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Interventions for replacing missing teeth: alveolar ridge preservation techniques for dental implant site development (Review)

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[Intervention Review]

Interventions for replacing missing teeth: alveolar ridge preservation techniques for dental implant site development

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ABSTRACT

Background

Alveolar bone changes following tooth extraction can compromise prosthodontic rehabilitation. Alveolar ridge preservation (ARP) has been proposed to limit these changes and improve prosthodontic and aesthetic outcomes when implants are used. This is an update of the Cochrane Review first published in 2015.

Objectives

To assess the clinical effects of various materials and techniques for ARP after tooth extraction compared with extraction alone or other methods of ARP, or both, in patients requiring dental implant placement following healing of extraction sockets.

Search methods

Cochrane Oral Health's Information Specialist searched the following databases: Cochrane Oral Health's Trials Register (to 19 March 2021), the Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library 2021, Issue 2), MEDLINE Ovid (1946 to 19 March 2021), Embase Ovid (1980 to 19 March 2021), Latin American and Caribbean Health Science Information database (1982 to 19 March 2021), Web of Science Conference Proceedings (1990 to 19 March 2021), Scopus (1966 to 19 March 2021), ProQuest Dissertations and Theses (1861 to 19 March 2021), and OpenGrey (to 19 March 2021). The US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) and the World Health Organization International Clinical Trials Registry Platform were searched for ongoing trials. No restrictions were placed on the language or date of publication when searching the electronic databases. A number of journals were also handsearched.

Selection criteria

We included all randomised controlled trials (RCTs) on the use of ARP techniques with at least six months of follow-up. Outcome measures were: changes in the bucco-lingual/palatal width of alveolar ridge, changes in the vertical height of the alveolar ridge, complications, the need for additional augmentation prior to implant placement, aesthetic outcomes, implant failure rates, peri-implant marginal bone level changes, changes in probing depths and clinical attachment levels at teeth adjacent to the extraction site, and complications of future prosthodontic rehabilitation.

Data collection and analysis

We selected trials, extracted data, and assessed risk of bias in duplicate. Corresponding authors were contacted to obtain missing information. We estimated mean differences (MD) for continuous outcomes and risk ratios (RR) for dichotomous outcomes, with 95% confidence intervals (95% CI). We constructed 'Summary of findings' tables to present the main findings and assessed the certainty of the evidence using GRADE.

Main results

We included 16 RCTs conducted worldwide involving a total of 524 extraction sites in 426 adult participants. We assessed four trials as at overall high risk of bias and the remaining trials at unclear risk of bias. Nine new trials were included in this update with six new trials in the category of comparing ARP to extraction alone and three new trials in the category of comparing different grafting materials.

ARP versus extraction: from the seven trials comparing xenografts with extraction alone, there is very low-certainty evidence of a reduction in loss of alveolar ridge width (MD -1.18 mm, 95% CI -1.82 to -0.54; P = 0.0003; 6 studies, 184 participants, 201 extraction sites), and height (MD -1.35 mm, 95% CI -2.00 to -0.70; P < 0.0001; 6 studies, 184 participants, 201 extraction sites) in favour of xenografts, but we found no evidence of a significant difference for the need for additional augmentation (RR 0.68, 95% CI 0.29 to 1.62; P = 0.39; 4 studies, 154 participants, 156 extraction sites; very low-certainty evidence) or in implant failure rate (RR 1.00, 95% CI 0.07 to 14.90; 2 studies, 70 participants/extraction sites; very low-certainty evidence). From the one trial comparing alloplasts versus extraction, there is very low-certainty evidence of a reduction in loss of alveolar ridge height (MD -3.73 mm; 95% CI -4.05 to -3.41; 1 study, 15 participants, 60 extraction sites) in favour of alloplasts. This single trial did not report any other outcomes.

Different grafting materials for ARP: three trials (87 participants/extraction sites) compared allograft versus xenograft, two trials (37 participants, 55 extraction sites) compared alloplast versus xenograft, one trial (20 participants/extraction sites) compared alloplast with and without membrane, one trial (18 participants, 36 extraction sites) compared allograft with and without synthetic cell-binding peptide P-15, and one trial (30 participants/extraction sites) compared alloplast with different particle sizes. The evidence was of very low certainty for most comparisons and insufficient to determine whether there are clinically significant differences between different ARP techniques based on changes in alveolar ridge width and height, the need for additional augmentation prior to implant placement, or implant failure.

We found no trials which evaluated parameters relating to clinical attachment levels, specific aesthetic or prosthodontic outcomes for any of the comparisons.
No serious adverse events were reported with most trials indicating that the procedure was uneventful. Among the complications reported were delayed healing with partial exposure of the buccal plate at suture removal, postoperative pain and swelling, moderate glazing, redness and oedema, membrane exposure and partial loss of grafting material, and fibrous adhesions at the cervical part of previously preserved sockets, for the comparisons xenografts versus extraction, allografts versus xenografts, alloplasts versus xenografts, and alloplasts with and without membrane.

Authors' conclusions

ARP techniques may minimise the overall changes in residual ridge height and width six months after extraction but the evidence is very uncertain. There is lack of evidence of any differences in the need for additional augmentation at the time of implant placement, implant failure, aesthetic outcomes, or any other clinical parameters due to lack of information or long-term data. There is no evidence of any clinically significant difference between different grafting materials and barriers used for ARP. Further long-term RCTs that follow CONSORT guidelines (www.consort-statement.org) are necessary.

PLAIN LANGUAGE SUMMARY

What works best to preserve the jaw bone after tooth extraction?

Why is this question important?

Tooth extraction is a common procedure that can be used for example to:

- remove damaged or diseased teeth;
- remove teeth that are in the wrong place; or
- make room for other teeth.

After a tooth extraction, the part of the jaw bone that used to hold the tooth shrinks because it is no longer needed to support the tooth. If the bone shrinks too much, this can:

- make it difficult or impossible to replace the missing tooth with an artificial one (an implant); and
- weaken the support and health of neighbouring teeth.

To limit bone loss after tooth extraction, dentists or surgeons can carry out a procedure called alveolar ridge preservation (ARP). ARP involves filling the hole left by the missing tooth (using a range of different materials and techniques), and leaving it to heal for several months. The hole can be filled with human, animal, or artificial bone. It can be covered over (to stop gums from growing into the hole) using:

- materials that, after some time, are naturally absorbed by the body; or
- materials that need to be removed with surgery once no longer needed.

To find out if ARP works to preserve jaw bone after tooth extraction, we reviewed the evidence from research studies. We also wanted to know if any materials and ARP techniques are better than others.

How did we identify and evaluate the evidence?

First, we searched the medical literature for studies that compared:

- ARP against no ARP; or
- different ARP materials or techniques.

We then compared the results, and summarised the evidence from all the studies. Finally, we rated our confidence in the evidence, based on factors such as study methods and sizes, and the consistency of findings across studies.

What did we find?

We found 16 studies that followed a total of 426 adults for at least six months. The studies took place in North America, South America, Europe, and Asia. Four studies were supported by pharmaceutical and medical device companies. The other studies either received public funding, no specific funding, or did not report funding source.

ARP compared to no ARP

Eight studies compared ARP against no ARP. In seven studies, animal bone was used to fill the hole left by the missing tooth. In one study, the hole was filled with an artificial bone.

Bone loss: evidence from studies suggests that ARP may prevent bone loss after tooth extraction. However, we are not confident about this finding. This is because studies reported conflicting findings and did not report their methods clearly.

Complications: the evidence about complications (such as discomfort or pain) was mixed. One study reported delayed healing in one person following ARP. In another, some people experienced pain and swelling after ARP. Others reported no complications.

Implications for tooth implants: evidence from studies where ARP used animal bones suggests that ARP may make little or no difference to the need to add more bone to the jaw before implants can be inserted. However, we are not confident about this finding. This is because studies reported conflicting findings and did not report their methods clearly.

It is unclear if ARP affects the success of implants, or the appearance of teeth after implantation. This is because too few robust studies have investigated this.

Comparisons between different materials

Eight studies compared the use of different ARP materials (animal bone against artificial bone). In general, these studies did not provide sufficiently robust evidence to determine which materials work best.

Bone loss: there was some evidence to suggest that there may be little or no difference in bone loss between animal bone and artificial bone. However, we are not confident about this finding. This is because studies reported conflicting findings and did not report their methods clearly.

Complications: the evidence about complications was mixed. Some studies reported redness, pain or swelling, but others did not report that any complications had occurred.

Implications for tooth implants: evidence suggests that the material used may make little or no difference to the need to add more bone to the jaw before implants can be inserted. However, we are not confident about this finding. This is because studies reported conflicting findings and did not report their methods clearly.

It is unclear if different ARP materials and methods have different effects on the success of implants, or the appearance of teeth after implantation. This is because too few robust studies have investigated this.

What does this mean?

We do not know what works best to preserve jaw bone after tooth extraction. It is not clear :

- if ARP is better than no ARP; or
- if some ARP materials and techniques are better than others.

This is because the evidence currently available is not sufficiently robust.

Future studies that report their methods clearly and follow people over long periods will help to strengthen the evidence and draw conclusions.

How-up-to date is this review?

The evidence is current to March 2021.

Summary of findings 1. Alveolar ridge preservation (ARP) versus extraction for replacing missing teeth

Alveolar ridge preservation (ARP) versus extraction for replacing missing teeth

Patient or population: adults requiring replacement of missing teeth
Setting: dental implantology
Intervention: alveolar ridge preservation (ARP) techniques (bone grafting (xenografts, alloplasts))
Comparison: extraction

Outcomes	Number of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Certainty of the evidence (GRADE)
			Risk with extraction	Risk difference with ARP	
Xenografts versus extraction					
Changes in width of alveolar ridge (mm) Follow-up: range 6 months to 36 months	184 (6 RCTs)	-	Risk with extraction: mean change in width of alveolar ridge (mm) was 3.40	Risk difference with xenografts: MD 1.18 lower (1.82 lower to 0.54 lower)	⊕⊖⊖⊖ VERY LOW[a,d]
Changes in height of alveolar ridge (mm) Follow-up: range 6 months to 36 months	184 (6 RCTs)	-	Risk with extraction: mean change in height of alveolar ridge (mm) was 2.40	Risk difference with xenografts: MD 1.35 lower (2.00 lower to 0.70 lower)	⊕⊖⊖⊖ VERY LOW[a,d]
Complications (e.g. discomfort, pain and swelling) Follow-up: range 6 months to 36 months	54 (2 RCTs)	1 trial (Cha 2019) reported delayed healing with partial exposure of the buccal plate at suture removal by 1 participant in the test group. Another trial (Festa 2013) reported pain and swelling			⊕⊕⊖⊖ LOW[a,f]
Need for additional augmentation prior to implant placement Follow-up: range 6 months to 36 months	154 (4 RCTs)	RR 0.68 (0.29 to 1.62)	Study population 383 per 1000	126 fewer per 1000 (199 fewer to 19 fewer)	⊕⊖⊖⊖ VERY LOW[a,c,f]
Aesthetic outcomes of future prosthodontic rehabilitation Follow-up: range 6 months to 36 months	Outcome not reported				
Implant failure rate Follow-up: range 6 months to 36 months	70 (2 RCTs)	RR 1.00 (0.07 to 14.90)	In 1 trial (Barone 2012) 2 implants failed, 1 in each group. Another trial (Pang 2014) reported no implant failures after 1-year follow-up		⊕⊖⊖⊖ VERY LOW[b,f]

Alloplasts versus extraction					
Changes in width of alveolar ridge (mm) Follow-up: 6 months	Outcome not reported				
Changes in height of alveolar ridge (mm) Follow-up: 6 months	15 (1 RCT)	-	Risk with extraction: mean change in height of alveolar ridge (mm) was 2.45	Risk difference with alloplasts: MD 3.73 lower (4.05 lower to 3.41 lower)	⊕⊖⊖⊖ VERY LOW[a,e]
Complications (e.g. discomfort, pain and swelling) Follow-up: 6 months	15 (1 RCT)	Included study (Madan 2014) reported there were no adverse effects			⊕⊖⊖⊖ VERY LOW[a,e]
Need for additional augmentation prior to implant placement Follow-up: 6 months	Outcome not reported				
Aesthetic outcomes of future prosthodontic rehabilitation Follow-up: 6 months	Outcome not reported				
Implant failure rate Follow-up: 6 months	Outcome not reported				

[*] **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a]Certainty of the evidence downgraded 1 level due to unclear risk of bias.
[b]Certainty of the evidence downgraded 2 levels due to high risk of bias.
[c]Certainty of the evidence downgraded 1 level due to inconsistency (moderate heterogeneity).
[d]Certainty of the evidence downgraded 2 levels due to inconsistency (substantial heterogeneity).
[e]Certainty of the evidence downgraded 2 levels due to imprecision (single study with limited number of participants).
[f]Certainty of the evidence downgraded 1 level due to imprecision (small studies and/or wide confidence intervals).

Summary of findings 2. Different grafting materials for alveolar ridge preservation

Different grafting materials for alveolar ridge preservation

Patient or population: adults requiring replacement of missing teeth
Setting: dental implantology
Intervention: grafting materials for alveolar ridge preservation
Comparison: other grafting materials for alveolar ridge preservation

Outcomes	Number of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Certainty of the evidence (GRADE)
			Risk with other grafting material for alveolar ridge preservation	Risk difference with one grafting material for alveolar ridge preservation	
Allografts versus xenografts					
Changes in width of alveolar ridge (mm) Follow-up: 6 months	87 (3 RCTs)	-	Risk with xenografts: mean change in width of alveolar ridge (mm) was -0.53	Risk difference with allografts: MD 0.40 lower (1.13 lower to 0.34 higher)	⊕⊖⊖⊖ VERY LOW[a,d]
Changes in height of alveolar ridge (mm) Follow-up: 6 months	60 (2 RCTs)	-	Risk with xenografts: mean change in height of alveolar ridge (mm) was -2.92	Risk difference with allografts: MD 0.45 lower (1.48 lower to 0.58 higher)	⊕⊖⊖⊖ VERY LOW[a,c,f]
Complications (e.g. discomfort, pain and swelling) Follow-up: 6 months	87 (3 RCTs)	1 trial (Scheyer 2016) reported moderate glazing, redness and oedema, while 2 trials (Santana 2019; Serrano Mendez 2017) reported there were no adverse events			⊕⊕⊖⊖ LOW[a,f]
Need for additional augmentation prior to implant placement Follow-up: 6 months	40 (1 RCT)	RR 6.36 (0.35 to 115.73)	Additional bone augmentation procedure was required for 3 sites in the allograft group, while none of the sites in the xenograft group required additional augmentation procedure before implant placement (Scheyer 2016)		⊕⊖⊖⊖ VERY LOW[a,e]
Aesthetic outcomes of future prosthodontic rehabilitation Follow-up: 6 months	Outcome not reported				
Implant failure rate Follow-up: 6 months	Outcome not reported				
Alloplasts versus xenografts					

Changes in width of alveolar ridge (mm) Follow-up: range 6 months to 8 months	37 (2 RCTs)	-	Risk with xenografts: mean change in width of alveolar ridge (mm) was -0.52	Risk difference with alloplasts: MD 0.31 lower (0.66 lower to 0.04 higher)	⊕⊖⊖⊖ VERY LOW[a,d]
Changes in height of alveolar ridge (mm) Follow-up: range 6 months to 8 months	25 (1 RCT)	-	Risk with xenografts: mean change in height of alveolar ridge (mm) was 0.25	Risk difference with alloplasts: MD 0.60 lower (1.27 lower to 0.07 higher)	⊕⊖⊖⊖ VERY LOW[a,e]
Complications (e.g. discomfort, pain and swelling) Follow-up: range 6 months to 8 months	37 (2 RCTs)	1 trial (Patel 2013) reported pain, swelling, membrane exposure and partial loss of grafting material, while the other trial (Gholami 2012) reported that the procedure was uneventful			⊕⊕⊖⊖ LOW[a,f]
Need for additional augmentation prior to implant placement Follow-up: range 6 months to 8 months	37 (2 RCTs)	RR 1.09 (0.65 to 1.83)	1 trial (Patel 2013) reported 9 events in the alloplasts groups and 8 events in the xenografts group, while the other trial (Gholami 2012) reported 3 events in the alloplasts group and 1 event in the xenograft group		⊕⊖⊖⊖ VERY LOW[a,c,f]
Aesthetic outcomes of future prosthodontic rehabilitation Follow-up: range 6 months to 8 months	Outcome not reported				
Implant failure rate Follow-up: range 6 months to 8 months	25 (1 RCT)	1 trial (Patel 2013) reported that none of the implants failed after 12 months of loading			⊕⊖⊖⊖ VERY LOW[a,e]
Alloplasts with membrane versus alloplasts without membrane					
Changes in width of alveolar ridge (mm) Follow-up: 9 months	20 (1 RCT)	-	Risk with alloplasts without membrane: mean change in width of alveolar ridge (mm) was 0.86	Risk difference with alloplasts with membrane: MD 0.43 higher (0.18 higher to 0.68 higher)	⊕⊖⊖⊖ VERY LOW[b,e]
Changes in height of alveolar ridge (mm) Follow-up: 9 months	20 (1 RCT)	-	Risk with alloplasts without membrane: mean change in height of alveolar ridge (mm) was 0.12	Risk difference with alloplasts with membrane: MD 0.38 higher (0.26 higher to 0.50 higher)	⊕⊖⊖⊖ VERY LOW[b,e]
Complications (e.g. discomfort, pain and swelling) Follow-up: 9 months	20 (1 RCT)	Fibrous adhesions at the cervical part of previously preserved sockets were observed in 2 participants (Brkovic 2012)			⊕⊖⊖⊖ VERY LOW[b,e]

Need for additional augmentation prior to implant placement Follow-up: 9 months	Outcome not reported				
Aesthetic outcomes of future prosthodontic rehabilitation Follow-up: 9 months	Outcome not reported				
Implant failure rate Follow-up: 9 months	Outcome not reported				
Allografts with versus allografts without synthetic cell-binding peptide P-15					
Changes in width of alveolar ridge (mm) Follow-up: 6 months	18 (1 RCT)	-	Risk with allografts without P-15: mean change in width of alveolar ridge (mm) was 3.40	Risk difference with allografts with P-15: MD 0.87 lower (1.61 lower to 0.13 lower)	⊕⊖⊖⊖ VERY LOW[b,e]
Changes in height of alveolar ridge (mm) Follow-up: 6 months	18 (1 RCT)	-	Risk with allografts without P-15: mean change in height of alveolar ridge (mm) was 1.50	Risk difference with allografts with P-15: MD 0.30 lower (1.06 lower to 0.46 higher)	⊕⊖⊖⊖ VERY LOW[b,e]
Complications (e.g. discomfort, pain and swelling) Follow-up: 6 months	18 (1 RCT)	Included study (Fernandes 2011) reported there were no adverse effects			⊕⊖⊖⊖ VERY LOW[b,e]
Need for additional augmentation prior to implant placement Follow-up: 6 months	Outcome not reported				
Aesthetic outcomes of future prosthodontic rehabilitation Follow-up: 6 months	Outcome not reported				
Implant failure rate Follow-up: 6 months	Outcome not reported				
Alloplasts single particle size versus alloplasts multiple particle size					
Changes in width of alveolar ridge (mm) Follow-up: 6 months	30 (1 RCT)	-	Risk with alloplasts multiple particle size:	Risk difference with alloplasts single particle size: MD 0.10 higher	⊕⊖⊖⊖ VERY LOW[a,e]

			mean change in width of alveolar ridge (mm) was 1.30	(0.97 lower to 1.17 higher)	
Changes in height of alveolar ridge (mm) Follow-up: 6 months	30 (1 RCT)	-	Risk with alloplasts multiple particle size: mean change in height of alveolar ridge (mm) was 0	Risk difference with alloplasts single particle size: MD 0.10 higher (1.22 lower to 1.42 higher)	⊕⊖⊖⊖ VERY LOW[a,e]
Complications (e.g. discomfort, pain and swelling) Follow-up: 6 months	30 (1 RCT)	Included study (Hoang 2012) reported there were no adverse effects			⊕⊖⊖⊖ VERY LOW[a,e]
Need for additional augmentation prior to implant placement Follow-up: 6 months	Outcome not reported				
Aesthetic outcomes of future prosthodontic rehabilitation Follow-up: 6 months	Outcome not reported				
Implant failure rate Follow-up: 6 months	Outcome not reported				

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CI: confidence interval; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** risk ratio

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[f]Certainty of the evidence downgraded 1 level due to imprecision (small studies and/or wide confidence intervals).

BACKGROUND

Description of the condition

The extraction of teeth is performed for a variety of reasons, often without any consideration for the preservation of the alveolar ridge. Following this, bone remodelling commences and continues for several months, with most changes occurring in the first three months (Schropp 2003). Post-extraction alveolar bone changes have been estimated to cause 50% reduction in the bucco-lingual width of alveolar bone (Camargo 2000; Iasella 2003; Lekovic 1997; Lekovic 1998; Schropp 2003), and a further loss in height has also been reported (Iasella 2003; Lam 1960). A systematic review evaluated the dimensional changes of the alveolar ridge following tooth extraction and showed a mean reduction of 3.8 mm in width and 1.24 mm in height in the first six months (Tan 2012). The predictable order of bone resorption is known, with the buccal aspect resorbing first (Cawood 1988; Soehren 1979), greater resorption in width than height (Johnson 1967), and with the mandibular bone resorbing faster than the maxillary bone (Atwood 1971; Tallgren 1972). Furthermore, a lingual shift of the crest of the bone, in relation to the original position of the tooth, has also been identified (Pietrokovski 1975). Disuse atrophy, inadequate vascularisation and inflammatory response have been implicated as causative factors for alveolar ridge resorption (Ashman 2000).

The overall alveolar changes following tooth extraction may compromise the prosthodontic rehabilitation using tooth-supported fixed or removable prostheses, as well as implant-supported prostheses. The alveolar bone resorption may not allow an optimal positioning of dental implants (John 2007; Mecall 1991). Therefore, the planning for a prosthodontically-driven implant placement may require preservation of the original alveolar ridge dimensions following tooth extraction. Postoperative care of extraction sockets to reduce pain, minimise complications and improve soft and hard tissue healing, has been previously investigated (Khosla 1971). The practice of bone preservation following tooth extraction in an attempt to maintain ridge height and width was first described as 'bone maintenance' (Ashman 1982; Greenstein 1985; Kentros 1985). Different terms were then used to describe the same procedure, such as 'socket preservation', 'socket augmentation', 'socket grafting', 'ridge preservation', 'alveolar bone grafting', and 'alveolar augmentation', which is defined by the Glossary of Prosthodontic Terms as "any surgical procedure employed to alter the contour of the residual alveolar ridge" (Academy of Prosthodontics 2005). To avoid ambiguity, the term 'alveolar ridge preservation' (ARP) will be used throughout this review. ARP is defined as the procedure of arresting or minimising the alveolar ridge resorption following tooth extraction for future prosthodontic treatment including placement of dental implants.

The purpose of ARP is to maintain a favourable alveolar ridge architecture for future dental implant placement. The timing of placement varies and may influence the final functional and aesthetic outcomes. Following ARP, delayed implant placement is considered to allow time for bone formation within the extraction socket. A recent consensus statement has limited the potential benefits of immediate implant placement particularly in the aesthetic zone where a high rate of mucosal recession is expected (Hämmerle 2012). Nevertheless, there remains a lack of evidence regarding the optimal timing for implant placement after ARP.

ARP techniques may include the placement of different grafting materials, with or without the use of membranes, to preserve and minimise ridge resorption for optimising future implant placement. Several systematic reviews (Avila-Ortiz 2014; Avila-Ortiz 2019; Bassir 2018; Hämmerle 2012; Iocca 2017; MacBeth 2017; Mardas 2015; Vignoletti 2012) were published and demonstrated a significantly smaller reduction in the vertical and horizontal dimensions in alveolar ridge following ARP. Two systematic reviews (Avila-Ortiz 2014; Avila-Ortiz 2019) compared different grafting materials with extraction alone and concluded that xenografts and allografts, use of barrier membrane, and flap elevation may achieve favourable outcomes in terms of minimizing changes in ridge dimensions following extraction. With regard to patient-reported outcomes, no significant changes were observed between patients having preserved or non-preserved extraction sites. Two systematic reviews by the same research group (MacBeth 2017; Mardas 2015) did not identify any advantage in using one particular type of ARP intervention but showed that ARP may reduce the need for additional augmentation at the time of implant placement. Another systematic review of six trials (Iocca 2017) referred to freeze-dried bone graft as the most effective grafting material for ARP but recommended further studies of high quality and large sample size. A recent systematic review (Bassir 2018), included 21 randomised and non-randomised trials published in English and showed positive effects when primary closure, barrier membrane, and recombinant human bone morphogenetic protein-2 were utilized.

Despite the abundance of published systematic reviews, clinicians' choice of ARP technique often relies on personal preference rather than evidence of efficacy. The clinical efficacy of grafting materials and procedures for ARP remains controversial with each claiming superiority in limiting the horizontal and vertical alveolar ridge resorption.

Description of the intervention

ARP techniques include the use of grafting materials of human, animal, or synthetic origin, with or without the use of barrier membranes, to further optimise the functional and aesthetic restoration of dental implants. The grafting materials include: particulate autogenous chips (Araujo 2011; Becker 1994), allografts (Iasella 2003), xenografts (Araujo 2010; Carmagnola 2003), and alloplasts (Norton 2002). Growth factors were also used for ARP including recombinant human bone morphogenetic protein-2 (Fiorellini 2005) and platelet-rich fibrin (Hauser 2013; Temmerman 2016).

In addition, the literature describes a variety of membranes for covering extraction sockets and preserving alveolar ridges. Barrier membranes can be classified into two main categories: the non-resorbable and resorbable membranes. The former is characterised by its larger bone fill and favourable marginal tissue response provided that the membrane is not exposed (e.g. expanded polytetrafluoroethylene (ePTFE)) (Bartee 1998). On the other hand, resorbable membranes do not require a second surgery and are characterised by significant improvement in soft tissue healing, with minimal tissue reaction to membrane exposure (e.g. bovine and porcine collagen matrices) (Iasella 2003).

ARP follows the same principles of guided bone regeneration (GBR) and has been described as a GBR procedure that is carried out at the time of tooth extraction (Lee 2018). Experimental animal studies

showed that following extraction and ARP, some grafting particles are initially surrounded by multinucleated cells, mostly osteoclasts that contribute to resorption and continuing elimination of the graft material, while other particles are coated with woven bone. New bone formation often starts in the apical portion of the grafted extraction site in the early stages of healing where a coagulum fills a void apical to the grafted particles which occupy most of the ridge volume (Araujo 2008; Araujo 2009). In fact, the placement of grafting material or barrier membrane following tooth extraction do not inhibit the process of early formation of woven bone (modelling) or the subsequent replacement of woven bone with lamellar bone and marrow (remodelling), but ARP can be considered as a modelling and remodelling modifier that may compensate for bone loss and ridge contraction (Araujo 2015).

How the intervention might work

Resorbable and non-resorbable membranes are thought to keep the grafting material in place and maintain the space to allow bone regeneration, thus preserving the shape of the alveolar ridge. Bone grafting materials with or without barrier membranes are also used for their osteoconductive and osteoinductive properties. Osteoinduction is the stimulation of bone growth by the use of grafting materials that activate the mesenchymal cells to differentiate into bone forming cells (Reddi 1981; Urist 1965). On the other hand, osteoconduction is the process of encouraging the formation of capillaries and progenitor cells from the recipient site, by using osteoconductive materials that act as a scaffold which allows the establishment of new bone (Buch 1986; Reddi 1987). A bone graft acts as a space-maintaining device which stabilises the blood clot, and prevents volume reduction and collapse of overlying soft tissue (Friedmann 2002).

Why it is important to do this review

Although several techniques and materials have been introduced to preserve the alveolar ridge, a lack of evidence exists with regard to the efficacy of these techniques and the superiority of one technique over the other. There are at present conflicting views with some authors considering the use of grafting material for ARP an effective technique in limiting alveolar ridge resorption (Barone 2008; Iasella 2003), while others argue that intra-socket grafts may compromise the normal healing process of the extraction socket, or be of no benefit in preserving the alveolar ridge (Becker 1998; Buser 1998). Further controversy is found determining the rate at which grafting material may resorb, with evidence that particles of different grafting material may remain within the extraction socket for more than six months following placement (Artizi 2000; Becker 1994; Carmagnola 2003). Several systematic reviews (Avila-Ortiz 2014; Avila-Ortiz 2019; Bassir 2018; Hämmerle 2012; Iocca 2017; MacBeth 2017; Mardas 2015; Vignoletti 2012) were published to evaluate the evidence on ARP, but none of these reviews have attempted to minimize the risk of bias by limiting their selection criteria to randomised trials and have mostly compared different grafting materials in one group against extraction alone. The aim of this review was to evaluate whether ARP techniques are effective in minimising post-extraction ridge resorption, and to identify whether any specific material or procedure could provide superior outcomes.This is an update of the Cochrane Review first published in 2015 (Atieh 2015).

OBJECTIVES

To assess the clinical effects of various materials (including grafting materials, biologics, and growth factors) and techniques (including guided bone regeneration (GBR) and socket seal) for alveolar ridge preservation (ARP) after tooth extraction compared with extraction alone in patients requiring dental implant placement following healing of extraction sockets.

To assess the clinical effects of various materials (including grafting materials, biologics, and growth factors) and techniques (including GBR and socket seal) for ARP after tooth extraction compared with other methods of ARP in patients requiring dental implant placement following healing of extraction sockets.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs) on the use of alveolar ridge preservation (ARP) techniques, with at least six months of follow-up. The follow-up was regarded as the period from tooth extraction until the final measurements of the alveolar ridge prior to or at the time of implant placement.

Types of participants

Adult participants aged 18 years or older, in good general health (including participants with well-controlled systemic disease), who required extraction of one or more permanent teeth involving the use of ARP techniques, including the use of barrier membrane or bone graft, or both, in mandibular or maxillary, molar or non-molar sites, with consideration of future delayed placement of dental implants.

We excluded participants who had undergone ARP procedures as part of non-implant related prosthodontic treatment.

Types of interventions

We accepted any method of ARP (including use of grafting materials, biologics, and growth factors) and techniques (including guided bone regeneration (GBR) and socket seal) with or without the use of any type of barrier membranes after tooth extraction. ARP was compared to either extraction alone (no ARP was performed), or another type of ARP.

Types of outcome measures

Primary outcomes

- Changes in the bucco-lingual/palatal width of alveolar ridge.
- Changes in the vertical height of the alveolar ridge.
- Complications (e.g. discomfort, pain, and swelling).
- Need for additional augmentation prior to implant placement.
- Aesthetic outcomes of future prosthodontic rehabilitation.
- Implant failure (defined as implant loss) rate.

Secondary outcomes

- Peri-implant marginal bone level changes.
- Changes in probing depth (PD) at teeth adjacent to the extraction site.

- Changes in clinical attachment level (CAL) at teeth adjacent to the extraction site.
- Prosthodontic outcomes of rehabilitation.

Search methods for identification of studies

Electronic searches

Cochrane Oral Health's Information Specialist conducted systematic searches in the following databases for randomised controlled trials and controlled clinical trials. There were no language, publication year, or publication status restrictions:

- Cochrane Oral Health's Trials Register (searched 19 March 2021) (Appendix 1);
- Cochrane Central Register of Controlled Trials (CENTRAL; 2021, Issue 2) in the Cochrane Library (searched 19 March 2021) (Appendix 2);
- MEDLINE Ovid (1946 to 19 March 2021) (Appendix 3);
- Embase Ovid (1980 to 19 March 2021) (Appendix 4);
- LILACS BIREME Virtual Health Library (Latin American and Caribbean Health Science Information database; from 1982 to 19 March 2021) (Appendix 5);
- Web of Science Conference Proceedings (1990 to 19 March 2021) (see Appendix 6);
- Scopus (1966 to 19 March 2021) (Appendix 7);
- ProQuest Dissertations and Abstracts service (1861 to 19 March 2021) (Appendix 8);
- OpenGrey (www.opengrey.eu/) (to 19 March 2021) (Appendix 9).

Subject strategies were modelled on the search strategy designed for MEDLINE Ovid. Where appropriate, they were combined with subject strategy adaptations of the highly sensitive search strategies designed by Cochrane for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions*, Version 6.1 (Lefebvre 2020)).

Searching other resources

The following trial registries were searched for ongoing studies, see Appendix 10 for details of the search strategies:

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov; searched 19 March 2021);
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch; searched 19 March 2021).

The following journals were handsearched for the period 2003 to 2020:

- *Clinical Oral Implants Research*
- *Clinical Implant Dentistry and Related Research*
- *International Journal of Oral Implantology*
- *International Journal of Oral and Maxillofacial Implants*
- *Journal of Clinical Periodontology*
- *Journal of Periodontology*
- *Clinical Trials in Dentistry* (2019 to 2020).

We contacted corresponding authors for further information. We also approached the manufacturers of different grafting materials in an attempt to identify any unpublished or ongoing studies.

We searched the reference lists of included studies and relevant systematic reviews for further studies.

We checked that none of the included studies in this review were retracted due to error or fraud.

We did not perform a separate search for adverse effects of interventions used, we considered adverse effects described in included studies only.

Data collection and analysis

Selection of studies

Three review authors (Momen A Atieh (MAA), Nabeel HM Alsabeeha (NHMA), and Sara Ali (SA)) independently screened the retrieved citations for relevance. The search results were printed off and checked on the basis of title first, then by abstract and keywords The search was designed to be sensitive and include controlled clinical trials, these were filtered out early in the selection process if they were not randomised. Irrelevant references were discarded, and those that were screened as relevant were obtained in full and assessed for inclusion in the review by using an eligibility form that was prepared and pilot tested in advance. Any disagreements were resolved by discussion and consultation with a third review author (Alan GT Payne (AGTP). In the presence of more than one publication of the same trial, all the publications were reviewed and relevant information were obtained from all related publications but the most relevant one was quoted. We recorded all rejected studies in the table of excluded studies giving reasons for exclusion.

No language restrictions were applied.

Data extraction and management

Three review authors (MAA, NHMA, and SA) used a piloted data extraction form to independently extract the data, in duplicate, from all the included studies. Any discrepancies were discussed with a third review author (AGTP). We contacted corresponding authors of studies to request missing data or for clarification. We excluded any studies that had insufficient data. The review authors were not blinded to the study authors' names, institutional affiliations, journal of publication, and the results of the study. The following data were recorded for each included trial according to the Cochrane review guidelines.

- Study characteristics: title, authors' names, contact address, study location, language of publication, year of publication, published or unpublished data, source of study funding, study design (parallel group or split-mouth), method of randomisation, duration of study, allocation concealment, and blinding (participants, investigators, outcome examiners).
- Participants: demographic characteristics, inclusion/exclusion criteria, number of participants in test and control groups, number of withdrawals and the reasons for dropouts.
- Interventions: types of ARP techniques and grafting materials.
- Comparison: extraction alone (no ARP is performed) or another method of ARP.
- Outcomes: the previously described outcomes in addition to any other outcomes evaluated in the study. The method of assessment, length of the observation period, and any adverse events were also recorded.

Assessment of risk of bias in included studies

Three review authors (MAA, NHMA, and SA) assessed the risk of bias independently, and in duplicate, for the included studies by using a two-part tool that addresses the specific domains set out in Section 8 of the *Cochrane Handbook for Systematic Reviews for Interventions* (Higgins 2011). The domains include sequence generation, allocation concealment, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other bias. In the 'Risk of bias' table, the first part of the tool involves a description for each entry, while the second part determines the risk of bias by assigning a judgment for each entry as 'low risk' of bias, 'high risk' of bias, and 'unclear risk' of bias indicating uncertainty or lack of information.

The overall risk of bias was assessed by completing a 'Risk of bias' table for each included study and then studies were grouped in the following categories.

- Low risk of bias: when all key domains were assessed as being at low risk of bias (a possible bias that was unlikely to alter the results).
- High risk of bias: when one or more domains were assessed as being at high risk of bias (a likely bias that seriously indicated less confidence about the results).
- Unclear risk of bias: when one or more key domains were assessed as unclear (a likely bias that raised doubts about the results).

Measures of treatment effect

Continuous data

We calculated the mean difference (MD) and 95% confidence interval (CI) for continuous outcomes such as changes in width and height of alveolar ridge. The reported mean changes from baseline as well as the final mean scores were combined as MD. In the event of combining studies using different scales of measurements, the standardised mean difference (SMD) was used.

Binary data

Risk ratios (RR) and 95% CIs were calculated for dichotomous outcomes such as implant failure rate.

Unit of analysis issues

The statistical unit of randomisation for parallel-group studies was the participant, and for split-mouth studies it was the site. The following issues were taken into account in data analysis.

- The errors related to the unit of analysis particularly in the presence of multiple treatment sites in split-mouth studies.
- The level of randomisation (i.e. cluster-randomised trials).
- Multiple observations (i.e. repetition of measurements of the same outcome).
- studies with multiple intervention groups to avoid a unit-of-analysis error in the Methods>Unit of analysis issues section.

Dealing with missing data

In the event of incompletely reported data regarding the study characteristics, methods, and results, we contacted the corresponding authors for clarification. We estimated the missing standard deviations of continuous variables using the methods detailed in Section 7.3.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of heterogeneity

We used Cochran's test for heterogeneity and the I^2 statistic to statistically determine the percentage variation across the studies. The tests for heterogeneity were interpreted according to the guidelines detailed in Section 9.5 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of reporting biases

A comprehensive search was adopted in an attempt to avoid reporting bias. The search included grey literature, non-English language publications, and contacting different manufacturers to identify ongoing and unpublished clinical trials. We did not use the funnel plot technique (Egger 1997) to assess publication and reporting bias because of the small number of included studies.

Data synthesis

Meta-analyses were conducted for trials of similar comparisons reporting the same outcome measures. The meta-analyses were used to quantitatively summarise the results using RevMan 5.4 (Review Manager 2020). In the presence of four or more trials, risk ratios were combined for dichotomous data, and mean differences for continuous data using a random-effects model. Otherwise, a fixed-effect model was used for combining three or less trials. The analysis of the split-mouth trials was undertaken using the generic inverse variance method in RevMan, taking into account the clustering of sites within participants. A correlation coefficient of 0.5 was imputed for split-mouth trials. The effect of ARP techniques for bone maintenance was assessed according to different outcomes (alveolar bone width and height, post-surgical complications, need for additional augmentation, and implant failure).

Subgroup analysis and investigation of heterogeneity

Subgroup analysis was to be performed to investigate the heterogeneity of the results and explore the effects of different methods of ARP across different methods of assessment and types of socket morphology. However, the subgroup analysis was not possible due to the small number of studies within each category of comparison.

Sensitivity analysis

Sensitivity analysis was planned to investigate the influence of methodological quality (such as excluding trials with overall high risk of bias or those with small sample size) on the robustness of our findings.

Summary of findings and assessment of the certainty of the evidence

We developed 'Summary of findings' tables for the main comparisons and primary outcomes of this review using GRADEPro software (GRADEpro GDT). The certainty of the body of evidence was assessed with reference to the overall risk of bias of the included studies, the directness of the evidence, the inconsistency of the results, the precision of the estimates, and the risk of publication bias. The certainty of the body of evidence for each of the primary outcomes was categorised as high, moderate, low, or very low.

RESULTS

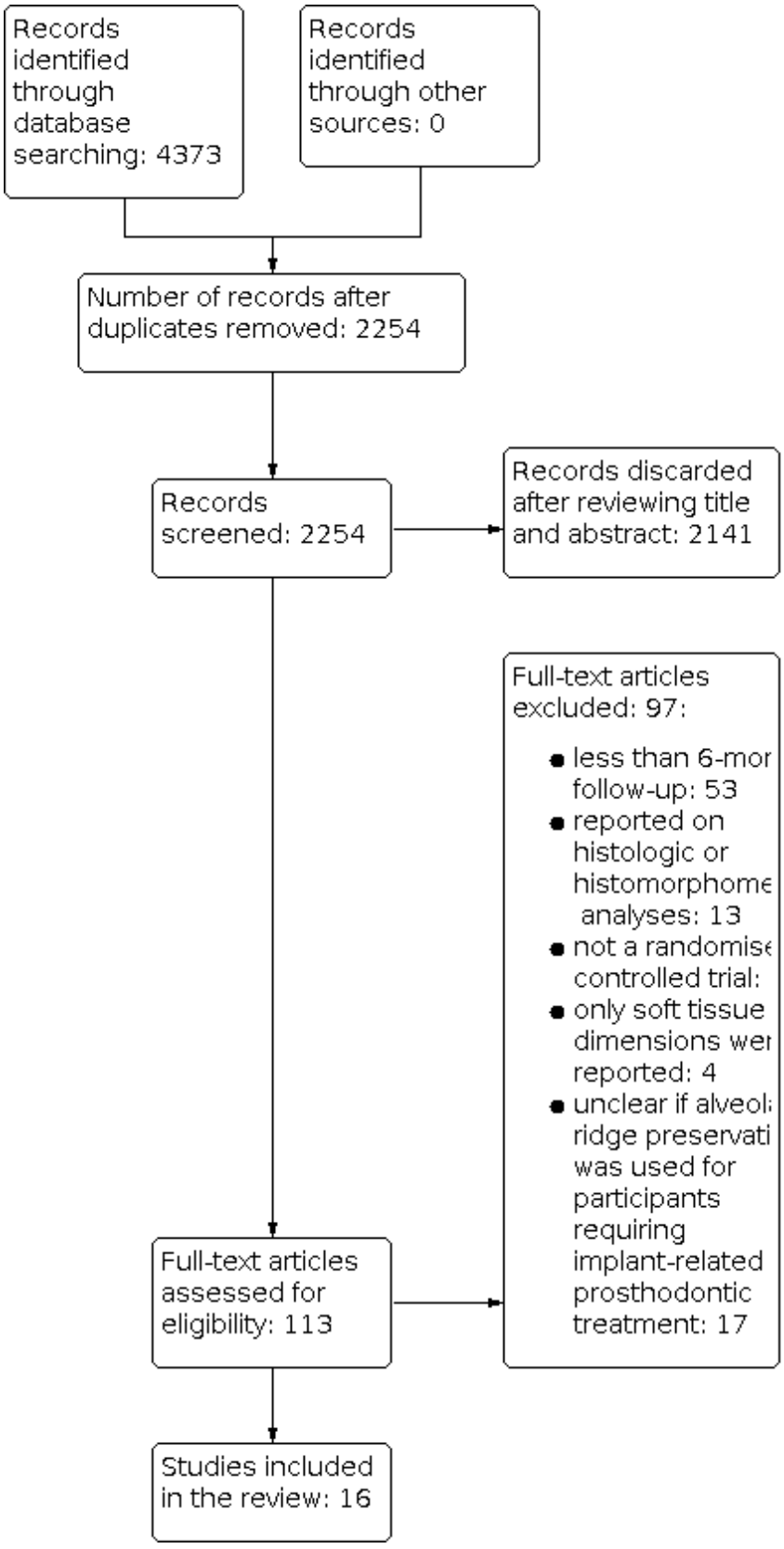
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies tables.

Results of the search

A total of 113 trials were potentially eligible for inclusion (Figure 1), of which we excluded 97. There were no non-English language studies included in this review. A total of 16 trials were included (Barone 2012; Brkovic 2012; Cha 2019; Fernandes 2011; Festa 2013; Fischer 2018; Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017). Nine new trials were included in this updated review, with six new trials (Cha 2019; Fischer 2018; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014) in the category of comparing alveolar ridge preservation (ARP) to extraction alone and three new trials (Santana 2019; Scheyer 2016; Serrano Mendez 2017) in the category of comparing different grafting materials. One trial (Iasella 2003) from the original review was excluded as some of the data were recorded at four months.

Figure 1. Study flow diagram.



Included studies

Characteristics of the trial settings and investigators

Of the 16 included trials, four trials were conducted in Italy (Barone 2012; Festa 2013; Iorio-Siciliano 2017; Iorio-Siciliano 2020), two trials in the USA (Hoang 2012; Santana 2019), one trial in Brazil (Fernandes 2011), one trial in the UK (Patel 2013), one trial in Serbia (Brkovic 2012), one trial in Iran (Gholami 2012), one trial in China (Pang 2014), one trial in South Korea (Cha 2019), one trial in Germany (Fischer 2018), one trial in India (Madan 2014), one trial in Colombia (Serrano Mendez 2017), and one multicentre trial in the USA and Germany (Scheyer 2016).

The study design was described as parallel group in 12 trials (Barone 2012; Brkovic 2012; Cha 2019; Fischer 2018; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017), whereas four trials had a split-mouth study design (Fernandes 2011; Festa 2013; Gholami 2012; Madan 2014).

The product used for ARP was supported by industry in four trials (Brkovic 2012; Fernandes 2011; Patel 2013; Scheyer 2016). Two trials (Cha 2019; Serrano Mendez 2017) were funded by a research grant, seven trials (Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014; Santana 2019) did not receive any support, and three trials (Barone 2012; Festa 2013; Fischer 2018) did not report on the source of funding.

All the trials were conducted at universities, except for two trials (Barone 2012; Scheyer 2016).

Characteristics of the interventions

1. Bone grafting versus extraction

Eight trials (Barone 2012; Cha 2019; Festa 2013; Fischer 2018; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014) compared the use of grafting materials with extraction alone.

i. Xenografts versus extraction

Four trials (Cha 2019; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014) compared deproteinised bovine bone mineral (DBBM) (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) or DBBM with 10% porcine collagen (Bio-Oss Collagen, Geistlich Pharma AG, Wolhusen, Switzerland) and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) with extraction alone.

Two trials (Barone 2012; Festa 2013) compared porcine-derived corticocancellous bone mix and collagen membrane (OsteoBiol, Coazze, Italy) with extraction alone.

One trial (Fischer 2018) compared DBBM (Endobon, Zimmer Biomet, West Palm Beach, Florida, USA) alone or with soft tissue punch or collagen barrier (OsseoGuard, Zimmer Biomet, West Palm Beach, Florida, USA) with extraction alone.

ii. Alloplasts versus extraction

One trial (Madan 2014) compared resorbable polylactide and polyglycolide (PLA-PGA) sponge (Fisiograft, Ghimas, Bologna, Italy) with extraction alone.

2. Different grafting materials

Eight trials (Brkovic 2012; Fernandes 2011; Gholami 2012; Hoang 2012; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017) compared different grafting materials.

i. Allograft versus xenograft

One trial (Santana 2019) compared a mineralised ground cancellous human allograft (AlloGraft, OCAN 250 to 1000 microns, Straumann AG, Basel, Switzerland) and synthetic polymeric polyethylene glycol (PEG) barrier (Straumann AG, Basel, Switzerland) versus DBBM (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) and PEG barrier (Straumann AG, Basel, Switzerland).

One trial (Scheyer 2016) compared demineralised allograft (OraGraft DGC, LifeNet Health Inc., Virginia Beach, Virginia, USA) and cross-linked bovine collagen barrier (BioMend Extend Zimmer Dental, Inc., Carlsbad, USA) versus DBBM with 10% porcine collagen (Bio-Oss Collagen, Geistlich Pharma AG, Wolhusen, Switzerland) and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland).

One trial (Serrano Mendez 2017) compared demineralised freeze-dried cortical bone allograft (600 to 800 µm, Banco de Tejidos Cosme y Damian, Bogota, Colombia) and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) versus DBBM with 10% porcine collagen (Bio-Oss Collagen, Geistlich Pharma AG, Wolhusen, Switzerland) and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland).

ii. Alloplast versus xenograft

One trial (Gholami 2012) compared nanocrystalline hydroxyapatite (NCHA) NanoBone 0.6 mm and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) versus DBBM (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland). Another trial (Patel 2013) compared Straumann bone ceramic (SBC) (Straumann AG, Basel, Switzerland) and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) versus DBBM (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland).

iii. Alloplast with and without membrane

One trial (Brkovic 2012) compared the use of beta-tricalcium phosphate with type I collagen (β-TCP/C1g) (Septodont, Saint-Maur-des-Fosses, France) with barrier membrane (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) versus β-TCP/C1g alone.

iv. Synthetic cell-binding peptide P-15 as adjunct to other grafting materials

One trial (Fernandes 2011) compared acellular dermal matrix (ADM) (AlloDerm, LifeCell Corporation, The Woodlands, Texas, USA), anorganic bovine bone matrix (ABM) and synthetic cell-binding peptide P-15 (PepGen P-15, DENTSPLY Friadent CeraMed, Lakewood, Colorado, USA) versus ADM alone.

v. Demineralised bone matrix single particle size versus demineralised bone matrix multiple particle size

One trial (Hoang 2012) compared demineralised bone matrix, single particle size (SPS) between 125 µm and 710 µm in a carrier

of bovine collagen and sodium alginate versus demineralised bone matrix multiple particle size (MPS) between 125 µm and 710 µm in a carrier of bovine collagen and sodium alginate.

Characteristics of the outcome measures

Primary outcomes

- Changes in the bucco-lingual/palatal width of the alveolar ridge were reported in 14 trials (Barone 2012; Brkovic 2012; Cha 2019; Fernandes 2011; Festa 2013; Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017).
- Changes in vertical height of the alveolar ridge were reported in 14 trials (Barone 2012; Brkovic 2012; Cha 2019; Fernandes 2011; Festa 2013; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017).
- Complications were reported in five trials (Brkovic 2012; Cha 2019; Festa 2013; Patel 2013; Scheyer 2016). The adverse events ranged from pain and swelling (Festa 2013; Patel 2013), moderate glazing, redness and oedema (Scheyer 2016), partial loss of grafting material (Patel 2013), membrane exposure (Patel 2013), fibrous adhesion (Brkovic 2012) to delayed healing with partial exposure of buccal plate (Cha 2019). Eleven trials reported that the procedure was uneventful (Barone 2012; Fernandes 2011; Fischer 2018; Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014; Santana 2019; Serrano Mendez 2017).
- Need for additional augmentation prior to implant placement was reported in seven trials (Barone 2012; Cha 2019; Fischer 2018; Gholami 2012; Iorio-Siciliano 2020; Patel 2013; Scheyer 2016).
- Aesthetic outcomes of future prosthodontic rehabilitation were not assessed in any trial.
- Implant failure rate was reported in three trials (Barone 2012; Pang 2014; Patel 2013).

Secondary outcomes

- Peri-implant marginal bone level changes were measured in one trial (Barone 2012) using standardised intraoral radiographs.
- Changes in probing depth (PD) at teeth adjacent to the extraction site were presented in one trial (Patel 2013).
- Changes in clinical attachment level (CAL) at teeth adjacent to the extraction site were not reported in any trial.
- Complications of prosthodontic rehabilitation were not reported in any trial.

Characteristics at baseline

Inclusion criteria

- Age ≥ 18 years of age (Barone 2012; Cha 2019; Festa 2013; Fischer 2018; Gholami 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Patel 2013; Santana 2019; Serrano Mendez 2017). In one trial, an age range of 20 and 55 was specified (Brkovic 2012).
- ≥ 20 teeth in both maxillary and mandibular arches (Fernandes 2011).
- Extraction of non-molars and subsequent single-tooth implant treatment (Barone 2012; Brkovic 2012; Fernandes 2011; Festa 2013; Fischer 2018; Gholami 2012; Madan 2014; Pang 2014; Patel 2013; Santana 2019; Serrano Mendez 2017).
- Extraction of one or more maxillary or mandibular molars and subsequent single-tooth implant treatment (Brkovic 2012; Cha 2019; Hoang 2012).
- Extraction of maxillary or mandibular non-molars and molars with subsequent implant treatment (Iorio-Siciliano 2017; Iorio-Siciliano 2020).
- Extraction of premolars or molars with subsequent implant treatment (Scheyer 2016).
- Radiographic bone height of 4 to 8 mm at the site intended for surgery (Cha 2019).
- Radiographic bone height of ≥ 7 mm at the site intended for surgery (Madan 2014).
- Full-mouth plaque and bleeding scores of less than 25% (Iorio-Siciliano 2017; Iorio-Siciliano 2020).
- Presence of at least 2 mm of keratinised tissue (Iorio-Siciliano 2017; Iorio-Siciliano 2020).
- Being in good general health (Brkovic 2012; Cha 2019; Fischer 2018; Madan 2014; Pang 2014).

Exclusion criteria

- Patients with acute periapical or periodontal infections (Brkovic 2012; Fernandes 2011; Fischer 2018; Gholami 2012; Iorio-Siciliano 2020; Pang 2014). Acute endodontic lesion in the test tooth or in the neighbouring areas (Patel 2013). Teeth with small apical lesions ≤ 3 mm were not excluded if it was determined that the lesion could be adequately debrided after extraction (Hoang 2012).
- Inability to maintain adequate oral hygiene (Brkovic 2012). Full-mouth plaque level of more than 30% (Patel 2013; Serrano Mendez 2017). Periodontally compromised teeth (Iorio-Siciliano 2020). Untreated periodontal disease (Fischer 2018).
- Third molars (Iorio-Siciliano 2020).
- Loss of buccal bone at the time of extraction (Scheyer 2016; Serrano Mendez 2017).
- Any medical condition that contraindicated surgery (Cha 2019; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Santana 2019).
- Compromised health that could affect the ability of the participants' tissues to heal (Barone 2012; Brkovic 2012; Fernandes 2011; Festa 2013; Gholami 2012; Hoang 2012; Patel 2013; Scheyer 2016; Serrano Mendez 2017). Immunosuppressive systemic diseases (Santana 2019).
- History of malignancy, radiotherapy, or chemotherapy (Cha 2019; Fischer 2018; Scheyer 2016).
- Pathologic condition of the maxillary sinus such as active sinusitis or cysts (Cha 2019).
- Use of medications that compromise healing (Pang 2014; Scheyer 2016). Use of intravenous bisphosphonates (Fischer 2018; Scheyer 2016).
- Long-term antibiotic therapy or the need for antibiotic prophylaxis (Fernandes 2011).
- Allergy to medications, grafting materials, or membranes used in the study (Barone 2012; Gholami 2012; Scheyer 2016).
- Pregnancy or lactation (Brkovic 2012; Cha 2019; Fernandes 2011; Festa 2013; Fischer 2018; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014; Patel 2013; Scheyer 2016; Serrano Mendez 2017).
- Occlusal considerations: lack of opposing occluding dentition in the area intended for extraction (Barone 2012), absence of

one or two of the adjacent teeth (Barone 2012; Cha 2019; Festa 2013; Patel 2013; Scheyer 2016; Serrano Mendez 2017), suitable occlusion for the planned prosthodontic treatment (Brkovic 2012), extensive parafunctional habits or bruxism (Patel 2013).

- Smoking habits: smokers (Brkovic 2012; Festa 2013; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014; Santana 2019; Scheyer 2016). Smoking more than 10 cigarettes per day (Barone 2012; Fischer 2018; Patel 2013; Serrano Mendez 2017). Smoking more than 20 cigarettes (Cha 2019).

Indications for tooth extraction

Several indications were listed in the selected trials including: inability to restore tooth (Brkovic 2012; Hoang 2012), endodontic reasons (e.g. failed treatment or root fracture) (Brkovic 2012; Cha 2019; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Santana 2019; Serrano Mendez 2017), cracked tooth (Cha 2019), prosthetic reasons (Santana 2019), caries (Iorio-Siciliano 2017; Iorio-Siciliano 2020; Serrano Mendez 2017), and periodontal disease (Brkovic 2012; Cha 2019; Hoang 2012; Santana 2019).

Method of assessment

All of the included trials used one or a combination of the following methods to record the dimensions of the preserved alveolar ridge: periodontal probe (Barone 2012; Brkovic 2012; Fernandes 2011; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017), caliper (Brkovic 2012; Festa 2013; Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Santana 2019; Serrano Mendez 2017), standardised radiograph (Barone 2012; Patel 2013; Serrano Mendez 2017), panoramic radiograph (Cha 2019; Pang 2014), computed tomography (Cha 2019; Madan 2014; Pang 2014), and template (Barone 2012; Fernandes 2011; Festa 2013; Madan 2014; Santana 2019; Scheyer 2016; Serrano Mendez 2017).

Type of socket

Twelve trials included four-wall socket (Barone 2012; Brkovic 2012; Festa 2013; Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014; Patel 2013; Santana 2019; Serrano Mendez 2017). Two trials evaluated three-wall socket (Fernandes 2011; Scheyer 2016), one trial evaluated both three- and four-wall sockets (Fischer 2018), while one trial evaluated one-, two-, three- and four-wall sockets (Cha 2019).

Surgical technique

Primary closure was not attempted in eight trials (Cha 2019; Fischer 2018; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Patel 2013; Scheyer 2016), whereas primary closure was achieved in eight trials (Barone 2012; Brkovic 2012; Fernandes 2011; Festa 2013; Gholami 2012; Pang 2014; Santana 2019; Serrano Mendez 2017).

Comparability of control and treatment groups at entry

At entry, the control and treatment groups were comparable for the baseline characteristics and outcomes used in all trials.

Timing of implant placement

- Six months (Cha 2019; Fernandes 2011; Festa 2013; Fischer 2018; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014; Santana 2019; Scheyer 2016; Serrano Mendez 2017).
- Six to eight months (Gholami 2012).
- Seven months (Barone 2012).
- Eight months (Patel 2013).
- Nine months (Brkovic 2012).

Duration of the studies

- Six months (Cha 2019; Fernandes 2011; Festa 2013; Fischer 2018; Hoang 2012; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014; Santana 2019; Scheyer 2016; Serrano Mendez 2017).
- Six to eight months (Gholami 2012).
- Eight and 12 months (Patel 2013).
- Nine months (Brkovic 2012).
- 36 months (Barone 2012).

Sample size

Eight trials reported a sample size calculation (Cha 2019; Fernandes 2011; Fischer 2018; Hoang 2012; Iorio-Siciliano 2020; Patel 2013; Scheyer 2016; Serrano Mendez 2017).

Excluded studies

We excluded 97 trials. Fifty-three trials had less than six months of follow-up (Aimetti 2009; Alkanan 2019; Araujo 2015; Arbab 2016; Areewong 2019; Barone 2016; Barone 2017; Borg 2015; Canellas 2020; Cardaropoli 2012; Cardaropoli 2014; Clark 2018; Clementini 2020; Cook 2013; Coomes 2014; Corning 2019; Demetter 2017; Eskow 2014; Fiorellini 2005; Fotek 2009; Guarnieri 2017; Hauser 2013; Iasella 2003; Jo 2019; Jonker 2020; Kim 2014; Kotsakis 2014; Kutkut 2012; Lai 2020; Lekovic 1998; Lim 2017; Lim 2019; Llanos 2019; Machtei 2019; Mandarino 2018; Marconcini 2018; Mayer 2016; Meloni 2015; Nart 2017; Nevins 2006; Oghli 2010; Ouyyamwongs 2019; Ovcharenko 2020; Parashis 2016; Pinho 2006; Poulias 2013; Sisti 2012; Spinato 2014; Sun 2019; Toloue 2012; Vance 2004; Walker 2017; Wood 2012); 13 trials only reported on histologic or histomorphometric analyses (Alkan 2013; Bakhshalian 2018; Barone 2013; Barone 2015; Calasans-Maia 2013; Checchi 2011; Froum 2002; Geurs 2014; Molly 2008; Nevins 2011; Pellegrini 2014; Perelman-Karmon 2012; Scheyer 2012), 10 trials were not randomised controlled trials (Casado 2010; Crespi 2009; Kim 2011; Lekovic 1997; Neiva 2011; Pelegrine 2010; Serino 2003; Shakibaie 2013; Shim 2018; Zhao 2018), four trials only reported soft tissue dimensions (Debel 2021; Flugge 2015; Schneider 2014; Thalmair 2013), and for 17 trials it was unclear whether ARP was used for participants requiring implant-related prosthodontic treatment (Abdelhamid 2016; Aimetti 2018; Al Qabbani 2018; Amirzargar 2018; Cavdar 2017; Fernandes 2016; Girish Kumar 2018; Hassan 2017; Jung 2013; Jung 2018; Karaca 2015; Lee 2020; Natto 2017; Rasperini 2010; Sbordone 2017; Temmerman 2016; Zadeh 2016).

Risk of bias in included studies

The assessment of risk of bias is summarised in Figure 2 and Figure 3. Some additional information was provided by corresponding authors. In summary, four trials were judged to be at high risk of bias overall (Barone 2012; Brkovic 2012; Fernandes 2011; Iorio-Siciliano 2020), whereas the remaining trials were judged to be at unclear risk of bias (Cha 2019; Festa 2013; Fischer 2018; Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Madan 2014; Pang 2014; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

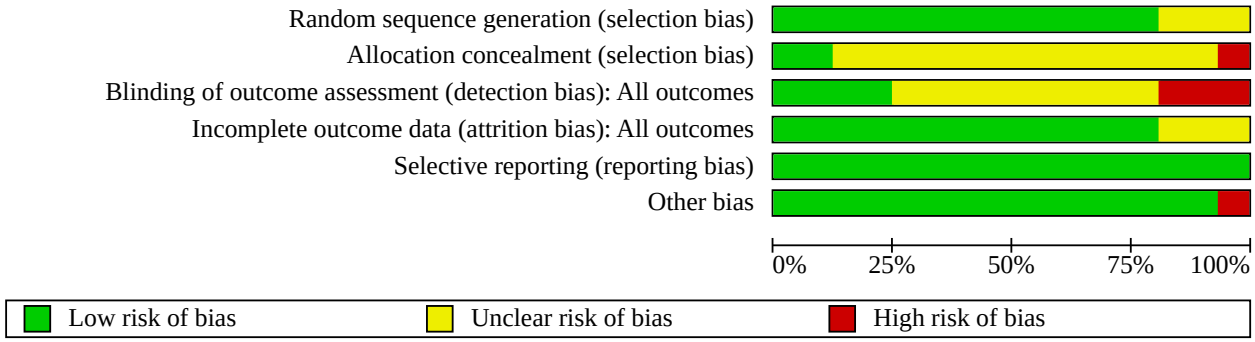
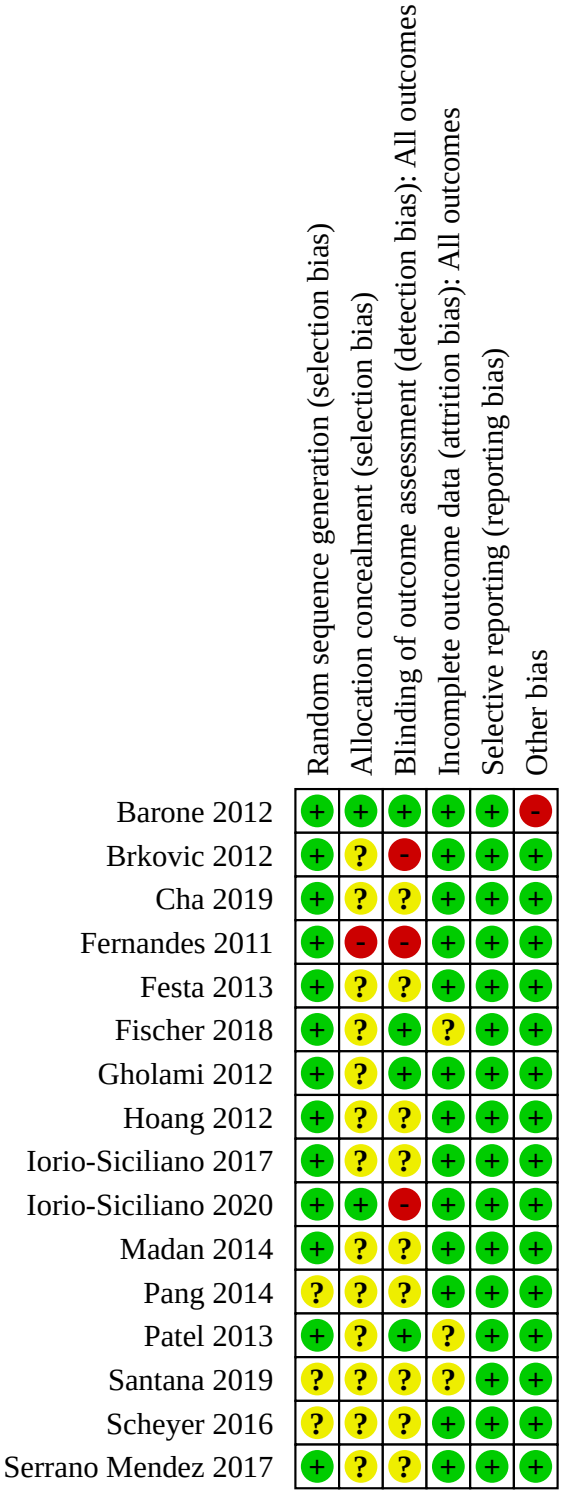


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

The random sequence generation was judged as adequate in all but three trials (Pang 2014; Santana 2019; Scheyer 2016) in which the method of randomisation was unclear. In one trial (Fernandes 2011) allocation was not concealed, while it was not clear how the allocation was concealed in 13 trials (Brkovic 2012; Cha 2019; Festa 2013; Fischer 2018; Gholami 2012; Hoang 2012; Iorio-Siciliano 2017; Madan 2014; Pang 2014; Patel 2013; Santana 2019; Scheyer 2016; Serrano Mendez 2017). Allocation was adequately concealed in two trials (Barone 2012; Iorio-Siciliano 2020).

Blinding

It is acknowledged that there is a risk of performance bias as it is not possible to blind the surgeon or the participant to the intervention. Therefore, the assessment of blinding was limited to assessing the blinding of outcome evaluation, which is a more practical way to minimise detection bias in these trials.

A blinded outcome assessor recorded the follow-up measurements in four trials (Barone 2012; Fischer 2018; Gholami 2012; Patel 2013). Blinding of assessors was not clear in nine trials (Cha 2019; Festa 2013; Hoang 2012; Iorio-Siciliano 2017; Madan 2014; Pang 2014; Santana 2019; Scheyer 2016; Serrano Mendez 2017). The blinding process was not attempted in three trials (Brkovic 2012; Fernandes 2011; Iorio-Siciliano 2020).

Incomplete outcome data

No withdrawals were reported in nine trials (Barone 2012; Brkovic 2012; Fernandes 2011; Festa 2013; Iorio-Siciliano 2017; Madan 2014; Pang 2014; Scheyer 2016; Serrano Mendez 2017).

Withdrawals and exclusions occurred in seven trials (Cha 2019; Fischer 2018; Gholami 2012; Hoang 2012; Iorio-Siciliano 2020; Patel 2013; Santana 2019).

Despite withdrawals, four trials (Cha 2019; Gholami 2012; Hoang 2012; Iorio-Siciliano 2020) were still judged to be at low risk of attrition bias as the number and reasons of withdrawals did not seem to affect the overall results. In Hoang 2012, nine participants were non-compliant with the trial protocol and one was excluded from the study at the time of surgery due to large buccal and palatal dehiscence after extracting the tooth. Another participant did not complete the radiographic part of the trial due to pregnancy. In Cha 2019, one out of the 40 participants dropped out due to personal reason following tooth extraction. One participant in Gholami 2012 withdrew and did not return to second-stage surgery. Five dropouts were recorded in Iorio-Siciliano 2020; two participants had medical reasons, one was pregnant, one moved to another town, and one was not compliant with the research protocol.

It was not clear whether the withdrawals in three trials (Fischer 2018; Patel 2013; Santana 2019) had any impact on the estimate of treatment effect. Fischer 2018 reported five dropouts, of which, two declined implant placement and the remaining three were non-compliant with the protocol. Patel 2013 reported five withdrawals and exclusions: two were excluded due to complete loss of buccal plate during extraction, one withdrew before randomisation, one quit the trial before implant placement, and one did not have the implant due to insufficient primary stability. Santana 2019 recorded four excluded sites but did not fully clarify all the reasons for dropouts apart from some inadequate sampling for histological evaluation. We assessed these three trials as at unclear risk of attrition bias.

Selective reporting

We assessed all trials as at low risk of reporting bias.

Other potential sources of bias

We judged one trial (Barone 2012) at high risk of other bias as the figures presented showed one molar site while the inclusion criteria in the text indicated that only non-molar sites were included in the trial. Authors did not reply to our request for clarification.

Effects of interventions

See: **Summary of findings 1** Alveolar ridge preservation (ARP) versus extraction for replacing missing teeth; **Summary of findings 2** Different grafting materials for alveolar ridge preservation

In total, 426 participants with 524 extraction sites were included in the analysis.

1. Bone grafting versus extraction

We found eight trials in this category: seven trials comparing xenografts versus extraction (Barone 2012; Cha 2019; Festa 2013; Fischer 2018; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014) and one trial comparing alloplasts versus extraction (Madan 2014).

i. Xenografts versus extraction

Changes in width and height of alveolar ridge

Meta-analyses of six trials (Barone 2012; Cha 2019; Festa 2013; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014) showed a significant reduction in the bucco-lingual/palatal width (mean difference (MD) -1.18 mm, 95% confidence interval (CI) -1.82 to -0.54; P = 0.0003, I^2 = 82%; 6 studies, 184 participants, 201 extraction sites) (Analysis 1.1), and height of the alveolar ridge (MD -1.35 mm, 95% CI -2.00 to -0.70; P < 0.0001, I^2 = 87%; 6 studies, 184 participants, 201 extraction sites) (Analysis 1.2). Both meta-analyses indicated a significant benefit for ARP using xenografts.

Complications

In one trial (Cha 2019) delayed healing with partial exposure of the buccal plate at suture removal was reported by one participant in the test group. Another trial (Festa 2013) reported postoperative pain and swelling without specifying the number of participants showing those symptoms.

Five trials (Barone 2012; Fischer 2018; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Pang 2014) reported that the procedure was uneventful.

Need for additional augmentation prior to implant placement

A meta-analysis of four trials (Barone 2012; Cha 2019; Fischer 2018; Iorio-Siciliano 2020) showed no evidence of a significant difference that ARP with xenograft reduced the need for additional augmentation (risk ratio (RR) 0.68, 95% CI 0.29 to 1.62; P = 0.39; 4 studies, 154 participants, 156 extraction sites) (Analysis 1.3).

Implant failure rate

One trial (Barone 2012) found no evidence of a difference between the use of xenograft and extraction. Two implants failed, one in

each group: one implant was not osseointegrated six months post-placement at the time of abutment connection, another implant failed and was removed as a result of mobility after 24 months of loading. Another trial (Pang 2014) reported no implant failures after one-year follow-up (Analysis 1.4).

Peri-implant marginal bone level changes

The data in relation to peri-implant marginal bone level changes were obtained from the results after seven months (Barone 2012). There were no statistically significant differences between the two groups for the marginal bone changes (Analysis 1.5).

Other outcomes

None of the studies comparing xenografts with extraction reported on aesthetic outcomes of future prosthodontic rehabilitation, changes in probing depth (PD) and changes in clinical attachment level (CAL) at teeth adjacent to the extraction site, or prosthodontic outcomes of rehabilitation.

ii. Alloplasts versus extraction

Changes in width and height of alveolar ridge

One trial (Madan 2014) of split-mouth design compared resorbable polylactide and polyglycolide (PLA-PGA) sponge (Fisiograft, Ghimas SpA, Italy) with extraction alone. The study evaluated 60 non-molar extraction sites in 15 participants at six months. No dropouts were reported. After six months, statistically significant differences were detected for ridge height in favour of ARP (Analysis 1.6).

Complications

Madan 2014 reported that the procedure was uneventful.

Other outcomes

No other primary or secondary outcomes were reported by the only trial included comparing alloplasts versus extraction.

2. Different grafting materials

We found eight trials in this category: three trials comparing allograft versus xenograft (Santana 2019; Scheyer 2016; Serrano Mendez 2017), two trials comparing alloplast versus xenograft (Gholami 2012; Patel 2013), one trial comparing alloplast with and without membrane (Brkovic 2012), one trial comparing allograft with and without synthetic cell-binding peptide P-15 (Fernandes 2011), and one trial comparing alloplast with different particle sizes (Hoang 2012).

i. Allografts versus xenografts

Changes in width and height of alveolar ridge

Meta-analyses of three trials (Santana 2019; Scheyer 2016; Serrano Mendez 2017) showed no significant differences between the two groups with regard to bucco-lingual/palatal width (MD -0.40 mm, 95% CI -1.13 to 0.34; P = 0.29, I^2 = 82%; 3 studies, 87 participants, 87 extraction sites; Analysis 2.1), and height of the alveolar ridge (MD -0.45 mm, 95% CI -1.48 to 0.58; P = 0.39, I^2 = 56%; 2 studies, 60 participants, 60 extraction sites; Analysis 2.2).

Complications

One trial (Scheyer 2016) reported moderate glazing, redness and oedema, while two trials (Santana 2019; Serrano Mendez 2017) reported there were no adverse events.

Need for additional augmentation prior to implant placement

Only Scheyer 2016 reported that additional bone augmentation procedure was required for three sites in the allograft group, while none of the sites in the xenograft required additional augmentation procedure before implant placement. No statistically significant difference was shown between the two groups (RR 6.36, 95% CI 0.35 to 115.73; P = 0.21; 1 study, 40 participants, 40 extraction sites; Analysis 2.3).

Other outcomes

None of the trials under this comparison reported on aesthetic outcomes of future prosthodontic rehabilitation, implant failure rate, peri-implant marginal bone level changes, changes in probing depth and changes in clinical attachment level at teeth adjacent to the extraction site, or prosthodontic outcomes of rehabilitation.

ii. Alloplasts versus xenografts

Changes in width and height of alveolar ridge

Meta-analysis of two studies (Gholami 2012; Patel 2013) showed that there were no statistically significant differences for changes in width and height of the alveolar ridge, with mean differences of -0.31 mm (95% CI -0.66 to 0.04; P = 0.08, I^2 = 73%; 2 studies, 37 participants, 55 extraction sites; Analysis 2.4) and -0.60 mm (95% CI -1.27 to 0.07; P = 0.08; 1 study, 25 participants, 25 extraction sites; Analysis 2.5), respectively.

Complications

One trial (Patel 2013) reported pain, swelling, membrane exposure, and partial loss of grafting material, while the other trial (Gholami 2012) reported that the procedure was uneventful.

Need for additional augmentation prior to implant placement

The meta-analysis included two trials (Gholami 2012; Patel 2013) and showed no evidence of a difference (RR 1.09, 95% CI 0.65 to 1.83; P = 0.75, I^2 = 0%; 2 studies, 37 participants, 55 extraction sites; Analysis 2.6).

Implant failure rate

One trial (Patel 2013) reported that none of the implants failed after 12 months of loading (Analysis 2.7).

Changes in probing depths (PD) at teeth adjacent to the extraction site

Meta-analyses showed no differences in PDs at the neighbouring teeth between the test groups. Only one trial (Patel 2013) reported the changes in PD at teeth adjacent to the extraction sites (MD -0.30 mm, 95% CI -0.61 to 0.01; P = 0.06; 1 study, 25 participants, 25 extraction sites; Analysis 2.8).

Other outcomes

None of the included studies reported on aesthetic outcomes of future prosthodontic rehabilitation, peri-implant marginal bone level changes, changes in CAL at teeth adjacent to the extraction site, and prosthodontic outcomes of rehabilitation.

iii. Alloplasts with and without membrane

Changes in width and height of alveolar ridge

One trial (Brkovic 2012) of parallel-group design compared beta-tricalcium phosphate with type I collagen (β-TCP/C1g)

(Septodont, Saint-Maur-des-Foses, France) versus β-TCP/C1g and barrier membrane (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland). Twenty participants enrolled in this study with each participant contributing to either non-molar or molar extraction site. All the sites healed uneventfully with no signs of inflammation. Significant reductions in the alveolar ridge height and width and height in the non-membrane group were observed (Analysis 2.9; Analysis 2.10).

Complications

Fibrous adhesions at the cervical part of previously preserved sockets were observed in two participants (Brkovic 2012).

Other outcomes

None of the trials reported on any other primary or secondary outcomes of this review.

iv. Allografts with and without synthetic cell-binding peptide P-15

Changes in width and height of alveolar ridge

One trial (Fernandes 2011) of split-mouth design compared acellular dermal matrix (ADM) (AlloDerm, LifeCell Corporation, The Woodlands, Texas, USA), anorganic bovine bone matrix (ABM) with synthetic cell-binding peptide P-15 (PepGen P-15, DENTSPLY Friadent CeraMed, Lakewood, Colorado, USA) versus ADM only. A total of 18 participants (36 maxillary anterior extraction sockets) completed the study with no postoperative complications. A reduction in alveolar ridge width in the allograft with synthetic cell-binding peptide P-15 group was observed, however, no statistically significant differences were found between the two groups in terms of ridge height (Analysis 2.11; Analysis 2.12).

Complications

Fernandes 2011 reported that the procedure was uneventful.

Other outcomes

Fernandes 2011 did not report on any other primary or secondary outcomes of this review.

v. Alloplasts with different particle sizes

Changes in width and height of alveolar ridge

One trial (Hoang 2012) of parallel-group design including 30 participants (30 extractions sites) compared demineralised bone matrix, single particle size (SPS) between 125 µm and 710 µm in a carrier of bovine collagen and sodium alginate versus demineralised bone matrix multiple particle size (MPS) between 125 µm and 710 µm in a carrier of bovine collagen and sodium alginate. No statistically significant differences were found between the two groups in terms of ridge width and height (Analysis 2.13; Analysis 2.14).

Complications

Hoang 2012 reported that the procedure was uneventful.

Other outcomes

Hoang 2012 did not report on any other primary or secondary outcomes of this review.

Sensitivity analysis

The planned sensitivity analysis was not performed due to the small number of trials and the fact that none of the trials were of high quality.

DISCUSSION

Summary of main results

See Summary of findings 1, Summary of findings 2.

The question of whether alveolar ridge preservation (ARP) does maintain valuable alveolar ridge bone following extractions is relevant to current 'state of the art' recommendations for prosthodontically-driven implant placement, with enhanced aesthetic outcomes. This applies whether delayed or immediate placement techniques are followed and regardless of the loading protocol used. A follow-up period of six months or more was considered suitable in this review to allow for most of the vertical and horizontal resorption of socket walls to occur, in order to provide a better understanding of the role of ARP in implant site development.

Nine new trials were included in this updated review, with six new trials (Cha 2019; Fischer 2018; Iorio-Siciliano 2017; Iorio-Siciliano 2020; Madan 2014; Pang 2014) in the category of comparing ARP to extraction alone and three new trials (Santana 2019; Scheyer 2016; Serrano Mendez 2017) in the category of comparing different grafting materials, bringing the total to 16 included studies. With the inclusion of more trials, there is very low-certainty evidence of a reduction in loss of alveolar ridge width and height in favour of ARP techniques, but we found no evidence of a significant difference for the need for additional augmentation at the time of implant placement. There is still a lack of evidence of any differences in other outcomes such as implant failure rate and peri-implant marginal bone level changes. There is also lack of information to evaluate other outcomes, especially changes in clinical attachment level, aesthetic, and prosthodontic outcomes. There is no evidence of any clinically significant difference between different grafting materials and barriers used for ARP in ridge width and height or the need for additional augmentation procedures even when a new comparison group (allograft versus xenograft) was included in this update. With only one trial (Brkovic 2012) at high risk of bias showing very low-certainty evidence that alloplastic materials with membrane resulted in less change in ridge height and width, compared with alloplastic materials alone.

Overall completeness and applicability of evidence

When ARP was compared to extraction alone, the inclusion of new trials further supported the use of ARP techniques to minimise changes in ridge width and height as well as the need for additional augmentation procedures. When different grafting materials for ARP were compared, new trials were included in a subgroup that compared allografts to xenografts. The variety of grafting materials and the limited number of participants per subgroup analysis did not provide any strong evidence on the use of a specific ARP technique. In addition, the small number of participants increased the risk of overestimation of intervention effects (Thorlund 2011). No sensitivity analysis was attempted due to the small number of included studies. The fact that over 100 trials were initially selected and considered eligible for further scrutinisation highlights the growing number of trials in this field of implant dentistry. However,

most studies did not meet the selection criteria of this review and therefore further studies with sufficient follow-up period are still needed. The influence of commercial funding and industry support remains an important factor that may increase the number of trials and introduce additional new materials for ARP that would potentially inflate heterogeneity further across the included trials in future reviews.

Quality of the evidence

The certainty of the evidence for ARP interventions when compared with extraction or with another ARP intervention was considered to be very low to low. We downgraded the included trials by one level for unclear risk of bias and by two levels for high risk of bias. We downgraded single trials with limited number of participants by two levels for imprecision. Small trials or trials with wide confidence intervals were downgraded by one level for imprecision. For inconsistency, further downgrades by one and two levels were considered for moderate and high heterogeneity, respectively.

Four out of 16 trials were judged to be at high risk of bias, largely due to lack of allocation concealment and blinding of outcome assessors. Twelve trials were judged to be at unclear risk of bias. As most of the studies failed to clarify the method of allocation concealment, one may question whether the participants might have been treated differently if the allocation of the participants was concealed from the operators. In exploring other potential sources of bias, authors were contacted to clarify inclusion criteria which only included non-molar sites, while the figures showed an ARP of molar site (Barone 2012).

It is acknowledged that all trials were judged to be at high risk of performance bias but blinding of participants and personnel was not considered as one of the main domains for assessing risk of bias in this review as neither participants nor personnel could be blinded to the intervention. However, we considered the blinded assessment of outcomes because having a blinded examiner to assess the outcomes is possible in these trials, particularly when the assessment is based on radiographic or cast analysis in which the examiner can be unaware of the interventions. Moreover, blinding the outcome assessor may eliminate the detection bias as measurements are made on a very narrow scale of millimetres which may have a significant effect on the results. In this context, 12 out of 16 trials were judged to be at unclear or high risk of bias in this domain.

In some instances, the information provided by the publications was not sufficient to reliably assess the quality of the trial. Some corresponding authors provided us with additional information that clarified the trials and allowed us to include them in the present review. This emphasises the importance of clearly reporting the results, including any attempt to conceal the allocation, along with dropouts and the reasons for exclusions, as recommended by CONSORT guidelines (www.consort-statement.org).

Fifty-three of 113 studies considered potentially eligible were excluded because their follow-up was less than six months and this was deemed insufficient to judge post-extraction ridge resorption. This indicates the need for further trials with long-term follow-up; see Implications for research.

Another important consideration that may affect the certainty of the evidence is the confounding variables across the included studies, such as: different tooth sites, anatomical factors, methods of assessment, and keratinised tissue at extraction sites. It is reasonable to assume that it is not possible to standardise all these variables, but one should consider that different determinants may affect the outcome of ARP. Research has suggested that healing time, clinical attachment level, and keratinised tissue at extraction site are possible determinants of ridge height preservation, whereas the buccal plate thickness and tooth root length are possible determinants of alveolar ridge width loss (Leblebicioglu 2013).

Potential biases in the review process

In addition to extensive searches of the electronic databases, we approached corresponding authors in an attempt to obtain additional information. Some corresponding authors did not reply to our requests and their trial data were therefore excluded from the analysis. With seven included trials either failing to report the source of funding or having commercial support for the ARP product used, publication bias is also suspected on research quality and outcomes.

Agreements and disagreements with other studies or reviews

The present review included all the randomised controlled trials (RCTs) available to date. The interaction of many variables and the lack of long-term data mean that it is not possible to determine whether the reduced loss in alveolar ridge height and width achieved by ARP is likely to improve implant treatment outcomes. Several systematic reviews (Avila-Ortiz 2014; Avila-Ortiz 2019; Bassir 2018; Canellas 2020; Chan 2013; Darby 2009; Del Fabbro 2017; Horváth 2013; Iocca 2017; Lee 2018; MacBeth 2017; Mardas 2015; Ten Heggeler 2011; Troiano 2018; Vignoletti 2012; Vittorini Orgeas 2013) were published on this topic, with almost half published in the last five years. They were not based on the most reliable clinical trials, and pooled different study designs, grafting materials, and therapeutic approaches in one comparison group against extraction alone. Nevertheless, they concluded that ARP may improve bone dimensions compared with extraction alone, but again questioned the long-term effects of ARP on implant success and peri-implant tissues.

Unlike other systematic reviews, Cochrane Reviews adopt stringent methodology in preparing protocols and reviews that go through internal and external thorough reviewing process prior to publication. In the current update of this Cochrane Review, we followed our original protocol by conducting a rigorous search strategy to identify only randomised trials and limiting our comparison groups to one ARP method or technique to minimise heterogeneity amongst included studies. Nevertheless, a small number of studies was analysed in many comparisons with general lack of long-term follow-up of implant outcomes.

There is general agreement that ARP may considerably enhance the site following extraction for future implant placement particularly when xenografts are compared to extraction alone. When different materials are compared in the absence of a control group of extraction alone, it is still premature to conclude which material is superior to others and whether barrier membranes provide any additional benefit.

AUTHORS' CONCLUSIONS

Implications for practice

Alveolar ridge preservation (ARP) techniques may minimise the loss of ridge width and height under ideal conditions in non-molar four-wall sockets, following extraction, but the evidence is very uncertain. There is a general agreement that implants can be placed six months after ARP, following a delayed placement procedure. However, there was no evidence that ARP would improve implant or prosthodontic success. There is also a lack of evidence of any significant differences in the need for additional augmentation at the time of implant placement. There are more trials to suggest that xenografts (one of the most studied materials) showed successful short-term ARP in terms of minimising loss of ridge width and height. However, clinicians should interpret the findings of this review with caution as the certainty of the evidence remains very low to low with all included studies judged to be at unclear or high risk of bias.

It is still not clear which ARP technique provides more predictable results. However, there is an indication that the need for primary closure is not warranted.

Implications for research

There is a need to conduct further long-term well-designed randomised controlled trials (RCTs), following the CONSORT guidelines (www.consort-statement.org) that not only report changes in ridge height and width, but also the achieved aesthetic/prosthodontic outcomes, the need for any additional augmentation, patient outcomes, and the long-term success rates of implants placed in preserved sites.

The analyses of cost-effectiveness and cost-benefit of ARP techniques are needed to compare the benefits of ARP and the cost of different grafting materials. As ARP is a relatively new intervention in dental care and the implementation of such procedure generates additional cost, an essential question to be answered resides mainly in the analysis of whether ARP can achieve tangible improvements of the clinical outcomes for the extra financial liability.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barone 2012

Study characteristics	
Methods	Trial design: randomised, parallel-group trial Location: Lucca, Italy Number of centres: single centre, Division of Dentistry, Versilia Hospital, Lido di Camaiore, Lucca, Italy Recruitment period: 2006 to 2007 Funding source: not stated
Participants	Inclusion criteria: patients 18 years of age and older that required 1 tooth extraction and requested implant restoration; had extraction sites with adjacent teeth; were able to sign an informed consent form Exclusion criteria: history of systemic diseases; long-term NSAID; required antibiotics prophylaxis; lack of opposite occluding dentition in the area intended for extraction and subsequent implant placement; presence of molar sites that required extraction; absence of adjacent teeth; absence of alveolar bone wall; unwillingness to return for follow-up examination; smoking > 10 cigarettes per day (participants smoking < 10 cigarettes per day were requested to stop smoking before and after surgery) Age at baseline: range 26 to 69 years Gender: M 16/F 24 Smokers: 12 (6 in each group) Teeth extracted: anterior and premolars Number randomised (participants/sites): 40/40 Number evaluated (participants/sites): 40/40
Interventions	**Comparison: ARP versus extraction alone**

Barone 2012 *(Continued)*

	Test group: (n = 20 extraction sockets) xenograft (corticocancellous porcine bone (mp3, OsteoBiol, Coazze, Italy)) and collagen membrane (Evolution, OsteoBiol) **Control group:** (n = 20 extraction sockets) extraction alone Surgical technique: primary closure Type of socket: 4-wall socket Duration of follow-up: 7 months until implant placement + 36 months
Outcomes	Plaque index, gingival index, bleeding on probing, width and height of alveolar ridge, implant failure, need for additional augmentation prior to implant placement Method of assessment: periodontal probe, standardised radiograph, template
Notes	Sample size calculation: not reported Data from same study (Barone 2008) were also used

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Extraction sockets were allocated to either a test (graft material) or control (spontaneous healing) group using a computerised random allocation process"
Allocation concealment (selection bias)	Low risk	Quote: "Only one of the investigators (BO), not involved in the selection and treatment of the patients, was aware of the randomisation sequence and had access to the randomisation list. The randomised codes were enclosed in sequentially numbered, identical, opaque, and sealed envelopes"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All radiographic measurements were taken by 1 masked examiner
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	High risk	The inclusion criteria included non-molar sites while the figures in the article showed an ARP of a molar site

Brkovic 2012

Study characteristics

Methods	Trial design: randomised, parallel-group trial Location: Belgrade, Serbia Number of centres: single centre, Clinic of Oral Surgery, Faculty of Dentistry, University of Belgrade, Belgrade, Serbia Recruitment period: January 2008 to March 2009

Brkovic 2012 *(Continued)*

	Funding source: the study was supported by Septodont, France, grant number 2207-2006
Participants	Inclusion criteria: age between 20 and 55 years; ASA I status as classified by the American Society of Anesthesiologists; good oral hygiene; indications for tooth extraction such as fracture of the tooth, non-vital tooth without the possibility of endodontic treatment and restoration, chronic periodontitis, endodontic treatment failure, and periodontal disease; extraction socket with 4 intact walls; occlusion suitable for the planned prosthodontic treatment; non-smokers or had quit smoking for at least 2 months prior to enrolment in study Exclusion criteria: presence of any chronic systemic disease, allergy, medication given within 48 hours pre-operatively; presence of purulent periodontal lesions as well as severe periodontal bone loss with a remaining alveolar bone height of less than 6 mm; history of chronic pain; pregnancy or nursing mothers; inability to comply with the study protocol Age at baseline: mean age 49 ± 15 (β-TCP/C1g); 46 ± 13 (β-TCP/C1g + membrane) years Gender: M 8/F 12 Smokers: 4 (β-TCP/C1g); 5 (β-TCP/C1g + membrane) Teeth extracted: canine, premolar, molar areas Number randomised (participants/sites): 20/20 Number evaluated (participants/sites): 20/20
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material and membrane)** **Test group:** (n = 11 extraction sockets) beta-tricalcium phosphate with type I collagen (β-TCP/C1g) (Septodont, Saint-Maur-des-Fosses, France) **Control group:** (n = 9 extraction sockets) β-TCP/C1g and collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) Surgical technique: flap, primary closure for the (graft and membrane) group Type of socket: 4-wall socket Duration of follow-up: 9 months
Outcomes	Width and height of alveolar ridge Method of assessment: periodontal probe, caliper
Notes	Sample size calculation: not reported but authors replied that sample size was based on practicality. This was the amount of material they had at their disposal, once it ran out the study was finished

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The authors replied that cue cards in sealed envelopes drawn from a jar at the time of acceptance of participant into the study
Allocation concealment (selection bias)	Unclear risk	Nothing reported in the article No clarifying reply
Blinding of outcome assessment (detection bias) All outcomes	High risk	Nothing reported in the article, but the authors replied that the nature of the appearance of the wound made it impossible to reliably blind the observer

Brkovic 2012 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Cha 2019

Study characteristics	
Methods	Trial design: randomised, parallel-group trial Location: Seoul, South Korea Number of centres: single centre, Yonsei University Dental Hospital, Seoul, Korea Recruitment period: January 2017 to June 2018 Funding source: this study was supported by a grant from the Osteology Foundation, Switzerland
Participants	Inclusion criteria: patients aged ≥ 18 years, required extraction of at least 1 maxillary posterior tooth with root apices projecting into the maxillary sinus and committed to replacement with dental implant after 6 months; radiographic bone height of 4 to 8 mm at the site intended for surgery; presence of at least 2 residual teeth after extraction to be used as references during image superimposition Exclusion criteria: systemic disease or bone metabolic disorder; any systemic condition that contraindicated surgery; history of malignancy, radiotherapy, or chemotherapy in the past 5 years; pathologic condition of the maxillary sinus such as active sinusitis or cysts; pregnant or lactating women; smoking > 20 cigarettes Age at baseline: 54.85 ± 8.37 (test group); 51.89 ± 12.08 (control group) years Gender: M 26/F 13 Smokers: not stated Teeth extracted: maxillary molar teeth Number randomised (participants/sites): 40/42 Number evaluated (participants/sites): 39/41
Interventions	**Comparison: ARP (grafting material) versus extraction alone** **Test group:** (n = 21 extraction sockets) deproteinised bovine bone mineral (DBBM) with 10% porcine collagen (DBBM-C; Bio-Oss Collagen, Geistlich Pharma AG, Wolhusen, Switzerland) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) **Control group:** (n = 20 extraction sockets) extraction alone Surgical technique: flapless, no primary closure Type of socket: 1-, 2-, 3- and 4-wall sockets Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge

Cha 2019 *(Continued)*

	Method of assessment: panoramic radiograph, computed tomography
Notes	Sample size calculation: reported The sample size was calculated with a power of 80% and an alpha level of 0.05. The calculations were based on previous literature and assumed mean vertical height changes for 6 months at 2.06% for the test group and 7.17% for the control group with standard deviation of 5.04%. A total of 20 participants per group was required based on an assumed dropout rate of 10%

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a web-based software"
Allocation concealment (selection bias)	Unclear risk	Insufficient information in the article
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information in the article
Incomplete outcome data (attrition bias) All outcomes	Low risk	Number and reasons for withdrawals were reported. It does not seem that the lost data had affected the results. 1 out of the 40 participants dropped out due to personal reason following tooth extraction
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Fernandes 2011

Study characteristics

Methods	Trial design: randomised, split-mouth trial Location: São Paulo, Brazil Number of centres: single centre, University of São Paulo, São Paulo, Brazil Recruitment period: February 2009 to March 2010 Funding source: BioHorizons, Birmingham, Alabama donated the grafting material used in this study
Participants	Inclusion criteria: systemic health; ≥ 20 teeth in both maxillary and mandibular arches; ≥ 2 hopeless, single-rooted and non-adjacent teeth in the maxilla Exclusion criteria: antibiotic therapy in the last 6 months; systemic involvement; smokers; pregnant or lactating patients Age at baseline: mean age 44.0 ± 8.10 years (33 to 58) Gender: M 5/F 13 Smokers: none Teeth extracted: maxillary anterior teeth

Fernandes 2011 *(Continued)*

	Number randomised (participants/sites): 18/36 Number evaluated (participants/sites): 18/36
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material)** **Test group:** (n = 18 extraction sockets) acellular dermal matrix (ADM) (AlloDerm, LifeCell Corporation, The Woodlands, Texas, USA) + anorganic bovine bone matrix (ABM) with synthetic cell-binding peptide P-15 (PepGen P-15, DENTSPLY Friadent CeraMed, Lakewood, Colorado, USA) **Control group:** (n = 18 extraction sockets) ADM only Surgical technique: flap, primary closure Type of socket: all alveolar sockets had buccal bone defects after extraction Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge Method of assessment: periodontal probe, template
Notes	Sample size calculation: reported The sample size was calculated with a power of 83%. A total of 18 participants per group was required to detect a difference in bucco-palatal alveolar ridge of 1.5 mm

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The sites for the test and control groups were randomly selected by a coin toss"
Allocation concealment (selection bias)	High risk	The authors replied that no allocation concealment was attempted
Blinding of outcome assessment (detection bias) All outcomes	High risk	The authors replied that examiners were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Festa 2013

Study characteristics

Methods	Trial design: randomised, split-mouth trial Location: Naples, Italy

Festa 2013 *(Continued)*

	Number of centres: single centre, Stomatology Department, Second University of Naples (SUN), Naples, Italy Recruitment period: June 2008 to March 2010 Funding source: unclear
Participants	Inclusion criteria: over 18 years of age; require double extraction of contralateral premolars located in symmetrical quadrants of maxillary or mandibular arches and requested an implant restoration; all extraction sites had adjacent teeth Exclusion criteria: systemic diseases that affect the periodontium or that contraindicate surgical treatment; long-term NSAID therapy; failure to sign an informed consent; smoking; pregnancy or lactating period; buccal or palatal/lingual bony wall fractured or completely lost during the extraction procedure Age at baseline: range 28 to 58 years Gender: M 6/F 9 Smokers: none Teeth extracted: premolars Number randomised (participants/sites): 15/30 Number evaluated (participants/sites): 15/30
Interventions	**Comparison: ARP (grafting material) versus extraction alone** **Test group:** (n = 15 extraction sockets) corticocancellous porcine bone xenograft (OsteoBiol Gen-Os) mixed granules with a diameter ranging from 250 to 1000 µm + soft cortical membrane (OsteoBiol Lamina) **Control group:** (n = 15 extraction sockets) extraction alone Surgical technique: flap, primary closure Type of socket: 4-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge Method of assessment: caliper, template
Notes	Sample size calculation: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The test and control sites were randomly selected using a coin toss"
Allocation concealment (selection bias)	Unclear risk	No information in the article and the authors did not provide further information
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information in the article and the authors did not provide further information
Incomplete outcome data (attrition bias)	Low risk	All data presented

Festa 2013 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Fischer 2018

Study characteristics	
Methods	Trial design: randomised, parallel-group trial Location: Würzburg, Germany Number of centres: single centre, Julius-Maximilians University, Würzburg, Germany Recruitment period: not stated Funding source: not stated
Participants	Inclusion criteria: patients aged ≥ 18 years, required extraction of non-molar tooth and committed to replacement with dental implant after 6 months Exclusion criteria: uncontrolled systemic disease; history of radiotherapy or chemotherapy; use of intravenous bisphosphonates; infectious diseases; untreated periodontal disease; multiple extraction sites; pregnant or lactating women; smoking > 10 cigarettes per day Age at baseline: range 18 to 80 years Gender: M 16/F 24 Smokers: not mentioned Teeth extracted: non-molar teeth Number randomised (participants/sites): 40/40 Number evaluated (participants/sites): 35/35
Interventions	**Comparison: ARP (grafting material) versus extraction alone** **Test group A:** (n = 9 extraction sockets) deproteinised bovine bone mineral (DBBM) (Endobon, 500 to 1000 µm particle size, Zimmer Biomet, West Palm Beach, Florida, USA) + soft tissue punch harvested from the palate **Test group B:** (n = 8 extraction sockets) DBBM (Endobon, 500 to 1000 µm particle size, Zimmer Biomet, West Palm Beach, Florida, USA) **Test group C:** (n = 10 extraction sockets) DBBM (Endobon, 500 to 1000 µm particle size, Zimmer Biomet, West Palm Beach, Florida, USA) + resorbable collagen membrane (OsseoGuard, Zimmer Biomet, West Palm Beach, Florida, USA) **Control group:** (n = 8 extraction sockets) extraction alone Surgical technique: flapless, no primary closure Type of socket: 3- and 4-wall socket Duration of follow-up: 6 months

Fischer 2018 *(Continued)*

Outcomes	Soft tissue volumetric analysis, need for additional augmentation at the time of implant placement
Notes	Sample size calculation: reported The sample size was calculated with a power of 90% and an alpha level of 0.05. The calculations were based on previous literature and assumed mean dimensional change of 0.75 mm with standard deviation of 0.50. A total of 40 participants per group was required

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was performed using a computerized randomization scheme"
Allocation concealment (selection bias)	Unclear risk	No information in the article
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: ".. blinded examiners performed data collection and analysis to avoid bias"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is not clear whether the number and reasons for withdrawals had affected the results. The trial reported 5 dropouts. Of which, 2 declined implant placement and the remaining 3 were non-compliant with the protocol
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Gholami 2012

Study characteristics

Methods	Trial design: randomised, split-mouth trial Location: Tehran, Iran Number of centres: single centre, Department of Periodontics, Dental School, Shaheed Beheshti University of Medical Sciences, Tehran, Iran Recruitment period: June 2009 to July 2010 Funding source: not supported or sponsored by any external resources
Participants	Inclusion criteria: over 18 years of age; requiring 1 or 2 pairs of non-molar teeth extraction and desired implant restoration; 4-wall sockets of the teeth with hopeless prognosis due to endodontic problems, trauma or prosthetic issues Exclusion criteria: history of systemic diseases that would contraindicate surgical treatment; acute infection in surgical sites; long-term non-steroidal anti-inflammatory drug therapy; periodontal disease with bone loss; known allergy to any of the materials used in the study; molar extraction sites; presence of inter-radicular septum in extraction sockets; failure to sign an informed consent Age at baseline: mean age 44.6 ± 11.4 years (21 to 60) Gender: M 4/F 8

Gholami 2012 *(Continued)*

	Smokers: none Teeth extracted: non-molar teeth Number randomised (participants/sites): 13/30 Number evaluated (participants/sites): 12/28
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material)** **Test group:** (n = 15 extraction sockets) deproteinised bovine bone mineral (DBBM) (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) (small particle size 0.25 mm to 1.0 mm)) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) (25 x 25 mm) **Control group:** (n = 15 extraction sockets) nanocrystalline hydroxyapatite (NCHA) (NanoBone 0.6 mm) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) (25 x 25 mm) Surgical technique: flap, primary closure Type of socket: 4-wall socket Duration of follow-up: 6 to 8 months (mean 6.9 ± 0.8 months)
Outcomes	Width and height of alveolar ridge, need for additional augmentation prior to implant placement Method of assessment: caliper
Notes	Sample size calculation: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Fifteen symmetrical pairs were randomly selected using a random number table"
Allocation concealment (selection bias)	Unclear risk	No information in the article. In their response, the authors did not provide more details to clarify this issue
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The horizontal ridge width was assessed blindly. The operator was blinded to the treatment groups during surgical re-entry, and the serial longitudinal sections were also coded and analysed by an examiner masked to the type of treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Number and reasons for withdrawals were reported. It does not seem that the lost data had affected the results
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Hoang 2012

Study characteristics

Methods	Trial design: randomised, parallel-group trial

Hoang 2012 *(Continued)*

	Location: San Antonio, Texas, USA Number of centres: single centre, University of Texas Health Science Center at San Antonio (UTHSCSA) Recruitment period: November 2008 to May 2010 Funding source: no funding was received for this study
Participants	Inclusion criteria: having 1 molar tooth requiring extraction, followed by replacement with a dental implant; adequate restorative space and height of alveolar bone; extracted teeth were removed as a result of non-restorability, fracture, periodontal disease, or failed endodontic procedures; teeth with small apical lesions ≤ 3 mm were not excluded if it was determined that the lesion could be adequately debrided after extraction Exclusion criteria: pregnant or planning to become pregnant within the study period; had any medical contraindications to dental surgery or any medical conditions that may affect wound healing after dental surgery, such as autoimmune disorders and immunosuppressive therapy; molar sites, with a buccal bony dehiscence extending > 50% of the length of socket Age at baseline: mean age 56.1 years; range 29 to 76 Gender: M 15/F 15 Smokers: all non-smokers Teeth extracted: molars Number randomised (participants/sites): 40/40 Number evaluated (participants/sites): 30/30
Interventions	**Comparison: ARP (grafting materials) versus ARP (grafting materials)** **Test group:** (n = 15 extraction sockets) demineralised bone matrix, single particle size (SPS) between 125 µm and 710 µm in a carrier of bovine collagen and sodium alginate **Control group:** (n = 15 extraction sockets) demineralised bone matrix, multiple particle size (MPS) between 125 µm and 710 µm in a carrier of bovine collagen and sodium alginate + additional particles measuring approximately 2 to 4 mm in length Surgical technique: flaps were not reflected to obtain primary closure of the wound Type of socket: 4-wall socket. 4 of the 16 subjects in the SPS group and 3 of the 14 subjects in the MPS group had a small dehiscence in the buccal wall (authors replied) Duration of follow-up: 6 months (time of implant placement)
Outcomes	Width and height of alveolar ridge Method of assessment: periodontal probe, caliper
Notes	Sample size calculation: reported The sample size was calculated with a power of 88.5% and an alpha level of 0.05. The calculations were based on detecting a clinically significant mean difference of 1 standard deviation or more. A total of 20 participants per group was required based on a dropout rate of 30%

Risk of bias

Bias	Authors' judgement	Support for judgement

Hoang 2012 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "Immediately preceding the start of the surgical procedure, an envelope was drawn from a stack of sealed envelopes with the name of either graft material written inside"
Allocation concealment (selection bias)	Unclear risk	No information in the article
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Histologic examination was conducted by masked examiners but not clear whether clinical parameters were recorded by masked examiners
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study excluded 10 participants. Of which, 9 were non-compliant with the trial protocol and 1 withdrew from the study at the time of surgery due to large buccal and palatal dehiscence after extracting the tooth Dropouts were equal in both groups
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Iorio-Siciliano 2017

Study characteristics	
Methods	Trial design: randomised, parallel-group trial Location: Naples, Italy Number of centres: single centre, University of Naples Federico II, Naples, Italy Recruitment period: not stated Funding source: self-funded
Participants	Inclusion criteria: patients aged ≥ 18 years, required extraction of maxillary or mandibular tooth and committed to replacement with dental implant after 6 months; full mouth plaque and bleeding scores of less than 25%; presence of at least 2 mm of keratinized tissue Exclusion criteria: any medical condition that contraindicated surgery; pregnant or lactating women; smoking Age at baseline: 38.2 ± 9.4 (test group); 40.2 ± 12.1 (control group) years Gender: M 11/F 9 Smokers: 0 Teeth extracted: maxillary or mandibular teeth Number randomised (participants/sites): 20/20 Number evaluated (participants/sites): 20/20
Interventions	**Comparison: ARP (grafting material) versus extraction alone**

Iorio-Siciliano 2017 *(Continued)*

	Test group: (n = 10 extraction sockets) deproteinised bovine bone mineral (DBBM) with 10% porcine collagen (Bio-Oss Collagen, Geistlich Pharma AG, Wolhusen, Switzerland) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) **Control group:** (n = 10 extraction sockets) extraction alone Surgical technique: flap, no primary closure Type of socket: 4-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge Method of assessment: periodontal probe, caliper
Notes	Sample size calculation: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The fresh alveolar sockets were randomly assigned to the test or control group with the allocation conducted using a commercially available computer software package"
Allocation concealment (selection bias)	Unclear risk	No information in the article
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information in the article
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Iorio-Siciliano 2020

Study characteristics

Methods	Trial design: randomised, parallel-group trial Location: Naples, Italy Number of centres: single centre, University of Naples Federico II, Naples, Italy Recruitment period: not stated Funding source: self-funded
Participants	Inclusion criteria: patients aged ≥ 18 years, required extraction of maxillary or mandibular posterior single- or multi-rooted tooth and committed to replacement with dental implant after 6 months; full

Iorio-Siciliano 2020 *(Continued)*

	mouth plaque and bleeding scores of less than 25%; presence of at least 2 mm of keratinized tissue; sound socket walls, signed consent form Exclusion criteria: any medical condition that contraindicate surgery; pregnant or lactating women; smoking; periodontally compromised; acute abscess, third molars Age at baseline: 38.9 ± 10.1 (test group A); 43.6 ± 14.2 (test group B); 38.4 ± 13.2 (control group) years Gender: M 22/F 18 Smokers: 0 Teeth extracted: single- and multi-rooted posterior teeth Number randomised (participants/sites): 45/45 Number evaluated (participants/sites): 40/40
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material) versus extraction alone** **Test group A:** (n = 12 extraction sockets) bovine-derived xenograft with 10% collagen (Bio-Oss Collagen, Geistlich Biomaterials, Wolhusen, Switzerland) + resorbable collagen membrane (Bio-Gide, Geistlich, Biomaterials, Wolhusen, Switzerland) **Test group B:** (n = 13 extraction sockets) bovine-derived xenograft (Bio-Oss, Geistlich Biomaterials, Wolhusen, Switzerland) + resorbable collagen membrane (Bio-Gide, Geistlich, Biomaterials, Wolhusen, Switzerland) **Control group:** (n = 15 extraction sockets) extraction alone Surgical technique: flap, no primary closure Type of socket: 4-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge, thickness of buccal wall Method of assessment: periodontal probe, caliper
Notes	Sample size calculation: reported The sample size was calculated with a power of 80% and an alpha level of 0.05. The calculations were based on previous literature and assumed mean horizontal bone difference of 17.3 ± 16.4% between test and control groups. A total of 15 participants per group was required based on possible dropouts

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization procedure was performed by single examiner using a commercially available computer software package"
Allocation concealment (selection bias)	Low risk	Quote: "Allocation was performed after tooth or root extraction by opening an opaque envelope"
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The principal investigator and co-investigators were not masked"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Number and reasons for withdrawals were reported. It does not seem that the lost data had affected the results. 5 dropouts were recorded; 2 participants

Iorio-Siciliano 2020 *(Continued)*

		had medical reasons, 1 was pregnant, 1 moved to another town, and 1 was not compliant with the research protocol
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Madan 2014

Study characteristics	
Methods	Trial design: randomised, split-mouth trial Location: Uttar Pradesh, India Number of centres: single centre, Saraswati Dental College and Hospital, Lucknow, Uttar Pradesh, India Recruitment period: not stated Funding source: self-funded
Participants	Inclusion criteria: patients required extraction of non-molar tooth and committed to replacement with dental implant after 6 months; systemically healthy, compliant Exclusion criteria: systemic disease; radiographic bone height of < 7 mm at the site intended for surgery Age at baseline: range 20 to 45 years Gender: M 7/ F8 Smokers: 0 Teeth extracted: non-molar teeth Number randomised (participants/sites): 15/60 Number evaluated (participants/sites): 15/60
Interventions	**Comparison: ARP (grafting material) versus extraction alone** **Test group:** (n = 30 extraction sockets) resorbable polylactide and polyglycolide (PLA-PGA) sponge (Fisiograft, Ghimas SpA, Italy) **Control group:** (n = 30 extraction sockets) extraction alone Surgical technique: flapless, no primary closure Type of socket: 4-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge, histologic analyses Method of assessment: periodontal probe, computed tomography, template
Notes	Sample size calculation: not reported
Risk of bias	

Madan 2014 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Extraction sockets were randomly allocated for test and control groups by the toss of a coin into equal numbers"
Allocation concealment (selection bias)	Unclear risk	No information in the article
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information in the article
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Pang 2014

Study characteristics	
Methods	Trial design: randomised, parallel-group trial Location: Xi'an, China Number of centres: single centre, Fourth Military Medical University, Xi'an, China Recruitment period: January 2010 to December 2012 Funding source: self-funded
Participants	Inclusion criteria: patients required extraction of single tooth and committed to replacement with dental implant after 6 months Exclusion criteria: systemic disease; acute inflammation; use of medications that compromise healing; pregnant or lactating women; smoking Age at baseline: range 22 to 47 years Gender: M 14/F 16 Smokers: 0 Teeth extracted: non-molar and molar teeth Number randomised (participants/sites): 30/30 Number evaluated (participants/sites): 30/30
Interventions	**Comparison: ARP (grafting material) versus extraction alone** **Test group:** (n = 15 extraction sockets) deproteinised bovine bone mineral (DBBM) (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland)

Pang 2014 *(Continued)*

	Control group: (n = 15 extraction sockets) extraction alone Surgical technique: flap, primary closure Type of socket: 4-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge, implant stability measurements Method of assessment: computed tomography
Notes	Sample size calculation: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The method of randomisation was not mentioned
Allocation concealment (selection bias)	Unclear risk	No information in the article
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information in the article
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Patel 2013

Study characteristics

Methods	Trial design: randomised, parallel-group trial Location: London, UK Number of centres: single centre, Clinical Investigation Centre, UCL Eastman Dental Institute, London, UK Recruitment period: 2006 to 2008 Funding source: the study was supported by a grant from the Institut Straumann AG, Basel, Switzerland
Participants	Inclusion criteria: age between 18 and 75 years; good general health; the presence of a hopeless tooth in the mandibular or the maxillary incisor, canine, or premolar region requiring extraction and would be suitable for replacement by a dental implant; the tooth to be extracted has at least 1 neighbouring tooth; the subject had voluntarily signed the informed consent Exclusion criteria: pregnancy or lactating period; chronic treatment with any medication known to affect oral status and bone turnover or contraindicate surgical treatment within 1 month of baseline visit;

Patel 2013 *(Continued)*

	concomitant anticoagulant therapy; any known diseases (not including controlled diabetes mellitus); infections or recent surgical procedures within 30 days of study initiation; HIV or hepatitis; administration of any other investigational drug within 30 days of study initiation; limited mental capacity or language skills or suffering from a known psychological disorder; heavy smoking (> 10 cigarettes per day); uncontrolled or untreated periodontal disease; full-mouth plaque level (FMPL) > 30% at the enrolment visit; severe bruxism; acute endodontic lesion in the test tooth or in the neighbouring areas; major part of the buccal or palatal osseous wall damaged or lost following tooth extraction Age at baseline: mean age 37.3 ± 11.4 years (20 to 58) Gender: M 6/F 21 Smokers: 3 Teeth extracted: non-molar sites Number randomised (participants/sites): 30/30 Number evaluated (participants/sites): 25/25 (radiographic evaluation 24/24)
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material)** **Test group:** (n = 13 extraction sockets) synthetic bone substitute-Straumann bone ceramic (SBC) (Straumann AG, Basel, Switzerland, granule size 400 µm to 1000 µm) + collagen barrier (Bio-Gide, Geistlich, Basel, Switzerland) **Control group:** (n = 12 extraction sockets) deproteinised bovine bone mineral (DBBM) (Bio-Oss, Geistlich Pharma AG, Basel, Switzerland) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Basel, Switzerland) Surgical technique: flap, no primary closure Type of socket: 4-wall socket Duration of follow-up: 8 months at implant placement (Mardas 2010); 12 months post-loading (Patel 2013)
Outcomes	Width and height of alveolar ridge, probing pocket depth, gingival recession, implant survival, need for additional augmentation prior to implant placement Method of assessment: periodontal probe, standardised radiograph
Notes	Sample size calculation: reported The sample size was calculated based on previous literature and assumed difference in observed radiographic bone changes of 1 mm and standard deviation of 0.05 mm

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The subjects were randomly assigned to the test or the control group by a computer-generated table. A balanced randomly permuted block approach was used to prepare the randomisation tables in order to avoid unequal balance between the two treatments"
Allocation concealment (selection bias)	Unclear risk	It is not clear whether the randomised codes were enclosed in sequentially numbered, identical, opaque, and sealed envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All the periodontal and surgical measurements were made by a single, blinded examiner

Patel 2013 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	It is not clear whether the number and reasons of withdrawals had any impact on the results and how the authors managed the dropouts
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Santana 2019

Study characteristics	
Methods	Trial design: randomised, parallel-group trial Location: Massachusetts, USA Number of centres: single centre, Boston University, Boston, Massachusetts, USA Recruitment period: not mentioned Funding source: self-funded
Participants	Inclusion criteria: patients aged ≥18 years, required extraction of single-rooted tooth and committed to replacement with dental implant after 6 months Exclusion criteria: any condition that contraindicated surgery; immunosuppressive systemic diseases; smoking Age at baseline: range 34 to 52 years Gender: M 14/F 18 Smokers: 0 Teeth extracted: single-rooted teeth Number randomised (participants/sites): 32/45 Number evaluated (participants/sites): 31/41 (27 included in our analyses)
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material)** **Test group A:** (n = 13 extraction sockets) mineralised ground cancellous human allograft (AlloGraft, OCAN 250-1000 microns; Straumann AG, Basel, Switzerland) + synthetic polymeric polyethylene glycol (PEG) barrier membrane (Straumann AG, Basel, Switzerland) **Test group B:** (n = 14 extraction sockets) deproteinised bovine bone mineral (DBBM) (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) + PEG barrier membrane (Straumann AG, Basel, Switzerland) **Test group C:** (n = 14 extraction sockets) PEG barrier membrane (Straumann AG, Basel, Switzerland) (not included in analyses) Surgical technique: flap, primary closure Type of socket: 4-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge, histologic analysis

Santana 2019 *(Continued)*

	Method of assessment: periodontal probe, caliper, template
Notes	Sample size calculation: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information in the article
Allocation concealment (selection bias)	Unclear risk	No information in the article
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information in the article
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	4 sites were excluded but authors did not fully clarify all the reasons for dropouts apart from some inadequate sampling for histological evaluation
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Scheyer 2016

Study characteristics

Methods	Trial design: randomised, parallel-group trial Location: USA and Germany Number of centres: multicentre, private practices (Texas, Washington, Illinois, Massachusetts, California, Virginia, Michigan, USA), University of Washington (USA), University of Illinois (USA), Harvard School of Dental Medicine (USA), Virginia Commonwealth School of Dentistry (USA), University of Michigan (USA), University of Freiburg (Germany) Recruitment period: November 2013 to February 2015 Funding source: this study was partly supported by a grant from Geistlich Pharma AG
Participants	Inclusion criteria: patients required extraction of premolar or molar tooth and committed to replacement with dental implant after 6 months; presence of neighbouring teeth; presence of buccal bone dehiscence of at least 1/3 of the socket height and width; signed an informed consent form Exclusion criteria: any systemic disease that may affect healing; use of immunosuppressive, systemic corticosteroids, intramuscular or intravenous bisphosphonates; radiotherapy or chemotherapy in the last 2 months; known allergy to materials used in this study; pregnant, lactating women or those intending to become pregnant; smoking in the last 6 months Age at baseline: range 18 to 70 years Gender: not mentioned Smokers: 0

Scheyer 2016 *(Continued)*

	Teeth extracted: premolar and molar teeth Number randomised (participants/sites): 40/40 Number evaluated (participants/sites): 40/40
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material)** **Test group A:** (n = 21 extraction sockets) demineralised allograft (OraGraft DGC, LifeNet Health Inc, Virginia Beach, Virginia, USA) + cross-linked bovine collagen membrane (BioMend Extend, Zimmer Dental Inc, Carlsbad, California, USA) **Test group B:** (n = 19 extraction sockets) deproteinised bovine bone mineral (DBBM) with 10% porcine collagen (Bio-Oss Collagen, Geistlich Pharma AG, Wolhusen, Switzerland) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) Surgical technique: flap, no primary closure Type of socket: 3-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge, soft tissue inflammation, histomorphometric analysis Method of assessment: periodontal probe, template
Notes	Sample size calculation: reported The sample size was calculated using statistical software to assess non-inferiority hypothesis. A total of 20 participants per group was required to account for possible dropouts

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Subjects were randomly assigned to either the control or test therapy in a block 1:1 ratio"
Allocation concealment (selection bias)	Unclear risk	No information in the article
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information in the article
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

Serrano Mendez 2017

Study characteristics

Methods	Trial design: randomised, parallel-group trial

Serrano Mendez 2017 *(Continued)*

	Location: Bogota, Colombia Number of centres: single centre, National University of Colombia, Bogota, Colombia Recruitment period: April 2012 to October 2015 Funding source: this study was supported by grants from vice-rectory for research (National University of Colombia), Colgate Palmolive (Colombia), Ariminum Research and Dental Education Centre (Rimini, Italy), and Clinical Research Foundation for the Promotion of Oral Health (Brienz, Switzerland)
Participants	Inclusion criteria: patients aged ≥ 18 years, required extraction of non-molar tooth and committed to replacement with dental implant after 6 months; presence of at least 1 neighbouring tooth Exclusion criteria: any medication compromising healing; periodontitis; plaque score > 30%; loss of buccal bone at the time of extraction; pregnant women, smoking > 10 cigarettes per day Age at baseline: mean age of 44 years Gender: M 10/F 10 Smokers: 2 Teeth extracted: non-molar teeth Number randomised (participants/sites): 20/20 Number evaluated (participants/sites): 20/20
Interventions	**Comparison: ARP (grafting material) versus ARP (grafting material)** **Test group A:** (n = 10 extraction sockets) demineralised freeze-dried cortical bone allograft (DFDBA) (600 to 800 µm, Banco de Tejidos Cosme y Damian, Bogota, Colombia) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) **Test group B:** (n = 10 extraction sockets) deproteinised bovine bone mineral (DBBM) with 10% porcine collagen (Bio-Oss Collagen, Geistlich Pharma AG, Wolhusen Switzerland) + collagen barrier (Bio-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) Surgical technique: flap, primary closure Type of socket: 4-wall socket Duration of follow-up: 6 months
Outcomes	Width and height of alveolar ridge, histomorphometric analysis Method of assessment: periodontal probe, caliper, standardised radiograph, template
Notes	Sample size calculation: reported The sample size was calculated with a power of 80% and an alpha level of 0.05. The calculations were based on previous literature and assumed a difference of 1 mm and standard deviation of 1.3 mm in ridge width. A total of 10 participants per group was required

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A randomization table was created electronically in blocks of two patients"
Allocation concealment (selection bias)	Unclear risk	Insufficient information in the article

Serrano Mendez 2017 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quotes: "The clinical measurements were performed by a different person that was not involved in any other section of the treatments" and "The histological assessments were performed by an operator not involved in any of the other parts"
Incomplete outcome data (attrition bias) All outcomes	Low risk	All data presented
Selective reporting (reporting bias)	Low risk	All outcomes appear to be reported
Other bias	Low risk	None detected

ARP = alveolar ridge preservation; F = female; M = male; NSAID = non-steroidal anti-inflammatory drugs.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abdelhamid 2016	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Aimetti 2009	The study followed up participants for less than 6 months
Aimetti 2018	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Alkan 2013	A histological study
Alkanan 2019	The study followed up participants for less than 6 months
Al Qabbani 2018	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Amirzargar 2018	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Araujo 2015	The study followed up participants for less than 6 months
Arbab 2016	The study followed up participants for less than 6 months
Areewong 2019	The study followed up participants for less than 6 months
Bakhshalian 2018	A histological and histomorphometrical study
Barone 2013	A histological study
Barone 2015	A histological and histomorphometrical study
Barone 2016	The study followed up participants for less than 6 months
Barone 2017	The study followed up participants for less than 6 months
Borg 2015	The study followed up participants for less than 6 months

Study	Reason for exclusion
Calasans-Maia 2013	A histological and histomorphometrical study
Canellas 2020	The study followed up participants for less than 6 months
Cardaropoli 2012	The study followed up participants for less than 6 months
Cardaropoli 2014	The study followed up participants for less than 6 months
Casado 2010	The study is not a randomised controlled trial
Cavdar 2017	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Checchi 2011	A histological and histomorphometrical study
Clark 2018	The study followed up participants for less than 6 months
Clementini 2020	The study followed up participants for less than 6 months
Cook 2013	The study followed up participants for less than 6 months
Coomes 2014	The study followed up participants for less than 6 months
Corning 2019	The study followed up participants for less than 6 months
Crespi 2009	The study is not a randomised controlled trial
Debel 2021	The study only reported the soft tissue volumetric changes
Demetter 2017	The study followed up participants for less than 6 months
Eskow 2014	The study followed up participants for less than 6 months
Fernandes 2016	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Fiorellini 2005	The study followed up participants for less than 6 months
Flugge 2015	The study only reported the soft tissue volumetric changes
Fotek 2009	The study followed up participants for less than 6 months
Froum 2002	A histological study
Geurs 2014	A histological and histomorphometrical study
Girish Kumar 2018	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Guarnieri 2017	The study followed up participants for less than 6 months
Hassan 2017	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Hauser 2013	The study followed up participants for less than 6 months

Study	Reason for exclusion
Iasella 2003	The study followed up some participants for less than 6 months. Some of the data were recorded at 4 months
Jo 2019	The study followed up participants for less than 6 months
Jonker 2020	The study followed up participants for less than 6 months
Jung 2013	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Jung 2018	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Karaca 2015	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Kim 2011	The study is not a randomised controlled trial
Kim 2014	The study followed up participants for less than 6 months
Kotsakis 2014	The study followed up participants for less than 6 months
Kutkut 2012	The study followed up participants for less than 6 months
Lai 2020	The study followed up participants for less than 6 months
Lee 2020	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Lekovic 1997	The study is not a randomised controlled trial
Lekovic 1998	The study followed up participants for less than 6 months
Lim 2017	The study followed up participants for less than 6 months
Lim 2019	The study followed up participants for less than 6 months
Llanos 2019	The study followed up participants for less than 6 months
Machtei 2019	The study followed up participants for less than 6 months
Mandarino 2018	The study followed up participants for less than 6 months
Marconcini 2018	The study followed up participants for less than 6 months
Mayer 2016	The study followed up participants for less than 6 months
Meloni 2015	The study followed up participants for less than 6 months
Molly 2008	A histological study
Nart 2017	The study followed up participants for less than 6 months
Natto 2017	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment

Study	Reason for exclusion
Neiva 2011	The study is not a randomised controlled trial
Nevins 2006	The study followed up participants for less than 6 months
Nevins 2011	A histological and histomorphometrical study
Oghli 2010	The study followed up participants for less than 6 months
Ouyyamwongs 2019	The study followed up participants for less than 6 months
Ovcharenko 2020	The study followed up participants for less than 6 months
Parashis 2016	The study followed up participants for less than 6 months
Pelegrine 2010	There were serious doubts if the study was actually a randomised controlled trial and the authors did not answer back and clarified the doubts
Pellegrini 2014	A histological and histomorphometrical study
Perelman-Karmon 2012	A histological and histomorphometrical study
Pinho 2006	The study followed up participants for less than 6 months
Poulias 2013	The study followed up participants for less than 6 months
Rasperini 2010	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Sbordone 2017	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Scheyer 2012	A histological study
Schneider 2014	The study only reported the soft tissue volumetric changes
Serino 2003	The study is not a randomised controlled trial
Shakibaie 2013	The study is not a randomised controlled trial
Shim 2018	The study is not a randomised controlled trial
Sisti 2012	The study followed up participants for less than 6 months
Spinato 2014	The study followed up participants for less than 6 months
Sun 2019	The study followed up participants for less than 6 months
Temmerman 2016	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Thalmair 2013	The study only reported the soft tissue volumetric changes
Toloue 2012	The study followed up participants for less than 6 months
Vance 2004	The study followed up participants for less than 6 months

Study	Reason for exclusion
Walker 2017	The study followed up participants for less than 6 months
Wood 2012	The study followed up participants for less than 6 months
Zadeh 2016	Unclear whether alveolar ridge preservation was used for participants requiring implant-related prosthodontic treatment
Zhao 2018	The study is not a randomised controlled trial

DATA AND ANALYSES

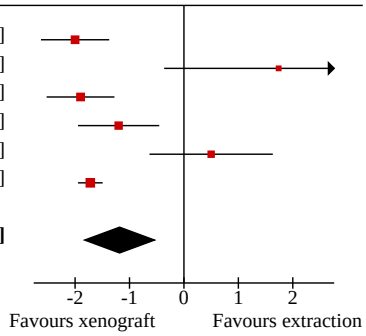
Comparison 1. Alveolar ridge preservation (ARP) versus extraction

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Xenograft versus extraction: changes in width of alveolar ridge (mm)	6	201	Mean Difference (IV, Random, 95% CI)	-1.18 [-1.82, -0.54]
1.2 Xenograft versus extraction: changes in height of alveolar ridge (mm)	6	201	Mean Difference (IV, Random, 95% CI)	-1.35 [-2.00, -0.70]
1.3 Xenograft versus extraction: need for additional augmentation prior to implant placement	4	156	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.29, 1.62]
1.4 Xenograft versus extraction: implant failures	2	70	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.07, 14.90]
1.5 Xenograft versus extraction: peri-implant marginal bone level changes	1	38	Mean Difference (IV, Fixed, 95% CI)	-0.02 [-0.18, 0.14]
1.6 Alloplast versus extraction: changes in height of alveolar ridge (mm)	1		Mean Difference (IV, Fixed, 95% CI)	-3.73 [-4.05, -3.41]

Analysis 1.1. Comparison 1: Alveolar ridge preservation (ARP) versus extraction, Outcome 1: Xenograft versus extraction: changes in width of alveolar ridge (mm)

Study or Subgroup	MD	SE	Xenograft Total	Extraction Total	Weight	Mean Difference IV, Random, 95% CI
Barone 2012	-2	0.32	20	20	19.3%	-2.00 [-2.63 , -1.37]
Cha 2019	1.74	1.0733	21	20	6.7%	1.74 [-0.36 , 3.84]
Festa 2013 (1)	-1.9	0.318	15	15	19.4%	-1.90 [-2.52 , -1.28]
Iorio-Siciliano 2017	-1.2	0.3808	10	10	17.9%	-1.20 [-1.95 , -0.45]
Iorio-Siciliano 2020	0.5	0.5779	25	15	13.6%	0.50 [-0.63 , 1.63]
Pang 2014	-1.72	0.1157	15	15	23.0%	-1.72 [-1.95 , -1.49]
Total (95% CI)			**106**	**95**	**100.0%**	**-1.18 [-1.82 , -0.54]**

Heterogeneity: Tau² = 0.45; Chi² = 27.38, df = 5 (P < 0.0001); I² = 82%
Test for overall effect: Z = 3.62 (P = 0.0003)
Test for subgroup differences: Not applicable

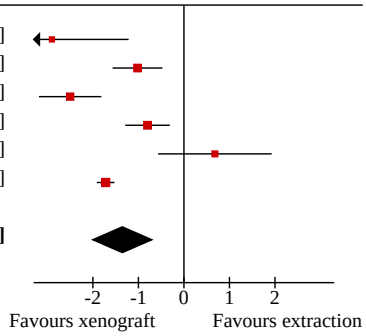


Footnotes
(1) For split-mouth trials the number of participants is double-counted.

Analysis 1.2. Comparison 1: Alveolar ridge preservation (ARP) versus extraction, Outcome 2: Xenograft versus extraction: changes in height of alveolar ridge (mm)

Study or Subgroup	MD	SE	Xenograft Total	Extraction Total	Weight	Mean Difference IV, Random, 95% CI
Barone 2012	-2.9	0.86	20	20	8.9%	-2.90 [-4.59 , -1.21]
Cha 2019	-1.02	0.2794	21	20	19.3%	-1.02 [-1.57 , -0.47]
Festa 2013 (1)	-2.5	0.35	15	15	17.9%	-2.50 [-3.19 , -1.81]
Iorio-Siciliano 2017	-0.8	0.25	10	10	19.8%	-0.80 [-1.29 , -0.31]
Iorio-Siciliano 2020	0.68	0.6364	25	15	12.2%	0.68 [-0.57 , 1.93]
Pang 2014	-1.72	0.0989	15	15	21.9%	-1.72 [-1.91 , -1.53]
Total (95% CI)			**106**	**95**	**100.0%**	**-1.35 [-2.00 , -0.70]**

Heterogeneity: Tau² = 0.49; Chi² = 37.61, df = 5 (P < 0.00001); I² = 87%
Test for overall effect: Z = 4.09 (P < 0.0001)
Test for subgroup differences: Not applicable

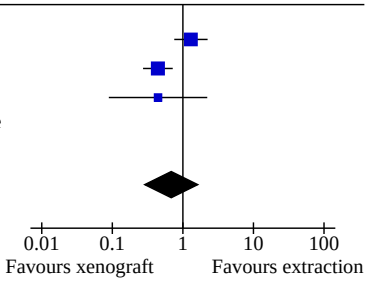


Footnotes
(1) For split-mouth trials, the number of participants is double-counted.

Analysis 1.3. Comparison 1: Alveolar ridge preservation (ARP) versus extraction, Outcome 3: Xenograft versus extraction: need for additional augmentation prior to implant placement

Study or Subgroup	Xenograft Events	Xenograft Total	Extraction Events	Extraction Total	Weight	Risk Ratio M-H, Random, 95% CI
Barone 2012	13	20	10	20	40.3%	1.30 [0.75 , 2.24]
Cha 2019	9	21	20	20	41.7%	0.44 [0.27 , 0.72]
Fischer 2018	3	27	2	8	18.0%	0.44 [0.09 , 2.21]
Iorio-Siciliano 2020	0	25	0	15		Not estimable
Total (95% CI)		**93**		**63**	**100.0%**	**0.68 [0.29 , 1.62]**
Total events:	25		32			

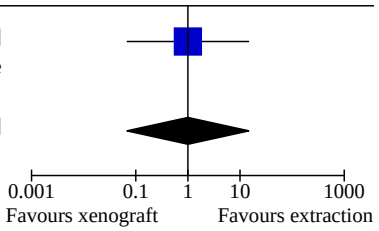
Heterogeneity: Tau² = 0.41; Chi² = 8.74, df = 2 (P = 0.01); I² = 77%
Test for overall effect: Z = 0.86 (P = 0.39)
Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1: Alveolar ridge preservation (ARP) versus extraction, Outcome 4: Xenograft versus extraction: implant failures

Study or Subgroup	Xenograft Events	Xenograft Total	Extraction Events	Extraction Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Barone 2012	1	20	1	20	100.0%	1.00 [0.07 , 14.90]
Pang 2014	0	15	0	15		Not estimable
Total (95% CI)		**35**		**35**	**100.0%**	**1.00 [0.07 , 14.90]**
Total events:	1		1			

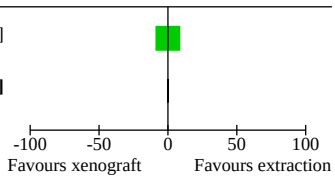
Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)
Test for subgroup differences: Not applicable



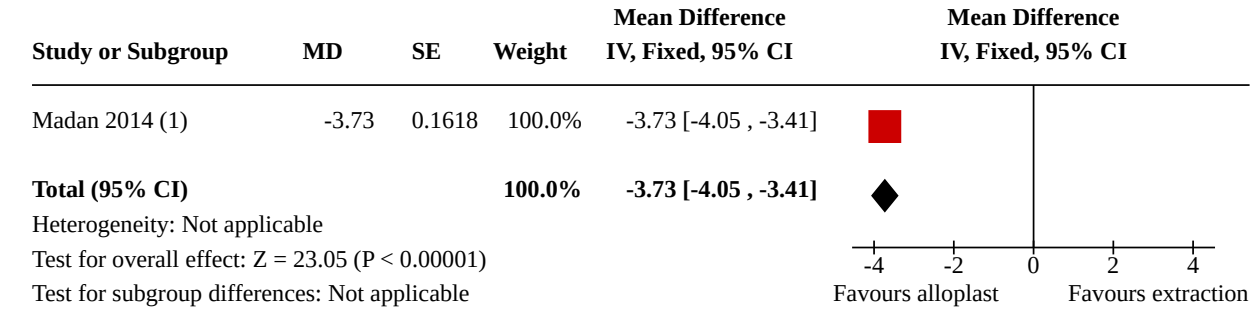
Analysis 1.5. Comparison 1: Alveolar ridge preservation (ARP) versus extraction, Outcome 5: Xenograft versus extraction: peri-implant marginal bone level changes

Study or Subgroup	Xenograft Mean	Xenograft SD	Xenograft Total	Extraction Mean	Extraction SD	Extraction Total	Weight	Mean Difference IV, Fixed, 95% CI
Barone 2012	1	0.2	19	1.02	0.3	19	100.0%	-0.02 [-0.18 , 0.14]
Total (95% CI)			**19**			**19**	**100.0%**	**-0.02 [-0.18 , 0.14]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)
Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1: Alveolar ridge preservation (ARP) versus extraction, Outcome 6: Alloplast versus extraction: changes in height of alveolar ridge (mm)



Footnotes

(1) For split-mouth trials, the number of participants is double-counted.

Comparison 2. Different grafting materials for alveolar ridge preservation

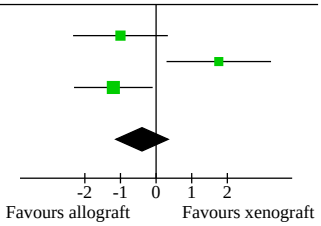
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Allograft versus xenograft: changes in width of alveolar ridge (mm)	3	87	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-1.13, 0.34]
2.2 Allograft versus xenograft: changes in height of alveolar ridge (mm)	2	60	Mean Difference (IV, Fixed, 95% CI)	-0.45 [-1.48, 0.58]
2.3 Allograft versus xenograft: need for additional augmentation prior to implant placement	1	40	Risk Ratio (M-H, Fixed, 95% CI)	6.36 [0.35, 115.73]
2.4 Alloplast versus xenograft: changes in width of alveolar ridge (mm)	2	55	Mean Difference (IV, Fixed, 95% CI)	-0.31 [-0.66, 0.04]
2.5 Alloplast versus xenograft: changes in height of alveolar ridge (mm)	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.27, 0.07]
2.6 Alloplast versus xenograft: need for additional augmentation prior to implant placement	2	55	Risk Ratio (IV, Fixed, 95% CI)	1.09 [0.65, 1.83]
2.7 Alloplast versus xenograft: implant failures	1	25	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
2.8 Alloplast versus xenograft: changes in probing pocket depth at teeth adjacent to the extraction site (mm)	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-0.61, 0.01]
2.9 Alloplast with membrane versus alloplast without membrane: changes in width of alveolar ridge (mm)	1	20	Mean Difference (IV, Fixed, 95% CI)	0.43 [0.18, 0.68]
2.10 Alloplast with membrane versus alloplast without membrane: changes in height of alveolar ridge (mm)	1	20	Mean Difference (IV, Fixed, 95% CI)	0.38 [0.26, 0.50]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.11 Allograft with P-15 versus allograft without P-15: changes in width of alveolar ridge (mm)	1	36	Mean Difference (IV, Fixed, 95% CI)	-0.87 [-1.61, -0.13]
2.12 Allograft with P-15 versus allograft without P-15: changes in height of alveolar ridge (mm)	1	36	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.06, 0.46]
2.13 Alloplast single particles versus alloplast multiple particles: changes in width of alveolar ridge (mm)	1	30	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.97, 1.17]
2.14 Alloplast single particles versus alloplast multiple particles: changes in height of alveolar ridge (mm)	1	30	Mean Difference (IV, Fixed, 95% CI)	0.10 [-1.22, 1.42]

Analysis 2.1. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 1: Allograft versus xenograft: changes in width of alveolar ridge (mm)

Study or Subgroup	Allograft Mean	Allograft SD	Allograft Total	Xenograft Mean	Xenograft SD	Xenograft Total	Weight	Mean Difference IV, Fixed, 95% CI
Santana 2019	1.5	1.9	13	2.5	1.6	14	30.5%	-1.00 [-2.33 , 0.33]
Scheyer 2016	-4.95	2.65	21	-6.71	2.07	19	25.1%	1.76 [0.29 , 3.23]
Serrano Mendez 2017	1.4	1.1	10	2.6	1.4	10	44.4%	-1.20 [-2.30 , -0.10]
Total (95% CI)			**44**			**43**	**100.0%**	**-0.40 [-1.13 , 0.34]**

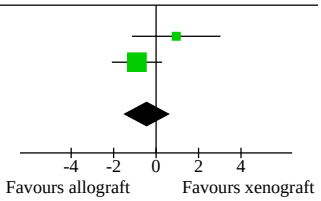
Heterogeneity: Chi² = 11.13, df = 2 (P = 0.004); I² = 82%
Test for overall effect: Z = 1.06 (P = 0.29)
Test for subgroup differences: Not applicable



Analysis 2.2. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 2: Allograft versus xenograft: changes in height of alveolar ridge (mm)

Study or Subgroup	Allograft Mean	Allograft SD	Allograft Total	Xenograft Mean	Xenograft SD	Xenograft Total	Weight	Mean Difference IV, Fixed, 95% CI
Scheyer 2016	-5.29	3.73	21	-6.24	2.98	19	24.4%	0.95 [-1.13 , 3.03]
Serrano Mendez 2017	-0.5	1.4	10	0.4	1.3	10	75.6%	-0.90 [-2.08 , 0.28]
Total (95% CI)			**31**			**29**	**100.0%**	**-0.45 [-1.48 , 0.58]**

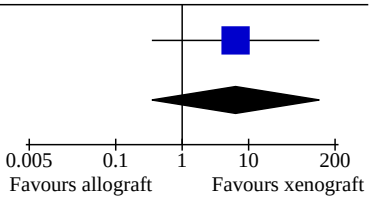
Heterogeneity: Chi² = 2.29, df = 1 (P = 0.13); I² = 56%
Test for overall effect: Z = 0.85 (P = 0.39)
Test for subgroup differences: Not applicable



Analysis 2.3. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 3: Allograft versus xenograft: need for additional augmentation prior to implant placement

Study or Subgroup	Allograft Events	Allograft Total	Xenograft Events	Xenograft Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Scheyer 2016	3	21	0	19	100.0%	6.36 [0.35 , 115.73]
Total (95% CI)		**21**		**19**	**100.0%**	**6.36 [0.35 , 115.73]**
Total events:	3		0			

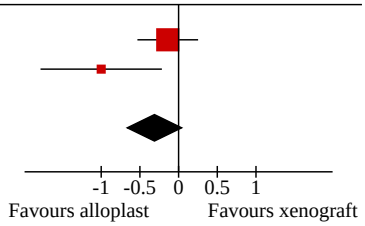
Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable



Analysis 2.4. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 4: Alloplast versus xenograft: changes in width of alveolar ridge (mm)

Study or Subgroup	MD	SE	Alloplast Total	Xenograft Total	Weight	Mean Difference IV, Fixed, 95% CI
Gholami 2012 (1)	-0.14	0.2	15	15	80.0%	-0.14 [-0.53 , 0.25]
Patel 2013	-1	0.4	13	12	20.0%	-1.00 [-1.78 , -0.22]
Total (95% CI)			**28**	**27**	**100.0%**	**-0.31 [-0.66 , 0.04]**

Heterogeneity: Chi² = 3.70, df = 1 (P = 0.05); I² = 73%
Test for overall effect: Z = 1.74 (P = 0.08)
Test for subgroup differences: Not applicable

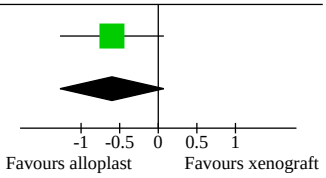


Footnotes
(1) For split-mouth trials the number of participants is double-counted.

Analysis 2.5. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 5: Alloplast versus xenograft: changes in height of alveolar ridge (mm)

Study or Subgroup	Alloplast Mean	Alloplast SD	Alloplast Total	Xenograft Mean	Xenograft SD	Xenograft Total	Weight	Mean Difference IV, Fixed, 95% CI
Patel 2013	-0.4	1	13	0.2	0.7	12	100.0%	-0.60 [-1.27 , 0.07]
Total (95% CI)			**13**			**12**	**100.0%**	**-0.60 [-1.27 , 0.07]**

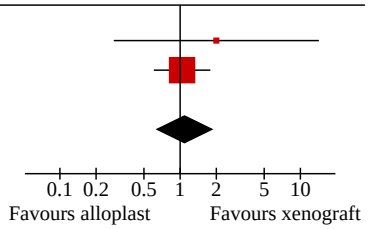
Heterogeneity: Not applicable
Test for overall effect: Z = 1.75 (P = 0.08)
Test for subgroup differences: Not applicable



Analysis 2.6. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 6: Alloplast versus xenograft: need for additional augmentation prior to implant placement

Study or Subgroup	log[RR]	SE	Alloplast Total	Xenograft Total	Weight	Risk Ratio IV, Fixed, 95% CI
Gholami 2012 (1)	0.693	1.002	15	15	7.1%	2.00 [0.28 , 14.25]
Patel 2013	0.037	0.276	13	12	92.9%	1.04 [0.60 , 1.78]
Total (95% CI)			**28**	**27**	**100.0%**	**1.09 [0.65 , 1.83]**

Heterogeneity: Chi² = 0.40, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.75)
Test for subgroup differences: Not applicable

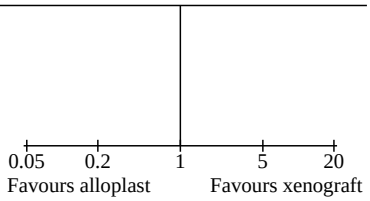


Footnotes
(1) For split-mouth trials the number of participants is double-counted.

Analysis 2.7. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 7: Alloplast versus xenograft: implant failures

Study or Subgroup	Alloplast Events	Alloplast Total	Xenograft Events	Xenograft Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Patel 2013	0	13	0	12		Not estimable
Total (95% CI)		**13**		**12**		**Not estimable**
Total events:	0		0			

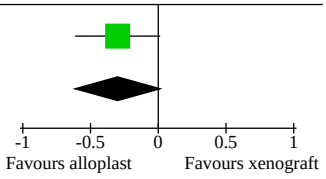
Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable



Analysis 2.8. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 8: Alloplast versus xenograft: changes in probing pocket depth at teeth adjacent to the extraction site (mm)

Study or Subgroup	Alloplast Mean	Alloplast SD	Alloplast Total	Xenograft Mean	Xenograft SD	Xenograft Total	Weight	Mean Difference IV, Fixed, 95% CI
Patel 2013	0	0.4	13	0.3	0.4	12	100.0%	-0.30 [-0.61 , 0.01]
Total (95% CI)			**13**			**12**	**100.0%**	**-0.30 [-0.61 , 0.01]**

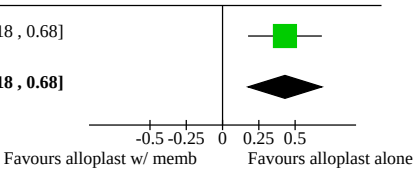
Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)
Test for subgroup differences: Not applicable



Analysis 2.9. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 9: Alloplast with membrane versus alloplast without membrane: changes in width of alveolar ridge (mm)

Study or Subgroup	Alloplast w/ membrane Mean	SD	Total	Alloplast w/o membrane Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brkovic 2012	1.29	0.32	11	0.86	0.26	9	100.0%	0.43 [0.18 , 0.68]
Total (95% CI)			**11**			**9**	**100.0%**	**0.43 [0.18 , 0.68]**

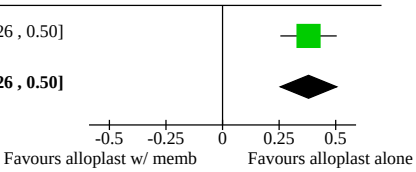
Heterogeneity: Not applicable
Test for overall effect: Z = 3.32 (P = 0.0009)
Test for subgroup differences: Not applicable



Analysis 2.10. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 10: Alloplast with membrane versus alloplast without membrane: changes in height of alveolar ridge (mm)

Study or Subgroup	Alloplast w/ membrane Mean	SD	Total	Alloplast w/o membrane Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Brkovic 2012	0.5	0.16	11	0.12	0.124	9	100.0%	0.38 [0.26 , 0.50]
Total (95% CI)			**11**			**9**	**100.0%**	**0.38 [0.26 , 0.50]**

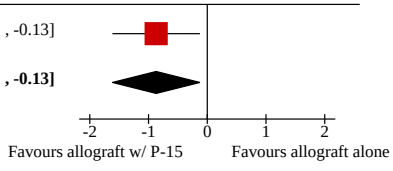
Heterogeneity: Not applicable
Test for overall effect: Z = 5.98 (P < 0.00001)
Test for subgroup differences: Not applicable



Analysis 2.11. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 11: Allograft with P-15 versus allograft without P-15: changes in width of alveolar ridge (mm)

Study or Subgroup	MD	SE	Allograft with P-15 Total	Allograft without P-15 Total	Weight	Mean Difference IV, Fixed, 95% CI
Fernandes 2011 (1)	-0.87	0.38	18	18	100.0%	-0.87 [-1.61 , -0.13]
Total (95% CI)			**18**	**18**	**100.0%**	**-0.87 [-1.61 , -0.13]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.29 (P = 0.02)
Test for subgroup differences: Not applicable

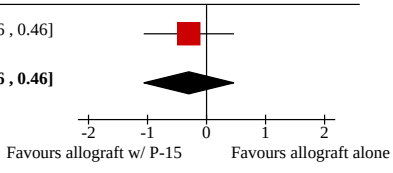


Footnotes
(1) For split-mouth trials the number of participants is double-counted.

Analysis 2.12. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 12: Allograft with P-15 versus allograft without P-15: changes in height of alveolar ridge (mm)

Study or Subgroup	MD	SE	Allograft with P-15 Total	Allograft without P-15 Total	Weight	Mean Difference IV, Fixed, 95% CI
Fernandes 2011 (1)	-0.3	0.39	18	18	100.0%	-0.30 [-1.06 , 0.46]
Total (95% CI)			**18**	**18**	**100.0%**	**-0.30 [-1.06 , 0.46]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.77 (P = 0.44)
Test for subgroup differences: Not applicable

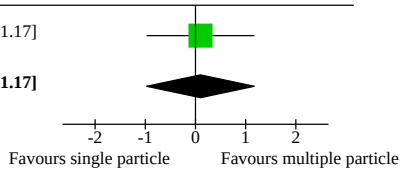


Footnotes
(1) For split-mouth trials the number of participants is double-counted.

Analysis 2.13. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 13: Alloplast single particles versus alloplast multiple particles: changes in width of alveolar ridge (mm)

Study or Subgroup	Alloplast single particle Mean	SD	Total	Alloplast multiple Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Hoang 2012	1.4	1.5	15	1.3	1.5	15	100.0%	0.10 [-0.97 , 1.17]
Total (95% CI)			**15**			**15**	**100.0%**	**0.10 [-0.97 , 1.17]**

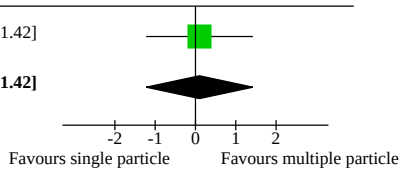
Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.86)
Test for subgroup differences: Not applicable



Analysis 2.14. Comparison 2: Different grafting materials for alveolar ridge preservation, Outcome 14: Alloplast single particles versus alloplast multiple particles: changes in height of alveolar ridge (mm)

Study or Subgroup	Alloplast single particle Mean	SD	Total	Alloplast multiple Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Hoang 2012	0.1	1.8	15	0	1.9	15	100.0%	0.10 [-1.22 , 1.42]
Total (95% CI)			**15**			**15**	**100.0%**	**0.10 [-1.22 , 1.42]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.15 (P = 0.88)
Test for subgroup differences: Not applicable



APPENDICES

Appendix 1. Cochrane Oral Health's Trials Register search strategy

Cochrane Oral Health's Trials Register is available via the Cochrane Register of Studies. For information on how the register is compiled, see oralhealth.cochrane.org/trials

From July 2014, searches of Cochrane Oral Health's Trials Register were conducted using the Cochrane Register of Studies and the search strategy below:

1. (((socket* or ridge* or alveolar) and (preserv* or augment*))) AND (INREGISTER)
2. ((graft* or autograft* or allograft* or "homologous bone" or DFDBA or FDBA or xenograft* or "heterologous bone" or "bovine bone" or "anorganic bone" or alloplast* or hydroxyapatite or ceramic* or polymer* or "calcium sulfate" or "calcium phosphate" or "tricalcium phosphate" or "calcium phosphosilicate" or "bioactive glass" or collagen* or "resorbable membrane*" or "non-resorbale membrane*" or "non resorbable membrane*" or "growth factor*" or "bone morphogenetic protein*" or BMP or rh-BMP)) AND (INREGISTER)
3. (#1 and #2) AND (INREGISTER)

Previous searches of Cochrane Oral Health's Trials Register were undertaken in February 2012 and January 2013 using the Procite software and the search strategy below:

(((socket* or ridge* or alveolar) and (preserv* or augment*)) AND (graft* or autograft* or allograft* or "homologous bone" or DFDBA or FDBA or xenograft* or "heterologous bone" or "bovine bone" or "anorganic bone" or alloplast* or hydroxyapatite or ceramic* or polymer* or "calcium sulfate" or "calcium phosphate" or "tricalcium phosphate" or "calcium phosphosilicate" or "bioactive glass" or collagen* or "resorbable membrane*" or "non-resorbale membrane*" or "non resorbable membrane*" or "growth factor*" or "bone morphogenetic protein*" or BMP or rh-BMP))

Appendix 2. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1 MeSH descriptor ALVEOLAR BONE LOSS this term only
#2 MeSH descriptor Alveolar Process explode all trees
#3 ((socket* in All Text or ridge* in All Text or alveolar in All Text) and (preserv* in All Text or augment* in All Text))
#4 (#1 or #2 or #3)
#5 MeSH descriptor BONE SUBSTITUTES explode all trees
#6 ((bone* in All Text near/5 graft* in All Text) or (socket* in All Text near/5 graft* in All Text))
#7 ("autogenous graft*" in All Text or "autologous graft*" in All Text or autograft* in All Text)

#8 (allograft* in All Text or "homologous bone" in All Text or DFDBA in All Text or FDBA in All Text)
#9 (xenograft* in All Text or "heterologous bone" in All Text or "bovine bone" in All Text or "anorganic bovine" in All Text)
#10 (alloplast* in All Text or hydroxyapatite in All Text or ceramic* in All Text or polymer* in All Text or "calcium sulfate" in All Text or "calcium phosphate" in All Text or "tricalcium phosphate" in All Text or "calcium phosphosilicate" in All Text or "bioactive glass*" in All Text)
#11 ((resorbable in All Text or non-resorbable in All Text or (“non in All Text and resorbable” in All Text)) and membrane* in All Text)
#12 (collagen in All Text and (plug* in All Text or fleece* in All Text or barrier* in All Text or seal* in All Text or matri* in All Text)) 639 edit delete
#13 ("growth factor*" in All Text or "bone morphogenetic protein*" in All Text or BMP in All Text or rh-BMP in All Text)
#14 (#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13)
#15 MeSH descriptor DENTAL IMPLANTS explode all trees
#16 MeSH descriptor DENTAL IMPLANTATION explode all trees
#17 (osseointegrated in All Text near/5 implant* in All Text)
#18 ((implant* in All Text near/5 dent* in All Text) or (implant* in All Text near/5 oral* in All Text))
#19 ((overdenture* in All Text or crown* in All Text or bridge* in All Text or prosthesis in All Text or restoration* in All Text) and (dental in All Text or oral in All Text) and implant* in All Text)
#20 "implant supported dental prosthesis" in All Text
#21 (#15 or #16 or #17 or #18 or #19 or #20)
#22 (#4 and #14 and #21)

Appendix 3. MEDLINE Ovid search strategy

1. ALVEOLAR BONE LOSS/
2. exp ALVEOLAR PROCESS/
3. ((socket$ or ridge$ or alveolar) and (preserv$ or augment$)).mp.
4. or/1-3
5. exp BONE SUBSTITUTES/
6. ((bone$ adj5 graft$) or (socket$ adj5 graft$)).mp.
7. (“autogenous graft$” or “autologous graft$” or autograft$).mp.
8. (allograft$ or “homologous bone” or DFDBA or FDBA).mp.
9. (xenograft$ or “heterologous bone” or “bovine bone” or “anorganic bovine”).mp.
10. (alloplast$ or hydroxyapatite or ceramic$ or polymer$ or “calcium sulfate” or “calcium phosphate” or “tricalcium phosphate” or “calcium phosphosilicate” or “bioactive glass$”).mp.
11. ((resorbable or non-resorbable or “non resorbable”) and membrane$).mp.
12. (collagen adj (plug$ or fleece$ or barrier$ or seal$ or matri$)).mp.
13. (“growth factor$” or “bone morphogenetic protein$” or BMP or rh-BMP).mp.
14. or/5-13
15. exp DENTAL IMPLANTS/
16. exp DENTAL IMPLANTATION/
17. (osseointegrated adj5 implant$).mp.
18. (implant$ adj5 (dent$ or oral$)).mp.
19. (((overdenture$ or crown$ or bridge$ or prosthesis or restoration$) adj5 (dental or oral)) and implant$).mp.
20. ("implant supported dental prosthesis").mp.
21. or/15-20
22. 4 and 14 and 21

The above subject search was linked with the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials in MEDLINE (as described in Lefebvre 2020, box 3b).

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/ not humans.sh.
11. 9 not 10

Appendix 4. Embase Ovid search strategy

1. ALVEOLAR BONE LOSS/
2. ((socket$ or ridge$ or alveolar) and (preserv$ or augment$)).mp.

3. or/1-2
4. BONE PROSTHESIS/
5. ((bone$ adj5 graft$) or (socket$ adj5 graft$)).mp.
6. (“autogenous graft$” or “autologous graft$” or autograft$).mp.
7. (allograft$ or “homologous bone” or DFDBA or FDBA).mp.
8. (xenograft$ or “heterologous bone” or “bovine bone” or “anorganic bovine”).mp.
9. (alloplast$ or hydroxyapatite or ceramic$ or polymer$ or “calcium sulfate” or “calcium phosphate” or “tricalcium phosphate” or “calcium phosphosilicate” or “bioactive glass$”).mp.
10. ((resorbable or non-resorbable or “non resorbable”) and membrane$).mp.
11. (collagen adj (plug$ or fleece$ or barrier$ or seal$ or matri$)).mp.
12. (“growth factor$” or “bone morphogenetic protein$” or BMP or rh-BMP).mp.
13. or/4-12
14. exp TOOTH IMPLANTATION
15. (osseointegrated adj5 implant$).mp.
16. (implant$ adj5 (dent$ or oral$)).mp.
17. (((overdenture$ or crown$ or bridge$ or prosthesis or restoration$) adj5 (dental or oral)) and implant$).mp.
18. ("implant supported dental prosthesis").mp.
19. or/14-18
20. 3 and 13 and 19

The above subject search was linked with the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials in Embase (as described in Lefebvre 2020, box 3e):

1. Randomized controlled trial/
2. Controlled clinical study/
3. random$.ti,ab.
4. randomization/
5. intermethod comparison/
6. placebo.ti,ab.
7. (compare or compared or comparison).ti.
8. ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.
9. (open adj label).ti,ab.
10. ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.
11. double blind procedure/
12. parallel group$1.ti,ab.
13. (crossover or cross over).ti,ab.
14. ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant $1)).ti,ab.
15. (assigned or allocated).ti,ab.
16. (controlled adj7 (study or design or trial)).ti,ab.
17. (volunteer or volunteers).ti,ab.
18. human experiment/
19. trial.ti.
20. or/1-19
21. random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.)
22. Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.)
23. (((case adj control$) and random$) not randomi?ed controlled).ti,ab.
24. (Systematic review not (trial or study)).ti.
25. (nonrandom$ not random$).ti,ab.
26. "Random field$".ti,ab.
27. (random cluster adj3 sampl$).ti,ab.
28. (review.ab. and review.pt.) not trial.ti.
29. "we searched".ab. and (review.ti. or review.pt.)
30. "update review".ab.
31. (databases adj4 searched).ab.
32. (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/
33. Animal experiment/ not (human experiment/ or human/)
34. or/21-33
35. 20 not 34

Appendix 5. LILACS BIREME Virtual Health Library search strategy

(Mh Alveolar bone loss or Mh Alveolar process or ((socket$ or ridge$ or alveolar or alveolo or rebordo or cresta) and (preserv$ or augment $ or aument$))) [Words] and ((Mh Bone substitutes or "bone graft$" or (socket$ and graft$) or (hueso and injerto) or (osso and enxerto) or allograft or aloinjerto or "homologous bone" or DFDBA or FDBA or "autogenous graft$" or "autologuous graft$" or autograft$ or xenograft$ or "bovine bone" or "anorganic bovine" or alloplast$ or hydroxyapatite or ceramic$ or polymer$ or "calcium sulfate" or "calcium phosphate" or "tricalcium phosphate" or "bioactive glass$" or "resorbable membrane$" or "non-resorbable membrane$" or "nonresorbable membrane$" or collagen$ or "growth factor" or "bone morphogenetic protein" or BMP) AND (Mh Dental implants or Mh Dental implantation or "ossointegrated implant" or (dent$ and implant$) or (oral and implant$) or overdenture$ or crown$ or bridge$ or prosthesis or restoration)) [Words]

The above subject search was linked to the Brazilian Cochrane Center filter for identifying randomised controlled trials in LILACS:

((Pt randomized controlled trial OR Pt controlled clinical trial OR Mh randomized controlled trials OR Mh random allocation OR Mh double-blind method OR Mh single-blind method) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Pt clinical trial OR Ex E05.318.760.535$ OR (Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR Tw experim$ OR Tw investiga$)) OR ((Tw singl$ OR Tw simple $ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) AND (Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR Tw mascar$)) OR Mh placebos OR Tw placebo$ OR (Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$ OR Tw azar OR Tw aleator$) OR Mh research design) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Ct comparative study OR Ex E05.337$ OR Mh follow-up studies OR Mh prospective studies OR Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$) AND NOT (Ct animal AND NOT (Ct human and Ct animal))) [Words]

Appendix 6. Web of Science Conference Proceedings search strategy

1 TS=(socket* or ridge* or alveolar)
2 TS=(preserv* or augment*)
3 #1 and #2
#4 TS=(bone and graft*)
#5 TS=(socket* and graft*)
#6 TS=("autogenous graft*" or "autologous graft" or autograft* or allograft* or "homologous bone" or DFDBA or FDBA or xenograft* or "heterologous bone" or "bovine bone" or "anorganic bovine" or alloplast* or hydroxyapatite or ceramic* or polymer* or "calcium sulfate" or "calcium phosphate" or "tricalcium phosphate" or "calcium phosphosilicate" or "bioactive glass*")
#7 TS=((resorbable or non-resorbable or "non resorbable") and membrane*)
#8 TS=(collagen and (plug* or fleece* or barrier* or seal* or matri*))
#9 TS=("growth factor*" or "bone morphogenetic protein*" or BMP or rh-BMP)
#10 #4 or #5 or #6 or #7 or #8 or #9
#11 TS=((osseointegrated or dent* or oral*) and implant*)
#12 TS=((overdenture* or crown* or bridge* or prosthesis or restoration*) and implant*)
#13 #11 or #12
#14 #3 and #10 and #13

Appendix 7. Scopus search strategy

TITLE-ABS-KEY(((socket* OR ridge* OR alveolar) AND (preserv* OR augment*)) AND (graft* OR autograft* OR allograft* OR "homologous bone" OR dfdba OR fdba OR xenograft* OR "heterologous bone" OR "bovine bone" OR "anorganic bone" OR alloplast* OR hydroxyapatite OR ceramic* OR polymer* OR "calcium sulfate" OR "calcium phosphate" OR "tricalcium phosphate" OR "calcium phosphosilicate" OR "bioactive glass" OR collagen* OR "resorbable membrane*" OR "non-resorbale membrane*" OR "non resorbable membrane*" OR "growth factor*" OR "bone morphogenetic protein*" OR bmp OR rh-bmp) AND ("clinical trial" OR random*))

Appendix 8. Proquest Dissertations and Theses search strategy

"alveolar ridge preservation" or "alveolar bone preservation" or "alveolar ridge augmentation" or "alveolar bone augmentation":TI

Appendix 9. OpenGrey search strategy

"alveolar ridge preservation" or "alveolar bone preservation" or "alveolar ridge augmentation" or "alveolar bone augmentation"

Appendix 10. Trials registries search strategies

US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) search strategy

"alveolar ridge preservation"
"alveolar bone preservation"
"alveolar ridge augmentation"
"alveolar bone augmentation"

World Health Organization International Clinical Trials Registry Platform search strategy

"alveolar ridge preservation"
"alveolar bone preservation"
"alveolar ridge augmentation"
"alveolar bone augmentation"

WHAT'S NEW

Date	Event	Description
19 March 2021	New citation required and conclusions have changed	Review update includes 9 new trials bringing the total to 16 included studies. New co-author.
19 March 2021	New search has been performed	Searches updated to 19 March 2021.

HISTORY

Protocol first published: Issue 11, 2012
Review first published: Issue 5, 2015

Date	Event	Description
9 February 2017	Amended	Minor edits. Reason for exclusion changed for Jung 2013.

CONTRIBUTIONS OF AUTHORS

- Drafting the protocol: Momen A Atieh (MAA), Nabeel HM Alsabeeha (NHMA), Alan GT Payne (AGTP).
- Developing search strategy: MAA.
- Searching for trials: MAA, NHMA, Sara Ali (SA), AGTP.
- Obtaining copies of trials: MAA, NHMA, SA.
- Selection of trials: MAA, NHMA, SA, AGTP.
- Data extraction: MAA, NHMA, SA, Clovis M Faggion Jr (CMFJr).
- Entering data into Review Manager 5: MAA, NHMA.
- Carrying out the analyses: MAA, NHMA, CMFJr.
- Interpretation of analyses: MAA, NHMA, SA, AGTP, Marco Esposito (ME).
- Drafting the final review: MAA, NHMA, SA, AGTP, ME.
- Updating the review: MAA, NHMA, SA, AGTP, ME.

DECLARATIONS OF INTEREST

None of the authors has any interests related to this review.

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- Cochrane Oral Health Global Alliance, Other

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- In terms of subgroup analysis, the effects of barrier membrane and site of alveolar ridge preservation (ARP) (molar versus non-molar) were omitted in the review due to lack of adequate number of studies to carry out the subgroup analysis.
- Different grafting materials were compared in addition to the type of grafting material versus extraction.
- The wording of two outcomes was changed:
  - 'complications' instead of 'post-surgical complications (i.e. discomfort, pain and swelling)' to include both intra- and postoperative complications;
  - 'prosthodontic outcomes of rehabilitation' instead of 'prosthodontic outcomes of future prosthodontic rehabilitation.'

INDEX TERMS

Medical Subject Headings (MeSH)

*Alveolar Process; Alveolar Ridge Augmentation; Bias; Biocompatible Materials [*administration & dosage]; Bone Regeneration; Bone Remodeling; Confidence Intervals; *Dental Implantation, Endosseous; Heterografts; Organ Sparing Treatments [*methods]; Randomized Controlled Trials as Topic; Time Factors; Tooth Extraction [*adverse effects] [methods]; *Tooth Socket; Treatment Outcome

MeSH check words

Adult; Humans; Middle Aged