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REVIEW ARTICLE

Alveolar ridge preservation: Complications and cost-effectiveness

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1 | INTRODUCTION

Tooth extraction triggers a sequence of biologic events that ultimately lead to dimensional alterations of the hard and soft tissues that constitute the alveolar ridge (Figure 1).[1–3] The result of this physiologic remodeling process varies from site to site and from individual to individual depending on systemic and local factors, such as the thickness of the facial alveolar bone wall, or other characteristics of the local/site phenotype.[4–6] Relative to tooth replacement therapy with dental implants, additional bone and/or soft tissue augmentation is often required for proper management of sites that undergo extensive ridge remodeling. Nonetheless, these procedures involve additional costs, elongated treatment time, and higher risk of morbidity.[7–9]

Different interceptive therapies to attenuate postextraction alveolar ridge resorption have been proposed over the past several decades, such as partial extraction protocols,[10,11] orthodontic extrusion,[12–14] and "alveolar ridge preservation" therapy,[15,16] which consists of filling the alveolus with biomaterials, such as bone graft particles, with or without application of a sealing material (socket sealing).[17–22] Over the past two decades, numerous alveolar ridge preservation modalities have been tested in randomized controlled trials.[23–26] Though the effectiveness of alveolar ridge preservation has been demonstrated compared with unassisted healing (ie, no further intervention beyond standard-of-care tooth extraction),[27,28] it is also known that it cannot completely eliminate a certain degree of postextraction ridge resorption.[3,29] Furthermore, despite the potential influence of the underlying properties of the applied biomaterials on the range of outcomes, a specific alveolar ridge preservation approach that patently and predictably renders superior outcomes has yet to be identified.

Thus far, clinical research in this area has been primarily focused on testing the efficacy of different alveolar ridge preservation therapies by assessing the degree to which a particular modality can prevent postextraction dimensional changes and, therefore, reduce the need for additional ridge augmentation for facilitating tooth replacement therapy. However, other relevant aspects pertaining to alveolar ridge preservation therapy, such as complications and analysis of costs, have often been overlooked and should also be carefully considered. A complication is an unanticipated adverse event that arises following, and as a direct outcome of, a procedure or illness. Complications may be

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caused by treatment errors made by members of the health-care team in the planning or execution of an intervention, or by other pertinent factors, an example of which can be the lack of patient compliance. Cost-effectiveness can be defined as the degree to which an intervention renders a favorable outcome as a function of its cost. Therefore, cost-effectiveness is null or low in scenarios where a therapeutic intervention leads to no or minimal benefit. Though low cost-effectiveness may not necessarily be considered a complication per se, it may indeed carry additional expenses and other detrimental effects in the continuum of care, such as patient dissatisfaction. With this review we provide an evidence-based analysis of the complications and cost-effectiveness of different modalities of alveolar ridge preservation.

2 | SELECTION OF EVIDENCE

Alveolar ridge preservation in this review was defined as a treatment performed immediately after complete tooth extraction with the purpose of reducing the dimensional changes of the alveolar ridge, using a biomaterial filler (socket grafting) with or without socket sealing.

We conducted a comprehensive systematic search with a predefined set of specific criteria, to identify human randomized controlled trials in the topic of alveolar ridge preservation published between 1 January 2001 and 1 January 2020. Medline, Embase, Web of Science, Cochrane Central, and the grey literature were searched using the following terms: "tooth extract*" OR "dental extract*" OR "tooth socket" OR "alveolar ridge*" OR "socket preservation*" OR "socket grafting," combined with a list of alveolar ridge preservation techniques and biomaterials commonly reported in the literature. All issues of selected journals in the fields of periodontology and implant dentistry published between 1 January 2010 and 1 June 2022 were hand-searched, and references of previously published reviews[3,28–45] were also cross-checked to supplement the electronic systematic search. No language limitation was set for the inclusion of articles. Data abstraction and assessment of reporting quality were independently performed by two calibrated reviewers (SB, JM) using a prestructured data extraction form. Further details with regard to the search strategy performed and selection of evidence can be found in Appendix S1.

3 | COMPLICATIONS

3.1 | Definition of complications in the context of the dental alveolus

In the scope of this review, we defined complications as any unanticipated adverse event that occurs as a direct manifestation of tooth extraction and/or alveolar ridge preservation therapy. Complications may occur because of a treatment planning error, inadequate biomaterial selection, improper technical execution, or other factors that may affect the healing process, such as uncontrolled systemic conditions or poor patient compliance.

3.2 | Results of the systematic search and description of complications

Our systematic search identified a total of 143 trials on alveolar ridge preservation that specified the postoperative healing conditions of extraction sockets, of which 49 described the occurrence of a complication or an adverse event.[22,46–93]

Overall, the majority of studies reported uneventful healing after tooth extraction and alveolar ridge preservation, with only minor adverse events, such as pain or swelling, occurring during the early healing phase.[46,56,66,68,73,76,79,82,89,91,94] As pain and localized swelling are, to an extent, expected outcomes of any surgical intervention, and their reporting tends to be largely subjective, we did not address them as complications specifically related to alveolar ridge preservation. For the rest, we described the reported complications and, when feasible, calculated their incidence relative to the total number of extraction sockets in that treatment arm. In addition, the need for staged or simultaneous bone augmentation procedures in the context of implant placement was noted and assessed as a separate outcome.

3.2.1 | Complications after tooth extraction

Common local complications related to tooth extraction and unassisted socket healing (without application of any bone grafting biomaterial or a membrane) include alveolar osteitis, also known as "dry socket" or "alveolar osteitis," which is characterized by severe postoperative pain and halitosis due to failure in the development of a stable blood clot, or an acutely infected alveolus, diagnosed by the presence of pain and edema with or without suppuration and/or fever.[47,94] The occurrence of these two complications after unassisted socket healing was reported in two studies with an incidence in 4% and 20% of the extraction sites, respectively.[22,47]

3.2.2 | Complications in the context of alveolar ridge preservation

Earlier onset of complications and adverse events

In the context of alveolar ridge preservation, complications can also be related to the use of biomaterials or the technical approach employed. The presence of an infection during the first two postoperative weeks was reported in six studies, with an incidence rate ranging from 2.8% to 9.1% of the total extraction sites.[60,62,84,88,92,93] An atypically delayed healing accompanied by persistent swelling, intense erythema, spontaneous bleeding, and ulceration that persisted after the first 2 weeks was also described in two studies.[78,89] Adverse events associated with a given

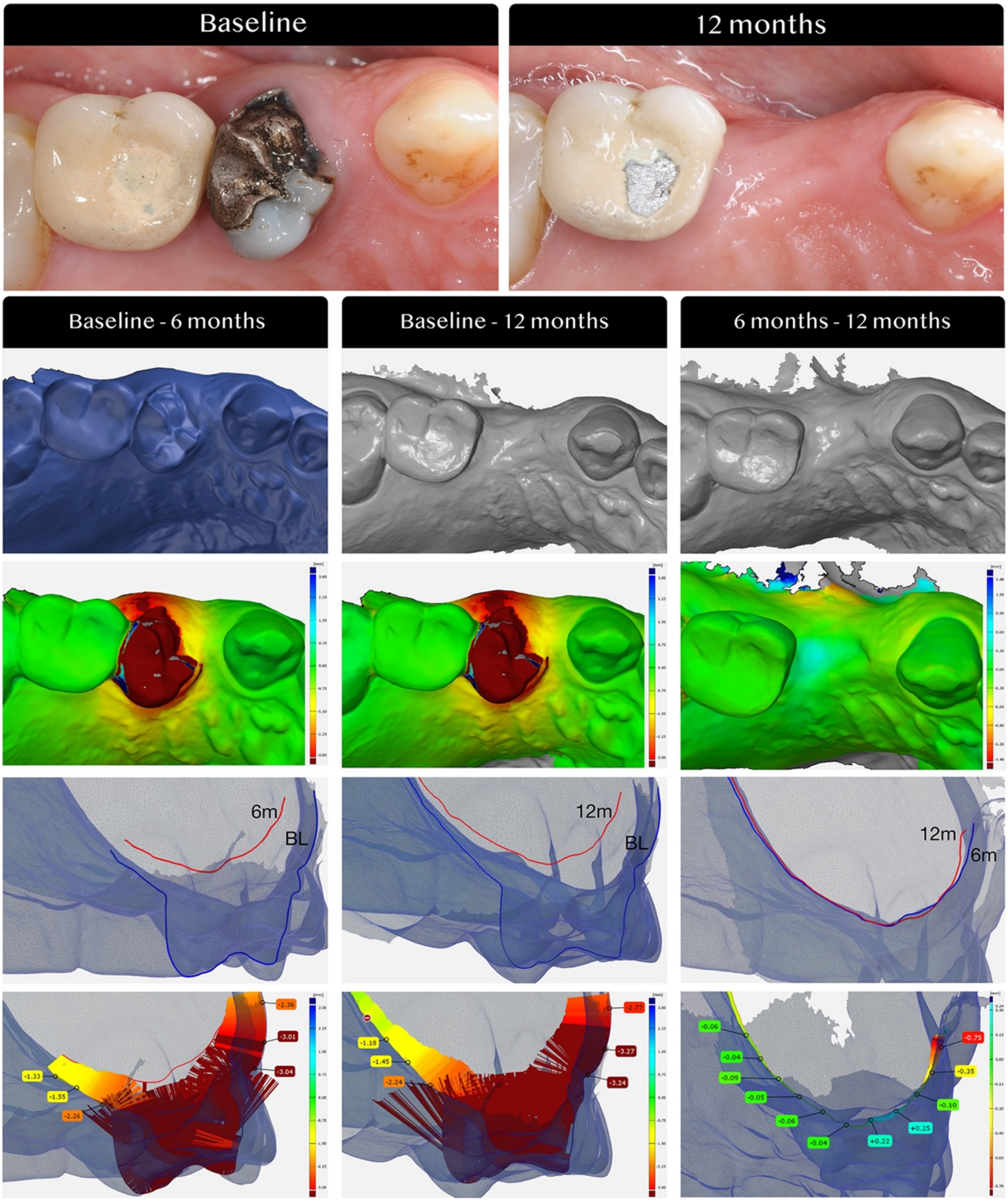

FIGURE 1 An example of linear and volumetric changes resulting from unassisted healing of an extraction socket throughout the initial 12-month healing period. The alveolar ridge has undergone significant reduction in total volume as a consequence of the significant resorption on the midcrestal horizontal (width) and midbuccal vertical (height) aspects, most of which was confined to the early healing stages, primarily affecting the facio-coronal region. BL, baseline

technique or biomaterial included the premature loss of bone graft particles with an incidence rate of 2.9%-14.3%,[66,74,84,89] membrane exposure when primary closure is attempted,[95] membrane perforation of the mucosa,[69] premature exfoliation of nonabsorbable membranes,[53,60,65,74,84,89] and loss of keratinized mucosal width.[65,80,90]

Barone et al[53] reported an incidence rate of 12.5% for membrane exposure at sites where a full-thickness flap was raised and approximated to achieve primary closure. The same study also reported an average loss of 1.7 mm in keratinized mucosal width, in contrast to the flapless treatment group that healed by secondary intention showing an increase of 1.8 mm in keratinized mucosa.[53] Similar findings were also described by Engler-Hamm et al,[65] who reported a loss of keratinized mucosa width in 100% of sites that underwent flap advancement and primary wound closure, averaging to approximately 4 mm. In molar sites, however, two studies reported a loss of keratinized mucosa after unassisted healing and no primary closure, because of a lingual and coronal shift of the mucogingival junction.[80,90]

Although these adverse events may not necessarily lead to unfavorable dimensional changes that would interfere with conventional implant placement or an alteration of the biologic characteristics of surrounding tissues, their occurrence may require additional treatment prior to, at the time of, or following implant placement. For example, given the emerging evidence supporting the importance of keratinized mucosa on peri-implant health and patient comfort,[96,97] an insufficient amount of keratinized mucosal width may warrant soft tissue augmentation in many clinical scenarios. Furthermore, despite reports stating that, after alveolar ridge preservation, periodontal parameters such as probing depth, recession, and clinical attachment level remain virtually unchanged,[67,84] some other studies have documented a minor increase in recession depth on teeth adjacent to the extraction site.[58,98] This correlates with results of clinical studies that documented the loss of vertical ridge height on the mesial and distal aspects of an extraction socket.[3,17,19,51]

Delayed adverse events and complications

In addition, the incidence of situations that require ridge augmentation and delayed implant placement or implant placement with simultaneous bone augmentation was assessed. The main goal of alveolar ridge preservation therapy is to attenuate alveolar ridge resorption and, in the context of delayed implant placement, to allow for proper implant placement in the ideal prosthetically planned position with no further augmentation. Therefore, the need for performing additional ridge augmentation indicates that the expected outcomes of alveolar ridge preservation therapy were not yielded, which can be considered a complication, in spite of not being an adverse event derived from pathologic inflammation or disease per se (such as an infection, etc).

The incidence of insufficient bone availability for a standard implant placement requiring staged implant placement or simultaneous bone augmentation at sites that had previously undergone alveolar ridge preservation ranged from 2.7% to 57%.[49,62,63,77]

Nonetheless, it must be acknowledged that a direct causal relationship between these occurrences and the alveolar ridge preservation modality cannot be established, as an unfavorable ridge remodeling may be associated with a wide range of local and systemic factors that are independent from the employed therapeutic approach. Though these numbers may carry a certain degree of selection bias, studies in this field have consistently described higher incidence rates of inadequate ridge dimensions for "control sites" that received no treatment beyond tooth extraction (unassisted healing), compared with sites that were assigned to the "test" group, and received alveolar ridge preservation therapy. In addition, delayed adverse events, such as encountering large amounts of nonintegrated bone graft particles at the time of surgical reentry, lack of implant primary stability (4%-10%), and failure of implant osseointegration (3.3%-20%) have also been reported in the literature.[63,74,77,85]

Lastly, another possible scenario, despite performing alveolar ridge preservation, is a dimensionally deficient ridge or an unfavorable situation at the time of implant surgery that warrants simultaneous bone augmentation.[50,52,53,59–62,64,65,70,77,79,81,85,86,88,90,92] In contrast to early implant placement protocols,[99] alveolar ridge preservation is particularly beneficial when surgical reentry for implant placement is planned after a minimum healing period of approximately 3 months.[100] A recent study found that 80% of extraction sites that were treated with a deproteinized bovine bone mineral and 10% collagen, covered with a collagen matrix, still required additional grafting at 2 months for an early implant placement (compared with 90% of sites in the unassisted healing group).[88]

Among selected comparative trials with at least a 3-month healing period between tooth extraction and implant placement, an average of 54% of sites that served as untreated controls required additional bone augmentation at the time of implant placement,[50,52,59,61,64,68,86,88,90] ranging from 25%[90] to 100%.[59] Conversely, extraction sites that were filled with either an allograft or a xenograft particulate material and covered with a barrier membrane or a fast-absorbing collagen dressing required significantly less additional bone augmentation at the time of implant placement (approximately 15% for xenografts,[52,53,59,60,70,77,80,85,88] and 27% for allografts[50,62,64,66,90,92]) (Figure 2). Though the feasibility to place an implant in an ideal prosthetic position and the need for additional bone augmentation are the prerogative of the clinician, and therefore subjective, it can be concluded that alveolar ridge preservation significantly decreases the need for additional bone grafting at the time of implant placement.

Table 1 displays a summary of the possible complications that may derive from tooth extraction and alveolar ridge preservation relative to their timeframe, as well as implant placement–related adverse events, as reported in the selected articles.

4 | COST-EFFECTIVENESS

4.1 | Methodology

4.1.1 | Restriction of evidence

For cost-effectiveness, to increase methodological rigor and clinical relevance, we substantially limited the original inclusion criteria to studies that uniformly reported changes in horizontal ridge width (within the most coronal 2 mm of the crest) and/or midbuccal

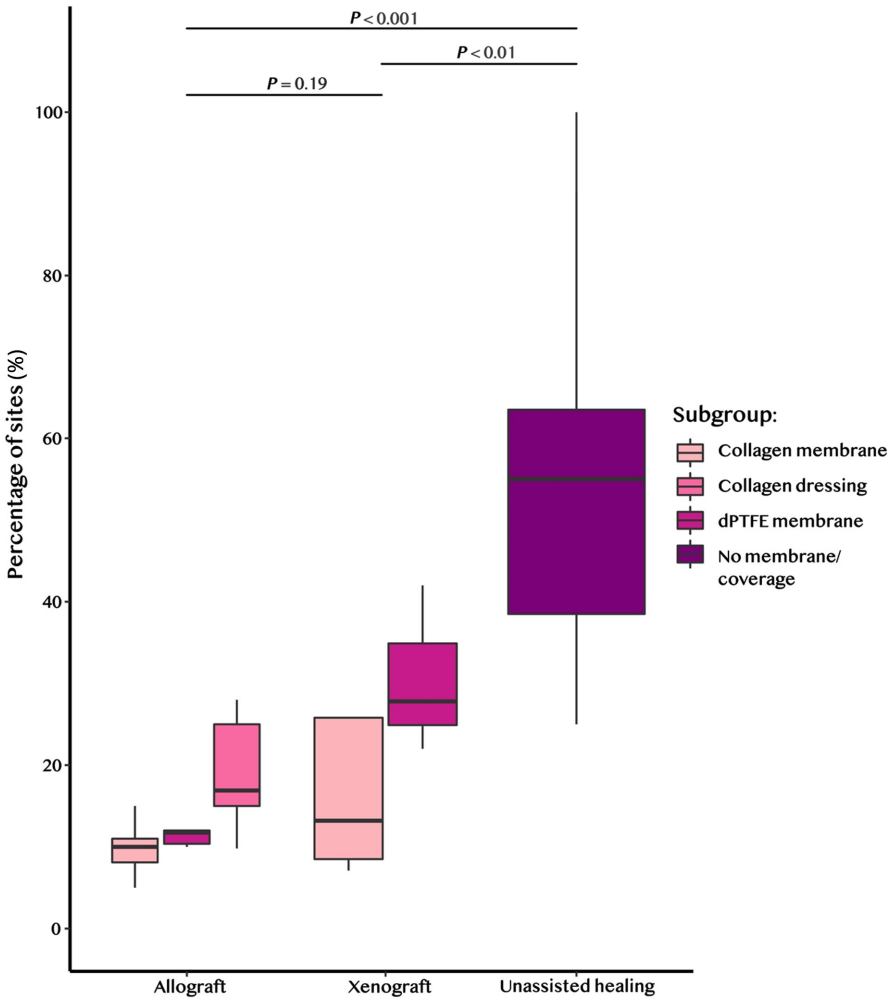

FIGURE 2 Percentage of sites requiring additional bone augmentation at the time of implant placement. dPTFE, dense polytetrafluoroethylene

vertical ridge height. To avoid collinearity, only data from nonmolar extraction sites that exhibited no more than 50% loss the of buccal plate after tooth extraction were considered. In addition, studies must have performed alveolar ridge preservation through utilization of a nonautogenous bone graft (either an allograft, a xenograft, or an alloplastic material) with or without socket sealing with a barrier membrane or a dressing and allowed for a minimal healing period of 3 months after tooth extraction.

Clinical outcomes must have been assessed in a standardized and reliable manner, either clinically or with the use of three-dimensional radiographic imaging. Owing to insufficient available data, treatments that involved the use of autogenous soft tissue grafts or substitutes in concomitance with alveolar ridge preservation were not included. Additionally, studies that involved the use of healing enhancers, biologics, or other interim interventions that may have interfered with the outcomes of interest were excluded.

Corresponding authors of studies with unclear methodology or missing critical information were contacted. If no response was received or the ambiguity was not resolved, the study was not included in the analysis.

Methodological quality of the included trials was evaluated using the Cochrane checklist[101] for incorporation into the analysis, along with information on study sponsorship for any potential influence of bias on the study results. However, no study was excluded solely based on the assessment of the risk of bias or information on sponsorship. Details pertaining to study exclusion are displayed in Appendix S1.

4.1.2 | Identification of costs

In a dental practice, the costs that arise from a treatment typically include the price of the materials utilized, as well as the reimbursement of time, staff, and the overhead.

In our analysis, as all the included trials described a minimally invasive tooth extraction protocol and the treatment of compromised extraction sockets was not allowed (those sites with more than 50% loss/damage to the buccal plate were not eligible), we considered the costs associated with standard minimally invasive tooth extraction (anesthesia, surgical instruments, suturing materials, etc) to be negligible. As it pertains to the aim of our cost-effectiveness analysis and within our criteria for study inclusion, these costs would not differ if alveolar ridge preservation were to be performed after tooth extraction, nor can they influence the treatment outcomes to a meaningful degree. We made these assumptions to facilitate precise accounting; therefore, we set the cost of unassisted socket healing

TABLE 1 Postoperative complications associated with alveolar ridge preservation reported among the selected randomized controlled trials from the systematic search, with their relative incidence per study, when available

Reported timeframe	Complication/adverse event	Study (relative incidence[a])
Within the first 2 wk	Infection	Cook and Mealey (2013)[60] (4.5%), Corning and Mealey (2019)[62] (2.3%), Parashis et al (2016)[84] (4.3%), Thoma et al (2020)[88] (2.8%), Wood and Mealey (2012)[92] (9.1%), Zwahlen et al (2009)[93] (20%)
	Membrane exfoliation, premature exposure or perforation	Barone et al (2014)[53] (12.5% in group with primary wound closure), Fotek et al (2009)[69] (70%), Cook and Mealey (2013)[60] (2.3%)
	Loss/extravasation of bone graft particles	Eskow and Mealey (2014)[66] (2.9%), Hoang and Mealey (2012)[74] (6.7%), Parashis et al (2016)[84] (4.3%), Toloue et al (2012)[89] (14.3%)
	Wound dehiscence	Cha et al (2019)[59] (2.6%)
After the initial 2 wk	Bleeding	Lee et al (2020)[78] (13.3%)
	Persistent mucosal ulceration	Lee et al (2020)[78] (3.3%), Toloue et al (2012)[89] (7.1%)
	Loss of keratinized mucosal width	Barone et al (2014),[53] Brkovic et al (2012)[54] (100% of cases with primary intention healing), Engler-Hamm et al (2011)[65] (NA), Walker et al (2017)[90] (NA), Lim et al (2019)[80] (NA)
	Increased recession depth on the adjacent sites	Cardaropoli et al (2012)[58] (NA)
Related to the implant therapy	Large amount of loose, nonintegrated biomaterial upon surgical reentry	De Coster et al (2011)[63] (NA)
	Lack of implant primary stability due to soft bone substrate	De Coster et al (2011)[63] (10%[b]), Lai et al (2020)[77] (56%[b]), Patel et al (2013)[85] (4%[b])
	Additional bone augmentation required at the time of implant placement (simultaneous approach)	Avila-Ortiz et al (2020)[50] (11.5%[b] and 48.1%[c]), Barone et al (2013)[52] (7.1%[b] and 46.4%[c]), Barone et al (2014)[53] (8.5%), Cha et al (2019)[59] (57.1%[b] and 100%[c]), Cook and Mealey (2013)[60] (13.2%[b]), Coomes et al (2014)[61] (43.7%[c]), Corning and Mealey (2019)[62] (8.1%[b]), Duong et al (2020)[64] (9.8%[b] and 25%[c]), Eskow and Mealey (2014)[66] (25.7%[b]), Gholami et al (2012)[70] (12.5%[b]), Lai et al (2020)[77] (27.8%), Lim et al (2020)[79] (77.8%), Llanos et al (2019)[81] (10.8%[b]), Neiva et al (2008)[83] (33%[c]), Patel et al (2013)[85] (68%[b]), Pelegrine et al (2010)[86] (33.3%[c]), Walker et al (2017)[90] (10%[b] and 25%[c]), Wood and Mealey (2012)[92] (15.2%[b])
	Bone augmentation required prior to implant placement (staged approach)	Arbab et al (2016)[49] (12.5%)[b], Coomes et al (2014)[61] (37.5%), Corning and Mealey (2019)[62] (2.7%[b]), De Coster et al (2011)[63] (33.3%[b] and 7%[c]), Kutkut et al (2012)[76] (12.5%[c]), Lai et al (2020)[77] (5.6%[b])
	Failure of osseointegration	De Coster et al (2011)[63] (20%[b] and 23.1%[c]), Hoang and Mealey (2012)[74] (3.3%[b])

Abbreviation: NA, NA refers to when the percentage of the incidence of the specific event could not be estimated.

[a]The relative incidence indicates the per study incidence rate of the event.

[b]Incidence following alveolar ridge preservation.

[c]Incidence in nongrafted sites.

without any other intervention as the initial starting point to zero. We valued the total cost of an alveolar ridge preservation modality per study arm to consist of the price of the bone grafting material used to fill the alveolar socket and the price of the socket sealing material/agent, if employed. The costs were obtained directly from the respective manufacturers according to the standard market price in North America in US dollars as of July 2020.

4.1.3 | Analysis of effectiveness and cost

The performance of each treatment modality was evaluated based on linear dimensional changes of crestal horizontal (width) and mid-buccal vertical (height) from baseline (tooth extraction and ridge preservation) until a minimum healing period of 3 months. A linear mixed-regression model was fit to the study arm–level results, using changes in ridge width and height as the outcomes, with reference costs for the bone graft and socket sealing materials as predictors, as well as the study arm's follow-up time. Study arms were weighted by sample size and clustered by publication. Similar to methodologies applied in previous work,[96,102–104] fixed covariates such as flap reflection and primary wound closure were included to explore interactions and control for potential influence on the results, and random effects to capture unique intercepts for study, study arm, and studies with a parallel arm vs a split-mouth design that contributed to the analysis with both treatment arms. Correlations with funding, study setting, the method of outcome assessment (cone-beam computed tomography vs clinical assessment), and the quality appraisal according to the Cochrane checklist (low, medium, high) were also tested and, if needed, controlled for in the model.

To test the robustness of our results with respect to the material costs and potential subsequent unbalanced inflation, additional sensitivity analyses were conducted, first based on the average product costs per types of bone graft and socket sealing agents, as well fractional increased costs for the two components, to observe for a significant shift in any of the comparisons. Rainforest and dot plots were used to illustrate the model results. Parallel coordinate plots were utilized to assess relationships in multivariate data and observe for patterns between components of cost and alveolar ridge resorption. The costs of the included composite treatment modalities as stated among study arms were plotted against their effectiveness in terms of the modeled expected reduction of alveolar ridge resorption for a nonmolar extraction site at 4 months. All model assumptions were tested and fixed for covariates.

To assess the relationship between different bone grafts and socket sealing materials, as well as the unique contribution of each biomaterial to the outcomes, a similar mixed model was fit using the desegregated costs to the study arm–level results, with the same outcomes (changes in ridge width and height) as predictors.

4.2 | Synthesis of evidence

A total of 60 eligible treatment arms from 36 randomized controlled trials that met the inclusion criteria were identified.[17–19,50,51,60,62,66,67,70,72,75–78,86,87,89,91,92,98,105–119] Seventeen studies had included a control group of unassisted healing after extraction,[17–19,50,51,67,75,76,86,87,98,105,106,108,109,111,118] whereas the rest compared different ridge preservation modalities. A particulate bone allograft, either a mineralized cancellous bone,[62,118] freeze-dried bone allograft,[62,66,92,107,110,112] demineralized freeze-dried bone allograft,[17,91,92,116,117] or a combination of the latter two,[50,72,107,115] was used in 23 study arms. Fifteen treatment arms involved the application of a xenograft, either bovine bone mineral,[60,70,77,106,114,116,119] porcine bone mineral,[51,77,111] or a bovine bone mineral with 10% collagen.[78,113,114,117] Lastly, four studies employed an alloplast, either calcium sulfate,[19,89] beta-tricalcium phosphate,[18] or a nanocrystalline hydroxyapatite.[70]

An absorbable barrier membrane was used in 20 arms,[17,51,60,62,70,78,106,111,112,114,116,117,119] whereas a nonabsorbable dense polytetrafluoroethylene membrane was utilized in 10 treatment groups.[50,72,77,107,110,115] An absorbable collagen dressing was used to cover the underlying bone graft in eight treatment arms,[66,92,109,113,118] whereas in three studies, in which an alloplastic material was used, no socket sealing was performed.[18,19,89] An overview of the characteristics of the selected studies is presented in Table 2.

4.2.1 | Effectiveness of alveolar ridge preservation

Dimensional changes after unassisted socket healing

Figure 3 illustrates the average dimensional changes after tooth extraction that typically follow unassisted socket healing of a well-preserved and uncompromised nonmolar socket (with intact, or at the most with 50% loss of buccal plate) compared with alveolar ridge preservation. Figure 4 displays the estimated amount of resorption in different dimensions of nonmolar sites that exhibited no more than 50% loss of buccal plate at the time of extraction after unassisted healing, based on the constructed model fixed for a healing time of 4 months. According to the evidence selected, the greatest linear resorption occurs on the most facial and coronal aspect of the alveolar ridge in the horizontal dimension for a mean loss of approximately 3.4 mm, which translates into approximately 40% of the initial ridge width, half of which

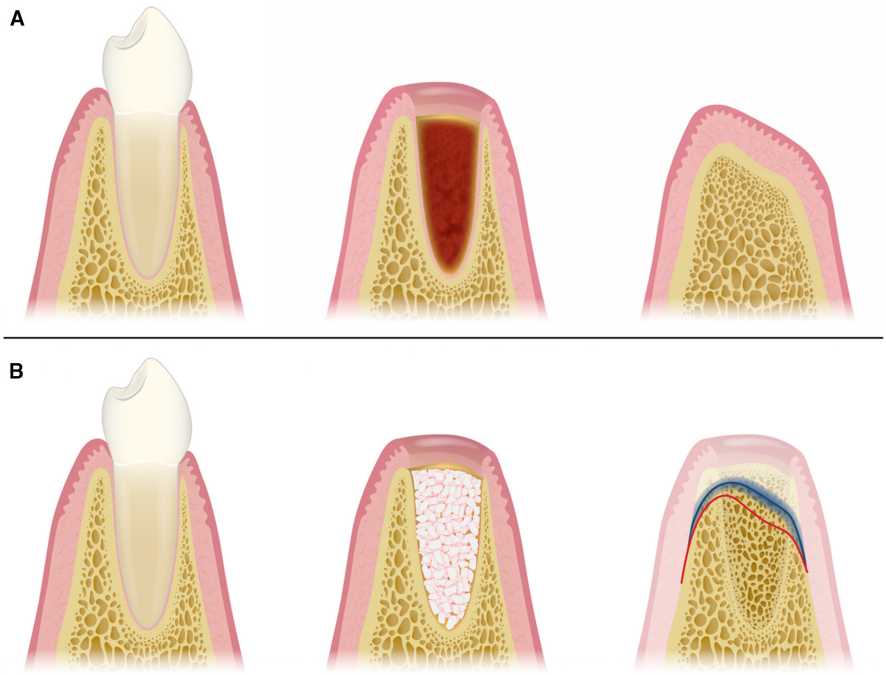

FIGURE 3 Illustration of the dimensional changes that typically follow, A, unassisted socket healing compared with, B, alveolar ridge preservation therapy after approximately 4 months of healing time. The red line in B illustrates an estimate of the expected alveolar ridge resorption following unassisted healing, and the blue line shows the average anticipated ridge resorption with alveolar ridge preservation, which may vary depending on the approach utilized (transparent blue shade represents the range of outcomes)

TABLE 2 Summarized characteristics of the selected randomized controlled trials, based on the systematic search and inclusion criteria, for the quantitative analyses and assessment of cost-effectiveness

Study	Final follow-up time point[a]	Mean age of patients (y)	Number of patients analyzed, extraction sockets	Treated sites	Flap elevation, primary wound closure	Treatment	Average baseline midcrestal (horizontal) width (mm)	Average midcrestal width (horizontal) changes (mm)[b]	Average midbuccal height (vertical) changes (mm)	Method of outcome assessment
Aimetti et al (2009)[19]	3 mo	50.8	18, 18	Anterior maxilla	No, no	Unassisted healing	10 (0.7)	−3.2	−1.2	Clinical (modified digital calipers and acrylic stents)
		51.8	22, 22	Anterior maxilla	No, no	Medical-grade calcium sulfate hemihydrate	9.4 (2.2)	−2	−0.5	
Araújo et al (2015)[105]	4 mo	NA	14, 14	Maxillary incisors, canines, premolars	No, no	Unassisted healing			−3.6	Cone-beam computed tomography
Avila-Ortiz et al (2020)[50]	14 wk	57.24	27, 27	Nonmolar and nonmandibular incisors	No, no	Unassisted healing	9.26 (0.37)	−1.68	−1.7	Cone-beam computed tomography
		58.37	26, 26	Nonmolar and nonmandibular incisors	No, no	70% cortical mineralized freeze-dried bone allograft and 30% cortical demineralized freeze-dried bone allograft + dense polytetrafluoroethylene membrane	9.36 (0.38)	−1.07	−0.9	
Azizi and Moghadam (2009)[106]	6 mo	37.5	15, 40	Nonmolar sites	No, no	Unassisted healing	11.2 (0.6)	−4.1	−4.2	Clinical (template and periodontal probe)
		37.5	15, 40	Nonmolar sites	No, no	Demineralized bovine bone mineral particles + non-cross-linked collagen membrane	10.9 (1.4)	−2.6	−0.9	
Barone et al (2008)[51]	7 mo	NA	20, 20	Maxillary incisors, canines, premolars; mandibular canines and premolars	Yes, yes	Unassisted healing	10.8 (0.8)	−4.5	−3.6	Clinical (periodontal probe and customized acrylic stents)
		NA	20, 20	Maxillary incisors, canines, premolars; mandibular canines and premolars	Yes, yes	Cortico-cancellous porcine-derived bone graft + non-cross-linked collagen membrane	10.6 (1)	−2.5	−0.7	

TABLE 2 (Continued)

Study	Final follow-up time point[a]	Mean age of patients (y)	Number of patients analyzed, extraction sockets	Treated sites	Flap elevation, primary wound closure	Treatment	Average baseline midcrestal (horizontal) width (mm)	Average midcrestal width (horizontal) changes (mm)[b]	Average midbuccal height (vertical) changes (mm)	Method of outcome assessment
Borg and Mealey (2015)[107]	21 wk (average 19 wk)	52	20, 20	Maxillary nonmolar	Yes, no	100% cortical mineralized freeze-dried bone allograft + dense polytetrafluoroethylene membrane	9.02 (1.57)	−1.19	0.26	Clinical (periodontal probe, stent, caliper)
	21 wk (average 18.6 wk)	52	21, 21	Maxillary nonmolar	Yes, no	70% cortical mineralized freeze-dried bone allograft and 30% cortical demineralized freeze-dried bone allograft + dense polytetrafluoroethylene membrane	9.07 (2.1)	−1.63	−0.25	
Brownfield and Weltman (2012)[108]	3 mo	NA	NA, 10	Maxillary and mandibular nonmolar	No, no	Collagen dressing				Cone-beam computed tomography (caliper for buccal plate measurement)
Clark et al (2018)[109]	3.5 mo	58	10, 10	Nonmolar sites	No, no	Collagen dressing		−2.9	−3.8	Clinical (periodontal probe and stent)
	3.6 mo	58	10, 10	Nonmolar sites	No, no	Freeze-dried bone allograft + collagen dressing		−2.5	−2.2	
Clementini et al (2019)[98]	4 mo	50.5	10, 10	Maxillary and mandibular anterior and premolars	Yes, no	Unassisted healing		−3.37	−0.83	Cone-beam computed tomography
Cook and Mealey (2013)[60]	5.18 mo	56	20, 21	Maxillary and mandibular incisors and premolars	Yes, no	Demineralized bovine bone mineral particles-C+non-cross-linked collagen membrane	9.1 (1.67)		−0.14	Clinical (periodontal probe, stent and caliper)
Corning and Mealey (2019)[62]	2.87 mo	59	20, 20	Nonmolar sites	Yes, no	Freeze-dried bone allograft + bovine pericardium membrane	9.8 (2.16)		−0.5	Clinical (acrylic stent and Castroviejo calipers)
	2.84 mo	59	17, 17	Nonmolar sites	Yes, no	Solvent-dehydrated bone allograft + bovine pericardium membrane	9.9 (2.12)		−0.2	

(Continues)

TABLE 2 (Continued)

Study	Final follow-up time point[a]	Mean age of patients (y)	Number of patients analyzed, extraction sockets	Treated sites	Flap elevation, primary wound closure	Treatment	Average baseline midcrestal (horizontal) width (mm)	Average midcrestal width (horizontal) changes (mm)[b]	Average midbuccal height (vertical) changes (mm)	Method of outcome assessment
Demetter et al (2017)[110]	18.4 wk	55.5	19, 19	Nonmolar sites	No, no	100% cortical freeze-dried bone allograft + dense polytetrafluoroethylene membrane	9.48 (1.76)		0.29	Clinical (periodontal probe, stent and calipers)
	18.7 wk	55.5	19, 19	Nonmolar sites	No, no	100% cancellous freeze-dried bone allograft + dense polytetrafluoroethylene membrane	9.71 (1.69)		−1	
	18.9 wk	55.5	20, 20	Nonmolar sites	No, no	50%/50% cortico-cancellous freeze-dried bone allograft + dense polytetrafluoroethylene membrane	8.93 (1.38)		0.1	
Eskow and Mealey (2014)[66]	21 wk (average 18.2 wk)	55.6	15, 15	Maxillary and mandibular premolars and incisors	No, no	Cortical freeze-dried bone allograft + collagen dressing	8.59 (1.36)		−0.5	Clinical (periodontal probe and calipers)
	21 wk (average 18.2 wk)	53.4	17, 17	Maxillary and mandibular premolars, canines and incisors	No, no	Cancellous freeze-dried bone allograft + collagen dressing	8.61 (1.5)		−1	
Festa et al (2013)[67]	6 mo		15, 15	Maxillary and mandibular premolars	Yes, yes	Unassisted healing	9.9 (1)	−3.7	−3.1	Clinical (acrylic template, K-files, calipers)
Gholami et al (2012)[70]	8 mo	44.6	12, 14	Nonmolar sites	Yes, yes	Demineralized bovine bone mineral particles + non-cross-linked collagen membrane	7.75 (1.55)	−1.07		Clinical (stent and caliper)
		44.6	12, 14	Nonmolar sites	Yes, yes	Nanocrystalline hydroxyapatite + non-cross-linked collagen membrane	7.36 (1.94)	−0.93		
Guarnieri et al (2017)[111]	3 mo	46.7	4, 4	Premolars	No, no	Unassisted healing		−3.51	−2.07	Clinical (probe and caliper)
		46.7	4, 4	Premolars	No, no	Porcine-derived bone graft + non-cross-linked collagen membrane		−0.47	−0.69	

TABLE 2 (Continued)

Study	Final follow-up time point[a]	Mean age of patients (y)	Number of patients analyzed, extraction sockets	Treated sites	Flap elevation, primary wound closure	Treatment	Average baseline midcrestal (horizontal) width (mm)	Average midcrestal width (horizontal) changes (mm)[b]	Average midbuccal height (vertical) changes (mm)	Method of outcome assessment
Hassan et al (2017)[72]	3 mo	54.8	9, 11	Nonmolar sites	No, no	Combination of demineralized freeze-dried bone allograft and freeze-dried bone allograft + dense polytetrafluoroethylene membrane	9.6 (1.6)	−2.72		Cone-beam computed tomography
Hong et al (2019)[112]	6 mo	48.5	14, 14	Nonmolar sites	Yes, yes	Freeze-dried bone allograft + non-cross-linked collagen membrane	8.61 (1.4)	−4.18	−0.95	Cone-beam computed tomography (caliper for buccal plate measurement)
		52.3	14, 14	Nonmolar sites	Yes, no	Freeze-dried bone allograft + cross-linked collagen membrane	8.43 (1.4)	−1.74	−0.6	
Iasella et al (2003)[17]	6 mo	56	12, 12	Nonmolar sites	Yes, no	Unassisted healing	9.1 (1)	−2.6	−0.9	Clinical (modified digital caliper and customized acrylic stents)
		56	12, 12	Nonmolar sites	Yes, no	Freeze-dried bone allograft + non-cross-linked collagen membrane	9.2 (1.2)	−1.2	1.3	
Jung et al (2013)[18]	6 mo	48	10, 40	Premolars, laterals incisors, central incisors, and canines	No, no	Unassisted healing	7.6	−3.3	−0.5	Cone-beam computed tomography
		59	10, 40	Premolars, laterals incisors, central incisors, and canines	No, no	Beta-tricalcium phosphate granules	7.87	−6.1	−2	
Karaca et al (2015)[75]	3 mo	46.7	10, 10	Anterior maxilla	No, no	Unassisted healing			−1.43	Cone-beam computed tomography
Kutkut et al (2012)[76]	3 mo	51	8, 8	Maxillary central and lateral incisors, canines, and premolars/ mandibular premolars	No, no	Collagen dressing		−1.7	−1.4	Clinical (probe and stent)

(Continues)

TABLE 2 (Continued)

Study	Final follow-up time point[a]	Mean age of patients (y)	Number of patients analyzed, extraction sockets	Treated sites	Flap elevation, primary wound closure	Treatment	Average baseline midcrestal (horizontal) width (mm)	Average midcrestal width (horizontal) changes (mm)[b]	Average midbuccal height (vertical) changes (mm)	Method of outcome assessment
Lai et al (2020)[77]	4.5 mo	57	16, 16	Single rooted teeth	Yes, no	Demineralized bovine bone mineral particles + dense polytetrafluoroethylene membrane	9.03 (0.83)			Clinical (probe with acrylic stents)
	4.4 mo	57	20, 20	Single rooted teeth	Yes, no	Porcine-derived bone graft + dense polytetrafluoroethylene membrane	0.74 (0.36)			
Lee et al (2020)[78]	3 mo	57.2	15, 15	Maxillary central and lateral incisors	No, no	Demineralized bovine bone mineral with 10% collagen + non-cross-linked collagen membrane		−1.57	−3.19	Cone-beam computed tomography
	5 mo	57.2	15, 15	Maxillary central and lateral incisors	No, no	Demineralized bovine bone mineral with 10% collagen + collagen dressing		−1.60	−3.30	
Morelli et al (2020)[113]	6 mo	56.4	12, 12	Nonmolar sites	No, no	Demineralized bovine bone mineral with 10% collagen + collagen dressing		−1.98		Cone-beam computed tomography
Nart et al (2017)[114]	5 mo	56.7	NA, 11	Maxillary central incisors/ mandibular canines/ maxillary and mandibular premolars	Yes, no	Demineralized bovine bone mineral particles + non-cross-linked collagen membrane	10.13 (0.74)	−0.91	−0.61	Cone-beam computed tomography
		56.7	NA, 11	Maxillary central incisors/ mandibular canines/ maxillary and mandibular premolars	Yes, no	Demineralized bovine bone mineral with 10% collagen + non-cross-linked collagen membrane	10.62 (2.15)	−1.53	−0.98	
Nelson and Mealey (2020)[115]	20 wk	59	19, 19	Single-rooted sites	Yes, no	70% cortical freeze-dried bone allograft, 30% cortical demineralized freeze-dried bone allograft + dense polytetrafluoroethylene membrane	10.76 (1.75)		−1	Clinical (probe, stent and calipers)

TABLE 2 (Continued)

Study	Final follow-up time point[a]	Mean age of patients (y)	Number of patients analyzed, extraction sockets	Treated sites	Flap elevation, primary wound closure	Treatment	Average baseline midcrestal (horizontal) width (mm)	Average midcrestal width (horizontal) changes (mm)[b]	Average midbuccal height (vertical) changes (mm)	Method of outcome assessment
Pelegrine et al (2010)[86]	6 mo	46.6	6, 15	Anterior maxilla	Yes, no	Unassisted healing		−2.46	−1.17	Clinical (titanium screw inserted in bone and probe)
Sadeghi et al (2016)[116]	6 mo	35.3	10, 10	Single-rooted sites	Yes, yes	Demineralized freeze-dried bone allograft + non-cross-linked collagen membrane	7.79 (0.89)	−2.3	−1.1	Clinical (probe, caliper, stent)
		35.35	10, 10	Single-rooted sites	Yes, yes	Demineralized bovine bone mineral particles + non-cross-linked collagen membrane	7.89 (0.63)	−2.26	−1.29	
Serrano Mendez et al (2017)[117]	6 mo	44	10, 10	Maxillary incisors, premolars; mandibular premolar	Yes, yes	Demineralized freeze-dried bone allograft + non-cross-linked collagen membrane	7.8 (1.5)	−1.4	0.5	Clinical (probe, stents, digital caliper)
		44.5	10, 10	Maxillary incisors, canine, premolars	Yes, yes	Demineralized bovine bone mineral with 10% collagen + non-cross-linked collagen membrane	8.7 (1.3)	−2.6	−0.4	
Spinato et al (2014)[118]	4 mo	48.5	11, 11	Anterior maxilla teeth, buccal bone thickness ≤1 mm	No, no	Solvent-dehydrated bone allograft + collagen dressing	7.18 (1.47)		−0.27	Clinical (probe, caliper)
		48.5	8, 8	Anterior maxilla teeth, buccal bone thickness >1 mm	No, no	Solvent-dehydrated bone allograft + collagen dressing	7.13 (0.83)		−0.38	
		48.5	6, 6	Anterior maxilla, buccal bone thickness ≤1 mm	No, no	Unassisted healing	8.17 (1.72)		−1.17	
		48.5	6, 6	Anterior maxilla, buccal bone thickness >1 mm	No, no	Unassisted healing	8.33 (1.36)		−0.50	

(Continues)

TABLE 2 (Continued)

Study	Final follow-up time point[a]	Mean age of patients (y)	Number of patients analyzed, extraction sockets	Treated sites	Flap elevation, primary wound closure	Treatment	Average baseline midcrestal (horizontal) width (mm)	Average midcrestal width (horizontal) changes (mm)[b]	Average midbuccal height (vertical) changes (mm)	Method of outcome assessment
Temmerman et al (2016)[87]	3 mo	54	11, 21	Maxillary and mandibular premolars and incisors	No, no	Unassisted healing		−5.4	−1.6	Cone-beam computed tomography
Toloue et al (2012)[89]	3 mo	49	12, 13	Nonmolar sites	No, no	Calcium sulfate	7.12 (1.6)			Clinical (probe, stents, caliper)
Vance et al (2004)[119]	4 mo	56	12, 12	Maxillary incisor, canine, premolars; mandibular canine, premolars	Yes, no	Demineralized bovine bone mineral particles + non-cross-linked collagen membrane	9.7 (1.2)	−0.5	0.7	Clinical (caliper, stent)
Whetman and Mealey (2016)[91]	19.1 wk	55.7	19, 19	Non-Molar sites	Yes, no	Demineralized freeze-dried bone allograft + collagen dressing	8.85		−1.18	Clinical (probe, stents and caliper)
Wood and Mealey (2012)[92]	19.8 wk	56.7	16, 16	Maxillary incisors, canines, premolars; Mandibular premolars	No, no	Demineralized freeze-dried bone allograft + collagen dressing	9.7 (1.13)	−2.18	−0.37	Clinical (probe, stents, caliper)
	19.2 wk	56.7	16, 16	Maxillary incisors, canine, premolars; mandibular premolars	No, no	Freeze-dried bone allograft + collagen dressing	9.97 (1.01)	−2.09	−0.57	

Note: Collagen dressing indicates utilization of a fast-absorbing collagen dressing.

[a]Note that though the final time point is mentioned in this table, in statistical modeling the average time point among the specific treatment arm was utilized.

[b]For crestal width changes of the alveolar ridge, values for up to the coronal 2 mm aspect of the alveolar ridge were considered.Abbreviations: CBCT, Cone-beam computed tomography; CM, Non cross-linked collagen Membrane; DBBM, demineralized bovine bone mineral particles; DBBM-C, demineralized bovine bone mineral with 10% collagen; DFDBA, Demineralized Freeze-Dried Bone Allograft; dPTFE, dense polytetrafluoroethylene membrane; FDBA, freeze-dried bone allograft; NA, Not available; SDBA, solvent-dehydrated bone allograft

Dimension	Millimeter resorption [95% CI]
Horizontal (width)	
Crest (up to 1 mm below)	3.38 [3.25, 3.52]
3 mm below crest	1.88 [1.50, 2.25]
5 mm below crest	1.02 [0.80, 1.24]
Vertical (height)	
Midbuccal	1.94 [1.70, 2.18]
Midlingual	1.33 [1.17, 1.49]
Mesial height changes	0.53 [0.43, 0.63]
Distal height changes	0.53 [0.43, 0.63]

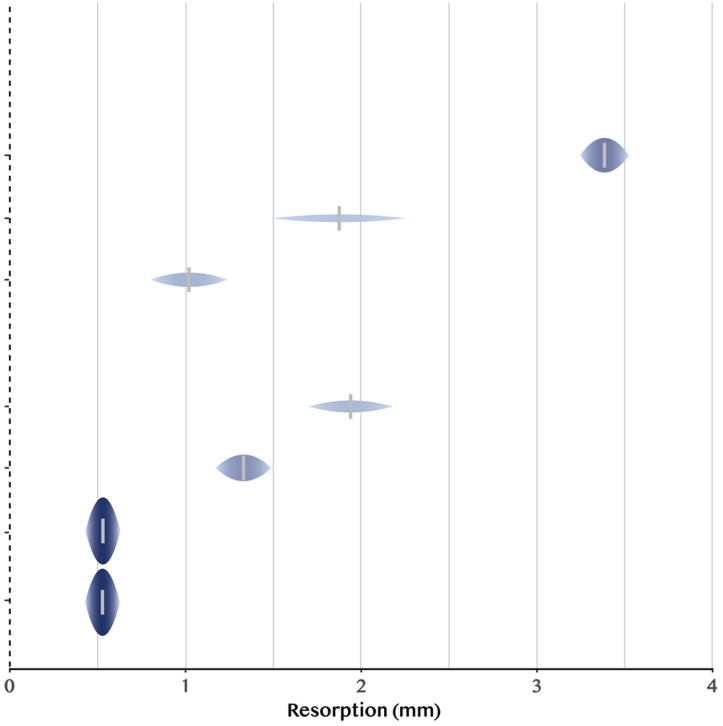

FIGURE 4 Linear dimensional changes that occur as a result of unassisted extraction socket healing, estimated at a fixed healing time of 4 months for a nonmolar site. CI, confidence interval

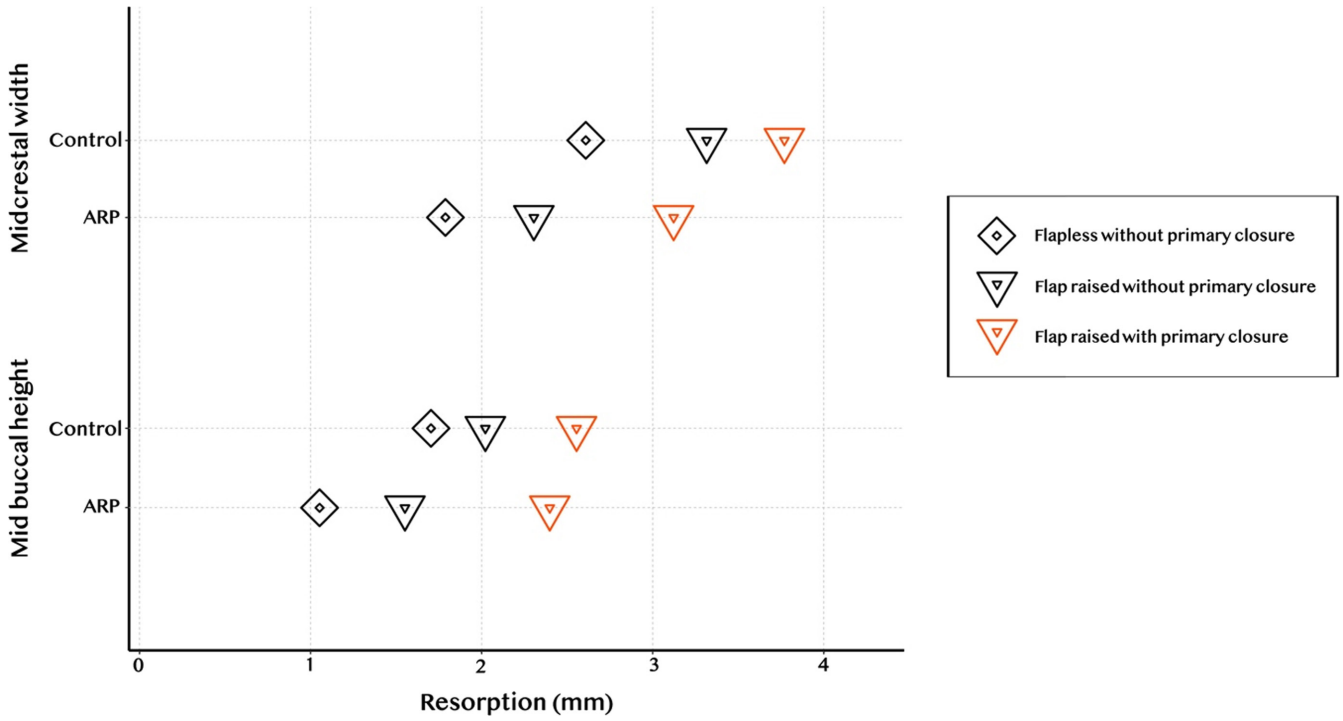

FIGURE 5 Conditional relationship of flap reflection and primary wound closure to ridge width and height changes. The dot plots depict the results of the mixed model. Note that these data and comparison pertain to analysis of only noncompromised extraction sockets. ARP, alveolar ridge preservation

can be prevented with alveolar ridge preservation. The reduction in ridge width is substantially reduced at an increasing distance from the crest (1.8 and 1.02 mm resorption at reference points approximately 3 and 5 mm below the crest, respectively). The reduction of the midbuccal height is less pronounced than the midcrestal horizontal reduction, for a mean value of 1.94 mm. Height

TABLE 3 Cost parameters for the biomaterials enlisted in the eligible trials for the alveolar preservation modalities considered. Note that the costs were obtained directly from manufactures based on standard market price on the current day (in July 2020) in North America

Biomaterial	Type	Product name	Amount/size	Cost [US$]
Bone graft	Allograft	AlloOss cancellous particulate bone	0.5 cm^3	90.79
		LifeNet mineralized cancellous bone	0.5 cm^3	92
		LifeNet mineralized cortical bone	0.5 cm^3	60
		LifeNet demineralized cortical bone	0.5 cm^3	63
		Maxxeus cortical mineralized/demineralized blend	0.5 cm^3	51
		enCore 70|30 combination of freeze-dried bone allograft and demineralized freeze-dried bone allograft	0.5 cm^3	97
		enCore 70|30 mineralized cortical allograft	0.5 cm^3	59
		enCore 50|50 cortical and cancellous allograft	0.5 cm^3	87
		Puros cancellous particulate allograft	0.5 cm^3	104
		Puros cortico-cancellous particulate allograft	0.5 cm^3	111
		RegenerOss allograft particulate	0.5 cm^3	70
	Alloplastic	GUIDOR Easy-Graft CLASSIC alloplastic bone	1 syringe	85
		DentoGen bone graft	1 cm^3	48.5
		IngeniOs HA synthetic bone particles	0.5 cm^3	70
		IngeniOs silicated beta-tricalcium phosphate synthetic bone particles	0.5 cm^3	80
	Xenograft	MinerOss XP cancellous	0.5 cm^3	46.2
		MinerOss cortical and cancellous blend	0.5 cm^3	47
		Zcore porcine particulate (0.25–1 mm particle size)	0.5 cm^3	76
		Zcore porcine particulate (0.25–1 mm particle size)	1 cm^3	112
		Endobon xenograft particulate	0.5 cm^3	72
		Bio-Oss	0.5 cm^3	140
		Bio-Oss Collagen	50 mg	69
Barrier membrane	Collagen	Mem-Lok Pliable	15 mm × 20 mm	71.4
		Mem-Lok Pericardium	15 mm × 20 mm	123.5
		Bio-Gide	13 mm × 25 mm	165
		Biomend	15 mm × 20 mm	144
		Biomend Extend	15 mm × 20 mm	165
		OssixPlus	15 mm × 25 mm	189
	Dense polytetrafluoroethylene	Cytoplast TXT-200 singles	12 mm × 24 mm	50
Absorbable collagen dressing		Zimmer collagen plug	1 piece	14.3
		Zimmer collagen tape	1 piece	22
		Salvin OraPlug	1 piece	12

Note: Costs were directly obtained from manufactures based on current North America market prices in USD in July 2020.Abbreviations: FDBA, Freeze-dried bone allograft; DFDBA, demineralized freeze-dried bone allograft; dPTFE, dense polytetrafluoroethylene

loss is also notably lower on the lingual, compared with the buccal, aspect (1.33 mm) and on the mesial and distal aspects of an extraction socket, particularly in tooth-bound sites, for an average magnitude of approximately 0.5 mm.

In our analysis, we also noticed a positive trend for time. This, in fact, aligned with the existing body of literature on healing of extraction sockets, indicates that most of the dimensional changes do occur within the first 3 months, however stabilization of bone remodeling may take up to 1 year to complete. Within the scope of the selected data that include studies with a minimum healing time of 3 months and a maximum of 8 months, we observed that dimensional ridge alterations continue beyond the 3-month time point, though to a relatively small amount of approximately 0.17 and 0.11 mm resorption in ridge width and height, respectively.

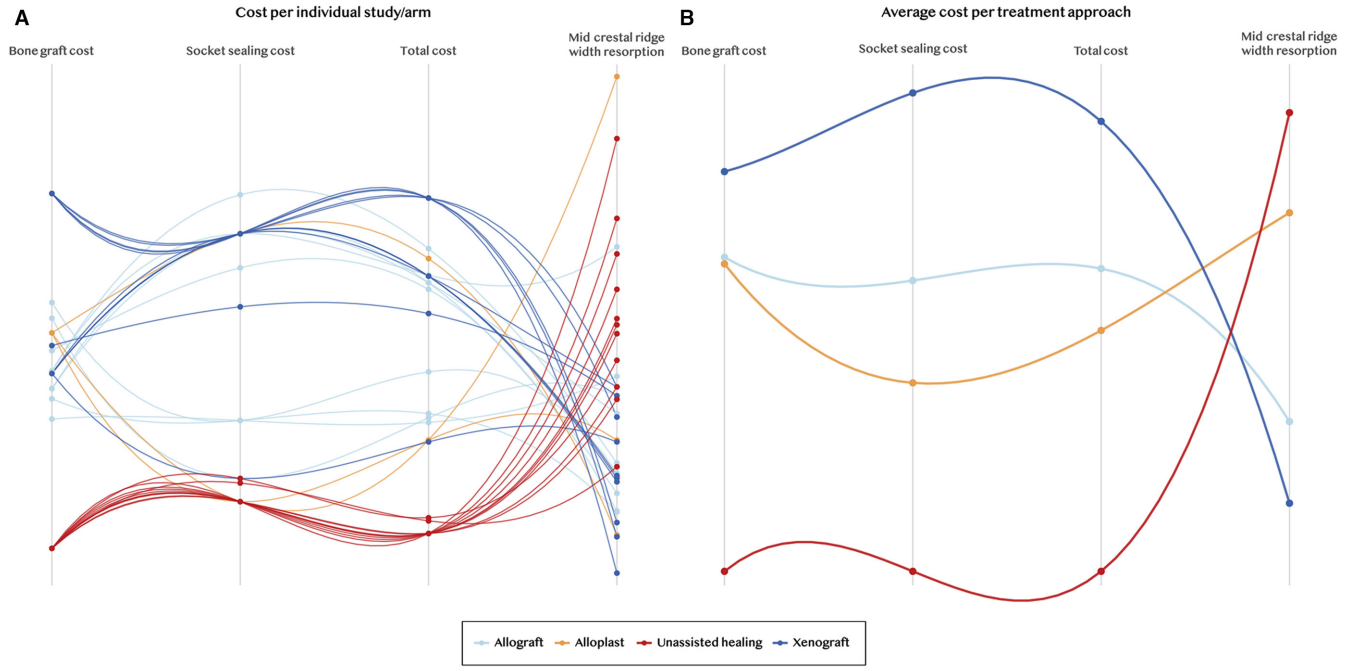

FIGURE 6 Parallel coordinates plots depicting the relationship between the costs associated with bone grafting and socket sealing materials, the total cost, and midcrestal ridge width resorption: A, per individual included study arm; B, arm-wise averages. Quantitative values on the vertical axes are scaled independently to visually encompass the range of data and display the standardized values of the corresponding variable. In A, points of the same study arm are connected with lines. In both A and B, colors differentiate unassisted healing and the types of bone grafting materials (allograft, alloplast, and xenograft)

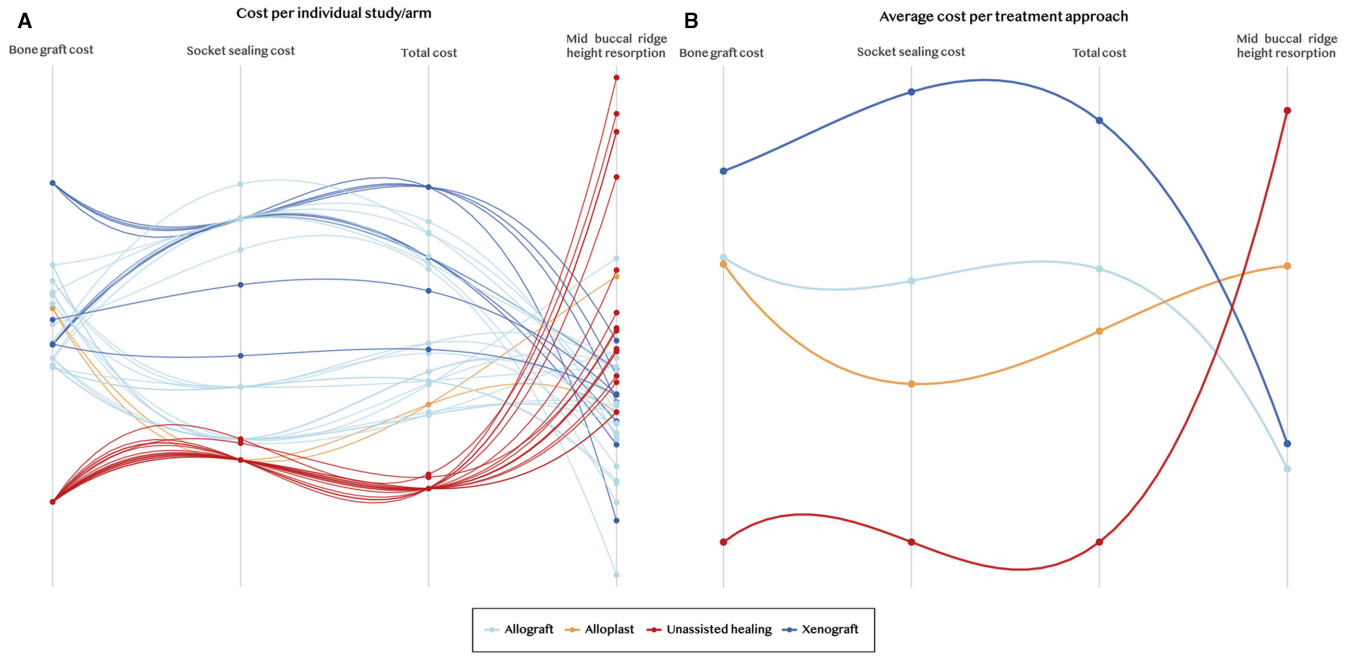

FIGURE 7 Parallel coordinates plots depicting the relationship between the costs associated with bone grafting and socket sealing materials, total cost, and midbuccal ridge height resorption: A, per individual included study arm; B, arm-wise averages. Quantitative values on the vertical axes are scaled independently to visually encompass the range of data and display the standardized values of the corresponding variable. In A, points of the same study arm are connected with lines. In A and B, colors differentiate unassisted healing and the types of bone grafting materials (allograft, alloplast, and xenograft)

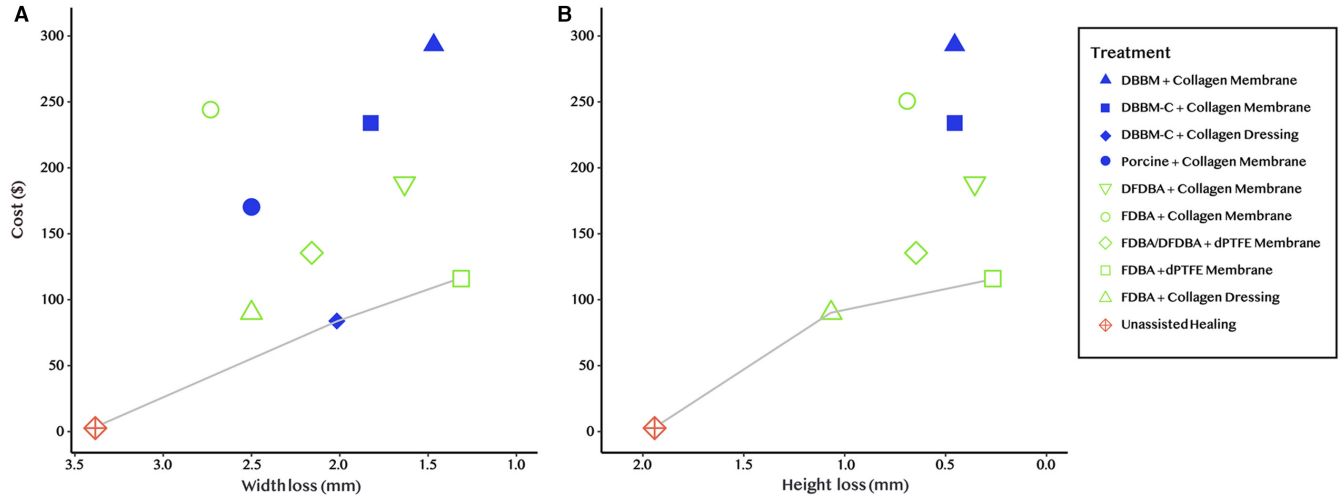

FIGURE 8 Cost-effectiveness plot for the included composite alveolar ridge preservation modalities for performance in, A, ridge width and, B, height maintenance. The plots present the relative efficacy of a specific treatment modality against its total cost, for the outcomes of interest. Generally, a more suitable treatment is positioned toward the lower right, as it would provide a superior ridge maintenance ability at a reduced cost, rendering it more cost-effective. The Pareto frontier (gray line) shows the most relevant treatments. Note that materials costs are based on standard market prices as obtained directly through the respective manufacturers in North America, in US dollars in July 2020. DBBM, demineralized bovine bone mineral particles; DBBM-C, demineralized bovine bone mineral with 10% collagen; DFDBA, demineralized freeze-dried bone allograft; dPTFE, dense polytetrafluoroethylene; FDBA, freeze-dried bone allograft

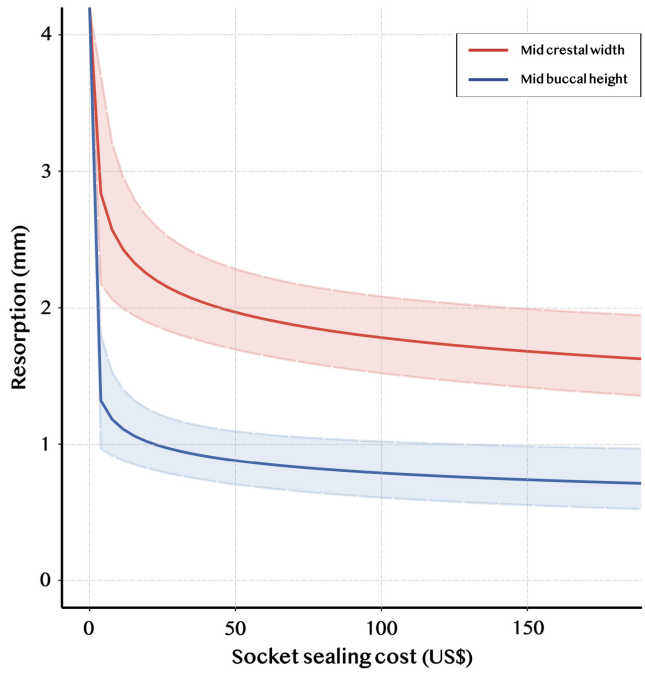

FIGURE 9 The estimated average alveolar ridge resorption in width and height against cost of the socket sealing material, fixed for an average bone graft price of US$85 and a healing time of 4 months. Note that materials costs are based on standard market prices as obtained directly through the respective manufacturers in North America in July 2020

Effect of technical variables on dimensional changes

Technical aspects can also influence the pattern of postextraction ridge remodeling, with flap elevation and primary closure being the most relevant.

Despite the general belief that flap elevation should be avoided whenever possible to minimize surgical trauma, owing to the notion that primary wound closure is beneficial for the outcomes of guided bone regeneration,[120–122] many have adopted this approach for the execution of alveolar ridge preservation. Hence, whether a primary wound closure is indeed beneficial to achieve more favorable ridge preservation outcomes has been a subject of debate in the literature and in scientific forums. Nonetheless, despite the similarities that exist between standard alveolar ridge preservation and alveolar ridge augmentation via guided bone regeneration in terms of the applied biomaterials (bone graft + membrane) and their comparable therapeutic goal (achieving favorable ridge dimensions), it must be acknowledged that important differences also exist among the two treatment concepts, as related to the primary therapeutic goal. Whereas alveolar ridge augmentation via guided bone regeneration is aimed at reconstructing healed atrophic alveolar bone ridges,[123–127] alveolar ridge preservation is performed immediately after tooth extraction to preserve as much of the alveolar ridge width and height as possible,[3,27–29,45] with the additional purpose of facilitating implant placement by reducing the need for ancillary ridge augmentation.

Although the specific mechanisms by which alveolar ridge preservation aids in the maintenance of bone volume are not yet fully known, it may be speculated that the biomaterial filler, owing to its differential resorption rate compared with a blood coagulum, contributes to slowing down the physiologic events that naturally follow tooth removal, which eventually leads to reduced dimensional changes compared with unassisted healing. However, the principles of guided bone regeneration rely on the combined use of barrier membranes to allow for compartmentalization of the oral mucosa and the underlying bone, thus preventing soft tissue ingrowth, graft

particle extravasation, bacterial colonization, and debris accumulation, ultimately creating a favorable environment for bone formation to occur.[128–133]

Indeed, a submerged healing through obtaining primary closure may contribute to an optimized healing process. Nevertheless, considering the confined nature of an extraction socket with well-preserved bony walls and the relatively small oral exposure of a barrier membrane to the oral cavity, obtaining a primary closure may not be justified. Particularly as flap release and successful achievement of primary closure would inadvertently lead to coronal advancement of the mucogingival junction, reduced keratinized tissue width, and increased swelling as its result.

By fitting a mixed model to the outcomes of midhorizontal and midbuccal vertical ridge resorption, we assessed the conditional relationship of flap reflection and primary wound closure relative to dimensional changes and bone remodeling. Flap elevation was significantly associated with increased horizontal (1.48 mm; 95% confidence interval [0.37 mm, 2.58 mm], $P = .01$) and midbuccal vertical (0.59 mm; 95% confidence interval [0.11 mm, 1.08 mm], $P = .01$) bone loss. Similarly, primary wound closure after flap reflection was also associated with increased ridge resorption in both dimensions: 0.71 mm (95% confidence interval [0.17 mm, 1.26 mm], $P = .02$) for horizontal and 0.68 mm (95% confidence interval [0.18 mm, 1.17 mm], $P = .01$) for midbuccal vertical ridge resorption. Figure 5 shows the observed conditional relationship between flap reflection, primary wound closure, and dimensional changes, based on the model for control (unassisted socket healing) and test (alveolar ridge preservation) sites. However, it is worth mentioning that, as reported among most of the individual studies included in this analysis, the teeth that were subjected to extraction were typically with intact crowns, which likely allowed for proper utilization and grasp of surgical and extraction instruments. In the case of a severely damaged or fractured crown or root that does not allow for a typical extraction, it is plausible to assume that reflection of a mucoperiosteal flap to gain access may not only be indicated but may also result in carrying out an overall less traumatic tooth extraction.

Apart from solely considering dimensional alterations of the alveolar ridge, other endpoints, such as the effect of primary closure on keratinized mucosal width and patient-centered outcomes, should also be considered. A split-mouth randomized controlled trial consisting of a combination of bone graft particles and an absorbable membrane assessed the influence of primary wound closure on the outcomes of alveolar ridge preservation for intact sockets.[65] Though the study reported no statistically significant differences between the test (no primary closure) and control (primary closure) groups in terms of alveolar ridge preservation, a significant coronal displacement of the mucogingival junction was observed in sites that healed after primary closure, and those patients also reported greater postoperative discomfort,[65] differences that achieved statistical significance with even a rather modest sample size (11 subjects).

Influence of local anatomical features on resorptive patterns

In recent years, the role of the periodontal phenotype, which consists of the bone morphotype (buccal bone) and its soft tissue phenotype (keratinized tissue width and gingival thickness), have attracted a great deal of attention by clinicians and researchers relative to the etiology of periodontal diseases and conditions, as well as its influence on the outcomes of therapy.[96,103,134,135]

Notably, the importance of the integrity and thickness of the facial bone plate on the outcomes of alveolar ridge preservation has been highlighted in several studies.[4,28,50,136] In a case series, Chappuis et al identified a threshold of 1 mm, below which the extraction sites underwent significantly greater volumetric changes after unassisted healing, leading to the conclusion that a thin facial bone phenotype (<1 mm) is predictive of more pronounced bone resorption.[4] Recently, findings from a randomized controlled trial revealed that a minimum 10% ridge volume reduction can be expected under a threshold crestal facial bone thickness of 1 mm with unassisted healing, and 0.6 mm for sites that received alveolar ridge preservation.[50]

In our analysis, a significant correlation was noticed between the average crestal buccal bone thickness (within the most coronal 2 mm) and linear bone changes, as well as an interaction between buccal bone thickness and the presence vs absence of treatment (alveolar ridge preservation vs unassisted healing). We observed a significant association between an increase in buccal bone thickness and attenuation in the amount of midcrestal horizontal (−1.22 mm, 95% confidence interval [−2.31 mm, −0.14 mm], $P = .03$) and midbuccal vertical ridge resorption (−0.93 mm, 95% confidence interval [−1.75 mm, −0.105 mm], $P = .01$) for sites that underwent unassisted healing compared with treated extraction sockets. This indicates that the detrimental impact of a thin buccal plate can be substantially mitigated by performing alveolar ridge preservation, highlighting the added benefit of performing ridge preservation for sites exhibiting thin facial bone phenotypes (<1 mm).[4,5,137,138]

Nonetheless, among the two constituents of the periodontal phenotype—the hard- and soft-tissue components—few studies have focused on the role of the soft tissue phenotype. As such, only three of our included trials[50,98,112] had assessed and numerically reported the parameters of gingival thickness and keratinized mucosal width; therefore, performing a pooled analysis to investigate variations in the soft tissue phenotype and their effect on bone remodeling after alveolar ridge preservation was not feasible.

Owing to anatomical differences between a molar and a nonmolar site (ie, socket morphology and size), it has been speculated that molar sites would require a longer healing time, which may result in an increased net amount of dimensional reduction upon complete maturation of the socket.[22,139–141] Nonetheless, it must be acknowledged that molar sites are also more likely to exhibit a thicker facial bone, which, as previously discussed, can substantially influence the pattern of resorption. These sites are also naturally wider in the facio-lingual dimension, which can reduce the need for ancillary bone augmentation at the time of implant placement. Given these

considerations and potential multicollinearity, study arms involving the treatment of molar sites were excluded from our analysis. Moreover, the notion that larger extraction sites may also require additional bone grafting material, which would affect the total cost, fortified our decision toward the inclusion of only nonmolar sites in the cost analysis.

4.2.2 | Cost-effectiveness of alveolar ridge preservation

Details on material expenses for the alveolar preservation modalities included are listed in Table 3. Since, at the time of this analysis, two bone grafting materials (a xenograft and an alloplast) and a collagen membrane were not approved by the Food and Drug Administration for dental application in the United States, the respective treatment arms were not included in the cost analysis.[51,70]

Figures 6 and 7 present the relationship between the rescaled and standardized levels of bone graft cost, socket sealing cost, the total treatment cost, and the amount of horizontal and vertical ridge resorption. The plots in Figures 6A and 7A show the relationship of the variables per individual study arm, and each line represents the treatment of an included study, whereas Figures 6B and 7B display the arm-wise averages.

The treatment arms that involved the use of a xenogeneic bone graft tend to be associated with the highest cost, followed by those that utilized an allograft and an alloplast. As some alloplastic materials tend to be used with no concomitant socket sealing, their projected overall cost is relatively lower, as seen in both arm-wise average plots for outcomes of horizontal and vertical ridge loss. Evidently, the lowest cost comes at a price of no treatment, though at the expense of the highest overall ridge resorption.

In general, it can be observed that approaches based on the allograft and xenograft treatments tend to be associated with higher costs but lead to superior performance (reduced ridge width and facial height resorption). As shown in the arm-wise average plots, a monotonic relationship can be appreciated between the relative total treatment costs and the amount of subsequent ridge resorption for the xenograft and allograft treatment groups, as well as for the unassisted healing sites. However, the alloplast-treated sites display nonmonotonicity due to the relationship between their cost (comparable to that of allograft materials) and their relatively lower performance (more horizontal and vertical ridge resorption).

Figure 8 presents the cost-effectiveness of the composite treatment modalities included. Treatments supported by fewer than three distinct study arms are not presented; also excluded from further analyses beyond this point were alloplast-treated sites due to the observed nonmonotonicity, the high disparity across their limited available data, and the seemingly lower relative performance. Here, the most relevant treatments are those that are not dominated in terms of both efficacy (ridge width and height maintenance) and cost by another other treatment. These relevant treatments lie on the "Pareto frontier" (optimal path).[142,143] In other words, a treatment with an equal or greater efficacy while simultaneously providing an equal or lesser cost dominates other treatments, whereas other therapies that would yield a lesser or equal performance while with equal or higher costs are considered inadmissible (Figure 8).

Nonetheless, relative to ridge preservation, aside from specific clinical factors (eg, socket dimensions and integrity) or medical contraindications, treatment selection among alternative choices is ultimately upon the decision-making clinician, considering their willingness toward additional expenditure for obtaining the anticipated return on investment, which in the context of alveolar ridge preservation refers to an enhanced therapeutic performance.

To overcome potential biases from composite treatment options and frequent biomaterial combinations (eg, certain types of membranes that are commonly used with specific types of bone grafts, and vice versa) and to explore the relationship of the monetary investment toward other treatment options, a desegregated model was utilized to investigate the relationship of study-level costs for bone grafts and socket sealing materials relative to the outcomes of horizontal and vertical ridge resorption.

The cost for the bone graft substitutes and socket sealing materials ranged from US$46.2 to US$140 and from US$12 to US$189, respectively. Within this range, for width and height changes, we observed a significant correlation between expenditure on a barrier membrane and less horizontal (−0.012, 95% confidence interval [−0.006, −0.018], $P = .003$) and vertical (−0.011, 95% confidence interval [−0.007, −0.015], $P < .001$) ridge resorption. Interestingly, the bone graft cost did not seem to significantly influence postextraction alveolar ridge resorption horizontally (0.002 mm, 95% confidence interval [−0.008, 0.012], $P = .57$) or vertically (−0.004 mm, 95% confidence interval [−0.01, 0.002], $P = .21$). Additionally, the correlations remained qualitatively unchanged, and the model gained no leverage on dropping control sites (ie, unassisted healing), further supporting the positive relationship between the use of a membrane and less ridge resorption.

Lastly, when the model was fit to log-scale data for capturing relative returns on membrane costs (using changes in log ridge width and height as the outcomes with log reference costs for the membrane), a diminishing return was observed for an additional dollar spent for a barrier membrane beyond approximately US$50 and gaining additional performance in ridge preservation (Figure 9). In this context, it is important to consider the therapeutic differences between proper barrier membranes, either absorbable or nonabsorbable, and rapidly absorbing collage sponges, which lack compartmentalization properties.

In summary, our results indicate that there is no statistically significant difference between allograft and xenograft materials relative to their capacity of attenuating postextraction ridge remodeling in terms of linear bone width and height reduction, whereas a correlation does exist between the use of a barrier membrane and ridge preservation efficacy in terms ridge width and midbuccal height reduction.

5 | DISCUSSION

Several forms of economic evaluations or cost analyses have been performed throughout the literature. Though these analyses traditionally stem from economics, they have been routinely implemented in the medical field,[144–147] and to some extent in the dental arena.[148–151] The cost-effectiveness of a therapeutic approach is recognized as an important aspect toward policy making, and for the assessment and formulation of a treatment plan. The economic assessment of interventions in the periodontal field is, in fact, not new.[151–157] However, to the best of our knowledge, no form of an economic evaluation has been performed in the topic of alveolar ridge preservation, an area that is of particular interest to clinicians, owing to its relevance in daily practice, and in which, despite numerous descriptions of treatment modalities and comparative trials, a gold standard protocol has not yet been identified.[27] Furthermore, a systematic assessment of the incidence of complications and adverse events in this field has also not yet been published.

5.1 | Complications and adverse events

In our systematic search and among the assessment of studies on alveolar ridge preservation, we found more than one-third (49 articles) of studies to report the occurrence of a postoperative adverse event or a complication. The most commonly observed events were incidence of a postoperative infection, extravasation of bone graft particles, membrane dislodgment, and unintentional membrane exposure.

Indeed, the first step to effectively manage any complication is efforts made towards its prevention. The importance of a thorough assessment of a patient's medical history to prevent intra- and postoperative complications cannot be overemphasized. Predisposing conditions such as previous head and neck radiation, intravenous bisphosphonate treatment, poorly controlled metabolic disorders (eg, diabetes mellitus), heavy smoking, and immune deficiencies may compromise the healing potential and, subsequently, increase the risk for developing complications. Prophylactic systemic antibiotic therapy may be considered in patients with a medical history predisposing to bacterial infections. A meticulous review of current medications should also be conducted, as it can hint toward a condition that may have been overlooked or possible adverse events of the pharmaceutical agent. For instance, patients on antithrombotic therapy are at risk for excessive bleeding, and individuals who use steroid inhalers may have compromised healing outcomes. Generally, if there are concerns or doubts regarding a patient's medical history, a medical consultation with the primary health care provider should be considered. Careful assessment of clinical and radiographic information should also be performed. Providing and reinforcing pertinent postoperative instructions is also crucial to avoid adverse events. Patients should refrain from smoking and be asked to avoid any disturbance of the surgical site (eg, brushing, chewing). Practicing strict surgical asepsis, as well as executing a minimally invasive surgical intervention, may also reduce the occurrence of unwanted events.

The oral cavity is a reservoir of bacterial pathogens, and bacterial contamination of the surgical site can result in infections. Prior to the procedures, patients should be asked to rinse with an antiseptic mouthwash (chlorhexidine).

Nonetheless, owing to the nature of the oral cavity (having a variety of bacterial species), and in spite of making preventive efforts, bacterial contamination of the surgical site can occur and result in a postoperative infection, typically characterized by localized swelling, redness, and tenderness, as well as suppuration. In the case of an early infection (within the first 2 weeks), thorough debridement of the socket, with supportive systemic antibiotic therapy, is recommended. If nonintentional exposure, partial tissue perforation, or dislodging of a nonresorbable membrane occurs, the membrane may be trimmed or removed. The patient can also be advised to use an antiseptic rinse twice daily until the membrane is removed and healing by secondary intention occurs. In case of extravasation of bone graft particles or premature loss of a membrane, the ridge maintenance capacity of the treatment performed may be reduced. Patients presenting complications should be closely monitored until the event is resolved.

5.2 | Cost-effectiveness

To the best of our knowledge, this article presents the first cost analysis on alveolar ridge preservation in the literature, involving both a comparison of unassisted healing vs alveolar ridge preservation therapy and an evaluation of the relative efficacy of different alveolar ridge preservation modalities. Owing to vast methodological heterogeneity across published trials in this topic, we set a series of strict criteria for selection of evidence and assessed performance of different treatments relative to linear dimensional changes of the alveolar ridge (ie, midcrestal width and midbuccal height). The rationale behind selection of these two outcomes was the fact that those are the dimensions that typically undergo the most resorption following tooth extraction and are also the most predominantly reported outcomes in clinical trials in this field.

Various metrics have been proposed to estimate the health-benefit facet in a cost analysis. One of the unique attributes of the present study is that there are two major components that comprise the total cost of a standard alveolar ridge preservation intervention: a bone grafting material (socket filler) and a barrier (socket sealer). Both these could potentially influence the outcomes of therapy. Though these two components can be combined in a variety of ways, in practice and in research certain membrane types are more often used in combination with specific types of bone graft (eg, porcine collagen membranes are often utilized with bovine bone graft particles, whereas dense polytetrafluoroethylene barriers are often combined with allograft particles). Hence, considering this duality of alveolar ridge preservation therapy, no specific resorption rate for a fixed total dollar amount spent toward the treatment of an extraction socket can be expected. Additionally, one could speculate whether a certain type of membrane would perform differently (better or worse) when paired with a specific type of bone graft.

To that end, aside from assessing the cost-effectiveness of routinely applied composite alveolar ridge preservation modalities, we sought to explore cost-effectiveness through additional modeling strategies. Owing to the latitude provided by mixed models, we disaggregated the effect of the membrane/socket sealing material from the bone graft component. By assuming varying levels of membrane cost, we explored their correlation with changes in ridge width and height after 4 months of healing time, adjusting for a fixed average bone graft price. In addition, the models allowed for the adjustment of width and height changes by covariates, such as time, flap reflection, and primary closure. Furthermore, as additional sensitivity analyses, we inflated the costs of the biomaterials applied by fractional inflation rates (both unequal and constant rates for membranes and bone graft materials) and noted that the main conclusions remained qualitatively unchanged (ie, the difference between fractional increased bone graft cost does not translate into increased effectiveness of alveolar ridge preservation therapy between an allograft and a xenograft, whereas the slightest expenditure on membranes yields reduction of ridge width and height, though only to a certain degree, beyond which the return on investment is significantly diminished). This indicates that our conclusions, based on 2020 US market price would hold true in the immediate future, assuming minor changes in market price and similar inflation rates among the different classes of biomaterials.

To properly interpret and apply the findings from our analysis, it is important to remark that only data from nonmolar sites were included. Aside from different healing dynamics compared with a nonmolar site, a molar site also generally requires more grafting material to fill the socket, which "unfairly" increases the cost, while the benefit of the extra expense may not translate into an added benefit in terms of superior ridge preservation outcomes. Additionally, except for studies on third molars, only a few clinical studies exclusively focus on the treatment of molar extraction sites,[64,80,90] and those that include treatment of both molar and nonmolars seldom report the stratified data.

Another aspect worth consideration is the histomorphometric outcome following alveolar ridge preservation and the "quality" of the bone that is obtained with various bone grafting materials and membranes.[60,92,110,158,159] Though the significance of the proportion of mineralized tissue, nonmineralized tissue, and remaining bone graft material after socket grafting relative to ridge maintenance or implant success has not yet been fully elucidated, some believe that a higher percentage of mineralized tissue is necessary to accelerate the process of osseointegration and ensure long-term peri-implant health.[160] In this sense, studies on the topic of alveolar ridge preservation have shown that allograft materials can lead to the formation of a higher proportion of mineralized tissue due to their rapid turnover, whereas xenografts, which exhibit a lower biodegradability, may maintain the ridge volume upon maturation for longer periods of time.[100,124]

Owing to the limited information available in the literature regarding long-term implant outcomes (eg, survival, success, marginal bone changes) in sites that received alveolar ridge preservation compared with control sites, the inclusion of these clinically relevant outcomes in the cost-effectiveness analyses was not feasible. As this pertains to the important outcome of additional bone augmentation at the time of or prior to implant placement in sites that underwent alveolar ridge preservation therapy and since there was no available information on the exact types or quantity of biomaterials applied, it was not feasible for us to quantify the associated costs and include this in the analysis.

6 | FUTURE DIRECTIONS

Effective translation of novel research findings into clinical practice often presents challenges. A singular therapeutic approach for the effective and predictable treatment of extraction sockets has not been identified yet, as many gaps remain unaddressed in the scientific literature. To date, many clinical studies on alveolar ridge preservation simply consist of the comparison of treatment A vs B (often an unassisted healing control) in a typical two-arm clinical trial. Beyond the methodological plausibility of including a control group and the common finding that alveolar ridge preservation is effective and beneficial, the vast majority of comparative studies are primarily centered on the outcome of dimensional ridge alterations and overlook other relevant facets, such as patient- and implant-centered outcomes,[161–163] soft tissue healing dynamics,[164,165] and the occurrence of early and late complications.[166,167] Extraction sites exhibit a wide range of anatomical variability, including phenotypic characteristics such as keratinized tissue width, gingival thickness, bone thickness, and integrity, which can largely influence the outcomes of therapy. Other aspects, such as systemic and patient-related factors, may also affect the healing process.

In consequence, future research in the topic of alveolar ridge preservation should test different treatment modalities with or without immediate implant placement in well-conducted, adequately powered, multiple-arm clinical trials to evaluate the effect of relevant local, systemic, and patient-related factors on the outcomes of therapy. Novel, real-time, and less invasive technologies should also be adopted for improving accuracy in the assessment of therapeutic outcomes.[168–171] This information would allow clinicians to make evidence-based decisions and refine case selection, hence maximizing treatment predictability, accuracy, and cost-effectiveness while minimizing errors and the onset of complications.

7 | CONCLUDING REMARKS AND IMPLICATIONS FOR DAILY PRACTICE

1. Although infrequent, the most common postoperative complications associated with alveolar ridge preservation include, but are not necessarily limited to, infection, membrane exposure, or membrane exfoliation, and extravasation of bone graft particles.
2. Complications may be prevented with meticulous preoperative planning, which includes a thorough review of the medical history,

current medications, and allergies, along with a comprehensive clinical and radiographic examination, as well as the adherence to proper minimally invasive surgical protocols and adequate postoperative care.

3. To reduce the incidence of complications and the extent of postextraction ridge resorption, clinicians should perform minimally invasive surgical procedures, including delicate, flapless tooth extraction and avoid flap advancement for healing by primary intention.
4. The thickness of the facial bone wall is a strong predictor of the extent and severity of postextraction ridge resorption. In particular, the benefit of alveolar ridge preservation is accentuated in sites with a thin bone phenotype (<1 mm).
5. Alveolar ridge preservation therapy consisting of a combination of socket grafting with allogeneic or xenogeneic bone particles and socket sealing with a barrier membrane can greatly reduce but may not completely eliminate the need for additional bone grafting at the time of implant placement, compared with unassisted healing.
6. Alveolar ridge preservation using allogeneic or xenogeneic bone grafts is associated with higher costs, but also superior preservation performance compared with the use of alloplastic materials or unassisted healing. However, current evidence indicates that the use of a particulate allograft vs a xenograft bone material renders similar clinical outcomes.
7. Clinicians should consider the use of barrier membranes for socket sealing over grafted sockets as these can aid in minimizing postextraction alveolar ridge resorption. Nonetheless, a diminishing return on the monetary investment for a barrier membrane was observed beyond US$50 relative to ridge preservation performance.

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CONFLICT OF INTEREST

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SUPPORTING INFORMATION

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

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