expanded autogenous bone cells a clinically reliable option for sinus grafting? Clin Oral Implants Res 2009;20:135–139.
98. Bettega G, Brun JP, Boutonnat J, et al. Autologous platelet concentrates for bone graft enhancement in sinus lift procedure. Transfusion 2009;49:779–785.
99. Anitua E, Prado R, Orive G. A lateral approach for sinus elevation using PRGF technology. Clin Implant Dent Relat Res 2009;11(1, suppl):e23–e31.
100. Yamada Y, Nakamura S, Ito K, et al. Injectable tissue-engineered bone using autogenous bone marrow-derived stromal cells for maxillary sinus augmentation: Clinical application report from a 2–6-year follow-up. Tissue Eng Part A 2008;14:1699–1707.
101. Shayesteh YS, Khojasteh A, Soleimani M, Alikhasi M, Khoshzaban A, Ahmadbeigi N. Sinus augmentation using human mesenchymal stem cells loaded into a β-tricalcium phosphate/hydroxyapatite scaffold. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:203–209.
102. Schaaf H, Streckbein P, Lendeckel S, et al. Sinus lift augmentation using autogenous bone grafts and platelet-rich plasma: Radiographic results. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;106:673–678.
103. Nikolidakis D, Meijer GJ, Jansen JA. Sinus floor elevation using platelet-rich plasma and β-tricalcium phosphate: Case report and histological evaluation. Dent Today 2008;27:66;68;70.
104. Beaumont C, Schmidt RJ, Tatakis DN, Zafiropoulos GG. Use of engineered bone for sinus augmentation. J Periodontol 2008;79:541–548.
105. Antoun H, Bouk H, Ameur G. Bilateral sinus graft with either bovine hydroxyapatite or β-tricalcium phosphate, in combination with platelet-rich plasma: A case report. Implant Dent 2008;17:350–359.
106. Aimetti M, Romano F, Dellavia C, De Paoli S. Sinus grafting using autogenous bone and platelet-rich plasma: Histologic outcomes in humans. Int J Periodontics Restorative Dent 2008;28:585–591.
107. Zizelmann C, Schoen R, Metzger MC, et al. Bone formation after sinus augmentation with engineered bone. Clin Oral Implants Res 2007;18:69–73.
108. Consolo U, Zaffe D, Bertoldi C, Ceccherelli G. Platelet-rich plasma activity on maxillary sinus floor augmentation by autologous bone. Clin Oral Implants Res 2007;18:252–262.
109. Whitesides LM, Radwan A, Sharawy M. Sinus floor augmentation using a composite graft of bone morphogenic protein-2 and allogenic cancellous bone (Puros): Case report. J Oral Implantol 2006;32:259–264.
110. Steigmann M, Garg AK. A comparative study of bilateral sinus lifts performed with platelet-rich plasma alone versus alloplastic graft material reconstituted with blood. Implant Dent 2005;14:261–266.
111. Raghoebar GM, Schortinghuis J, Liem RS, Ruben JL, van der Wal JE, Vissink A. Does platelet-rich plasma promote remodeling of autologous bone grafts used for augmentation of the maxillary sinus floor? Clin Oral Implants Res 2005;16:349–356.
112. Philippart P, Daubie V, Pochet R. Sinus grafting using recombinant human tissue factor, platelet-rich plasma gel, autologous bone, and anorganic bovine bone mineral xenograft: Histologic analysis and case reports. Int J Oral Maxillofac Implants 2005;20:274–281.
113. Kassolis JD, Reynolds MA. Evaluation of the adjunctive benefits of platelet-rich plasma in subantral sinus augmentation. J Craniofac Surg 2005;16:280–287.
114. Graziani F, Ducci F, Tonelli M, El Askary AS, Monier M, Gabriele M. Maxillary sinus augmentation with platelet-rich plasma and fibrinogen cryoprecipitate: A tomographic pilot study. Implant Dent 2005;14:63–69.
115. Mazor Z, Peleg M, Garg AK, Luboshitz J. Platelet-rich plasma for bone graft enhancement in sinus floor augmentation with simultaneous implant placement: Patient series study. Implant Dent 2004;13:65–72.

116. Degidi M, Piattelli M, Scarano A, Iezzi G, Piattelli A. Maxillary sinus augmentation with a synthetic cell-binding peptide: Histological and histomorphometrical results in humans. J Oral Implantol 2004;30:376–383.
117. Wiltfang J, Schlegel KA, Schultze-Mosgau S, Nkenke E, Zimmermann R, Kessler P. Sinus floor augmentation with β-tricalciumphosphate (β-TCP): Does platelet-rich plasma promote its osseous integration and degradation? Clin Oral Implants Res 2003;14:213–218.
118. Schmelzeisen R, Schimming R, Sittinger M. Making bone: Implant insertion into tissue-engineered bone for maxillary sinus floor augmentation-a preliminary report. J Craniomaxillofac Surg 2003;31:34–39.
119. Rodriguez A, Anastassov GE, Lee H, Buchbinder D, Wettan H. Maxillary sinus augmentation with deproteinated bovine bone and platelet rich plasma with simultaneous insertion of endosseous implants. J Oral Maxillofac Surg 2003;61:157–163.
120. Philippart P, Brasseur M, Hoyaux D, Pochet R. Human recombinant tissue factor, platelet-rich plasma, and tetracycilne induce a high-quality human bone graft: A 5-year survey. Int J Oral Maxillofac Implants 2003;18:411–416.
121. Froum SJ, Wallace SS, Tarnow DP, Cho SC. Effect of platelet-rich plasma on bone growth and osseointegration in human maxillary sinus grafts: Three bilateral case reports. Int J Periodontics Restorative Dent 2002;22:45–53.
122. van den Bergh JP, ten Bruggenkate CM, Groeneveld HH, Burger EH, Tuinzing DB. Recombinant human bone morphogenetic protein-7 in maxillary sinus floor elevation surgery in 3 patients compared to autogenous bone grafts. A clinical pilot study. J Clin Periodontol 2000;27:627–636.
123. Rosenberg ES, Torosian J. Sinus grafting using platelet-rich plasma—initial case presentation. Pract Periodontics Aesthet Dent 2000;12:843–850.
124. Boyne PJ, Marx RE, Nevins M, et al. A feasibility study evaluating rhBMP-2/absorbable collagen sponge for maxillary sinus floor augmentation. Int J Periodontics Restorative Dent 1997;17:11–25.
125. Ueda M, Yamada Y, Ozawa R, Okazaki Y. Clinical case reports of injectable tissue-engineered bone for alveolar augmentation with simultaneous implant placement. Int J Periodontics Restorative Dent 2005;25:129–137.
126. Maiorana C, Sommariva L, Brivio P, Sigurta D, Santoro F. Maxillary sinus augmentation with anorganic bovine bone (Bio-Oss) and autologous platelet-rich plasma: Preliminary clinical and histologic evaluations. Int J Periodontics Restorative Dent 2003;23:227–235.
127. Krauser JT, Rohrer MD, Wallace SS. Human histologic and histomorphometric analysis comparing OsteoGraf/N with PepGen P-15 in the maxillary sinus elevation procedure: A case report. Implant Dent 2000;9:298–302.
128. Froum SJ, Wallace S, Cho SC, et al. Histomorphometric comparison of different concentrations of recombinant human bone morphogenetic protein with allogeneic bone compared to the use of 100% mineralized cancellous bone allograft in maxillary sinus grafting. Int J Periodontics Restorative Dent 2013;33:721–730.
129. Jensen OT, Cottam JR, Ringeman JL, et al. Experience with bone morphogenetic protein-2 and interpositional grafting of edentulous maxillae: A comparison of Le Fort I downfracture to full-arch (horseshoe) segmental osteotomy done in conjunction with sinus floor grafting. Int J Oral Maxillofac Implants 2013;28:e331–e348.
130. Jensen OT. Segmental alveolar split combined with dental extractions and osteotome sinus floor intrusion in posterior maxilla using BMP-2/ACS allograft for alveolar reconstruction: Technical note and report of three cases. J Oral Maxillofac Surg 2013;71:2040–2047.
131. Simion M, Rocchietta I, Fontana F, Dellavia C. Evaluation of a resorbable collagen matrix infused with rhPDGF-BB in peri-implant soft tissue augmentation: A preliminary report with 3.5 years of observation. Int J Periodontics Restorative Dent 2012;32:273–282.
132. Schuckert KH, Jopp S, Osadnik M. Modern bone regeneration instead of bone transplantation: A combination of recombinant human bone morphogenetic protein-2 and platelet-rich plasma for the vertical augmentation of the maxillary bone-a single case report. Tissue Eng Part C Methods 2010;16:1335–1346.
133. Urban I, Caplanis N, Lozada JL. Simultaneous vertical guided bone regeneration and guided tissue regeneration in the posterior maxilla using recombinant human platelet-derived growth factor: A case report. J Oral Implantol 2009;35:251–256.
134. Simion M, Rocchietta I, Monforte M, Maschera E. Three-dimensional alveolar bone reconstruction with a combination of recombinant human platelet-derived growth factor BB and guided bone regeneration: A case report. Int J Periodontics Restorative Dent 2008;28:239–243.
135. Schaaf H, Streckbein P, Lendeckel S, et al. Topical use of platelet-rich plasma to influence bone volume in maxillary augmentation: A prospective randomized trial. Vox Sang 2008;94:64–69.
136. Filho Cerruti H, Kerkis I, Kerkis A, et al. Allogenous bone grafts improved by bone marrow stem cells and platelet growth factors: Clinical case reports. Artif Organs 2007;31:268–273.
137. Thor A, Wannfors K, Sennerby L, Rasmusson L. Reconstruction of the severely resorbed maxilla with autogenous bone, platelet-rich plasma, and implants: 1-year results of a controlled prospective 5-year study. Clin Implant Dent Relat Res 2005;7:209–220.
138. Thor A. Reconstruction of the anterior maxilla with platelet gel, autogenous bone, and titanium mesh: A case report. Clin Implant Dent Relat Res 2002;4:150–155.
139. Reddi AH, Cunningham NS. Recent progress in bone induction by osteogenin and bone morphogenetic proteins: Challenges for biomechanical and tissue engineering. J Biomech Eng 1991;113:189–190.
140. Giannobile WV. Periodontal tissue engineering by growth factors. Bone 1996;19(1, suppl):23S–37S.
141. Bartold PM, McCulloch CA, Narayanan AS, Pitaru S. Tissue engineering: A new paradigm for periodontal regeneration based on molecular and cell biology. Periodontol 2000 2000;24:253–269.
142. Amini AR, Laurencin CT, Nukavarapu SP. Bone tissue engineering: Recent advances and challenges. Crit Rev Biomed Eng 2012;40:363–408.
143. Bichara DA, O'Sullivan NA, Pomerantseva I, et al. The tissue-engineered auricle: Past, present, and future. Tissue Eng Part B Rev 2012;18:51–61.
144. Ohya M, Yamada Y, Ozawa R, Ito K, Takahashi M, Ueda M. Sinus floor elevation applied tissue-engineered bone. Comparative study between mesenchymal stem cells/platelet-rich plasma (PRP) and autogenous bone with PRP complexes in rabbits. Clin Oral Implants Res 2005;16:622–629.
145. Park CH, Rios HF, Taut AD, et al. Image-based, fiber guiding scaffolds: A platform for regenerating tissue interfaces. Tissue Eng Part C Methods 2014;20:533–542.
146. Elangovan S, D'Mello SR, Hong L, et al. The enhancement of bone regeneration by gene activated matrix encoding for platelet derived growth factor. Biomaterials 2014;35:737–747.

Clinical Practice Guidelines: Role of Biologics to Assist in Ridge Development

SCOPE

This clinical practice guidelines (CPG) document is an official statement of the Academy of Osseointegration (AO) regarding the effectiveness and efficacy of different tissue engineering–based therapies for implant site development in atrophic maxillary segments prior to dental implant placement.

Target condition or procedures: Complete or partial maxillary edentulism in association with horizontal, vertical, or combined hard or soft tissue defects, which require implant site development therapy prior to implant placement and subsequent prosthetic rehabilitation.

Target population: Adult completely or partially edentulous patients who desire an implant-supported prosthesis and are in need of bone and/or soft tissue augmentation due to maxillary atrophy.

Clinical practice setting: Secondary or tertiary dental care provided by general dentists and specialists in private practice, academic institutions, military and/or civil hospital settings.

Interventions: Tissue engineering–based therapies that involve the clinical application of at least one of the following elements: pluripotential/stem cells (cell therapy), molecular mediators (eg, growth factors, bone morphogenetic proteins, biomimetic peptides, etc), and gene therapy, with or without scaffolds or matrices.

Outcome measures:

1. Clinical: Incidence of complications, dimensional changes of the ridge, implant primary stability, need of additional grafting at the time of implant placement, implant survival and success rate.
2. Radiographic: Dimensional changes (linear or volumetric) and densitometry of the grafted area, and marginal bone loss around implants.
3. Histologic: Evidence of bone formation, characteristics of the tissues, and proportion of different tissue compartments.
4. Patient-centered: Safety, perceived benefit, and changes in quality of life.

doi: 10.11607/jomi.16suppl.g4.cpg

INTRODUCTION

The past two decades have demonstrated the potential of applying concepts from the regenerative medicine arena, such as bone bioengineering for implant site development, into dentistry in order to allow more predictable, strategic, and idealized implant-supported prostheses that restore both function and esthetics. In recent years, and following rigorous preclinical and clinical evaluation, the application of tissue engineering therapies in dentistry to enhance soft and hard tissue augmentation procedures has become a reality in daily clinics.[1–7] These clinical practice guidelines (CPGs) are an official statement of the AO regarding the effectiveness and efficacy of both current and emerging tissue engineering strategies for implant site development in atrophic maxillary segments prior to dental implant placement.

PURPOSE

The purpose is to guide dental implant surgeons on the indications of tissue engineering therapies for implant site development in atrophic maxillary segments in order to optimize patient care through accurate case and therapy selection.

HEALTH CARE BURDEN

Unsuccessful implant site development procedures in maxillary atrophic ridges, due to either insufficient augmentation, failure to obtain an adequate substrate, and/or complications, has a significant financial impact in health care in the dental office setting, since it often implies an increase in the overall cost of therapy and longer treatment times, as well as patient dissatisfaction. The concomitant use of tissue engineering therapies may enhance the predictability and clinical efficacy of conventional implant site development approaches.

METHODS

Prior to the 2014 AO Summit, a systematic review was conducted on the basis of the following PICO question: In human subjects who desire an implant-supported prosthesis and are in need of bone and/or soft tissue augmentation due to maxillary atrophy, what is the effectiveness and/or efficacy of tissue engineering–based therapies compared to conventional site development approaches considering clinical, radiographic, histologic, and patient-centered outcomes?

Six electronic databases were searched for articles relevant in the context of this systematic review (SR): National Library of Medicine (MEDLINE – PubMed), Web of Knowledge, Scopus, Embase, Cochrane Library/Wiley, and ProQuest Dissertations and Theses (in an attempt to capture gray literature). No limits regarding language of the article, publication date, or status were set in order to conduct a search as comprehensive as possible. The last search was conducted on March 17, 2014. The terms and strategy used to search each individual database are displayed in Tables 2 through 7 of the systematic review. To complement the database search, cited reference searching was also performed. Pertinent articles for the review were selected by two independent examiners (G.A. and H.R.) following a set of predetermined eligibility criteria. One reviewer (G.A.) extracted the data of the studies in the final selection. In order to assess and report in a standardized manner the level of evidence of each one of the individual studies selected in this SR, the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence scale was applied.[8] On the other hand, for the assessment of the body of evidence, the 'SORT' grading and scoring system was followed at the AO Summit.[9] The methodology to distinguish between efficacy and effectiveness in clinical studies proposed by Gartlehner and collaborators[10] was followed to comprehensively determine the efficacy and effectiveness of the different therapeutic approaches included in the evidence selected in this SR. At the Summit, the SR and other sources of evidence were considered by a group of 16 experts to define the CPG.

GUIDELINE KEY ACTION STATEMENTS

The following clinical practice guidelines were developed at the 2014 AO Summit by a group of 14 experts on the basis of the best available evidence:

Recommendation 1: For maxillary buccal wall extraction socket defects, the evidence suggests that rhBMP-2/ACS may be considered by dental implant surgeons to promote bone repair and to facilitate implant placement (SORT score: B).[2]

Recommendation 2: Limited evidence suggests that autologous stem cell delivery in a gelatin foam may be considered by dental implant surgeons to accelerate bone formation and minimize ridge height reduction to enable implant placement in extraction sockets (SORT score: B).[3]

Recommendation 3: Limited evidence suggests that rhPDGF-BB combined with FDBA or βTCP may be considered by dental implant surgeons to accelerate bone formation in extraction sockets (SORT score: B).[6]

Recommendation 4: For maxillary sinus floor augmentation, evidence supports that rhBMP-2/ACS should be considered by dental implant surgeons as an alternative to bone autografts in promoting bone formation to enable implant placement and reduce patient morbidity associated with graft harvest (SORT score: A).[5,11,12]

IMPLEMENTATION CONSIDERATIONS

Given their novelty and, in some instances, recent experimental status, the cost of most tissue engineering approaches is relatively high. Additionally, the application of some of the aforementioned tissue engineering therapies requires advanced surgeon and staff training, as well as specific infrastructure and equipment that are not generally available in the majority of dental offices. Another factor to take into consideration are regulatory aspects that may influence the adoption of tissue engineering therapies by some clinicians. Although there is sufficient evidence to support the aforementioned guidelines, there is a paucity of robust evidence supporting the superiority of tissue engineering approaches as compared to conventional augmentation therapies in certain clinical applications, such as augmentation of horizontal, vertical, and/or combined defects. In summary, the acceptance of the recommendations hereby presented may be highly determined by financial and regulatory aspects of health care, and the level of expertise and comfort with new therapies of the surgeon.

ACKNOWLEDGMENTS

The authors would like to thank Julie Schiavo and Chris White, Specialist Librarians at Lousiana State University School of Dentistry and at the University of Iowa College of Dentistry, respectively, for their valuable assistance in the conduction of the search and finding full text versions of multiple articles. The authors G.A. and H.R. would like to acknowledge the American Academy of Periodontology Foundation (AAPF) for the support provided to pursue an academic career.

The development of these clinical practice guidelines was exclusively supported by the 2014 Academy of Osseointegration (AO) Summit operating budget.

Drs Gustavo Avila-Ortiz, Mark Bartold, Rolf Ewers, Alan Herford, Wataru Katagiri, Salvador Nares, Hector Rios, Gilbert Triplett, and Mark Wong declare no conflictS of interest with regards to the conduction of this systematic review. Dr William Giannobile declares having consulted for Osteohealth, Medtronic Spine & Biologics, Geistlich Pharma, and Straumann. Dr Marc Nevins declares having received research and lecture support from Osteohealth Co. Dr Anton Sculean declares having received support for research and lecturing from Straumann, Geistlich Pharma, Osteology Foundation, ITI Foundation, Botiss, and Helbo. Dr Daniel Spagnoli declares having consulted, done clinical research, and received lecture support from Medtronic Spine & Biologics. Dr Ulf ME Wikesjö was part of the team at Genetics Institute/Wyeth Research that provided the evidence and background for the development and registration of recombinant human bone morphogenetic protein-2 (rhBMP-2; brand name Infuse). He directed the preclinical/clinical development of recombinant human growth/differentiation factor-5 (rhGDF-5) for periodontal indications as a consultant to Scil Technology. Moreover, he has conducted research studies for/provided consultation services to WL Gore & Associates, Genetics Institute/Wyeth Research, Nobel Biocare, Medtronic Spine & Biologics, Osstem, Scil Technology, Daewoong Pharmaceuticals, OraPharma, and Dentsply International in corporate and academic settings.

REFERENCES

1. de Freitas RM, Susin C, Spin-Neto R, et al. Horizontal ridge augmentation of the atrophic anterior maxilla using rhBMP-2/ACS or autogenous bone grafts: A proof-of-concept randomized clinical trial. J Clin Periodontol 2013;40:968–975.
2. Fiorellini JP, Howell TH, Cochran D, et al. Randomized study evaluating recombinant human bone morphogenetic protein-2 for extraction socket augmentation. J Periodontol 2005;76:605–613.
3. Kaigler D, Pagni G, Park CH, et al. Stem cell therapy for craniofacial bone regeneration: A randomized, controlled feasibility trial. Cell Transplant 2013;22:767–777.
4. Simion M, Rocchietta I, Fontana F, Dellavia C. Evaluation of a resorbable collagen matrix infused with rhPDGF-BB in peri-implant soft tissue augmentation: A preliminary report with 3.5 years of observation. Int J Periodontics Restorative Dent 2012;32:273–282.
5. Triplett RG, Nevins M, Marx RE, et al. Pivotal, randomized, parallel evaluation of recombinant human bone morphogenetic protein-2/absorbable collagen sponge and autogenous bone graft for maxillary sinus floor augmentation. J Oral Maxillofac Surg 2009;67:1947–1960.
6. Geurs N, Ntounis A, Vassilopoulos P, Van der Velden U, Loos BG, Reddy M. Using growth factors in human extraction sockets: A histologic and histomorphometric evaluation of short-term healing. Int J Oral Maxillofac Implants 2014;29:485-496.
7. Pagni G, Kaigler D, Rasperini G, Avila-Ortiz G, Bartel R, Giannobile WV. Bone repair cells for craniofacial regeneration. Adv Drug Deliv Rev 2012;64:1310–1319.
8. Oxford Center for Evidence-Based Medicine 2011 Levels of Evidence. http://www.cebm.net/index.aspx?o=5653. Accessed 14 April 2014.
9. Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): A patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548–556.
10. Gartlehner G, Hansen RA, Nissman D, Lohr KN, Carey TS. A simple and valid tool distinguished efficacy from effectiveness studies. J Clin Epidemiol 2006;59:1040–1048.
11. Boyne PJ, Marx RE, Nevins M, et al. A feasibility study evaluating rhBMP-2/absorbable collagen sponge for maxillary sinus floor augmentation. Int J Periodontics Restorative Dent 1997;17:11–25.
12. Boyne PJ, Lilly LC, Marx RE, et al. De novo bone induction by recombinant human bone morphogenetic protein-2 (rhBMP-2) in maxillary sinus floor augmentation. J Oral Maxillofac Surg 2005;63:1693–1707.

Role of Prosthetic Management

Group Co-Chairs

James Taylor, DMD, MA
Lyndon F. Cooper, DDS, PhD

Group Participants

Avinash Bidra, BDS, MS
Marco Degidi, DDS, MD
Julie Elpers, DMD. MS
German Gallucci, DMD
Robert Jaffin, DMD
Henny Meijer, DDS, PhD
Stephen Parel, DDS
Stephen Porter, DDS
Steven Sadowsky, DDS
Wim Slot, DDS
Christian Stappert, MS, DDS, PhD
Thomas Taylor, DDS, MSD
Ghadeer Thalji, BDS, PhD
Nicola Zitzmann, MD

Maxillary Complete Denture Outcomes: A Systematic Review of Patient-Based Outcomes

Ghadeer Thalji, BDS, PhD[1]/Kate McGraw, MA, MLS[2]/Lyndon F. Cooper, DDS, PhD[3]

Purpose: *The aim of this systematic review is to report on the current knowledge regarding patient satisfaction as a primary outcome for maxillary complete denture therapy. We asked, "For the maxillary edentulous patient treated using maxillary dentures, what are the patient-based outcomes regarding quality of life and treatment satisfaction."* ***Materials and Methods:*** *An electronic search of publications up to March 2014 was established using four databases: PubMed, Web of Science, Scopus, and Embase. To meet the ultimate goal of establishing clinical guidelines based on available information, prospective comparative studies, cohort prospective studies, and retrospective studies on more than 10 subjects were included. The electronic search identified 4,530 articles that were evaluated at the title, abstract, and article level to include 31 articles of interest. The patient-based outcomes and satisfaction data included were examined and reported.* ***Results:*** *The studies included 5,485 participants. Of these, 2,685 were identified as wearing maxillary complete dentures. Reported mean ages ranged from 59.7 to 73.6 years. A systematic review indicated that the provision of new maxillary complete dentures for edentulous patients results in improved self-reported satisfaction and oral health–related quality of life. The included reports, while providing evidence that complete denture satisfaction of participants and new dentures improve self-reported outcomes, did not include variables that influence these positive outcomes.* ***Conclusion:*** *A broad range of evidence supports the use of complete dentures for rehabilitation of the edentulous maxilla. When considering treatment of the edentulous maxilla, the expectations of patients for esthetic and phonetic (social) rehabilitation are high and can be met using maxillary complete dentures as the mode of prosthetic rehabilitation. Patients dissatisfied with new complete dentures may be referred for dental implant therapies involving fixed or removable prostheses.* Int J Oral Maxillofac Implants 2016;31(suppl):s169–s181. doi: 10.11607/jomi.16suppl.g5.1

Keywords: *complete dentures, edentulism, edentulous maxilla, esthetic satisfaction, implant overdenture, implant-supported fixed prosthesis, OHIP-EDENT, OHQoL*

Edentulism is prevalent in the developed world. Populations around the world demonstrate adult tooth loss due, in part, to biofilm-mediated diseases of caries and periodontitis. In the United States, edentulism for individuals ranging from 50 to 85 years of age was reported as 23.98% for Native Americans, 19.39% for African Americans, 16.90% for Whites, 14.22% for Asians, and 14.18% for Hispanics (data from the National Health Interview Survey [1999–2008]). Although recent data indicate that, when controlling for time, age, gender, and whether the respondent was born in the United States, the odds of edentulism has declined in the past decades by 3% per year. More recently, this decline has slowed.

Associated with the existing edentulous population is an acknowledged increase in the number of older individuals with retained teeth at risk. For example, a study conducted in France concluded that the main biological reasons for tooth extraction in individuals younger than 50 years was caries; those older than 50 years underwent extraction because of periodontitis.[1] Irrespective of the biological reasons for tooth extraction/loss, an important factor in the decision to remove rather than preserve teeth is the individual's socioeconomic status. Included here are data on both income and educational status.[2]

Tooth extraction is often a choice made deliberately and for economic reasons. Sociodemographic factors, dental-related behaviors, and the types of dental services selected are all significantly related.[3] In a recent survey of 184 community-dwelling senior adults, 89% needed dental treatment and within 6 weeks, nearly one half had not received treatment. Those unable to access treatment were more likely to be referred for dentures. Self-reported reasons for not accessing care included lack of finances, transportation, or assistance in navigating dental service. Borreani et al[4] demonstrated that the costs of dental treatment, fear

[1]Assistant Professor, Department of Prosthodontics, University of Iowa, Iowa City, Iowa, USA.
[2]Librarian, School of Dentistry, Health Sciences Library, University of North Carolina, Chapel Hill, North Carolina, USA.
[3]Associate Dean for Research; Head, Department of Oral Biology, University of Illinois at Chicago, College of Dentistry, Chicago, Illinois, USA.

Correspondence to: Dr Lyndon F. Cooper, 330 Brauer Hall, CB#7450, University of North Carolina School of Dentistry, Chapel Hill, NC 27599. Email: lyndon_cooper@dentistry.unc.edu

of care, and perceived availability represented barriers to dental care. In an interesting report of estimated need vs actual treatment among 16 to 24 year olds, the mean number of teeth extracted was greater than the estimated need (27.4% vs 7.9%; $P = .0001$).[5] This was gr eatest for "less-well-off" adults. These observations regarding tooth extraction led to a conclusion that *(1)* dental extractions continue to exceed estimates based solely on disease prevalence, and *(2)* selection of extractions (leading to edentulism) is often an economic compromise.

Cost of tooth replacement or tooth repair is an important pragmatic factor influencing the individual patient outcome that often leads to edentulism. The initial cost of replacing teeth with dentures or various dental implant strategies is significant, and represents a factor in patient treatment. These costs include the materials, professional and laboratory fees, travel costs, and travel and clinic visit times. For example, Zitzmann et al[6] reported that implant-supported and implant-retained overdentures were 6.25 times and 2.75 times more costly, respectively, than conventional new dentures. Although there were apportioned benefits to the implant-associated treatments, these were associated with significant financial burden over an assumed 10-year time horizon.

There is ample evidence to support the many benefits of mandibular implant overdentures over conventional mandibular dentures, but the literature evaluating patient-centered benefits for maxillary implant overdentures is limited. In fact, several investigations have shown that there is no significant improvement for implant overdentures compared with complete dentures in patient-reported mastication, stability, retention, function, or speech. It has been stated that patients who are not satisfied with their maxillary complete dentures should investigate implants in efforts to improve satisfaction.[7] Overall, the literature shows both a significant negative impact of (old) dentures on a patient's quality of life and an improvement in life quality when patients are provided with new dentures. [8] A high-quality denture is a prosthesis that offers improvements in esthetics, phonetics, and related self-image.[9] It was concluded that the conventional maxillary denture is a prosthesis that affords individuals social and physical function, albeit with significant maintenance requirements, at a relatively low cost. In light of the prevalence of edentulism and the relative impact of socioeconomic status, age (birth year), and education on its distribution within populations, it is likely that the complete denture remains an important and relevant option for treatment of the edentulous maxilla.

The aim of this systematic review is to report on the current knowledge regarding patient satisfaction as a primary outcome for complete maxillary denture therapy. Further, investigation regarding the common complications encountered with this therapy will be discussed. The primary biological consequence of stomatitis will be reported elsewhere.

MATERIALS AND METHODS

An electronic search of publications up to March 2014 was established using four databases: PubMed, Web of Science, Scopus, and Embase. The aim of the search was to report on the current knowledge on the outcomes of rehabilitation in the edentulous maxilla. The intent of this review included deriving clinical guidelines for treatment of the edentulous maxilla. Thus, a broad search and wi de inclusion criteria (Table 1) were established.

The search included peer-reviewed publications in the English language. MeSH and free-text terms were used in the search. Search terms used in the different databases were as follows:

1. PubMed: ((implant*[text word] AND dental[text word] AND (full arch[text word] OR full mouth[text word] OR hybrid[text word] OR edentulous[text word])) OR (Denture*[text word] AND (complete[text word] OR full arch[text word] OR full mouth[text word] OR overlay[text word])) OR (overdenture*[text word] OR over denture*[text word])) AND (cohort studies[mesh] OR cohort[text word] OR longitudinal[text word] OR follow up[text word] OR followup[text word] OR prospective[text word] OR case control[text word] OR retrospective[text word] OR case comparison[text word] OR cross sectional[text word] OR comparative[text word] OR evaluat*[text word] OR survey*[text word] OR questionnaire*[text word] OR scale*[text word] OR clinical trial*[text word] OR random*[text word]) AND (fail*[text word] OR complication*[text word] OR surviv*[text word] OR longevity[text word] OR outcome*[text word] OR masticat*[text word] OR chew*[text word] OR wear[text word] OR attrition[text word] OR repair*[text word] OR nutrition*[text word] OR complain*[text word] OR patient satisfaction[text word] OR quality of life[text word] OR speech[text word] OR appearance*[text word] OR esthetic*[text word] or aesthetic*[text word]) Filters: English.
2. Web of Science: (implant* AND dental AND ("full arch" OR "full mouth" OR hybrid OR edentulous)) OR (Denture* AND (complete OR "full arch" OR "full mouth" OR overlay)) OR (overdenture* OR "over denture*")AND (cohort OR longitudinal OR "follow up" OR followup OR prospective OR "case control" OR retrospective OR "case comparison" OR "cross sectional" OR comparative OR evaluat* OR survey* OR questionnaire* OR scale* OR "clinical trial*" OR random*) AND (fail* OR complication* OR surviv* OR longevity OR outcome* OR masticat* OR chew* OR wear OR attrition OR repair* OR nutrition* OR complain* OR "patient satisfaction" OR "quality of

Table 1 Inclusion Criteria

Human clinical study; prospective, retrospective, randomized clinical trial, cross-sectional observational study
Investigation including maxillary complete denture, not including maxillary implants
If rehabilitation for the maxillary arch involved treatment modalities other than a maxillary complete denture, data were stratified to allow analysis of outcomes of the complete denture separately
Follow-up period defined after denture insertion
Publication in peer-reviewed journal
Inclusion of at least 10 participants
In English

life" OR speech OR appearance* OR esthetic* or aesthetic*)

3. Scopus: (implant* AND dental AND ("full arch" OR "full mouth" OR hybrid OR edentulous)) OR (Denture AND (complete OR "full arch" OR "full mouth" OR overlay)) OR (overdenture OR "over denture") AND (cohort OR longitudinal OR "follow up" OR followup OR prospective OR "case control" OR retrospective OR "case comparison" OR "cross sectional" OR comparative OR evaluat* OR survey OR questionnaire OR scale OR "clinical trial" OR random*) AND (fail* OR complication OR surviv* OR longevity OR outcome OR masticat* OR chew OR wear OR attrition OR repair* OR nutrition* OR complain* OR "patient satisfaction" OR "quality of life" OR speech OR appearance OR esthetic or aesthetic)
   ((TITLE-ABS-KEY(implant* AND dental AND ("full arch" OR "full mouth" OR hybrid OR edentulous)) OR TITLE-ABS-KEY(denture AND (complete OR "full arch" OR "full mouth" OR overlay)) OR TITLE-ABS-KEY(overdenture OR "over denture"))) AND (TITLE-ABS-KEY(cohort OR longitudinal OR "follow up" OR followup OR prospective OR "case control" OR retrospective OR "case comparison" OR "cross sectional" OR comparative OR evaluat* OR survey OR questionnaire OR scale OR "clinical trial" OR random*)) AND (TITLE-ABS-KEY(fail* OR complication OR surviv* OR longevity OR outcome OR masticat* OR chew OR wear OR attrition OR repair* OR nutrition* OR complain* OR "patient satisfaction" OR "quality of life" OR speech OR appearance OR esthetic OR aesthetic)) AND (LIMIT-TO(DOCTYPE, "ar") OR LIMIT-TO(DOCTYPE, "re") OR LIMIT-TO(DOCTYPE, "cp")) AND (LIMIT-TO(LANGUAGE, "English"))
4. Embase: Search ((implant*:de,ti,ab AND dental:de,ti,ab AND ("full arch":de,ti,ab OR "full mouth":de,ti,ab OR hybrid:de,ti,ab OR edentulous:de,ti,ab)) OR(Denture*:de,ti,ab AND (complete:de,ti,ab OR "full arch":de,ti,ab OR "fullmouth":de,ti,ab OR overlay:de,ti,ab)) OR (overdenture*:de,ti,ab OR "overdenture":de,ti,ab OR "over dentures":de,ti,ab)) AND (cohort:de,ti,ab OR longitudinal:de,ti,ab OR "follow up":de,ti,ab OR followup:de,ti,ab OR prospective:de,ti,ab OR "case control":de,ti,ab OR retrospective:de,ti,ab OR "case comparison":de,ti,ab OR "cross sectional":de,ti,ab OR comparative:de,ti,ab OR evaluat*:de,ti,ab OR survey*:de,ti,ab OR questionnaire*:de,ti,ab OR scale*:de,ti,ab OR "clinical trial":de,ti,ab OR "clinical trials":de,ti,ab OR random*:de,ti,ab) AND (fail*:de,ti,ab OR complication*:de,ti,ab OR surviv*:de,ti,ab OR longevity:de,ti,ab OR outcome*:de,ti,ab OR masticat*:de,ti,ab OR chew*:de,ti,ab OR wear:de,ti,ab OR attrition:de,ti,ab OR repair*:de,ti,ab OR nutrition*:de,ti,ab OR complain*:de,ti,ab OR "patient satisfaction":de,ti,ab OR "quality of life":de,ti,ab OR speech:de,ti,ab OR appearance*:de,ti,ab OR esthetic*:de,ti,ab or aesthetic*:de,ti,ab)

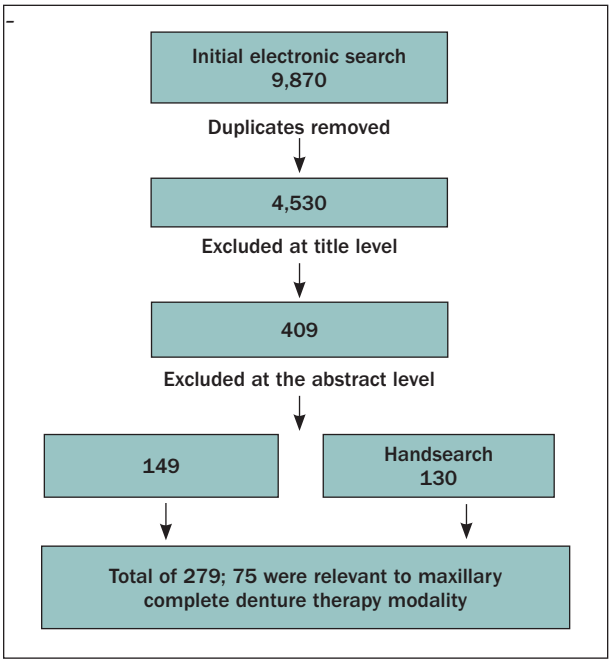


Fig 1 Flowchart of the article selection process.

Search of the four databases identified 9,870 references (Fig 1), of which 5,340 duplicates were removed. Titles and abstracts were screened for possible inclusion in the review. Treatment modalities for rehabilitation of the edentulous maxilla were then subdivided into conventional maxillary denture, implant overdenture, and implant-supported fixed prosthesis. The aim of this review (part 1) was to report on the outcomes of maxillary complete denture therapy. The full text of the articles judged to be relevant by the title and abstract was read and independently evaluated against the eligibility criteria (Table 1). In addition, a hand search was conducted of the reference lists of original studies found to be relevant.

Table 2 Studies Included That Evaluated Patient-Centered Outcomes for Maxillary Complete Dentures

Study	Study Design	Comparison	Time of Follow-up	No. of Patients Included (No. of Edentulous Maxilla)
Chandra et al (2013)[18]	Prospective	Masticatory problems of dentures made by postgraduate and undergraduate students	≤ 30 days	160
Celebic and Knezovic-Zlataric (2003)[17]	Retrospective	Satisfaction with dentures between complete denture wearers and Kennedy class I RDP wearers	Dentures 1–4 years old	268 (165)
Allen (2005)[36]	Prospective	Impact of provision of new complete dentures on nutritional risk (within group) and OHQoL	2 months	35 patients
Bradbury et al (2008)[23]	Cross-sectional observational	Intake and perceived chewing ability between edentulous and dentate individuals	N/A	131 (79)
Veyrune et al (2005)[37]	Prospective	OHRQoL with old dentures and after placement of new complete dentures in edentulous patients	12 weeks	26
Ozdemir et al (2006)[13]	Cross-sectional observational	Denture satisfaction according to personality type, sex, age, patients' perception of their income, denture usage period, and denture type	N/A	239 (216)
Psillakis et al (2004)[24]	Cross-sectional observational	Denture performance, patient perceptions, and bite force to denture dislodgement before and after the application of a denture adhesive on a maxillary complete denture	N/A	194
Vervoorn et al (1988)[38]	Cross-sectional observational	Complete denture satisfaction among patients with old dentures who were on the waiting list to get new dentures fabricated at the same clinic 2–5 years ago	N/A	213
Weinstein et al (1988)[21]	Cross-sectional observational	Patients' acceptance of their new dentures related to their age and past denture experience	60 days	135
Farias Neto A et al (2010)[10]	Double-blind controlled crossover clinical trial	Masticatory efficiency in complete denture wearers with bilateral balanced occlusion-BBO and canine guidance-CG	6 months	24
Ha et al (2012)[39]	Prospective	Oral health–related quality of care at baseline and after 3 months from provision of new dentures	3 months	439

RDP = removable dental prosthesis; CD = complete dentures; OHQoL = oral health quality of life; OHIP = Oral Health Impact Profile; EDENT = edentulous; GOHAI = Global Oral Health Assessment Index; BBO = bilateral balanced occlusion; CG = Canine guidance; N/A = not applicable; FDP = fixed dental prosthesis; WA = word accuracy; PEAKS = Program for the evaluation and analysis of all kinds of speech disorders; OVD = Occlusal vertical dimension; EMG = Electromyography.

Assessed Covariables	Outcomes
Self-rated satisfaction	Dentures made by postgraduates revealed less masticatory problems than those made by undergraduates at all visits.
Self-rated satisfaction Denture quality score	Patient assessment for CDs rated from best to worst were as follows: maxillary denture retention > speech > esthetics > chewing > overall satisfaction > retention of mandibular denture. Patient assessment of pain sensation under the CDs and RDPs: Highest % of grades—0 (no pain at all—was ascribed to maxillary CD (~ 90% of patients) & the lowest was ascribed to mandibular CD (~ 60%). Second was maxillary RDP (~ 90%) and 3rd was mandibular RDP (~ 75%). CD wearers were significantly more satisfied than RDP wearers with speech, chewing, and retention of maxillary dentures.
OHIP-EDENT Self-rated satisfaction Mini Nutritional Assessment Patterns	Nutritional risk category did not change with provision of new dentures—patients indicated that their general health and taste were important when making food choices. An association between OHIP scores and satisfaction with dentures. No association between Mini Nutritional Assessment Patterns and OHQoL. Patients were able to chew food reasonably well with their new dentures but with greater difficulty with hard foods.
Sociodemographic variables—BMI Food diary Questionnaire	BMI was not significantly different between denture wearers and dentate. Avoidance of certain foods was positively associated with perceived chewing ability but not with total fruit and vegetable intake. Perceived chewing ability was lower with poor/very poor rating for general health, in older patients and in denture wearers even after adjusting for age and health.
GOHAI Self-rated satisfaction Clinician assessment for quality of old dentures	An improvement was observed 12 weeks after the participants received their new dentures. There was a relationship between patients' satisfaction with their new dentures and change in GOHAI scores.
Type behavior pattern test Self-rated satisfaction	Personality type affected denture satisfaction related to esthetics, mastication, and speaking ability. Patients older than 65 years were less satisfied with their dentures. Patients who thought they had low income were less satisfied with denture esthetics. Patients with denture usage for less than 3 months had the lowest denture satisfaction. No statistically significant difference between esthetic satisfaction with regard to sex
Self-rated satisfaction	Improvement in bite force to dislodgement was observed with the use of adhesive. Most patients perceived better denture performance; improved speaking, chewing, fit, and comfort; and improved confidence
Age, sex, number of years with complete dentures Denture quality scores Denture complaint questionnaire Self-rated satisfaction	Lower denture satisfaction in patients on the waiting list to get new dentures. Patients were less satisfied with their lower dentures than their maxillary dentures. No correlation of satisfaction was seen with denture history, age, sex, or denture quality scores.
Self-rated satisfaction	Patients with no previous experience expressed a significant decrease in denture satisfaction than other complete denture wearers. Age was not a significant factor in predicting patient satisfaction.
Objective assessment for masticatory efficiency-colorimetric method with the beads Subjective data of patients' rating for their chewing function Satisfaction questionnaire	No statistically significant difference was found for masticatory efficiency between the 2 occlusal concepts studied. No significant relationship was found between masticatory efficiency and chewing ratings. No significant difference for overall patient satisfaction.
OHIP-14 K and self-rated satisfaction	Improved quality of life after provision of new dentures. Good or very good satisfaction with dentures showed greater improvement in the OHQoL.

Table 2 ***Continued*** **Studies Included That Evaluated Patient-Centered Outcomes for Maxillary Complete Dentures**

Study	Study Design	Comparison	Time of Follow-up	No. of Patients Included (No. of Edentulous Maxilla)
Viola et al (2013)[25]	Prospective	OHQoL and satisfaction of edentulous patients 3 months after provision with new dentures	3 months	70
Komagamine et al (2012)[19]	Prospective	OHQoL at baseline and after provision of new dentures	Following completion of adjustments with new complete dentures	75
Adam et al (2007)[8]	Prospective	OHQoL before and 2–3 months after provision of new dentures	2–3 months	76
Yoshinaka et al (2007)[40]	Cross-sectional observational	Subjective dissatisfaction with taste ability and factors such as age, sex, and oral status among independently living elderly individuals > 60 years old	N/A	640 (52)
Wolff et al (2003)[22]	Cross-sectional observational	Correlation between patient satisfaction with complete dentures and parameters of oral condition, and flow rate of the submandibular and sublingual salivary glands	N/A	50
Szentpetery et al (2005)[41]	Prospective	Problems reported by patients before and after prosthodontic treatment in patients receiving FDP vs RDP vs CD	6–12 months	107 (32)
Larsson et al (2014)[42]	Cross-sectional observational	Oral health-related quality of care in people with own teeth and/or fixed dental prosthesis; own teeth and RDPs; or edentulous and CDs	N/A	1,366 (21)
Nuñez et al (2013)[12]	Randomized controlled clinical trial	The effectiveness of a traditional and simplified protocol (only alginate impressions and no facebow) for construction of conventional CD	6 months	50
Ellis et al (2007)[11]	Randomized controlled clinical trial	Patient satisfaction and OHQol effects on patients restored with complete conventional or duplicate dentures	1 month	40
Miyaura et al (2000)[43]	Cross-sectional observational	Biting forces and pressure in patients with different types of prosthesis, complete dentures, RDP, FPD, and full natural dentition	N/A	590 (93)

RDP = removable dental prosthesis; CD = complete dentures; OHQoL = oral health quality of life; OHIP = Oral Health Impact Profile; EDENT = edentulous; GOHAI = Global Oral Health Assessment Index; BBO = bilateral balanced occlusion; CG = Canine guidance; N/A = not applicable; FDP = fixed dental prosthesis; WA = word accuracy; PEAKS = Program for the evaluation and analysis of all kinds of speech disorders; OVD = Occlusal vertical dimension; EMG = Electromyography.

Assessed Covariables	Outcomes
OHIP-EDENT and self-rated satisfaction	All domains of OHIP-EDENT showed significant improvements in addition to satisfaction with dentures. No association was found between patients' satisfaction of upper denture and gender. Association between upper denture satisfaction and age group was found. Patients older than 60 years were more satisfied with their upper dentures than younger patients.
OHIP-EDENT-Japanese version Self-rated satisfaction Objective test for masticatory performance using color changeable chewing gum	Significant improvement in OHQoL. Masticatory performance was not identified as a significant independent variable of change in OHIP-EDENT. Esthetics and speech were significant independent variables with negative correlation with OHIP-EDENT.
OHIP-EDENT before treatment and 2–3 months after treatment. Data regarding gender, age, education, and employment was recorded	New set of complete dentures improved the OHQoL significantly. The mean domain scores were similar by sex both at the pre- and post treatment evaluations, except for psychological disability at follow-up, which was significantly higher in women. Those < 60 years reported significantly higher mean for psychological disability than those aged > 60 years at post-treatment. At post-treatment evaluation, those with higher education reported higher scores for functional limitation and physical disability. At pretreatment evaluation, employed patients had higher means compared with pensioners and unemployed. At post-treatment evaluation, those differences were no longer significant.
Questionnaire on general health, dry mouth and taste dissatisfaction and chewing ability Examination of dental status Simulated salivary flow rate Gustatory response (filter paper disc method)	Factors associated significantly with dissatisfaction with taste ability were age, satisfaction with chewing, dry mouth during eating, and wearing dentures covering the entire hard palate; but not with simulated salivary flow.
Self-rated satisfaction Assessment of denture quality Assessment of oral condition; residual ridge shape, resilience, and musculature of tongue, lips and cheek; Salivary flow rate for sublingual and submandibular glands	A significant impact of reduced flow was seen on chewing, speech abilities, comfort of both dentures, and retention of both dentures. A positive correlation was found between oral musculature and retention of maxillary denture and between shape of the mandibular residual ridge and comfort of the mandibular denture.
OHIP-G	The largest number was reported with RDP group
OHIP-S49 OHIP-14 OHIP-5	Subjects who were edentulous had the highest oral health burden.
OHIP-EDENT-Brazilian version Self-rated satisfaction	A significant reduction in the impacts on OHQoL for both groups. Reduction was significant for all domains ranging from 59% reduction in masticatory discomfort and disability at 30 days to a 94.9% reduction on the social disability domain at 6 months. No significant differences were found between groups. Satisfaction with upper dentures was greater than with lower dentures regardless of period of evaluation and treatment group. Same number of adjustments was required for both groups. One patient from the simplified protocol group required rebase of the maxillary denture because of lack of retention.
OHIP-20 Self-rated satisfaction	No significant difference between the groups in OHIP and general satisfaction ratings. Statistically significant improvement in the OHIP domains of functional limitation and physical and psychological disability was seen in both groups. The duplication technique resulted in patients being less satisfied with the esthetics of their dentures.
Biting force and pressure were assessed with a pressure detecting sheet (prescale)	Biting forces of the fixed partial, removable partial, and complete denture wearers were 80%, 35%, and 11%, respectively, when expressed as a percentage of the subjects with a natural dentition.

Table 2 ***Continued*** **Studies Included That Evaluated Patient-Centered Outcomes for Maxillary Complete Dentures**

Study	Study Design	Comparison	Time of Follow-up	No. of Patients Included (No. of Edentulous Maxilla)
Knipfer et al (2014)[44]	Prospective	Speech intelligibility through prosthetic rehabilitation of patients with inadequate prosthesis with new maxillary complete dentures	6 months	68
Knipfer et al (2012)[45]	Prospective	Speech intelligibility in patients with a toothless or interrupted maxillary arch before and after rehabilitation with a maxillary complete denture or telescopic prosthesis compared with those with full natural dentition	6 months	85 (20)
Stelzle et al (2010)[46]	Prospective	Speech intelligibility through prosthetic rehabilitation of patients with inadequate prosthesis with new maxillary complete dentures and those with full natural dentition	1 month	68 (28)
Garrett et al (1996)[47]	Prospective	Satisfaction of patients with poorly fitting dentures before and after dentures were modified to improve occlusion, OVD, retention, and stability after new dentures	12 weeks	21
Silverman et al (1976)[20]	Cross-sectional observational	Correlate self-image and the extent of denture acceptance	N/A	50
Bilhan et al (2013)[16]	Cross-sectional observational	Satisfaction as well as frequency and type of prosthetic complications in patients with CDs that had been supplied at private clinics	N/A	64
Perea et al (2013)[30]	Cross-sectional observational	Differences in impact of OHQoL among complete denture wearers depending on their sociodemographic characteristics, prosthetic-related factors, and oral status	N/A	51 (39)
De Lucena et al (2011)[48]	Cross-sectional observational	Correlation between patients' and dentist's assessment of dentures and to correlate these variables with objective measures of masticatory function	N/A	28
Niedermeier and Kramer (1992)[49]	Cross-sectional observational	Correlate the retention of complete dentures and flow rates of the palatal and parotid glands	N/A	86
Wegner et al (2011)[14]	Prospective	Impact of 2 border-molding techniques (dentist-manipulated and patient-manipulated) on patient satisfaction, the occlusal force at denture dislodgement, and number of pressure sores	4 weeks	36

RDP = removable dental prosthesis; CD = complete dentures; OHQoL = oral health quality of life; OHIP = Oral Health Impact Profile; EDENT = edentulous; GOHAI = Global Oral Health Assessment Index; BBO = bilateral balanced occlusion; CG = Canine guidance; N/A = not applicable; FDP = fixed dental prosthesis; WA = word accuracy; PEAKS = Program for the evaluation and analysis of all kinds of speech disorders; OVD = Occlusal vertical dimension; EMG = Electromyography.

Assessed Covariables	Outcomes
WA: 2 times 1 with inadequate prosthesis and with new maxillary CD after 6 months post-treatment (using automatic speech recognition systems PEAKS) OHIP-G14	WA was significantly lower compared with 6 months after rehabilitation with adequate maxillary denture. Significantly improved OHIP scores were reported 6 months after new prosthesis compared with pretreatment.
WA: 2 times 1 with inadequate prosthesis and with new maxillary CD 6 months after treatment (using automatic speech recognition systems PEAKS)	For edentulous patients, WA was significantly lower when not wearing prosthesis at all compared with wearing an inadequate denture or a new CD 6 months after fabrication. Wearing an inadequate CD showed significantly lower WA than a new CD 1 week and 6 months after insertion. Within 6 months, speech intelligibility did not significantly improve from level found 1 week after insertion of new prosthesis for both groups.
Subjective assessment of speech by 3 therapists with and without prosthesis WA assessed by computer-based system with and without prosthesis	High correlation between subjective and objective measures. WA was significantly reduced in edentulous speakers than in control group. Wearing CD significantly improved WA.
Denture quality score Self-rated satisfaction Masticatory performance (peanuts and carrots) EMG activity	More than 55% of patients were moderately to fully satisfied with their poorly fitting dentures. Most patients perceived improvements in chewing comfort, chewing ability, eating enjoyment, food choices, security, and speech after each denture modification and with new dentures. Improvements in chewing function were perceived by most patients despite the lack of improvement in masticatory performance or masseter muscle activity with modified or new dentures.
Self-image was assessed using 3 methods: focused interview, by embedded figure test, or projective figure drawings Denture acceptance rating: no. of complaints, nature of complaints, and length of adjustment period	Men appeared to accept dentures more readily than the women. Employed subjects, compared with unemployed, showed significantly greater denture acceptance, higher morale, and self-image.
Self-rated satisfaction Complications—technical and biological	Biological complications: 44.2% ulceration, 8.3% denture stomatitis, 4.2% epulis fissuratum, 1.2% inflammatory papillary hyperplasia. Technical complications: 85.6% loss of retention, 31.4% loss or fracture of artificial teeth, 27.5% denture base fracture. Routine recalls are important for wearers of complete dentures.
OHIP-14 (Spanish version)	No significant differences were recorded according to sociodemographic factors (age, gender, marital, education, drinking, or smoking). The prosthesis location significantly influenced patient overall satisfaction. The lower denture being less comfortable. Functional limitation and physical pain dimensions showed significantly higher prevalence in patients who wore lower complete dentures. Significant differences were found depending on type of opposite prosthetic treatment with lower complete dentures resulting in lower patient satisfaction.
Self-rated satisfaction Masticatory performance and swallowing threshold using artificial test food Denture quality score	No significant correlation between patients' and dentist's assessment of dentures. Data on both masticatory tests showed no significant correlation with patients' satisfaction or with dentist's evaluation of dentures. Significant difference was reported in patient's satisfaction with stability of maxillary CD compared with mandibular CD.
Flow rates of parotid and palatal glands measured Retention of maxillary and mandibular denture was measured by means of dynamometer	A narrow correlation ($r = 0.83$) between the secretion of palatal glands and the retention of maxillary dentures. The medicinal stimulation of salivation showed that an increase of mucus secretion induced improved retention of maxillary complete dentures.
Salivary flow rate Patients were grouped according to jaw atrophy OHIP-G baseline and 1 week after treatment Occlusal force at dislodgement of maxillary denture Number of pressure sores over a 4-week period	Patient satisfaction increased significantly using both techniques. There was a low negative though significant correlation between salivary flow rate and occlusal force at dislodgement whereas jaw atrophy was not influential. Neither patient satisfaction nor occlusal force at dislodgement or number of sore spots was significantly influenced by the technique.

RESULTS

Study Search

The electronic search identified 4,530 articles, after which the analysis of the abstracts resulted in exclusion of 260 articles. After reading these articles, 31 were included (Table 2).

Description of Studies

To meet the ultimate goal of establishing clinical guidelines based on available information, prospective comparative studies, cohort prospective studies, and retrospective studies on more than 10 subjects were included. The topic of investigation was patient satisfaction and related objective clinical measures ranging from mastication to retention to occlusion.

Summary of Studies

The studies included are summarized in Table 2. They ranged from prospective and retrospective cohort investigations, to cross-sectional observational studies to a double-blinded, controlled, crossover trial. The populations and data collection were markedly heterogeneous, which precluded statistical analysis. Among the 31 studies included, seven invoked a randomization protocol and no masking was enforced, with the exception of the investigation of occlusal schemes.[10] Two studies were randomized, prospective, clinical studies[11,12] and one was a double-blinded, crossover designed, clinical trial.[10]

The studies included 5,485 participants. Among these, 2,685 were identified as wearing complete maxillary dentures. These publications included both male and female participants ranging in age from 39 to 89 years. Reported mean ages ranged from 59.7 to 73.6 years. Four of 31 studies recorded residual ridge conditions; one excluded "severe" ridge resorption.[13] One of the studies grouped individuals according to the extent of resorption.[14] Participants were typically edentulous for more than 5 years. Dentures were fabricated in undergraduate dental clinics (n = 10), private practice or faculty practices (n = 11), or not reported (n = 12). No study reported on the transition to immediate dentures. The duration of study or time to last follow-up ranged from 30 days to typically 2 to 6 months. Few reports included data from follow-up of more than 1 year (18 months [Diehl et al[15]; 3 years [Bilhan et al[16]; 1–4 years [Celebic and Knezovic-Zlataric[17]). Six authors described maintenance and follow-up care in terms of the number of adjustments made during the follow-up period.[12,15,18–20]

The primary goals of these studies varied (Table 2); however, their inclusion required measurement of patient satisfaction. The evaluation of studies included revealed several different primary outcomes reflecting the goals of the investigators among the 31 studies, 10 focused on oral health–related quality of life (OHQoL) using different instruments (Table 3). Four studies reported on objective measures that include body mass index, retention, masticatory function, and salivary flow rates vs denture satisfaction. The remaining studies included patient-reported outcomes focused on mastication, retention, speech, esthetics, comfort, and xerostomia.

The general finding of these studies was that patients receiving new dentures displayed an increase in their reported OHQoL. Comparisons were made between complete dentures and removable partial dentures,[17] affirming the greater patient satisfaction with complete dentures. Investigators sought to define the impact of age and denture experience on new denture acceptance,[8,21] the role of denture quality on satisfaction,[22] and the influence of dentures on mastication.[18,23,24]

Komagamine et al[19] assessed the association of OHQoL and masticatory performance using the Oral Health Impact Profile (OHIP) for edentulous patients (OHIP-EDENT) to assess dentures in the context of masticatory performance using a color change chewing gum. The 10-point reduction in OHIP-EDENT scores from before to after treatment was significant ($P = .000$) and related to the patient's self-assessment of the denture. Importantly, the authors concluded that lower denture, esthetic, and speech assessments accounted for much of the improvement, underscoring the importance of maxillary dentures in providing the social functions of esthetics and speech. Masticatory function was little changed, yet denture satisfaction and reported OHQoL improved. A second recent report indicated that a new conventional denture was associated with improvements in OHIP-EDENT scores and associated improvements in satisfaction with both new upper and lower dentures. However, satisfaction was lower for the new lower dentures. Satisfaction with the upper denture may be influenced by social functions, particularly esthetic satisfaction.[25]

These investigations, while providing evidence that participants are generally satisfied with complete dentures and that new dentures improve self-reported outcomes, did not report on variables of possible influence. For example, 27 of the 31 reports did not identify the denture occlusal scheme. Two studies indicated use of bilateral balanced occlusion and one compared bilateral balance vs canine-guided occlusion. No biological complications were reported in the context of patient satisfaction. Technical complications were not reported.

DISCUSSION

This systematic review focused on information pertaining to patient satisfaction and OHQoL related to maxillary complete denture therapy. Although many primary investiga tions and several systematic reviews have focused on the mandibular edentulous state and implant therapy, attention to the treatment of the edentulous maxillary arch using conventional dentures is largely absent. This is of importance to developed populations in which social interaction requires the esthetic and functional attributes of the dentition and for which edentulism afflicts 10% to 22% of the population older than 50 years of age.[2] For this population, the complete maxillary denture remains relevant. As stated by Carlsson and Omar,[26] the need for complete dentures remains, and improving the conventional management of edentulous patients is a necessity.

Ten of the 31 studies involved the treatment of patients in undergraduate dental clinics. The outcomes were positive. However, the impact of clinician experience may be questioned. In a comparative study of satisfaction among patients with dentures constructed by experienced vs inexperienced dentists, the general satisfaction was generally greater for patients treated by experienced dentists ($P = .05$).[18]

This systematic review affirms that new maxillary denture construction results in patients perceiving benefits and satisfaction. Higher satisfaction with maxillary dentures is recorded; this reflects little pain reported and little movement recorded in comparison to conventional mandibular dentures. Importantly, the provision of a new (maxillary) denture is associated with the reproducible measurement in quality of life. Taken at this coarse level, this is important. Looking at a more granular level, it becomes challenging to address the features of denture fabrication or provision that result in satisfaction or dissatisfaction. There is no published correlation between the quality of denture-supporting tissues and denture treatment outcomes. Further, data supporting the technical specifications of the denture and the degree of reported satisfaction are limited.[27] Most recently, an explanatory effort to link therapeutic goals to patient satisfaction was reported. A statistical model may account for 37% of the variation in satisfaction and more than one half of the OHIP-EDENT summary score. The explanatory variables, however, were largely focused on the mandibular denture. Social function and esthetics were not included.[28] However, they also concluded that a favorable oral condition and denture quality are important for successful complete denture therapy.

Studies have concluded that patients' and dentists' perception of denture quality and function are incongruent, and that denture quality estimates do not predict patient satisfaction.[29] Most complaints of discomfort are directed toward mandibular complete dentures.[30] Takamiya et al[31] concluded that complaints center around lack of retention and stability of the mandibular dentures and esthetics of maxillary dentures; esthetics are a decisive factor for treatment success and acceptance of complete dentures. Importantly, denture appearance is a determinant of how individuals emotionally respond to tooth loss.[32] When the associations between self-assessment and OHQoL were considered, "esthetics and speech" were significant independent variables.

Table 3 Instruments Used in Recording Oral Health Quality of Life in Denture Satisfaction Reports

OHIP-49
GOHAI
OHIP-EDENT (various languages)
OHIP-20
OHIP-14
OHIP-5

OHIP = Oral Health Impact Outcomes; EDENT = edentulous patients; GOHAI = Global Oral Health Assessment Index.

The studies included offer the clinician little guidance on what features of the patient, dentist, or prosthesis lead to greater satisfaction. Regarding the maxillary complete denture, the influence of esthetics on satisfaction cannot be overlooked. This point was recently highlighted by comparing the expectations and post-treatment ratings of dentists, patients, and technicians for new dentures. Patients displayed higher expectations and post-treatment completion ratings for esthetics and function than did the dentists and technicians. Only dentists reported higher esthetic outcomes than their expectations.[33] When considering the potential advantages of complete denture vs implant-based therapies for the edentulous maxilla, the relative absence of complications related to complete denture esthetics and/or phonetics should not be underestimated when offering alternative treatments to individual patients.

This systematic review did not directly address technical complications of complete dentures, but it is worth noting that denture base fracture and denture tooth fracture are common complications. More than one third of patients will experience denture tooth fracture or denture base fracture, the majority of which occur in the maxillary denture.[31,34] Biological complications with dentures also were not considered. Bilhan et al[16] reported that the most common complication associated with complete dentures was loss of retention, followed by ulceration in nearly half of all individuals seeking new

dentures. A recent report states that 45% of denture wearers presented with denture-related mucosal lesions including ulcers and denture stomatitis.[35] Denture stomatitis is another complication affecting denture use and is predominantly recognized in the maxilla. Denture stomatitis is associated with the age of the denture, type 2 diabetes, denture hygiene, and nocturnal denture use. The primary etiologic factor is Candida albicans; treatment or replacement of the denture is valuable for the resolution of stomatitis.[29]

CONCLUSIONS

This systematic review indicated that the provision of new maxillary complete dentures for edentulous patients results in improved self-reported satisfaction and OHQoL. There exists little information to direct clinicians to the improvement of one or other aspect of denture therapy (eg, impressions, tooth arrangement, etc) that influences patient satisfaction. When considering the treatment of the edentulous maxilla, the expectations of patients for esthetic and phonetic (social) rehabilitation are high and can be met using complete maxillary dentures as the mode of prosthetic rehabilitation. Patients dissatisfied with new complete dentures may be referred for dental implant therapies involving fixed or removable prostheses.

ACKNOWLEDGMENTS

The authors declare no conflicts of interest related to this systematic review.

REFERENCES

1. Cahen PM, Frank RM, Turlot JC. A survey of the reasons for dental extractions in France. J Dent Res 1985;64:1087–1093.
2. Jimenez M, Dietrich T, Shih MC, Li Y, Joshipura KJ. Racial/ethnic variations in associations between socioeconomic factors and tooth loss. Community Dent Oral Epidemiol 2009;37:267–275.
3. Ramraj C, Quiñonez CR. Self-reported cost-prohibitive dental care needs among Canadians. Int J Dent Hyg 2013;11:115–120.
4. Borreani E, Wright D, Scambler S, Gallagher JE. Minimising barriers to dental care in older people. BMC Oral Health 2008;8:7.
5. Guiney H, Felicia P, Whelton H, Woods N. Comparing epidemiologically estimated treatment need with treatment provided in two dental schemes in Ireland. BMC Oral Health 2012;12:31.
6. Zitzmann NU, Marinello CP, Sendi P. A cost-effectiveness analysis of implant overdentures. J Dent Res 2006;85:717–721.
7. Sadowsky SJ. Treatment considerations for maxillary implant overdentures: A systematic review. J Prosthet Dent 2007;97:340–348.
8. Adam RZ, Geerts GA, Lalloo R. The impact of new complete dentures on oral health-related quality of life. SADJ 2007;62:264–266;268.
9. Roumanas ED. The social solution-denture esthetics, phonetics, and function. J Prosthodont 2009;18:112–115.
10. Farias Neto A, Mestriner Junior W, Carreiro Ada F. Masticatory efficiency in denture wearers with bilateral balanced occlusion and canine guidance. Braz Dent J 2010;21:165–169.
11. Ellis JS, Pelekis ND, Thomason JM. Conventional rehabilitation of edentulous patients: The impact on oral health-related quality of life and patient satisfaction. J Prosthodont 2007;16:37–42.
12. Nuñez MC, Silva DC, Barcelos BA, Leles CR. Patient satisfaction and oral health-related quality of life after treatment with traditional and simplified protocols for complete denture construction [epub ahead of print 21 October 2013]. Gerodontology doi:10.1111.ger12078.
13. Ozdemir AK, Ozdemir HD, Polat NT, Turgut M, Sezer H. The effect of personality type on denture satisfaction. Int J Prosthodont 2006;19:364–370.
14. Wegner K, Zenginel M, Buchtaleck J, Rehmann P, Wostmann B. Influence of two functional complete-denture impression techniques on patient satisfaction: Dentist-manipulated versus patient-manipulated. Int J Prosthodont 2011;24:540–543.
15. Diehl RL, Foerster U, Sposetti VJ, Dolan TA. Factors associated with successful denture therapy. J Prosthodont 1996;5:84–90.
16. Bilhan H, Geckili O, Ergin S, Erdogan O, Ates G. Evaluation of satisfaction and complications in patients with existing complete dentures. J Oral Sci 2013;55:29–37.
17. Celebic A, Knezovic-Zlataric D. A comparison of patient's satisfaction between complete and partial removable denture wearers. J Dent 2003;31:445–451.
18. Chandra G, Agarwal S, Gupta A, Chandra S. New dentures: Mastication and post insertion phase. Int J Clin Dent 2013;6:131.
19. Komagamine Y, Kanazawa M, Kaiba Y, Sato Y, Minakuchi S, Sasaki Y. Association between self-assessment of complete dentures and oral health-related quality of life. J Oral Rehabil 2012;39:847–857.
20. Silverman S, Silverman SI, Silverman B, Garfinkel L. Self-image and its relation to denture acceptance. J Prosthet Dent 1976;35:131–141.
21. Weinstein M, Schuchman J, Lieberman J, Rosen P. Age and denture experience as determinants in patient denture satisfaction. J Prosthet Dent 1988;59:327–329.
22. Wolff A, Gadre A, Begleiter A, Moskona D, Cardash H. Correlation between patient satisfaction with complete dentures and denture quality, oral condition, and flow rate of submandibular/sublingual salivary glands. Int J Prosthodont 2003;16:45–48.
23. Bradbury J, Thomason JM, Jepson NJ, et al. Perceived chewing ability and intake of fruit and vegetables. J Dent Res 2008;87:720–725.
24. Psillakis JJ, Wright RF, Grbic JT, Lamster IB. In practice evaluation of a denture adhesive using a gnathometer. J Prosthodont 2004;13:244–250.
25. Viola AP, Takamiya AS, Monteiro DR, Barbosa DB. Oral health-related quality of life and satisfaction before and after treatment with complete dentures in a dental school in Brazil. J Prosthodont Res 2013;57:36–41.
26. Carlsson GE, Omar R. The future of complete dentures in oral rehabilitation. A critical review. J Oral Rehabil 2010;37:143–156.
27. Carlsson GE. Facts and fallacies: An evidence base for complete dentures. Dent Update 2006;33:134–136;138–140;142.
28. Yamaga E, Sato Y, Minakuchi S. A structural equation model relating oral condition, denture quality, chewing ability, satisfaction, and oral health-related quality of life in complete denture wearers. J Dent 2013;41:710–717.
29. Fenlon MR, Sherriff M. Investigation of new complete denture quality and patients' satisfaction with and use of dentures after two years. J Dent 2004;32:327–333.
30. Perea C, Suárez-García MJ, Del Río J, Torres-Lagares D, Montero J, Castillo-Oyagüe R. Oral health-related quality of life in complete denture wearers depending on their socio-demographic background, prosthetic-related factors and clinical condition. Med Oral Patol Oral Cir Bucal 2013;18:e371–e380.
31. Takamiya AS, Monteiro DR, Marra J, Compagnoni MA, Barbosa DB. Complete denture wearing and fractures among edentulous patients treated in university clinics. Gerodontology 2012;29:e728–e734.
32. Papadaki E, Anastassiadou V. Elderly complete denture wearers: A social approach to tooth loss. Gerodontology 2012;29:e721–e727.

33. Marachlioglou CR, Dos Santos JF, Cunha VP, Marchini L. Expectations and final evaluation of complete dentures by patients, dentist and dental technician. J Oral Rehabil 2010;37:518–524.
34. Darbar UR, Huggett R, Harrison A. Denture fracture—a survey. Br Dent J 1994;176:342–345.
35. Jainkittivong A, Aneksuk V, Langlais RP. Oral mucosal lesions in denture wearers. Gerodontology 2010;27:26–32.
36. Allen PF. Association between diet, social resources and oral health related quality of life in edentulous patients. J Oral Rehabil 2005;32:623–628.
37. Veyrune JL, Tubert-Jeannin S, Dutheil C, Riordan PJ. Impact of new prostheses on the oral health related quality of life of edentulous patients. Gerodontology 2005;22:3–9.
38. Vervoorn JM, Duinkerke AS, Luteijn F, van de Poel AC. Assessment of denture satisfaction. Community Dent Oral Epidemiol 1988;16:364–367.
39. Ha JE, Heo YJ, Jin BH, Paik DI, Bae KH. The impact of the National Denture Service on oral health-related quality of life among poor elders. J Oral Rehabil 2012;39:600–607.
40. Yoshinaka M, Yoshinaka MF, Ikebe K, Shimanuki Y, Nokubi T. Factors associated with taste dissatisfaction in the elderly. J Oral Rehabil 2007;34:497–502.
41. Szentpetery AG, John MT, Slade GD, Setz JM. Problems reported by patients before and after prosthodontic treatment. Int J Prosthodont 2005;18:124–131.
42. Larsson P, John MT, Hakeberg M, Nilner K, List T. General population norms of the Swedish short forms of oral health impact profile. J Oral Rehabil 2014;41:275–281.
43. Miyaura K, Morita M, Matsuka Y, Yamashita A, Watanabe T. Rehabilitation of biting abilities in patients with different types of dental prostheses. J Oral Rehabil 2000;27:1073–1076.
44. Knipfer C, Riemann M, Bocklet T, et al. Speech intelligibility enhancement after maxillary denture treatment and its impact on quality of life. Int J Prosthodont 2014;27:61–69.
45. Knipfer C, Bocklet T, Noeth E, et al. Speech intelligibility enhancement through maxillary dental rehabilitation with telescopic prostheses and complete dentures: A prospective study using automatic, computer-based speech analysis. Int J Prosthodont 2012;25:24–32.
46. Stelzle F, Ugrinovic B, Knipfer C, et al. Automatic, computer-based speech assessment on edentulous patients with and without complete dentures—preliminary results. J Oral Rehabil 2010;37:209–216.
47. Garrett NR, Kapur KK, Perez P. Effects of improvements of poorly fitting dentures and new dentures on patient satisfaction. J Prosthet Dent 1996;76:403–413.
48. De Lucena SC, Gomes SG, Da Silva WJ, Del Bel Cury AA. Patients' satisfaction and functional assessment of existing complete dentures: Correlation with objective masticatory function. J Oral Rehabil 2011;38:440–446.
49. Niedermeier WH, Kramer R. Salivary secretion and denture retention. J Prosthet Dent 1992;67:211–216.

Protocols for the Maxillary Implant Overdenture: A Systematic Review

Steven J. Sadowsky, DDS[1]/Nicola U. Zitzmann, DDS, PhD[2]

Purpose: *To evaluate patient-related outcomes in restoring the edentulous maxilla with an implant overdenture.* ***Materials and Methods:*** *A comprehensive systematic review of the literature was conducted. Publications reporting patient-based outcomes with concomitant data on implant and/or prosthetic success were selected using predetermined inclusion criteria that were agreed upon by the two reviewers.* ***Results:*** *Twenty-three publications related to 20 study cohorts were identified to meet the inclusion criteria for maxillary implant overdentures: two randomized controlled trials (RCTs), 13 prospective case series including two crossover trials, and five retrospective studies.* ***Conclusion:*** *An implant overdenture offers a stabilized removable solution for the edentulous maxilla, which provides increased patient satisfaction and quality of life improvement. A palateless design supported by four to six implants with a wide anteroposterior span has been successfully applied in some investigations. A higher failure rate was experienced with machined implants, particularly with short implants (length < 10 mm). Although both splinted and solitary anchorage systems are advocated, maintenance is higher for solitary attachments and inflammation is increased beneath the bars. Long-term maintenance care is essential for all designs. Well-designed RCTs with larger sample cohorts with longer follow-up periods are required to amplify patient- and clinician-based outcomes.*
Int J Oral Maxillofac Implants 2016;31(suppl):s182–s191. doi: 10.11607/jomi.16suppl.g5.2

Keywords: *implant/prosthetic survival/success, maintenance, maxillary implant overdentures, patient satisfaction*

Implant overdenture treatment in the edentulous maxilla (max IOD) was first reported in the 1980s.[1–3] Notably, this prosthetic design was frequently applied as a rescue operation when the implant number was limited after early failures and fabricating a fixed restoration was no longer feasible.[4–6] Hence, the max IOD has been considered a second choice offering limited retention and comfort compared with implant-supported fixed dental prostheses (IFDP). The max IOD was originally selected in cases of severe vertical bone resorption that allowed only short implants in dominantly cancellous bone, and offering minimal primary stability for implants with machined surfaces in early studies.[4,7] Because the max IOD was often not planned at the outset of treatment but selected after implant failure, risk factors were potentiated, leading to higher implant failure rate and prosthetic complications. For instance, interarch space allowance, interimplant distances, and angulations were frequently not considered, which led to material fatigue and inadequate bar clip length.

After the introduction of the max IOD, its application has evolved over the last two decades to offer specific advantages over fixed implant restorations. A removable implant design may circumvent extensive and costly augmentation procedures required for fixed restorations. More than a third of patients are unwilling to undergo autologous grafting even from an intraoral donor site.[8] In addition, it has been reported that treatment with IFDP is accompanied with higher patient expectations.[8] For some patients, the max IOD is most appropriate because it provides facial scaffolding; covers the prosthesis-tissue junction, particularly in patients with a wide smile and/or high smile line; assists in reconciling adverse ridge relations or discrepancies; and allows more latitude in adjusting palatal contour for phonation.[9,10] Further, cleaning the implants restored with an IFDP in patients with severe maxillary resorption can be challenging.[10] Rosén and Gynther[11] reported phonetic disturbances in 42% and esthetic problems in 37% of patients treated with four to six implants supporting an IFDP. Reinforcing patient preferences, a removable implant design was more often selected over a fixed prosthesis, in a crossover study, because of ease of cleaning and improved speech.[12] Moreover, patients with heavy parafunction may benefit from removing their prosthesis nocturnally as well as allowing greater ease in repair compared with a fixed restoration.

[1]Associate Professor, Department of Integrated Reconstructive Dental Science, University of the Pacific, Arthur A. Dugoni School of Dentistry, San Francisco, California, USA.
[2]Professor, Clinic for Periodontology, Endodontology and Cariology, School of Dental Medicine, University of Basel, Basel, Switzerland.

Correspondence to: Dr Steven J. Sadowsky, University of the Pacific Arthur A. Dugoni School of Dentistry, 155 5th Street, San Francisco, CA 94103. Email: ssadowsky@pacific.edu

The incidence of edentulism has been shown to occur earlier and more frequently in the maxilla than in the mandible (40% vs 27% in patients > 65 years of age).[13,14] Patients with complete dentures must make accommodations for palatal coverage and a sensitive interaction of several retention mechanisms at the periphery which is facilitated by tongue pressure during function. Therefore most conventional denture users remain satisfied and only a small percentage opt to pursue implant treatment.[15] When comparing quality of life (QoL) outcomes in a systematic review of complete dentures and max IODs, no significant differences were found in overall ratings.[16] Furthermore, a crossover study failed to yield substantive functional differences.[17] Despite these findings, patients may be motivated to undergo a max IOD restoration when anatomic deficiencies are linked to inadequate retention and/or stability, when gagging is refractory because of palatal coverage, and/or there is a psychogenic barrier to palatal coverage.[18] Zitzmann and Marinello[19] investigated psychosocial embarrassment stemming from the use of a conventional removable prosthesis. Significant self-esteem improvements were documented with implant treatment supporting fixed or removable restorations. Factors excluding subjects from implant therapy include financial constraints (despite the fact that cost estimates are less in removable compared with fixed prostheses[19]), unwillingness to undergo surgery or medically compromised for surgery, and the possibility of achieving marked improvements in the conventional prosthesis to meet patients' expectations.[20]

In addition to implant and prosthetic survival and success, patient satisfaction with the restoration and QoL effects are significant outcomes and described as patient-reported outcome measurements. McGrath et al[21] underscored the subjective nature of patient perceptions, which should complement clinical outcome data rather than be a standalone reflection of treatment. The purpose of this study was to complete a systematic review of articles evaluating patient-based outcomes after max IOD treatment.

MATERIALS AND METHODS

Search Strategy and Procedures

A critical review of the literature including relevant articles published in English was conducted. The most recent article included in this search was published before August 2014. The search was performed using the MEDLINE (PubMed) electronic database. Key words were maxillary implant overdentures, patient satisfaction, implant/prosthetic survival, success, and complications.

A hand search was also conducted for publications from 1986 to the present. The following journals were culled: *Clinical Oral Implants Research, Journal of Prosthetic Dentistry, International Journal of Prosthodontics, Clinical Implants and Related Dental Research, British Dental Journal, International Journal of Oral & Maxillofacial Implants, Journal of Clinical Periodontology, Practical Periodontics and Aesthetic Dentistry, Clinical Oral Investigation, Journal of Periodontology,* and *Vital Health Statistics*.

The levels of hierarchy of evidence accepted were randomized controlled trials, prospective studies, and retrospective studies. When multiple studies used the same population, only the more pertinent publication was entered into the database. The original search was limited to studies of human subjects published in English that included max IOD treatment and reported patient-based outcomes with concomitant data on implant and/or prosthetic success. Reporting of as little as a 2-month follow-up was accepted in crossover studies.

Full-text analysis of 40 initially retrieved articles was performed, and 20 publications relating to 18 study cohorts were identified as reporting max IOD patient-related outcomes. Two articles each reported data from a similar group.[7,22–24] In addition, three articles were retrieved by hand searching and were related to two study cohorts.[12,19,25] Among the 20 study cohorts, only two study designs were RCTs.[26,27] Thirteen were prospective case series,[12,17,19,22,23,28–35] and five were retrospective studies.[9,36–39]

Data Analysis

The studies included varied in the design of the questionnaires in terms of the wording of the questions and measures applied. In general, the most common items identified to assess patient-related outcomes were general satisfaction, comfort, stability/retention/fit, function, esthetics, ability to speak/phonetics, ability to chew (hard and soft food), ease of cleaning, food retention, lip, cheek and tongue biting, ease of removing and inserting prosthesis, self-esteem, and embarrassment. Additional data retrieved in some studies included incidence of food retention under prosthesis and impaired confidence in the retention of the max IOD.[7,35] Some studies recorded the patients' willingness to undergo treatment again, or recommend it to a friend or relative, and the preference of a fixed or removable implant restoration.[7,19,39]

Studies with longer observational follow-up indicated an unchanging perception of the evaluated parameters, or even a slight improvement in comfort and phonetics, which has been related to additional adaptation over the years.[7,22] The same investigators compared patients' and practitioners' assessments of esthetics and phonetics and documented slightly better scorings by professionals.[7,22]

Potential for Error

Questionnaires inherently do not account for language or cultural differences, especially when psychosocial issues are investigated. For example, when patients are asked whether intimacy is affected by prosthesis removal, their answer may be guarded or misinterpreted.

The strategy of assessing patient-mediated outcomes after prosthesis delivery can be problematic because of an inadequate adaptation period. A number of studies did not specify the time point at which the questionnaires were administered. Furthermore, assessing only post treatment data allows cross-sectional analysis, but not comparisons before and after treatment. Baseline patient perceptions before treatment, assessment of prosthetic status, how long patients used conventional dentures, and whether adjustments were made before their evaluation, all were not standardized among studies, which may lead to confounding of the outcome measurements. The methodologies of the investigations also differed in terms of being prospective or retrospective, measuring patient-based data as primary or secondary outcomes, and how the treatment was selected (preselected or after within-subject comparisons). Within-subject patient assessment may be influenced by cognitive dissonance if additional implants were placed for one design which the patient may attempt to justify.[12] Finally, individualized psychometric response scales were used in studies assessing patient satisfaction which may not allow for uniformity in a cross-sectional analysis. Because most outcomes relevant to patient satisfaction with a max IOD cannot be directly measured by a binary scale (yes/no response), instruments for subjective assessment were favored such as the visual analogue scale (VAS), or Likert scale. Using the VAS, respondents specify their level of agreement with a statement by indicating a position along a continuous line between two endpoints.[17,19] The endpoints should be clearly defined (eg, "worst possible pain," "no pain"). The Likert scale records levels of agreement by having patients select different numbers relating to their finding (eg, a three-point rating for degree of satisfaction or dissatisfaction).[29] Other studies[24,27] used a version of the Oral Health Impact Profile (OHIP or OHIP Edent) with selected domains to identify the impact of the prosthetic result on their QoL.

RESULTS

The 20 publications identified which met the inclusion criteria of studies in English reporting both patient- and clinician-based data are enumerated in Table 1. Three additional publications reporting data from the same study group are included in the same row as the selected pertinent article. The indicated number of patients treated relates to the study cohort on which outcome data are documented, thereby excluding dropouts or double registration. A total of 530 patients had been treated with max IOD prostheses between 1993 and 2014. Although a range of 1 to 10 implants was used for prosthesis retention or support, most concepts used 4 to 6 implants. Prosthesis retention was mainly designed with bars, either milled or using prefabricated bar segments. In four studies, different retentive elements were applied, one study used ball attachments only, and one study used solely double crowns (Table 1).

The earliest report on patient-related outcomes with max IOD was made by Smedberg et al[7,22] who treated 28 patients with a bar and additional CEKA REVAX attachment (Alphadent NV). A questionnaire with VAS ratings was given to the patients immediately after treatment and after a 2- and 6-year period, but no baseline data before implant treatment were available. Although overall satisfaction was high, some patients perceived uncertainty with the retention of the IOD and preferred a fixed implant restoration. Over time the subjective assessment of phonetics improved, which may be related to the adaptive capacity. Using machined implant surfaces, implant survival was 84% and most failures were related to short implants (7 mm in length). Stomatitis was the most frequent biological complication and affected 50% of patients.[7,22] In a report on 30 patients treated with bar-retained max IOD, Watson et al[33] found that more than 80% had mucosal problems. During the observation period of 5 years, each patient had on average one occasion per year of superstructure maintenance complications (such as clip activation or fracture, bar fracture, acrylic resin fracture, relining).[33] High incidence of technical and mucosal complications were also reported by Pieri et al[34] who performed immediate implant loading with bar-retained max IOD on four to five implants. Although comfort, chewing ability, esthetics, ability to speak, and general satisfaction were improved after treatment, cleaning feasibility was rated lower compared with the pretreatment assessment. Visser et al[32] summarized the prosthodontic aftercare as 443 minutes per patient over a 10-year observation period, albeit with a milled bar mesostructure.

In a retrospective study with a mean observation period of 2.5 years, Ekfeldt and coworkers[37] treated 38 patients with max IODs initially, and after four withdrawals divided them into group A (n = 7), originally planned for max IOD, and group B (n = 27), originally planned for IFDP but restored with IOD. The implant success rate in group A was 87.9% and in group B, 79.3%. Prosthodontic complications were mainly related to change of clips and more prevalent in group B. Most of these maintenance incidents occurred in bruxers (62%). Patient reactions to treatment with max IOD using a VAS were positive regarding esthetics, but more negative views were registered in group B in response to function and retention, and were possibly related to their initial expectation for a fixed restoration.

Slot et al[28] reported performing max IOD service on six implants, connected with a bar, with implants either

placed in the anterior (incisal and premolar region) or posterior region (canine to molar) with 25 patients each in a 1-year prospective case series. Group assignment was based on the bone volume and the intermaxillary space in the anterior region. The antagonist was a natural dentition. The authors found 98% implant survival (11 mm length) in the anterior sites and 99.3% in the posterior region (12 mm length). High patient satisfaction was recorded for both regimens. The same research group conducted a randomized trial among 49 fully edentulous patients and provided them with four or six implants in the anterior maxillary region.[26] After 1 year, one implant was lost in the six-implant group, bone resorption around the implants was similar in both groups, and overdenture survival was 100% in both groups. In addition, patient satisfaction had improved similarly irrespective of whether the max IOD was supported by four or six implants.[26]

Zou and coworkers[29] evaluated three different anchorage systems to retain a max IOD on four implants. Ten patients each were designed with telescopic crowns, bar, or Locator attachments (Zest Anchors). After 3 years, all patients were seen for recall. The implant survival and success was 100% for all groups. The Locator system had the least postinsertion visits for maintenance. Using a Likert scale, four patient-mediated parameters were recorded: facial contour, comfort, phonetics, and functional results. No significant differences were found in patient satisfaction among the groups. Double crowns (telescopes) for max IOD support were also used by Bernhart et al,[35] who observed biological (peri-implantitis) or technical complications (veneering fracture and retention loss of cemented telescopes) during the 2-year observation period.

Al-Zubeidi and associates[27] treated 40 patients with a three-implant max IOD using different attachment systems and palatal coverage designs, opposing a mandibular two-implant overdenture. Patients were randomly assigned to groups with either splinted (bar) or unsplinted (ball attachments) retentive systems and patient satisfaction was evaluated after 2 years of service. The OHIP-14 showed patients significantly more satisfied with the max IOD than with their pretreatment maxillary denture, whereas no differences were found between the two retentive systems. After the first year in function, the palatal coverage of the max IOD was reduced. Approximately 80% of patients preferred this palatally reduced design over a complete coverage.[27]

de Albuquerque et al[17] conducted a crossover trial to assess patient preferences for a long-bar max IOD with and without palatal coverage opposing a mandibular IFDP. Thirteen participants experienced both designs after a 2-month evaluation period. General satisfaction was high and VAS results showed no significant differences between the two treatments. Of note, the ratings for the long-bar max IOD were no better than those for a new conventional denture. The length of service with a conventional denture before implant placement was not reported.[17] The same research group conducted a within-subject crossover trial, in which 16 patients received either a max IOD supported by a long-bar or an IFDP on four to six implants. Prostheses were changed after a 2-month period and patient assessment recorded after another 2-month period.[12] Patients were on average more satisfied with the removable long-bar IOD and rated their ability to speak and ease of cleaning as better. Nine patients chose to keep the removable prosthesis and four preferred to keep the IFDP.[12] Removable and fixed maxillary implant restorations were also compared by Zitzmann and Marinello,[19] who conducted a self-selected trial, in which patients received a treatment recommendation based on their anatomic situations and need for lip and cheek support. Although patients treated with max IOD had poorer pretreatment ratings of their overall satisfaction and functional and psychological parameters, outcomes after treatment were similar in both groups with 10 patients each. So comfort and retention, function, esthetics and appearance, taste, speech, and self-esteem were significantly improved 6 months after rehabilitation compared with their pretreatment assessment.[19] Allen et al[20] also found that patients requesting dental implants perceive their impairment to be greater than those asking for new complete dentures. Sanna et al[38] compared patient satisfaction with bar-retained max IOD and IFDP in 44 patients provided with four to six implants. High ratings were given to all parameters except food impaction which affected both groups. Retention and fit of the restoration was rated better with IFDP than with IOD (Table 1). Although IOD supported by four to six implants revealed implant survival rates of 99% at 15 years, more implant failures were observed when only two implants were used either splinted (83% at 22 years) or unsplinted (74% at 17 years).[38]

Although Sanna et al[38] did not report patient-related outcome measures from the 12 additional patients treated with two implants, this design was also applied by Zembic et al[23,24] who assessed patient satisfaction with a VAS questionnaire and OHIP-20E. Before implant placement, edentulous patients received new complete dentures or relining of the existing dentures to have comparable conditions for the pretreatment questionnaire. A within-subject comparison was conducted and two implants were restored with max IOD with palatal coverage, which was removed after a 2-month period. Comparison of patient satisfaction before implant treatment, after restoration with IOD with palatal coverage, and without palatal coverage revealed improvements after IOD treatment for most parameters except for cleaning ability, comfort, and esthetics.

Table 1 Studies Evaluating Patient-Centered Outcomes for Implant Overdentures in the Maxilla (Max IOD)

Authors	Study design	Aim/comparison	Time of follow-up (assessment of PROM after max IOD insertion	No. of patients assessed/No. of implants in the maxilla/length
Smedberg et al (1999)[22] (1993)[7]	Prospective	Max IOD with bar and Ceka	Obs: 82 mo for pilot group, 35 mo for routine group; questionnaire given immediately after prosthesis delivery and after 2 y	28 (14 in pilot group from 1993; 14 in routine group)/2–6/7–13 mm (machined); 2 additional in pilot group lost all implants and received a CD (no IOD Tx)
Ekfeldt et al (1997)[34]	Retrospective	Group A: max IOD (originally planned) vs group B: max IOD (initially planned for IFDP); bar or ball attachments	Mean obs: 30 mo	38/1–4/10–18 mm (machined)
Watson et al (1997)[33]	Prospective (9 centers)	Max IOD with bar	Obs: 5 y; questionnaire given before Tx, after 1 mo, after 5 y	30 (16 available at 5 y)/3–4/7–15 mm (machined)
Naert et al (1998)[30]	Prospective	Hinging max IOD on rigid cast bar	48 mo	13/4/7 mm (1x), 10 mm (14x), 13 mm (17x), 15 mm (20x), 18 mm (1x) (machined)
de Albuquerque et al (2000)[17]	Prospective; within-subject crossover	Max IODs with long-bar; with vs without palatal coverage, opposed by mand IFDP	2 mo after new CDs and 2 mo after each long-bar max IOD (with/without palatal coverage) for crossover	13/4/length not defined
Zitzmann & Marinello (2000)[19] (2000)[25]	Prospective; self-selected Tx; fixed (n = 10) vs OD bar (n = 10)	Max IOD with bar vs IFDP	Obs: 39 mo fixed, 27 mo IOD; questionnaire before and 6 months after treatment	10/5 to 10 (plus 10 patients with IFDP)/ 10 mm (11x), 11.5–13.5 mm (39x), 15–18 mm (21x) (mainly machined)
Närhi et al (2001)[36]	Retrospective	Max IOD retained by splinted vs un-splinted implants	Bar-retained max IOD: mean Obs 32 mo; ball-retained max IOD: 54 mo	16/4–7/at least 12 mm
Heydecke et al (2003)[12]	Prospective; within-subject crossover trial	Long-bar IOD vs IFDP	2 mo with each prosthesis	13/4–6/length not indicated (machined)
Raghoebar et al (2003)[31]	Prospective	Augmented maxilla (3 mo before implant placement), loading after 2 mo, milled bar and Ceka	12 mo (questionnaire before and after Tx, timepoint not specified)	10/6 or 8/≥ 10 mm (moderately rough)
Kronström et al (2006)[9]	Retrospective	Planned max IOD (group 1) vs max IOD originally planned for IFDPs (group 2); rigid cast bar (with ball attachments)	12-month cycles	19/mean of 3.3 implants in planned max IODs, mean of 3.7 in cases of max IODs originally planned for fixed/length not defined
Krennmair et al (2008)[39]	Retrospective	Max IODs with 4 implants in anterior (group 1) vs 3–4 bilaterally in posterior (group 2) with sinus graft; rigid milled bar	42 months	34/4 anterior, 6–8 posterior/13–16 mm (anterior)/13 mm (posterior)
Visser et al (2008)[32]	Prospective	Max IODs with milled bar, mesostructure with Ceka	10 y	39/6/10–15 mm (machined)
Pieri et al (2009)[34]	Prospective	Immediate loading with bar-retained max IOD; rigid-cast bar with a < 10 mm distal cantilever	Pre-Tx: 2 mo; post-Tx: 12 mo	22/4–5/10–15 mm (moderately rough)
Sanna et al (2009)[38]	Retrospective	Max IOD with bar, comparison to fixed group (IFDP)	Obs: 1–22 y (average 9 y); timepoint of questionnaire not specified	44/4–6 (32x), 2 implants with bar (n = 8), 2 implants single attachments (n = 4)/> 6–18 mm (machined)
Al-Zubeidi et al (2012)[27]	Prospective RCT	Max IOD on 3 implants with splinted vs unsplinted ball attachments; opposing mand IOD on 2 implants	24 mo	39/3/10 mm (34x), 11.5 mm (17x), 13 mm (15x), 15 mm (51x) (roughened)
Bernhart et al (2012)[35]	Prospective	Max IOD with double crowns	2 y, no information about timepoint of questionnaire	12/4.4/range 3–6 mm (moderately rough)

Max = maxillary; IOD = implant overdenture prosthesis; PROM = patient-reported outcome measurement; CD = complete denture; Tx = treatment; Obs = observation time; VAS: visual analog scale; mand = mandibular; IFDP = implant fixed dental prosthesis; OD = overdenture; CAT = category scale; GI = gingival index; PI = plaque index; NA= not applicable; RCT = randomized controlled trial; BoP = bleeding on probing; ND = not defined; OHIP = oral health impact profile.

PROM measure	Outcomes PROM	Survival of implants and prosthesis/complications
10 questions yes/no (related to esthetics, phonetics, comfort, satisfaction, chewing, easily removable, and reinsertable, cleaning (0 = total discomfort; 10 = total satisfaction); and VAS esthetics 8.0/8.6, phonetics 9.3/9.7, comfort 8.3/– (filled out by patient/examiner); immediately after and 2 years after Tx	Most patients completely satisfied with reconstruction; improvement in phonetics and comfort after 2 y compared to prosthesis delivery; uncertainty related to IOD retention (n = 6); food sticking under IOD (n = 10); preferred fixed (n = 6); 1999 similar results in the VAS as in 1993, only phonetics improved at 6 y to 9.2/9.9	84% (pilot), 85% (routine); most failures with 7-mm implant length/24 adjustments, in 50% stomatitis
VAS (10-point scale) appearance, mastication, retention, esthetics, function	Group A: 8.5–9.1; group B: 7.1–9.0; group B had more negative experiences regarding ability to chew and retention	Group A: 85%, group B: 56.4%/prosthetic complications (n = 8, group A; n = 20, group B); retentive clip fractures (n = 7, group A; n = 5, group B); retentive clip changes; all single implant-retained overdentures failed (n = 4)
Questions with VAS (1 = very bad; 5 = average; 9 = excellent) overall satisfaction, retention/stability, function in chewing and speech, appearance; frequency of prosthesis removal because of discomfort	Retention, stability, chewing ability, speech improved	78% at 5 y/81% had mucosal problems, each patient had on average 5 occasions for maintaining superstructure complications (fractures denture, relining, bar fracture, clip fracture, or activation)
VAS questionnaire (0–9 Likert scale)	General satisfaction 8–9, ease of chewing 8–9, appearance 4–9 (most responses 8–9), retention 8–9, speaking ability 8–9	88.6%/ technical (n = 32), mucosal complications (n = 11)
VAS questionnaire and CAT scale, general satisfaction, stability, retention, esthetics, comfort, ease of cleaning, speaking ability, eating ability	No significant difference in long-bar max IOD with or without palate and new conventional dentures except for chewing nuts which was significantly better with implant support	96.7%
VAS questionnaire assessing comfort & retention, function, esthetics & appearance, taste, speech & self-esteem	All parameters improved in both groups, greatest improvements in self-esteem; IOD patients experienced greater differences between pre- & post-Tx scores for esthetics, taste & speech; Tx costs per unit significantly higher for fixed than OD	IFDP: 98%, IOD: 94% IOD; time until retreatment after prostheses insertion was 23.4 mo for fixed and 19.8 mo for IOD/higher GI and PI with IOD than with fixed
4-point Likert scale (0–3)	General satisfaction, esthetics, phonetics, chewing ability, pain, fit all not significantly different between bar/ball anchorage system	92%/most Obs times were within 2 y of treatment; hyperplasia (n = 9); inflamed soft tissue (n = 8); prosthetic adjustments (n = 7)
VAS for psychometric measurements of general satisfaction, comfort, ability to speak, stability, esthetics, ease of cleaning and occlusion; chewing ability with 7 types of food; CAT questions related to patients' physical & psychological function and general health (4-point Likert scale)	IOD higher VAS ratings of general satisfaction, ability to speak, & ease of cleaning than fixed; greater negative impact on psychological function of fixed, importance of esthetics & speech; 9 patients selected IOD, 4 preferred IFDP	NA
VAS (1–10) for overall satisfaction; 5-point rating scale (very satisfied to very dissatisfied) for 8 items (satisfaction with function of prosthetic construction & with esthetics)	VAS mean satisfaction with total Tx 7.9 ± 0.9 (1.85 ± 0.9 with previous denture); 5-point rating scale 7.9 ± 0.9	95.6%
VAS questionnaire (10-point scale), mastication, phonetics, esthetics, retention, satisfaction	Group A: 7.1–9.7; group B: 6.0–8.3, both groups had similar outcomes with patient satisfaction but speech problems more prevalent in group B	Not defined/5 patients lost all implants before 19 patients selected for study
Likert scale (1 = not satisfactory, 2 = adequate, 3 = satisfactory, 4 = good, 5 = excellent)	Mean scores were 5.0 for general satisfaction, chewing ability, denture stabilization, 4.6/4.7 for esthetic results and speech respectively with no difference between groups	Group A: 98.4%, group B: 97.4%/low prosthodontic complication rate (possibly because of rigid bar/metal reinforced prosthesis); adjustment of denture margin (n = 11); matrix activation (n = 8); abutment screw loosening (n = 6); fracture/renewal of antagonist denture (n = 5); no significant difference between group A and B
VAS for overall satisfaction (score 0 = low, 10 = high); 4 questions yes/no on more satisfied than with CD, Tx worthwhile, Tx again, advise to friends	Overall satisfaction 8.9 ± 1.1 (median 9, range 7–10)	86% at 10 y/more intensive pros aftercare (443 min/patient) than surgically (40 min/patient)
Questionnaire with VAS	At 2 mo and 12 mo significant increase in comfort, chewing ability, esthetics, ability to speak, and general satisfaction, but significant decrease in cleaning feasibility	97%/technical (n = 20), mucosal complications (n = 6)
Satisfaction only evaluated among the OD 4–6; questionnaire: comfort, ability to speak, stability, ease of cleaning, ability to chew soft & hard food (0 = totally dissatisfied; 10 = satisfied; 0–10 Likert scale)	Ratings of ≥ 8, except of food impaction (rating of 6) in both groups (fixed and IOD); better rating of retention/fit with fixed (9.7/9.8) vs IOD (8.9/8.6); no data on 2-implant IOD	99% at 15 y with 4–6 implants; 83% with 2 splinted implants at 22 y; 74% at 17 y with 2 unsplinted implants; 24% BoP
VAS pain reduction, comfort, stability and function; OHIP-14, OHIP-20	Post-Tx significantly more satisfaction; no difference between splinted and unsplinted groups; patient preferred reduced palatal coverage (1st year with palatal coverage, subsequent years reduced palatal coverage)	ND
Function & esthetics rated by patient & practitioner on a numerical rating scale (0–10)	Patient reported high satisfaction with function & esthetics	78% implant-supported IOD after 2 y/biological (peri-implantitis) & technical complications (veneering fracture, loss of cemented telescopes)

Table 1 *Continued* **Studies Evaluating Patient-Centered Outcomes for Implant Overdentures in the Maxilla (Max IOD)**

Authors	Study design	Aim/comparison	Time of follow-up (assessment of PROM after max IOD insertion	No. of patients assessed/No. of implants in the maxilla/length
Slot et al (2013)[26]	Prospective RCT	Max IOD with bar	Obs: 1 y; questionnaire given pre-Tx and 12 mo post-Tx	49/4 vs 6/≥ 11 mm (moderately rough)
Zembic et al (2015)[23](2014)[24]	Prospective	Within-subject comparison of max IOD with and without palatal coverage; ball attachments	2 mo with each IOD design; before implant placement (n = 12); new set of CDs (n = 9) relining or rebasing of existing CDs	21/2/length not indicated (moderately rough)
Zou et al (2013)[29]	Prospective	Max IOD with telescopic crowns vs bars vs locator attachments	36 mo	30/4/10–12 mm
Slot et al (2014)[28]	Prospective	Max IOD with implants placed in anterior or posterior region, opposed by natural dentition; bar	12 mo	50/6/11 mm (anterior), 12 mm (posterior)
Sum of 20 study cohorts (23 publications)	2 RCTs, 13 prospective, 5 retrospective studies	14 bar retention (milled or prefabricated); 3 bar or single; 1 balls; 1 telescopes, 1 bar or locator or telescopes	2 mo–22 y	530/1–10 (mainly 4–6 mm)

Max = maxillary; IOD = implant overdenture prosthesis; PROM = patient-reported outcome measurement; CD = complete denture; Tx = treatment; Obs = observation time; VAS: visual analog scale; mand = mandibular; IFDP = implant fixed dental prosthesis; OD = overdenture; CAT = category scale; GI = gingival index; PI = plaque index; NA= not applicable; RCT = randomized controlled trial; BoP = bleeding on probing; ND = not defined; OHIP = oral health impact profile.

A better perception of taste was documented for the IOD without palatal coverage than with palatal coverage. Although 16 patients chose an open palate, five selected palatal closure.

Krennmair and associates[39] conducted a retrospective study with a mean observation period of 42 months to compare a group of 16 patients with four implants placed in the anterior region with a group of 18 patients with six to eight implants placed in augmented posterior sites. A split milled bar was used in the posterior region whereas a continuous bar was used in the anterior site. No differences were seen in implant survival. The rigid construction using milled bars led to healthy soft tissue indices and low mechanical maintenance. General satisfaction, prosthesis stability, and esthetics all scored high on the VAS in both groups.[39] A similar design was applied by Raghoebar et al,[31] who placed six to eight implants in the augmented sinuses of 10 patients in a two-stage procedure and inserted a max IOD on bilateral milled bars with Ceka attachments. After 1 year, three implants were lost (implant survival 95.6%), but overall patient satisfaction was high.

Kronström et al[9] retrospectively compared two groups of patients (group 1 with 10 patients planned for max IOD and group 2 with nine patients planned for IFDP) with a mean follow-up of 6 to 7 years. Patients planned for a max IOD reported fewer speech problems than those planned for a fixed prosthesis. Some patients restored with IFDP reported cleansing difficulties. No other significant differences were discerned.

Naert and coworkers[30] conducted a prospective study on 13 patients restored with four implants with a rigid bar and a hinging max IOD design. After a mean loading time of 3 years, a cumulative implant success rate of 88.6% was reported. Attachment servicing was the most frequent maintenance problem. Strong improvement in patient satisfaction was recorded compared with the previous conventional denture.

Narhi et al[36] retrospectively compared splinted and unsplinted implants in max IOD prostheses in 16 patients with a mean follow-up of 32 to 54 months. Eleven patients were treated with a bar design (three to six clips) and five patients were restored with two to six ball attachments. Both palatal and reduced palatal coverage was split among the subjects. Notwithstanding a small sample size and lack of implant number standardization, no differences in marginal bone loss between the groups were noted. Cumulative implant survival after 72 months was 90%. Outcomes of patient satisfaction, esthetics, comfort, and phonetics were similar. The bar group expressed more difficulty in hygiene.

DISCUSSION

Despite the heterogeneity of the studies included, in terms of sample size, follow-up periods, implant macro- and microstructure, number of implants, prosthetic design, anchorage system, and method of data collection, trends were identified assisting the practitioner in treatment planning for max IODs.

PROM measure	Outcomes PROM	Survival of implants and prosthesis/complications
Questionnaire with 54 questions and 4-point rating (0 = no complaints, 3 = severe complaints) focused on complaints (functional problems with lower and upper denture, complaints in general, facial esthetics, accidental lip, cheek & tongue biting, esthetic of denture plus chewing ability questionnaire (0 = good, 2 = bad)	In both groups: all scores improved significantly between pre-Tx and 12 months post-Tx, but no group differences	100% with 4 implants, 99% with 6 implants
VAS (satisfaction and perception of IOD); and OHIP-20E on functional limitation, physical pain, psychological discomfort, physical, psychological & social disability & handicap; questions on cleaning ability, general satisfaction, speech, comfort, esthetics, stability, chewing ability	No significant differences between IOD with & without palatal coverage for any of the OHIP domains; higher satisfaction for esthetics & taste without palatal coverage; open palate (n = 16); palatal closure (n = 5); better results for IOD than for adjusted CD except for cleaning ability, better results for IOD than for new CD except for cleaning ability, comfort, and esthetics	100% (not specifically indicated) Caveat: Mainly patients with well-preserved alveolar ridges
Likert scale (0–2) with 0 = unsatisfied and 2 = fully satisfied, evaluating facial contour, comfort, pronunciation, and functional results	No differences detected between 3 groups; all patients recorded fully satisfied except 1 which was partially satisfied	100%/locator group had least prosthetic complications and telescopic group the most; telescopic crowns (n = 8), bar (n = 7), locator (n = 4); most common was denture margin adjustment
VAS comfort, esthetics, general satisfaction	No significant differences between anterior/posterior groups; satisfaction indices of max IOD comparable to data on mand IODs	98% anterior group, 99.3% posterior group
VAS, Likert scales, OHIP	Patient satisfaction and QoL	Implant survival, complications

Investigations using turned/machined surfaces demonstrated reduced implant survival. This was borne out by results from Jemt et al,[4] Widbom et al,[6] Naert et al,[30] Ekfeldt et al,[37] and Bergendal et al.[40] A recent Cochrane analysis[41] evaluated the clinical impact of microstructure of implants and noted that implants with turned surfaces tended to fail early more often than did implants with moderately rough surfaces and an additional surface coating after loading. However, rough implants tended to have a 20% increase in risk of peri-implantitis 3 years after loading (relative risk, 0.80; 95% confidence interval 0.67–0.96).[41] Overall, implants with moderately rough surfaces demonstrate a higher survival rate than those with machined surfaces.

Many of the studies that included short implants of less than 10 mm demonstrated lower implant survival rates than those that restricted placement to implants longer than 10 mm.[4,5,37,40,42] When two-thirds of the implants were 7 mm in length, the 5-year cumulative implant success rate was only 72.4%.[43] This was in contradistinction to the results reported with implants longer than 10 mm.[28,39] However, there appears to be a link between short/machined implants and implant loss. Meriscske-Stern et al,[44] Kiener et al,[45] and Mangano et al[46] all used less than 10-mm long moderately rough implants and reported better outcomes than the studies that used short machined implants. Van Assche et al[47] designed two extra-short (6 mm) moderately rough posterior implants and four longer (10–14 mm) anterior implants for a maxillary overdenture and also achieved good implant survival over the short term (2 years), though the 6-mm implants did display more marginal bone loss. The use of moderately rough implants of sufficient length (> 10 mm) and diameter may provide a higher survival rate after successful osseointegration.[39]

With regard to the minimum number of implants and anchorage system recommended for a max IOD, early studies on machined implants (< 4 implants) clearly demonstrated that less was not more.[37,40] Payne et al[48] reported using three-implant maxillary IODs and noted that short-term survival was less than 85% even with moderately rough implants. Sanna et al[38] demonstrated significant differences in long-term survival between six implants and two, though the latter anchorage system was unconnected. A number of studies have shown no difference in implant outcomes between splinted and unsplinted designs, but the sample sizes were low and the outcomes may be tied to other variables such as recall regimen, implant length, anteroposterior span, or suprastructure design.[27,29,36,44] Rigid milled bar designs appear to have lower implant failure and prosthodontic aftercare maintenance (mechanical and soft tissue indices) compared with resilient bars for max IODs or solitary anchors.[32,39] Raghoebar et al,[49] in a systematic review, reported an increased risk of implant loss when 4 or less implants with an unsplinted anchorage were used, while implant and max IOD survival rates were higher with splinted anchorage with 4 or more implants. Parel and Phillips[50] have reported that more than four implants may be appropriate for patients with associated risk factors such as reduced bone quality, opposing

natural dentition, and parafunction when assessing implant success with maxillary implant-fixed prostheses. Although there is no distinct evidence that implant splinting with a bar is superior to single attachments in terms of implant survival, the bar design facilitates compensation of nonaligned implant angulations, particularly in patients with severely resorbed maxillae with reduced arch circumference. As a consequence, detrimental forces, for example, from removing the prosthesis with uneven forces, are more likely to occur with stud abutments than with a bar providing an equal path of insertion. Care must be taken that the bar, either individually milled or prefabricated, is designed in a way to enable cleaning underneath to avoid mucosal inflammation.

Patients have demonstrated preference for reduced palatal coverage in the area of esthetics and taste reflected in the OHIP.[23,27] Successful outcomes have been demonstrated using a metal reinforcement with larger sample sizes.[26] On the other hand, horseshoe-shaped maxillary IODs do not offer the flexibility that palatal coverage offers if an implant is lost, but possibly can be adjusted accordingly.

Patient-based outcomes can best be assessed when a pretreatment questionnaire is used to elaborate the patient's requirements and select the appropriate rehabilitation. According to Zitzmann and Marinello,[19] patients were asked to indicate their preference between fixed or removable (with or without palatal coverage) and 80% wished to receive the fixed restoration. Based on their requests but taking the clinical indications into account, a recommendation was given with comprehensive informed consent. Among those initially requesting a fixed restoration, 38% were inclined to accept a max IOD after their specific local factors were reviewed. It has to be noted that post treatment patient-based outcomes are best documented after a 2- to 6-month follow-up period to allow for adaptation to the new restoration, and to overcome potential burdens of a long phase with temporary prostheses.

CONCLUSIONS

Outcomes

- A max IOD offers a stabilized removable solution for the edentulous maxilla that provides increased patient satisfaction and oral health QoL.
- A higher failure rate is experienced with machined implants.
- Four to six implants are widely applied in successful cohort studies.
- When four or less implants are used for max IODs, unsplinted designs have a higher implant/prosthetic failure rate than splinted implants.
- In general, both splinted and solitary anchorage systems are advocated. Maintenance may be higher for solitary attachments. Increased soft tissue inflammation has been reported under bars.
- Palateless design offers better patient satisfaction.

Guidelines (Consensus Group 5)

- When considering a max IOD design, the practitioners' team and the patient must understand the importance of long-term regular maintenance care.
- In the diagnostic phase, clinicians must identify systemic, local (eg, vertical space requirements) and patient-based factors to best select the adequate treatment regimen.
- The max IOD prosthesis should be designed to be maintainable, retrievable, repairable, or replaceable.
- Placing a minimum of four implants with a wide anteroposterior distribution of optimal support is recommended. Consider more implants when associated risk factors are present. Implants less than 10 mm in length challenge initial stability but implants with moderately rough surfaces may provide similar success rates irrespective of implant length.

ACKNOWLEDGMENTS

The authors declare no conflicts of interest related to this systematic review.

REFERENCES

1. Parel SM. Implants and overdentures: The osseointegrated approach with conventional and compromised applications. Int J Oral Maxillofac Implants 1986;1:93–99.
2. Parel SM, Balshi TJ, Sullivan DY. Modifications of existing prosthesis with osseointegrated implants. J Prosthet Dent 1986;56:61–65.
3. Watson PA, Listrom RD, Symington JM. Treatment of the edentulous maxillary arch using osseointrgrated implants supporting a fixed-removable prosthesis. J Can Dent Assoc 1988;54:119–121.
4. Jemt T, Book K, Lindén B, Urde G. Failures and complications in 92 consecutively inserted overdentures supported by Brånemark implants in severely resorbed edentulous maxillae: A study from prosthetic treatment to first annual check-up. Int J Oral Maxillofac Implants 1992;7:162–167.
5. Palmqvist S, Sondell K, Swartz B. Implant-supported maxillary overdentures: Outcome in planned and emergency cases. Int J Oral Maxillofac Implants 1994;9:184–190.
6. Widbom C, Söderfeldt B, Kronström M. A retrospective evaluation of treatments with implant-supported maxillary overdentures. Clin Implant Dent Relat Res 2005;7:166–172.
7. Smedberg JI, Lothigius E, Bodin I, Frykholm A, Nilner K. A clinical and radiological two-year follow-up study of maxillary overdentures on osseointegrated implants. Clin Oral Implants Res 1993;4:39–46.

8. Hof M, Tepper G, Semo B, et al. Patients' perspectives on dental implant and bone graft surgery: Questionnaire-based interview survey. Clin Oral Implants Res 2014;25:42–45.
9. Kronström M, Widbom C, Soderfeldt B. Patient evaluation with maxillary implant-supported overdentures. Clin Oral Implants Res 2006;8:39–43.
10. Zitzmann NU, Marinello CP. Treatment plan for restoring the edentulous maxilla with implant-supported restorations: Removable overdenture versus fixed partial denture design. J Prosthet Dent 1999;82:188–196.
11. Rosén A, Gynther G. Implant treatment without bone grafting in edentulous severely resorbed maxillas: A long-term follow-up study. J Oral Maxillofac Surg 2007;65:1010–1016.
12. Heydecke G, Boudrias P, Awad MA, De Albuquerque RF, Lund JP, Feine JS. Within-subject comparisons of maxillary fixed and removable implant prostheses: Patient satisfaction and choice of prosthesis. Clin Oral Implants Res 2003;14:125–130.
13. Dye BA, Tan S, Smith V, et al. Trends in oral health status: United States, 1988-1994 and 1999-2004. Vital Health Stat 11 2007;11:1–92.
14. Wu B, Liang J, Plassman BL, Remle C, Luo X. Edentulism trends among middle-aged and older adults in the United States: Comparison of five racial/ethnic groups. Community Dent Oral Epidemiol 2012;40:145–153.
15. Henry PJ. A review of guidelines for implant rehabilitation of the edentulous maxilla. J Prosthet Dent 2002;87:281–288.
16. Thomason JM, Heydecke G, Feine JS, Ellis JS. How do patients perceive the benefit of reconstructive dentistry with regard to oral health-related quality of life and patient satisfaction? A systematic review. Clin Oral Implants Res 2007; 18(suppl 3):168–188.
17. de Albuquerque Júnior RF, Lund JP, Tang L, et al. Within-subject comparison of maxillary long-bar implant-retained prostheses with and without palatal coverage: Patient-based outcomes. Clin Oral Implants Res 2000;11:555–565.
18. Zitzmann NU, Marinello CP. Fixed or removable implant-supported restorations in the edentulous maxilla: Literature review. Pract Periodontics Aesthet Dent 2000;12:599–608.
19. Zitzmann NU, Marinello CP. Treatment outcomes of fixed or removable implant supported prostheses in edentulous maxilla. Part I: Patients' assessments. J Prosthet Dent 2000;83:424–433.
20. Allen PF, McMillan AS, Walshaw D. Patient expectations of oral implant-retained prostheses in a UK dental hospital. Br Dent J 1999;186:80–84.
21. McGrath C, Lam O, Lang N. An evidence-based review of patient-reported outcome measures in dental implant research among dental subjects. J Clin Periodontol 2012;39(suppl 12):193–201.
22. Smedberg JI, Nilner K, Frykholm A. A six-year follow-up study of maxillary overdentures on osseointegrated implants. Eur J Prosthodont Restor Dent 1999;7:51–56.
23. Zembic A, Tahmaseb A, Wismeijer D. Within-subject comparison of maxillary implant-supported overdentures with and without palatal coverage. Clin Implant Dent Relat Res 2015;17:570–579.
24. Zembic A, Wismeijer D. Patient-reported outcomes of maxillary implant-supported overdentures compared to conventional dentures. Clin Oral Implants Res 2014;25:441–450.
25. Zitzmann NU, Marinello CP. Treatment outcomes of fixed or removable implant-supported prostheses in the edentulous maxilla. Part II: Clinical findings. J Prosthet Dent 2000;83:434–442.
26. Slot W, Raghoebar GM, Vissink A, Meijer HJ. A comparison between 4 and 6 implants in the maxillary posterior region to support an overdenture: 1-year results from a randomized controlled trial. Clin Oral Implants Res 2014;25:560–566.
27. Al-Zubeidi MI, Alsabeeha NH, Thomson WM, Payne AG. Patient satisfaction with maxillary 3-implant overdentures using different attachment systems opposing mandibular 2-implant overdentures. Clin Implant Dent Relat Res 2012;14(suppl 1):1–9.
28. Slot W, Raghobar GM, Vissink A, Meijer HJ. Maxillary overdentures supported by anteriorly or posteriorly placed implants opposed by natural dentition in the mandible: A 1-year prospective case series study. Clin Implant Dent Relat Res 2014;16:51–61.
29. Zou D, Wu Y, Huang W, et al. A 3-year prospective clinical study of telescopic crown, bar, locator attachments for removable four implant-supported maxillary overdentures. Int J Prosthodont 2013;26:566–573.
30. Naert I, Gizani S, van Steenberghe D. Rigidly splinted implants in the resorbed maxilla to retain a hinging overdenture: A series of clinical reports for up to 4 years. J Prosthet Dent 1998;79:156–164.
31. Raghoebar GM, Schoen P, Meijer HJ, Stellingsma K, Vissink A. Early loading of endosseous implants in augmented maxilla: A 1-year prospective study. Clin Oral Implants Res 2003;14:697–702.
32. Visser A, Raghoebar GM, Meijer HJ, Vissink A. Implant-retained maxillary overdentures on milled bar superstructures: A 10-year follow-up of surgical and prosthetic care and aftercare. Int J Prosthodont 2009;22:181–192.
33. Watson RM, Jemt T, Chai J, et al. Prosthodontic treatment, patient response, and the need for maintenance of complete implant-supported overdentures: An appraisal of 5 years of prospective study. Int J Prosthodont 1997;10:345–354.
34. Pieri F, Aldini NN, Fini M, Marchetti C, Corinaldesi G. Immediate functional loading of dental implants supporting a bar-retained maxillary overdenture: Preliminary 12-month results. J Periodontol 2009;80:1883–1893.
35. Bernhart G, Koob A, Schmitter M, Gabbert O, Stober T, Rammelsberg P. Clinical success of implant-supported and tooth-implant supported double crown-retained dentures. Clin Oral Investig 2012;16:1031–1037.
36. Närhi TO, Hevinga M, Voorsmit RA, Kalk W. Maxillary overdentures retained by splinted and unsplinted implants: A retrospective study. Int J Oral Maxillofac Implants 2001;16:259–266.
37. Ekfeldt A, Johansson LA, Isaksson S. Implant-supported overdenture therapy: A retrospective study. Int J Prosthodont 1997;10: 366–374.
38. Sanna A, Nuytens P, Naert I, Quirynen M. Successful outcome of splinted implants supporting a planned maxillary overdenture: A retrospective evaluation and comparison with fixed full dental restoration. Clin Oral Implants Res 2009;20:406–413.
39. Krennmair G, Krainhöfner M, Piehslinger E. Implant-supported maxillary overdentures retained with milled bars: Maxillary anterior versus maxillary posterior concept- a retrospective study. Int J Oral Maxillofac Implants 2008;23:343–352.
40. Bergendal T, Engquist B. Implant-supported overdentures: A longitudinal prospective study. Int J Oral Maxillofac Implants 1998;13:253–262.
41. Esposito M, Ardebili Y, Worthington HV. Interventions for replacing missing teeth: Different types of dental implants. Cochrane Database Syst Rev 2014;7:CD003815.
42. Suzuki Y, Osada H, Kobayashi M, et al. Long-term evaluation of implant over denture. J Prosthodont Res 2012;56:32–36.
43. Jemt T, Chai J, Harnett J, et al. A 5-year prospective multicenter follow-up report on overdentures supported by osseointegrated implants. Int J Oral Maxillofac Implants 1996;11:291–298.
44. Mericske-Stern R, Oetterli M, Keiner P, Mericske E. A follow-up study of maxillary implants supporting an overdenture: Clinical and radiographic results. Int J Oral Maxillofac Implants 2002;17:678–686.
45. Keiner P, Oetterli M, Meriske E, Meriske-Stern R. Effectiveness of maxillary overdentures supported by implants: Maintenance and prosthetic complications. Int J Prosthodont 2001;14:133–140.
46. Mangano C, Mangano F, Shibli JA, et al. Morse taper connection implants supporting "planned" maxillary and mandibular bar-retained overdentures: A 5-year prospective study. Clin Oral Implants Res 2011;22:1117–1124.
47. Van Assche N, Michels S, Quirynen M, Naert I. Extra short dental implants supporting an overdenture in edentulous maxilla: A proof of concept. Clin Oral Implants Res 2012;23:567–576.
48. Payne AG, Tawse-Smith A, Thomson WM, Duncan WD, Kumara R. One-stage surgery and early loading of three implants for maxillary overdentures: A 1-year report. Clin Implant Dent Relat Res 2004;6:61–74.
49. Raghoebar GM, Meijer HJ, Slot W, Slater JJ, Vissink A. A systematic review of implant-supported overdentures in the edentulous maxilla, compared to the mandible: How many implants? Eur J Oral Implantol 2014;7(suppl 2):S191–S201.
50. Parel SM, Phillips WR. A risk assessment treatment planning protocol for the four implant immediately loaded maxilla: Preliminary findings. J Prosthet Dent 2011;106:359–366.

Maxillary Implant-Supported Fixed Prosthesis: A Survey of Reviews and Key Variables for Treatment Planning

German O. Gallucci, DMD, PhD[1]/Marianna Avrampou, DDS, MSc[2]/James C. Taylor, DMD, MA[3]/
Julie Elpers, DMD, MS[4]/Ghadeer Thalji, DDS, PhD[5]/Lyndon F. Cooper, DDS, PhD[6]

Purpose: *This review was conducted to provide information to support the establishment of clinical guidelines for the treatment of maxillary edentulism using implant-supported fixed dental prostheses.* ***Materials and Methods:*** *Initial efforts were directed toward a systematic review with a defined PICO question: "For maxillary edentulous patients with dental implants treated using a fixed prosthesis, what is the impact of prosthesis design on prosthesis survival and complications?" Following a title search of more than 3,000 titles identified by electronic search of PubMed, 180 articles were identified that addressed the clinical evaluation of maxillary dental implant prostheses. The broad methodologic heterogeneity and clinical variation among reports precluded this approach for a systematic review. The information was extracted using a standardized extraction table by two pairs of investigators, and the reported outcomes were then summarized according to reported outcomes for implant prostheses supported by four, six, or eight implants using unitary or segmented prostheses.* ***Results:*** *This review indicated that high prosthetic survival is observed using all approaches. The advantages of using fewer implants and a unitary prosthesis are revealed in the surgical phases, and complications commonly involve the fracture or detachment of acrylic teeth and reduced access for proper oral hygiene and related biologic complications. Using six implants typically involved grafting of posterior regions with advantages of reduced cantilevers and redundancy of implant support. Reduced prosthesis survival in these cases was associated with poor implant distribution. Segmented prostheses supported by six or more implants offered greater prosthetic survival, perhaps due to posterior implant placement. Advantages of a segmented prosthesis included pragmatic issues of accommodating divergent implants, attaining passive fit, combining prosthetic materials, and relative simplicity of repair.* ***Conclusion:*** *The existing literature demonstrated that maxillary edentulism may be treated successfully using alternative approaches involving four, six, or more implants. The procedural diagnostics, treatment, and maintenance for these different approaches all require advanced knowledge and careful communication among the therapeutic team. The prosthetic therapeutic success requires maintenance, repair, and possible multiple replacements within the patient's lifetime.* Int J Oral Maxillofac Implants 2016;31(suppl):s192–s197. doi: 10.11607/jomi.16suppl.g5.3

[1]Raymond J. and Elva Pomfret Nagle Associate Professor and Chair, Department of Restorative Dentistry and Biomaterials Sciences, Harvard School of Dental Medicine, Boston, Massachusetts, USA.
[2]Assistant Professor, Department of Prosthodontics, Tufts School of Dental Medicine, Boston, Massachusetts, USA.
[3]Formerly Chief Dental Officer, Royal Canadian Dental Corps, Ottawa, Ontario, Canada.
[4]Private Practice, Sowles Trauring Dental Partners of Brookline, Boston, Massachusetts; Adjunct Assistant Professor, Department of Prosthodontics, University of North Carolina School of Dentistry, Chapel Hill, North Carolina, USA.
[5]Director, Advanced Prosthodontics, University of Iowa College of Dentistry, Iowa City, Iowa, USA.
[6]Associate Dean for Research; Head, Oral Biology, University of Illinois at Chicago College of Dentistry, Chicago, Illinois, USA.

Correspondence to: Dr German O. Gallucci, Department of Restorative Dentistry and Biomaterials Science, Harvard School of Dental Medicine, 188 Longwood Avenue, Boston, MA 02115. Email: german_gallucci@hsdm.harvard.edu

The restoration of the edentulous maxilla using dental implants is often challenged by multiple factors that influence clinical decision-making. Recent systematic reviews suggest that the overall implant survival and the extent of prosthetic complications differ. In fact, compared with implant survival rates of approximately 90% to 95%, the complication rates for maxillary implant fixed prostheses are higher.[1,2] The possible scope of treatment was revealed by Att et al,[1] who included implant rehabilitations without bone augmentation (implants > 10 mm, tilted implants, or zygoma implants) and implant rehabilitation with bone augmentation (sinus floor elevation and interpositional bone grafting). There was little data reported for prosthesis survival, but where reported, implant-supported fixed prosthesis (ISFP) survival in the maxilla was high. Quantification of complications was not achieved, however. This has been borne out by other systematic reviews.[1–3]

The edentulous maxilla presents several challenges for implant therapy. Principal among them is relatively low bone quality as compared with the edentulous mandible. Bone volume also varies remarkably throughout the maxilla and among individuals. Solutions to the bone volume problems fall into three categories: *(1)* grafting, *(2)* the use of shorter implants with enhanced surface topographies, and *(3)* the use of tilted implants or extra-alveolar implants (including pterygoid and zygomatic implants). In this context, the primary outcome for this specific report is a successful, stable, and predictable prosthetic restoration that makes use of whatever implant configuration is placed, with patient-oriented positive outcomes associated with esthetics, phonetics, function, comfort, lip support, ease of hygiene, and patient-perceived value for the treatment outcome.

Major maxillary bone grafting procedures may solve some of the clinical limitations and enable the otherwise unavailable implant solutions to patients. However, implant survival in grafted bone has been repeatedly demonstrated to be lower than implant survival in native bone.[4–8] Regarding short implants, several systematic reviews reveal high success.[9–13] Surface roughness contributes to improved implant survival in the lower-density bone of the maxilla, and several retrospective studies demonstrate higher survival of rough versus machined implants placed in the edentulous maxilla.[14,15] Zygomatic and pterygoid implants offer high implant survival[16–18]; however, complications associated with zygomatic implants are reportedly higher than for conventional implants. It is important to recognize that challenges and complications accompany this restoration and include unhygienic contours with palatal position of the implants, phonetic challenges with palatal contours, and vertical space limitations where the implants pass into the oral cavity. Additional training is required for appropriate utilization of these extra-alveolar implant types. Thus, the approaches offered to the patient for treatment of the edentulous maxilla using implant-supported fixed prostheses are dependent on the initial clinical situation of the edentulous maxilla.

Secondarily, the clinical team must consider either a grafting approach to provision of sufficient implants or a nongrafting approach utilizing short, angled, or extra-alveolar implants. Finally, once the patient has selected one of the presented possible treatment options, the clinical and laboratory teams must have the combined skillset to provide it safely and predictably. Another surgical variable presented in the literature is time of loading for dental implants. Suggested is an incrementally higher risk for immediate loading of implants in the edentulous maxilla compared with immediate loading of implants in the edentulous mandible.[19]

The original intent of this review was to explore the restorative options available for treatment of the edentulous maxilla using an implant-supported fixed prosthesis with guidance from existing clinical studies and published systematic reviews. Our initial efforts explored the potential of a systematic review to determine the extent of knowledge regarding the PICO question, "For maxillary edentulous patients with dental implants treated using a fixed prosthesis, what is the impact of prosthesis design on prosthesis survival and complications?" Following a title search of more than 3,000 titles identified by an electronic search of PubMed, 180 articles were found that addressed the clinical evaluation of maxillary dental implant prostheses. It became apparent that the broad methodologic heterogeneity and clinical variation among reports precluded this approach for a systematic evaluation of the literature. A further limitation in seeking an answer to this question was that the concept of a prosthesis complication has not been fully explored and a definition is lacking. Survival of the prosthesis connotes its use over time without replacement or loss. Complications have included extremes such as mechanical failure requiring replacement to chipping of porcelain veneers or wear of acrylic resin.

Therefore, the intent of this review was to explore the restorative options available for treatment of the edentulous maxilla using an implant-supported fixed prosthesis with guidance from existing clinical studies and published systematic reviews. In seeking to simplify our approach, we focused on the key factors demonstrated in the literature to drive a restorative strategy: the number, distribution, and orientation of implants that have been placed in the maxilla. Secondarily, it was possible to distinguish a difference for greater than six implants and for the provision of a one-piece versus a segmented prosthesis. Differences in the application of a screw-retained versus cement-retained approach were also discussed.

LESS THAN SIX IMPLANTS WITH A ONE-PIECE PROSTHESIS

Brånemark's initial conceptualization of treatment of the edentulous maxilla involved placement of five or six implants in the region of the maxilla anterior to the maxillary sinuses and restoring the patient with a one-piece acrylic-veneered gold prosthesis. The initial 1995 report of Brånemark et al indicated relatively low prosthesis survival that may have been associated with the 80.3% implant survival rate.[20] One prosthesis supported by four implants failed, while six prostheses supported by six implants failed. The use of four tilted implants to support the maxillary implant-supported fixed prosthesis was also proposed[21] using an immediate function protocol. The initial reported cohort of 23 patients demonstrated high implant survival,[22] and a

subsequent 5-year report demonstrated that 93% of 252 patients experienced no implant failures with a 100% prosthesis survival.[23] For 300 maxillary implants in 75 maxillae, similar high success was revealed at the implant level, but no information regarding prosthesis outcome was reported.[24] The use of less than four implants may not be feasible.

However, evidence on the complication rates associated with tilted implants using at least four implants is scarce and inconsistently reported. The technical challenges of this approach include increased difficulty in surgery and overcoming limited anterior/posterior distribution of supporting implants. It is noted that guided surgical approaches may aid in placement of implants to facilitate prosthesis construction and longevity.[25]

Central to choosing to use four implants, implant loss results in failure of the prosthesis. When acrylic veneered metal frameworks are used for restoration, there is a high likelihood of complications. An up to 5-year retrospective study of 34 maxillary prostheses revealed that approximately 20% of patients experienced fracture or detachment of acrylic teeth and nearly 40% experienced hygienic complications.[26] Further, there is little knowledge regarding the prosthetic complications for the monolithic zirconia alternatives. Mechanical risks to the prosthesis may be accentuated with increased cantilever lengths.

The advantages of using fewer (four or five) implants and a one-piece prosthesis include reduced surgical costs to the patient and potentially reduced surgical time, with no prior bone grafting experience necessary. Based on these features of this approach, it may be recommended that this is a complex procedure that should be conducted by an experienced team with a comprehensive knowledge of both the surgical and restorative aspects of care. Additionally, there is a requirement for experienced laboratory support. The risks and benefits of this approach call for a careful examination to consider the use of an implant-retained overdenture as a viable, less complex alternative implant prosthetic protocol.

SIX OR MORE IMPLANTS WITH A ONE-PIECE PROSTHESIS

Treatment using six or more implants may provide for 5 to 10 years of implant survival.[27] The related prosthesis survival for full-arch fixed dental prostheses was also high at 10 years (95% CI 88.5% to 97.9%). The placement of six or more implants distributed anteriorly and posteriorly in the maxilla often involves grafting of the alveolus and or the maxillary sinuses. The prosthesis construction involving more implants can become complex, particularly if malposition of implants is encountered.

The potential complications identified by review of the related literature include those associated with reduced implant survival in grafted bone, screw loosening, and prosthetic complications of acrylic wear and acrylic tooth chipping, as well as chipping of ceramic-veneered prostheses. The advantages of this approach include avoiding cantilevers, incorporating cross-arch stabilization of stress distribution, and redundancy of implant support, which prevents prosthesis loss if a single implant is lost. In a structured review that compared outcomes based on the number of implants per patient,[3] prosthesis survival tended to be lower when fewer than six implants supported the prosthesis from 1 to 10 years (at 5 years 92.6% versus 92.7%, $P = .05$, for < 6 or > 6 implants, respectively). The authors also described an impact on implant distribution; lower prosthesis survival was found when implants were not distributed anteriorly and posteriorly beyond the second premolar.[3]

Based on these observations, the recommendations for treatment include: an experienced team with comprehensive knowledge of surgical/restorative aspects related to this advanced procedure, a detailed presurgical analysis based on prosthetically driven implant position, selection of prosthetic materials based on patient-centered parameters (patient preference, age, esthetic requirement, bruxism, etc), and careful, robust prosthesis design and proper manufacturing technique to preclude chipping or fracture. The restorative process should involve an experienced laboratory and requires careful evaluation and adjustment of the occlusion upon delivery and throughout the periodic recall program.

SIX OR MORE IMPLANTS WITH A SEGMENTED PROSTHESIS

While no studies comparing the number of implants (four, six, or more than six) have been reported for the segmented maxillary implant-supported fixed prostheses, one systematic review suggested that the prosthodontic survival rates were significantly greater for restorations supported by six or more implants compared with those supported by fewer than six implants.[3] The summary data demonstrated no difference in prosthesis survival for one-piece versus segmented prostheses. It was argued that using more implants to achieve implant distribution beyond the first premolar was associated with increased prosthodontic survival ($P < .001$).

Many of the potential complications of the segmented prosthesis reflect those of one-piece prostheses supported by six or more implants. Included are the reduced implant survival in grafted bone, screw loosening and fracture, and prosthetic complications. The key advantage of a segmented prosthesis is that the loss of one implant may not result in loss of the

entire reconstruction. Additional advantages of using a segmented prosthesis for restoration of the edentulous maxilla include the pragmatic issues that address divergent angulation of implants in the anterior versus posterior maxilla, associated simplification of laboratory procedures and attainment of passive fitting prostheses, the use of different prosthetic materials in the anterior and posterior regions, and possibly simpler procedures by using cement-retained prostheses.

The difficulties inherent to this approach are not unique either. The possible need for bone grafting to support additional implants, the need to create complex prosthetic solutions including custom abutments, and related phonetic or esthetic complications have all been reported.

Based on the limited available data and information regarding the segmented restoration on more than six implants, it is recommended that patients be treated by an experienced team with a comprehensive knowledge of surgical/restorative aspects of therapy following a detailed presurgical analysis that leads to prosthesis-directed implant placement. A highly experienced laboratory should be engaged in assisting in the selection of patient-specific materials (based on patient preference, age, function, esthetic requirements, opposing arch status) and the fabrication of a well-designed prosthesis that can avoid chipping or catastrophic failure. The insertion requires verification and adjustment of the occlusion and regular evaluation and maintenance.

PROSTHESIS VARIABLES INFLUENCING OUTCOMES

This review identified two general categories of prosthesis variables that may influence maxillary implant-supported fixed prostheses: *(1)* screw-retained versus cement-retained and *(2)* prosthetic material selection. The results suggest that no prosthesis is yet to be proven free from complications. However, the reasons for catastrophic failure may be attributed to planning, prosthesis design, or execution factors. The main complication influencing the use of screw or cement retention involves screw loosening and fracture versus de-cementation. The difficulties, advantages, and recommendations are enumerated in Table 1. When considering prosthetic material selection, the prominent choices include metal-acrylic, metal-ceramic (PFM), zirconia-feldspathic ceramic, and monolithic zirconia. The relative complications, difficulties, advantages, and recommendations are enumerated in Table 2.

There are only limited long-term data concerning the treatment of the edentulous maxilla using implant-supported fixed prostheses. Jemt and Johansson[28] published a 15-year report of 76 patients treated with 450 machined implants. The 15-year implant and fixed prosthesis cumulative survival rates were 90.9% and 90.6%, respectively. Resin veneer fractures and severe wear were the main complications recorded. Interestingly, loosening of abutment/bridge locking screws was noted. These results should be compared to the 1991 1-year report of implants placed in 391 edentulous maxillae and mandibles, for which Jemt[29] recorded 98.1% and 99.5% success for the implants and prostheses, respectively. In a study recording the outcomes of 46 edentulous patients treated with maxillary prostheses 12 to 15 years after treatment, one framework fracture with acrylic veneer fracture was reported with a second having severe tooth wear, seven ceramic prostheses demonstrated chipping, and one abutment screw fractured.[30]

A recent systematic review of studies (including both maxillary and mandibular implant-supported fixed prostheses) with 5 to 10 or $>$ 10 years follow-up, reported the most commonly observed prosthetic complications were fracture or loosening of abutment and prosthesis screws and fracture of acrylic resin or acrylic resin teeth.[31] These complications appear to continue with time, and the data reinforce the observations made in an early systematic review.[2] Longer-term data will continue to inform the profession of its responsibilities regarding careful planning, providing opportunities for repair and revision, and maintaining implant health for longer than the commonly reported 1- to 5-year outcomes.

A comprehensive assessment of prosthodontic complication rates of maxillary implant-supported fixed prostheses demonstrated the time-dependent nature of the phenomenon. In a meta-analysis of 19 selected reports, there was limited comparison among types of restorations; however, the review demonstrated that within 10 years, a large number of veneer fractures and wear problems were encountered. By 15 years, over 50% of studied prostheses demonstrated fracture or wear of the veneering material.[32] Papaspyridakos et al[2] reported less than 10% prosthetic success (a prosthesis without complication) for implant-supported fixed prostheses at 10 years. The possible improvement of outcomes using ceramic maxillary implant-supported fixed prostheses has received some attention; however, fracture and chipping of crowns and fracture of gingival ceramic remained, particularly in a "development group" of prostheses.[33] Thus, long-term maxillary implant-supported fixed prosthesis success requires maintenance, repair, and possible replacements within the patient's lifetime. This should not be viewed as a limitation of this approach but instead with a rational understanding that the prosthesis has a lifespan and that the patient can be best served by prosthesis designs that are age-appropriate in regard to hygiene, esthetics, phonetics, function, and patient-based expectations, and with the knowledge that these expectations and their priority will change over the lifespan of the patient.

Table 1 Comparison of Implant Retention Mechanisms

Retention mechanism	Potential complications	Difficulties	Advantages	Recommendations
Screw-retained	Screw loosening, screw fracture	Requires ideal implant placement (prosthetically driven) or complex prosthesis	Easy retrieval, extraoral repairs, easier follow-up visits and maintenance	Complex procedure requires experienced team with comprehensive understanding of surgical/restorative aspects Highly experienced dental laboratory with access to CAD/CAM
Cement-retained	Debonding, cement retention, risk of peri-implantitis	Positioning of the crown margin, remaining cement, higher cost when individualized abutments are used, intraoral repairs/limited retrieval options	Better occlusal anatomy	

Table 2 Prosthetic Material Selection

Prosthetic material	Potential complications	Difficulties	Advantages	Recommendations
Metal-acrylic	Frequent fracture of the acrylic teeth, fracture of the pink acrylic material, fracture of the prosthesis when metal reinforcement is not used, discoloration, unstable occlusal contacts (wear)	Long-term survival without complications (fractures, discoloration)	Easy to repair, lower cost	Better for provisional phase Use higher-quality acrylic teeth
Porcelain fused to zirconia	Chipping of the prosthesis veneering material	Esthetics when implants are not correctly placed Difficult to repair	Long-term stability	Control design of the framework and space required for the veneering material Control the occlusion Segmentation of the prosthesis with ideal number of supporting implants
Monolithic zirconia	Unknown long-term results (aging of the material?)	Advanced technology is needed, experienced laboratory is needed, intraoral occlusal adjustments may diminish long-term stability of the material	Reduced possibility for chipping, as there is no need for veneering material	Include prototype prosthesis Lab finishing that avoids adjustments No intraoral occlusal adjustments Segmentation of the prosthesis with ideal number of implants

CONCLUSIONS

The aggregate evidence presented among different prospective studies and existing systematic reviews that reported on prosthetic survival and prosthesis complications permits clinical recommendations regarding the challenges presented in prosthetic rehabilitation of the edentulous maxilla using an implant-supported fixed prosthesis. Based on the reported evidence and expert opinions, it can be stated that:

- Four, six, or more than six implants can be undertaken to provide a maxillary fixed implant prosthesis when rough-surfaced implants, which have survival rates above 95% after 5 years, are used.
- The relative risks of using fewer implants in a tilted array versus distributing more implants, which is often dependent on bone grafting procedures, must be considered at individual patient and clinician levels.
- The use of a one-piece prosthesis is required when few implants are included. The pragmatic advantages of using more implants to support a segmented prosthesis should be included in decision-making for individual patients.
- The procedural diagnostics, treatment, and maintenance for these different approaches all require advanced knowledge and careful communication among the therapeutic team.
- Emerging long-term data on implant-supported fixed prosthesis treatment of the edentulous maxilla suggest that with possible long-term implant survival, the prosthetic therapeutic success requires maintenance, repair, and possible multiple replacements within the patient's lifetime.

ACKNOWLEDGMENTS

The authors wish to express their gratitude to all participants of AO Summit group 5. The authors declare no conflicts of interest related to this systematic review.

REFERENCES

1. Att W, Bernhart J, Strub JR. Fixed rehabilitation of the edentulous maxilla: Possibilities and clinical outcome. J Oral Maxillofac Surg 2009; 67(11 suppl):60–73.
2. Papaspyridakos P, Chen CJ, Singh M, Weber HP, Gallucci GO. Success criteria in implant dentistry: A systematic review. J Dent Res 2012;91:242–248.
3. Lambert FE, Weber HP, Susarla SM, Belser UC, Gallucci GO. Descriptive analysis of implant and prosthodontic survival rates with fixed implant-supported rehabilitations in the edentulous maxilla. J Periodontol 2009;80:1220–1230.
4. Chiapasco M, Casentini P, Zaniboni M. Bone augmentation procedures in implant dentistry. Int J Oral Maxillofac Implants 2009; 24(suppl):237–259.
5. Bector JP, Isakkson S, Sennerby L. Survival analysis of endosseous implants in grafted and nongrafted edentulous maxillae. Int J Oral Maxillofac Implants 2004;19:107–115.
6. Esposito M, Grusovin MG, Felice P, Karatzopoulos G, Worthington HV, Coulthard P. The efficacy of horizontal and vertical bone augmentation procedures for dental implants—A Cochrane systematic review. Eur J Oral Implantol 2009;2:167–184.
7. Pjetursson BE, Tan WC, Zwahlen M, Lang NP. A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation. J Clin Periodontol 2008:35(suppl 8):216–240.
8. Rocchietta I, Fontana F, Simion M. Clinical outcomes of vertical bone augmentation to enable dental implant placement: A systematic review. J Clin Periodontol 2008;35(suppl 8):203–215.
9. Annibali S, Cristalli MP, Dell'Aquila D, Bignozzi I, La Monaca, G, Pilloni A. Short dental implants: A systematic review. J Dent Res 2012:91:25–32.
10. Neldam CA, Pinholt EM. State of the art of short dental implants: A systematic review of the literature. Clin Implant Dent Relat Res 2012;14:622–632.
11. Telleman G, Raghoebar GM, Vissink A, den Hartog L, Huddleston Slater JJ, Meijer HJ. A systematic review of the prognosis of short (<10 mm) dental implants placed in the partially edentulous patient. J Clin Periodontol 2011;38:667–676.
12. Sun HL, Huang C, Wu YR, Shi B. Failure rates of short (≤ 10 mm) dental implants and factors influencing their failure: A systematic review. Int J Oral Maxillofac Implants 2011;26:816–825.
13. Kotsovilis S, Fourmousis I, Karoussis IK, Bamia C. A systematic review and meta-analysis on the effect of implant length on the survival of rough-surface dental implants. J Periodontol 2009;80:1700–1718.
14. Jemt T, Stenport V, Friberg B. Implant treatment with fixed prostheses in the edentulous maxilla. Part 1: Implants and biologic response in two patient cohorts restored between 1986 and 1987 and 15 years later. Int J Prosthodont 2011;24:345–355.
15. Malo P, Nobre Mde A, Lopes A. Immediate rehabilitation of completely edentulous arches with a four-implant prosthesis concept in difficult conditions: An open cohort study with a mean follow-up of 2 years. Int J Oral Maxillofac Implants 2012;27:1177–1190.
16. Curi MM, Cardoso CL, Ribeiro Kde C. Retrospective study of pterygoid implants in the atrophic posterior maxilla: Implant and prosthesis survival rates up to 3 years. Int J Oral Maxillofac Implants 2015;30:378–383.
17. Prithviraj DR, Vashisht R, Bhalla HK. From maxilla to zygoma: A review on zygomatic implants. J Dent Implant 2014;4:44–47.
18. Chrcanovic BR, Abreu MH. Survival and complications of zygomatic implants: A systematic review. Oral Maxillofac Surg 2013;17:81–93.
19. Andersson P, Degasperi W, Verrocchi D, Sennerby L. A retrospective study on immediate placement of Neoss implants with early loading of full-arch bridges. Clin Implant Dent Relat Res 2015;17:646–657.
20. Brånemark PI, Svensson B, Van Steenberghe D. Ten-year survival rates of fixed prostheses on four or six implants ad modum Brånemark in full edentulism. Clin Oral Implants Res 1995;6:227–231.
21. Maló P, Rangert B, Nobre M. "All-on-Four" immediate-function concept with Brånemark System implants for completely edentulous mandibles: A retrospective clinical study. Clin Implant Dent Relat Res 2003;5(suppl 1):2–9.
22. Maló P, Rangert B, Nobre M. All-on-4 immediate-function concept with Brånemark System implants for completely edentulous maxillae: A 1-year retrospective clinical study. Clin Implant Dent Relat Res 2005;7(suppl 1):S88–S94.
23. Maló P, de Araújo Nobre M, Lopes A, Francischone C, Rigolizzo M. "All-on-4" immediate-function concept for completely edentulous maxillae: A clinical report on the medium (3 years) and long-term (5 years) outcomes. Clin Implant Dent Relat Res 2012;14(suppl 1): e139–e150.
24. Balshi TJ, Wolfinger GJ, Slauch RW, Balshi SF. A retrospective analysis of 800 Brånemark System implants following the All-on-Four™ protocol. J Prosthodont 2014;23:83–88.
25. Pomares C. A retrospective study of edentulous patients rehabilitated according to the 'all-on-four' or the 'all-on-six' immediate function concept using flapless computer-guided implant surgery. Eur J Oral Implantol 2010;3:155–163.
26. Cavalli N, Barbaro B, Spasari D, Azzola F, Ciatti A, Francetti L. Tilted implants for full-arch rehabilitations in completely edentulous maxilla: A retrospective study. Int J Dent 2012;2012:180379. doi: 10.1155/2012/180379.
27. Heydecke G, Zwahlen M, Nicol A, et al. What is the optimal number of implants for fixed reconstructions: A systematic review. Clin Oral Implants Res 2012;23(suppl 6):217–228.
28. Jemt T, Johansson J. Implant treatment in the edentulous maxillae: A 15-year follow-up study on 76 consecutive patients provided with fixed prostheses. Clin Implant Dent Relat Res 2006;8:61–69.
29. Jemt T. Failures and complications in 391 consecutively inserted fixed prostheses supported by Brånemark implants in edentulous jaws: A study of treatment from the time of prosthesis placement to the first annual checkup. Int J Oral Maxillofac Implants 1991;6:270–276.
30. Ravald N, Dahlgren S, Teiwik A, Gröndahl K. Long-term evaluation of Astra Tech and Brånemark implants in patients treated with full-arch bridges. Results after 12–15 years. Clin Oral Implants Res 2012;24:1144–1151.
31. Kwon T, Bain PA, Levin L. Systematic review of short- (5-10 years) and long-term (10 years or more) survival and success of full-arch fixed dental hybrid prostheses and supporting implants. J Dent 2014;42:1228–1241.
32. Bozini T, Petridis H, Garefis K, Garefis P. A meta-analysis of prosthodontic complication rates of implant-supported fixed dental prostheses in edentulous patients after an observation period of at least 5 years. Int J Oral Maxillofac Implants 2011;26:304–318.
33. Maló P, de Araújo Nobre M, Borges J, Almeida R. Retrievable metal ceramic implant-supported fixed prostheses with milled titanium frameworks and all-ceramic crowns: Retrospective clinical study with up to 10 years of follow-up. J Prosthodont 2012;21:256–264.

Clinical Practice Guidelines: Role of Prosthetic Management of the Edentulous Maxilla

THE COMPLETE DENTURE

Scope: Interim or definitive replacement of teeth and alveolus in the edentulous maxilla
Target conditions of procedures: Socioeconomic, psychologic, or pragmatic limitations to implant placement
Target population: Edentulous maxilla
Target audience: General dentists, prosthodontists, denturists, laboratory technicians
Identify interventions: Immediate complete denture, interim complete denture, definitive complete denture
Measured outcomes: Patient satisfaction, oral mucosal health, prosthesis survival

Introduction

A maxillary complete denture is a minimal prosthesis required for maxillary edentulous patients. It is a necessary social and functional prosthesis provided as an immediate, interim, or definitive solution pending or following tooth loss.

Purpose

The purpose is to guide general dentists, prosthodontists, denturists, and laboratory technicians on the need to provide complete dentures for maxillary edentulism that fulfill minimal functional, biologic, and esthetic criteria.

Health Care Burden

Edentulism is prevalent in the United States; maxillary edentulism affects > 20 million individuals. The cost of a complete denture represents the minimal expenditure for providing a minimal yet satisfactory solution addressing individuals' functional and social needs imposed by edentulism.
Methods: systematic review and clinical experience

Key Action Statements

Prosthodontists and restorative dentists should provide all patients with immediate, interim, or complete dentures when patients will become or are edentulous.

A maxillary denture can provide rehabilitation without dental implants and represents a treatment choice when complex restorative needs cannot be met by the professional team or addressed financially by the patient.

The maxillary denture should be stable and retentive; function to satisfy patients' phonetic, esthetic, and masticatory needs; and be in sufficient physical state to support hygiene and oral mucosal health. Dentures not meeting these therapeutic goals should be replaced, or alternative reconstruction using implants should be considered.

Dentures provide functional and esthetic diagnostic guidelines for additional implant-supported prostheses.

Any decision to withhold a denture following surgical intervention should be a joint decision made by the surgical dentist, restorative dentist, and patient.

THE IMPLANT-SUPPORTED OVERDENTURE

Scope: Interim or definitive replacement of teeth and alveolus in the edentulous maxilla
Target conditions of procedures: Patients with physical limitations to denture use, patients who are accepting of removal prosthetic solutions, patients with marked alveolar resorption requiring prosthetic replacement of the alveolus, patients unable to achieve (for anatomical, pragmatic, or financial reasons) an implant-retained fixed prosthesis.
Target population: Edentulous maxilla
Target audience: General dentists, prosthodontists, denturists, laboratory technicians
Identify interventions: Implant-supported overdenture retained by bar or solitary attachment mechanisms
Measured outcomes: Patient satisfaction, component complications, prosthesis survival

Introduction

A maxillary implant-supported overdenture offers a stabilized removable solution for the edentulous maxilla. Sufficient vertical restorative dimension is required to manage construction of a durable, esthetic, and phonetic prosthesis. Support of two to six implants is required. The prosthesis may be bar or solitary attachment retained. Splinting of implants may not be required.

doi: 10.11607/jomi.16suppl.g5.cpg

Purpose
The purpose is to guide general dentists, prosthodontists, denturists, and laboratory technicians on the need to provide implant-supported overdentures for maxillary edentulism that fulfill minimal functional, biologic, and esthetic criteria.

Health Care Burden
Edentulism is prevalent in the United States; maxillary edentulism affects > 20 million individuals. Among individuals treated with dentures, a minority are unable to adapt to conventional denture use. Additionally, the benefits of denture stability afforded by implants are desirable, especially when palatal coverage is eliminated. The implant-supported overdenture is a less expensive prosthesis than an implant-retained fixed prosthesis restoring maxillary edentulism.
Methods: systematic review and clinical experience

Guideline Key Action Statements
Prosthodontists and restorative dentists should provide the option of an implant-supported maxillary overdenture to patients who *(1)* are unable to adapt to maxillary denture use (psychologic or physiologic), *(2)* have a desire for or will benefit from greater denture stability, *(3)* cannot afford the expense of an implant-supported fixed prosthesis.

A maxillary implant-supported overdenture can provide rehabilitation with as few as two unsplinted implants, thus avoiding more complex restorative implant-related needs that cannot be met by the professional team or addressed financially by the patient.

The maxillary implant overdenture should be stable and retentive; function to satisfy patients' phonetic, esthetic, and masticatory needs; and be in sufficient physical state to support hygiene and oral mucosal health. The patient must be able to place and remove the prosthesis competently without assistance.

The provision of implants and the implant overdenture should not interfere with or preclude the provision of phonetics, mastication, and esthetics.

Any decision to proceed with implant overdenture therapy should be a joint decision made by the surgical dentist, restorative dentist, and patient that is informed by the provision or presence of an ideal conventional denture.

THE FIXED IMPLANT-RETAINED PROSTHESIS

Scope: definitive replacement of teeth and alveolus in the edentulous maxilla
Target conditions or procedures: patients with physical limitations to denture use, patients who are not accepting of removable prosthetic solutions, patients willing to accept the responsibility for lifelong maintenance of the fixed prosthesis and abutments.
Target population: edentulous maxilla
Target audience: general dentists, prosthodontists, denturists, laboratory technicians
Identify interventions: implant-retained fixed prosthesis supported by four or more implants
Measured outcomes: patient satisfaction, component complications, prosthesis survival

Introduction
A maxillary implant-retained fixed prosthesis provides a fixed prosthetic solution for the edentulous maxilla. Support of four or more implants is required. Sufficient vertical restorative dimension is required to manage construction of a durable, esthetic, and phonetic prosthesis.

Purpose
The purpose is to guide general dentists, prosthodontists, denturists, and laboratory technicians on the appropriate provision of implant-retained fixed prostheses for maxillary edentulism that fulfill minimal functional, biologic, and esthetic criteria.

Health Care Burden
Among the many people afflicted with maxillary edentulism (> 20 million), some will pursue comprehensive rehabilitation using a fixed prosthetic solution. Compared to removable solutions using conventional dentures or implant-supported overdentures, this treatment is complex and significantly more expensive. The potential complications that influence biologic responses to implants, component failure, esthetic limitations, and phonetic complications add to the burden of care. A limited subset of the edentulous population will accept the financial burdens associated with this treatment.
Methods: systematic review and clinical experience

Key Action Statements
Prosthodontists and restorative dentists should provide the option of a maxillary implant-retained fixed prosthesis to patients who *(1)* are unable to adapt to a removable prosthesis (psychologic or physiologic), *(2)* have a desire for or will benefit from a fixed solution, and *(3)* can afford the expense of acquiring an implant-supported fixed prosthesis, and then maintaining it for their lifetime.

A maxillary implant-retained fixed prosthesis can provide rehabilitation with as few as four splinted implants. Greater numbers of implants are used to account for generalized low bone quality, greater function (eg, bruxers), and segmented prostheses.

The prosthesis may be constructed using cement retention or screw retention.

The maxillary implant-retained fixed prosthesis should function to satisfy patients' phonetic, esthetic, and masticatory needs, and be designed in a manner that supports long-term hygiene and oral mucosal health.

Any decision to proceed with maxillary implant-retained fixed prosthesis therapy should be a joint decision made by the surgical dentist, restorative dentist, and patient that is informed by the provision or presence of an ideal conventional denture or overdenture.

CLINICAL PRACTICE GUIDELINES

- Prosthodontists and restorative dentists should provide all patients with immediate, interim, or complete dentures when patients will become or are edentulous.
- A maxillary denture can provide rehabilitation without dental implants and represents a treatment choice when complex restorative needs cannot be met by the professional team or addressed financially.
- The maxillary denture should be stable and retentive; function to satisfy patients' phonetic, esthetic, and masticatory needs; and be in sufficient physical state to support hygiene and oral mucosal health. Dentures not meeting these therapeutic goals should be replaced or alternative reconstruction using implants should be considered.
- Dentures provide functional and esthetic guidelines for additional implant-supported prostheses.

ACKNOWLEDGMENTS

The authors reported no conflicts of interest related to these clinical practice guidelines.

AO 2014 Summit Attendees

Tara Aghaloo, DDS, MD, PhD
UCLA School of Dentistry
Los Angeles, California

Veeratrishul Allareddy, BDS, MS
University of Iowa College of Dentistry
Iowa City, Iowa

Edward Amet, DDS, BS, MSD
Overlook Park, Kansas

Gustavo Avila-Ortiz, DDS, MS, PhD
University of Iowa College of Dentistry
Iowa City, Iowa

Barry Bartee, DDS, MD
Osteogenics (Observer)

P. Mark Bartold, DDS, PhD
University of Adelaide
Adelaide, SA, Australia

Francesco Bassi, MD, DDS
University of Turin Dental School
Torino, Italy

Lori Bateman
Quintessence (Observer)

Francine Berkey
The Avenues Co
Flagstaff, Arizona

Ed Bedrossian, DDS
San Francisco, California

Avinash Bidra, BDS, MS
University of Connecticut
School of Dental Medicine
Farmington, Connecticut

Bradley Bockhorst, DMD
Zimmer (Observer)

Michael Bornstein, DMD, PhD
University of Bern
Bern, Switzerland

Lawrence Brecht, DDS
New York, New York

Nancy Deal Chandler, MA
ACP (Observer)

David Cochran, DDS, MS, PhD
University of Texas
Health Science Center
San Antonio, Texas

Paulo G. Coelho, DDS, MS, PhD
NYU College of Dentistry
New York, New York

Lyndon Cooper, DDS, PhD
UIC College of Dentistry
Chicago, Illinois

Susan Cutler, DMD
OraPharma
Bridgewater, New Jersey

C. Edgar Davila, DDS, MS, CDT
Tampa, Florida

Marco Degidi, DDS, MD
Bologna, Italy

George Duello, DDS, MS
St Louis, Missouri

Steven Eckert, DDS, MS
Byron, Minnesota

Julie Elpers, DMD
Somerville, Massachusetts

Rolf Ewers, MD, DMD, PhD
Vienna, Austria

John Forbes
AAP (Observer)

Luis Fujimoto, DMD
New York, New York

German Gallucci, DMD
Harvard School of Dental Medicine
Boston, Massachusetts

Scott Ganz, DMD
Fort Lee, New Jersey

Joseph Gian-Grasso, DMD
Philadelphia, Pennsylvania

William Giannobile, DDS, DMSc
University of Michigan
School of Dentistry
Ann Arbor, Michigan

Rand Harlow, DDS
UIC School of Dentistry
Chicago, Illinois

Alan Herford, DDS, MD
Loma Linda University School of Dentistry
Loma Linda, California

Steve Herrington
Biomet (Observer)

Vincent Iacono, DMD
Stony Brook University
School of Dental Medicine
Stony Brook, New York

Robert Jaffin, DMD
Hackensack, New Jersey

Ole Jensen, DDS, MS
Denver, Colorado

Asbjørn Jokstad, DDS, PhD
UiT: The Arctic University of Norway
Tromsø, Norway

Darnell Kaigler, DDS, MS
Detroit, Michigan

Wataru Katagiri, DDS, PhD
Nagoya University
Nagoya, Aichi, Japan

Hideaki Katsuyama, DDS, PhD
Yokohama, Japan

Fouad Khoury, DMD, PhD
Olsberg, Germany

Kent Knoernschild, DMD, MS
UIC College of Dentistry
Chicago, Illinois

Ernest Lam, BSc, DMD, MSc, PhD
University of Toronto
Toronto, Ontario, Canada

Bach Le, DDS, MD
Whittier, California

Liran Levin, DMD
Givat-Shmuel, Israel

Anna-Karin Lundegren, DDS, PhD
Dentsply
Molndal, Sweden

Sanjay Mallya, BDS, MDS, PhD
UCLA School of Dentistry
Los Angeles, California

Jay Malmquist, DMD
Portland, Oregon

Paulo Malo, DMD
Lisbon, Portugal

William Martin, DMD, MS
University of Florida
College of Dentistry
Gainesville, Florida

Thomas McGarry, DDS
Oklahoma City, Oklahoma

Ed McGlumphy, DDS, MS
Ohio State University
College of Dentistry
Columbus, Ohio

Henny Meijer, PhD
University Medical Center Groningen
Groningen, The Netherlands

Luiz Meirelles, DDS, PhD
University of Rochester Medical Center
Rochester, New York

Michael Miloro, DMD, MD
UIC College of Dentistry
Chicago, Illinois

Craig Misch, DDS, MDS
Sarasota, Florida

Pablo Galindo Moreno, DDS, PhD
Granada, Spain

Dean Morton, BDS, MS
Indiana University School of Dentistry
Indianapolis, Indiana

Peter Moy, DMD
UCLA School of Dentistry
Los Angeles, California

Salvador Nares, DDS
UIC College of Dentistry
Chicago, Illinois

Richard Nejat, DDS
New York, New York

William Nelson, DDS
AAOMS (Observer)

Marc Nevins, DMD, MMSc
Boston, Massachusetts

Russell Nishimura, DDS
Westlake Village, California

Michael Norton, BDS, FDS
London, England

Tom Olsen
Nobel Biocare (Observer)

Tak Ogawa, DDS, PhD
UCLA School of Dentistry
Los Angeles, California

Joan Otomo-Corgel, DDS, MPH
AAP (Observer)

Abigail Ovlinger
Straumann (Observer)

Stephen Parel, DDS
Dallas, Texas

Michael Pikos, DDS
Palm Harbor, Florida

Alan Pollack, DDS
New York, New York

Stephen Porter, DDS
West Palm Beach, Florida

Marc Quirynen, DDS
Catholic University Leuven
Leuven, Belgium

Franck Renouard, DDS
Paris, France

Robert Riley, CDT
Henry Schein (Observer)

Hector Rios, DDS
University of Michigan
School of Dentistry
Ann Arbor, Michigan

George Romanos, DDS, DMD, PhD
Stony Brook University
School of Dental Medicine
Stony Brook, New York

Scott Root
Dentsply (Observer)

Steven Rosenstein, DMD
Aventura, Florida

Julie Rule
Quintessence (Observer)

Steven Sadowsky, DDS
University of the Pacific
School of Dentistry
San Francisco, California

Thomas Salinas, DDS
Mayo Clinic
Rochester, Minnesota

Mariano Sanz, DDS, PhD
Complutense University of Madrid
Madrid, Spain

Paul Schnitman, DDS, MSD
Wellesley Hills, Massachusetts

Anton Sculean, DMD, MS, PhD
Radboud University Medical Center
Nijmegen, The Netherlands

Steve Sembler
OraPharma (Observer)

Edward Sevetz, DMD
Orange Park, Florida

Wim Slot, DDS, PhD
University Medical Center Groningen
Groningen, The Netherlands

Amerian Sones, DDS, MS
Baylor University College of Dentistry
Dallas, Texas

Daniel Spagnoli, DDS, PhD
LSU School of Dentistry
New Orleans, Louisiana

Clark Stanford, DDS, PhD
UIC College of Dentistry
Chicago, Illinois

Christian Stappert, MS, DDS, PhD
University of Maryland
School of Dentistry
Baltimore, Maryland

Rick Sullivan, DDS
Nobel Biocare (Observer)

Robert Taft, DDS
Bethesda, Maryland

James Taylor, DMD, MA
Ottawa, Ontario, Canada

Thomas Taylor, DDS, MSD
University of Connecticut
School of Dental Medicine
Farmington, Connecticut

Ghadeer Thalji, BDS, PhD
University of Iowa College of Dentistry
Iowa City, Iowa

Cristiano Tomasi, DDS, MSc, PhD
Salgrenska Academy at
University of Gothenburg
Göteborg, Sweden

Gil Triplett, DDS, PhD
Baylor University College of Dentistry
Dallas, Texas

Frank Tuminelli, DMD
ACP (Observer)

Istvan Urban, DMD, MD, PhD
Budapest, Hungary

Stephen Wallace, DDS
Waterbury, Connecticut

Hom-Lay Wang, DDS, MSD, PhD
University of Michigan
School of Dentistry
Ann Arbor, Michigan

Haibo Wen, PhD
Zimmer
Carlsbad, California

Ann Wennerberg, DDS, PhD
Malmo University
Malmo, Sweden

Stephen Wheeler, DDS
Encinitas, California

Ulf Wikesjo, DDS, DMD, PhD
Georgia Health Sciences University
Augusta, Georgia

Johan Wolfaardt, BDS, MD, PhD
University of Alberta
Edmonton, Alberta, Canada

Mark Wong, DDS
University of Texas
Houston, Texas

Nicola Zitzmann, MD
University of Basel Dental School
Basel, Switzerland

Yuval Zubery, DMD
Ramat HaSharon, Israel