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Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment (Review)

Coulthard P, Esposito M, Jokstad A, Worthington HV

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Abstract
Background
Dental implants require sufficient bone to adequately stabilise. For some patients implant treatment would not be an option without bone augmentation. A variety of materials and surgical techniques are available for use in bone augmentation.

Objectives
To test the null hypothesis of no difference in the success, function, morbidity and patient satisfaction between different bone augmentation techniques for dental implant treatment.

Search strategy
The Cochrane Oral Health Group's Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE were searched. Several dental journals were handsearched. The bibliographies of review articles were checked, and personal references were searched. Implant manufacturing companies were also contacted.

Selection criteria
Randomised controlled trials (RCTs) of different techniques and materials for augmenting bone for implant treatment.

Data collection and analysis
Quality assessment was carried out and authors were contacted for any missing information. Data were independently extracted in duplicate.

Main results
Four RCTs (n = 95) were suitable for inclusion in this review, assessing three different aspects of bone augmentation techniques: onlay grafting with and without a barrier membrane, grafting with a resorbable and non-resorbable membrane, and membranes for guided bone regeneration (GBR). Trials reported on augmentation procedures up to abutment connection only. At the patient level there were no statistically significant differences for the alternative techniques for onlay grafting with respect to the degree of bone graft resorption and wound dehiscence. One trial showed statistically significantly more infections in the non-resorbable group compared to the resorbable group, relative risk 0.05 (95% confidence interval (CI): 0.00 to 0.74). One study of GBR with a resorbable versus non-resorbable membrane indicated no statistically significant difference in early implant failure, reduction in bone defect or wound dehiscence. The other GBR study compared a non-resorbable membrane with no membrane and reported no statistically significant difference in wound infection or dehiscence but a significant increase in per cent bone gain for the test group compared to control, mean difference = 70 (95% CI: 36 to 104, p = 0.002).

Authors’ conclusions
There is no evidence from available RCTs supporting superior success with one or other of the alternative techniques examined. There was weak evidence that a non-resorbable membrane was better than no membrane for permitting bone growth about dental implants, and that a resorbable membrane over a bone graft may allow healing with fewer infections than a non-resorbable membrane.
SYNOPSIS

There is no evidence that some of the different techniques for increasing bone volume for implant placement have superior success rates.

Missing teeth can sometimes be replaced with dental implants placed into the jaw. A crown, bridge or denture can then be attached to the implant. Some patients have insufficient bone present to place dental implants but there are many surgical techniques to increase the bone volume making implant treatment possible. However, this review found few trials and these evaluated only three different techniques. There is not enough evidence to demonstrate superiority of any particular technique other than weak evidence that a membrane may be better than no membrane to allow bone growth around an implant, and that a dissolving membrane over a bone graft may allow healing with less infections than a non-dissolving membrane.

BACKGROUND

Missing teeth and supporting oral tissues have traditionally been replaced with dentures or bridges permitting restoration of chewing function, speech, and aesthetics. Dental implants offer an alternative. These implants are inserted into the jawbones to support a dental prosthesis and are retained because of the intimacy of bone growth on to their surface. This direct structural and functional connection between living bone and implant surface, termed osseointegration, was first described by (Brånemark 1977) and has undoubtedly been one of the most significant scientific breakthroughs in dentistry over the past 30 years.

Teeth may have been lost through dental disease or trauma or they may be congenitally absent. In addition, teeth may be lost as part of a surgical procedure to resect part of a jaw because of pathology such as cancer. Sometimes, there is a lack of supporting bone in addition to the absent teeth because of atrophy, trauma, failure to develop or surgical resection. Dental implants can only be placed if there is sufficient bone to adequately stabilise them, and bone augmentation permits implant treatment that would otherwise not be an option for some of these patients. Bone augmentation procedures may be carried out some time prior to implant placement, or at the same time as implant placement, using various materials and techniques. When carried out prior to placement, this necessitates an additional surgical episode and then the area is left to heal for a period of time before the implants are placed.

Some materials used to augment the bone volume may be described as follows:

- Autogenous bone grafts
  These are bone grafts taken from an adjacent or remote site in the same patient and used to build up the deficient area and are considered to be the material of choice (Palmer 2000). They are biologically compatible as they are from the same patient and provide a scaffold into which new bone may grow. Sites from within the mouth may be used for relatively small graft requirements or sites such as the hip bone (iliac crest) for larger bone volumes. All of these require surgery at a second site and therefore the morbidity must be considered. Of the many possible sites, each has its own merits and disadvantages. Sometimes it may be possible to recycle bone taken from the site of implant placement when preparing the hole by using a special filter to collect bone particles that would otherwise be lost and use this to build up a deficient area.
- Allografts
  These are bone grafts harvested from cadavers and processed by methods such as freezing or demineralising and freezing. The grafts are then sterilised and supplied by specially licensed tissue banks in several convenient ways such as bone particles or large blocks. They are resorbable. There may be some concern regarding their absolute non-infectivity.
- Xenografts
  These are graft materials derived from animals such as cow or coral. Bio-Oss is bovine bone that is processed to completely remove the organic component. Coral has been advocated because of a pore size suitable for permitting bone ingrowth. There has been concern regarding the absolute non-infectivity of bovine-derived materials although this has been disputed (Wenz 2001).
- Alloplastic graft materials
  These synthetic bone substitutes include calcium phosphates and bioactive glasses. Alloplasts provide a physical framework for bone ingrowth. Some surgeons use these materials in combination with autogenous bone grafts. These materials resorb completely or to some degree or not at all with time.
- Barrier membranes for guided bone regeneration (GBR)
  This technique uses special barrier membranes to protect defects from the ingrowth of soft tissue cells so that bone progenitor cells may develop bone uninhibited. Ingrowth of soft tissue may disturb or totally prevent osteogenesis in a defect or wound. Examples of membrane are expanded polytetrafluoroethylene (Gore-Tex), porcine collagen (Bio-Gide) and polyglyactin (Vicryl). Membranes can be resorbable or non-resorbable.
- Bone promoting molecules
  Bone morphogenic proteins (BMPs) are a family of proteins naturally present in bone and responsible for activation of bone de-
Some surgical techniques used to augment bone volume include:

- **Onlay grafting**
  
  The graft material is laid over the defective area to increase width or height or both of the alveolar jawbone. The host bed is usually perforated with a small bur to encourage the formation of a blood clot between the graft and recipient bed. The graft is immobilised with screws or plates or with dental implants (Kahnberg 1989).

- **Inlay grafting**
  
  One type of inlay graft is a sinus lift or sinus elevation procedure in which graft material is inserted inside the floor of the maxillary sinus to increase bone volume (Tatum 1986; Tong 1998). Also the floor of the nose may be grafted (Higuchi 1992). In another type of inlay grafting procedure, a section of jawbone is surgically separated and graft material sandwiched between two sections. The now established Le Fort I osteotomy and interpositional bone graft procedure (Obwegeser 1969) has been used for patients requiring implant treatment (Keller 1992).

- **Ridge expansion**
  
  The alveolar ridge is split longitudinally and parted to widen it and allow placement of an implant or graft material or both in the void. The longitudinal split is limited by placing transverse cuts in the bone.

- **Distraction osteogenesis**
  
  The principals of distraction osteogenesis in which a gradual, controlled displacement of a surgically prepared fracture is used to increase bone volume, are not new but have recently been introduced into implant surgery to increase alveolar bone volume (Chin 1999). The gap created during the displacement of the bone segment fills with immature non-calcified bone that matures during a subsequent fixation period. The associated soft tissues are also expanded as the bone segment is transported.

A long implant may be placed to the upper jaw passing through the sinus into the body of the zygomatic bone. This surgical technique is an alternative to bone augmentation in those patients with insufficient bone for placement of the usual type of dental implant. This comparison is not included in this review as the zygoma implant technique is not a technique for bone augmentation but is evaluated in another Cochrane review (Esposito 2003).

Each type of augmentation material may be used in combination with a variety of different surgical techniques, so many permutations of treatment are possible and the situation is rather complicated. Particular treatment options have strong proponents with surgeons claiming that a particular material or technique offers improved implant success. This review aims to compare different bone augmentation techniques against each other. The effect of the timing of the augmentation is also of interest to this review.

**OBJECTIVES**

To test the null hypothesis of no difference in the success, function, side effect and patient satisfaction between different bone augmentation techniques for dental implant treatment, against the alternative hypothesis of a difference.

**CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW**

Types of studies
Randomised controlled clinical trials including split mouth studies.

Types of participants
Patients with missing teeth who require alveolar bone augmentation for dental implant treatment. Patients who had undergone radiotherapy were excluded from this review and are the subject of a separate review (Coulthard 2002).

Types of intervention
Dental implant treatment with different techniques and materials for augmenting bone.

Types of outcome measures
Outcome measures included:

- Prosthesis failure due to implant failure (binary)
- Implant failure (mobility and removal of stable implants dictated by progressive marginal bone loss) (binary)
- Marginal bone levels on intraoral radiographs taken with a paralleling technique (continuous)
- Bone graft size (continuous)
- Bone graft failure (binary)
- Side effects (pain, infection, dehiscence, nerve injury, gait disturbance) (continuous on VAS scale and binary)
- Patient satisfaction (both binary and continuous on VAS scale).

**SEARCH STRATEGY FOR IDENTIFICATION OF STUDIES**

See: Oral Health Group search strategy

For the identification of studies included or considered for this review, detailed search strategies were developed for each
database searched. These were based on the search strategy developed for MEDLINE but revised appropriately for each database. The search strategy combined a sensitive search strategy for randomised controlled clinical trials (RCTs) revised from phases 1 and 2 of the Cochrane Sensitive Search Strategy for RCTs (as published in Appendix 5c in the Cochrane Reviewers’ Handbook). The subject search used a combination of controlled vocabulary and free text terms based on the following search strategy for searching MEDLINE:

#1 randomized controlled trial.pt.
#2 controlled clinical trial.pt.
#3 randomized controlled trials.sh.
#4 random allocation.sh.
#5 double blind method.sh.
#6 single blind method.sh.
#7 latin square.ti,ab.
#8 crossover.ti,ab.
#9 (split adj (mouth or plot)).ti,ab.
#10 or/1-9
#11 (ANIMAL not HUMAN).sh.
#12 10 not 11 #
#13 clinical trial.pt.
#14 exp clinical trials/
#15 (clin$ adj25 trial$).ti,ab.
#16 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
#17 placebo.sh.
#18 placebo$.ti,ab.
#19 random$.ti,ab.
#20 research design.sh.
#21 or/13-20
#22 21 not 11
#23 22 not 12
#24 12 or 22
#25 exp Dental Implants/
#26 exp Dental Implantation/ or dental implantation.mp.
#27 exp Dental Prosthesis, Implant-Supported/
#28 ((osseointegrated adj implant$) and (dental or oral)).mp. [mp=title, abstract, registry number word, mesh subject heading]
#29 dental implant$.mp. [mp=title, abstract, registry number word, mesh subject heading]
#30 (implant$ adj5 dent$).mp. [mp=title, abstract, registry number word, mesh subject heading]
#31 dental-implant$.mp. [mp=title, abstract, registry number word, mesh subject heading]
#32 ((overdenture$ or crown$ or bridge$ or prosthesis or restoration$) adj5 (Dental or oral)) and implant$.mp. [mp=title, abstract, registry number word, mesh subject heading]
#33 “implant supported dental prosthesis” .mp. [mp=title, abstract, registry number word, mesh subject heading]
#34 (“blade implant$” and (dental or oral)).mp. [mp=title, abstract, registry number word, mesh subject heading]

DATABASES SEARCHED
The Cochrane Oral Health Group’s Trials Register (December 2002)
The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 4, 2002)
MEDLINE (1966 to December 2002)
EMBASE (1980 to December 2002)
The bibliographies of papers were checked for studies outside the handsearched journals. Personal references were also searched.

HANDSEARCHING

UNPUBLISHED STUDIES
First named authors of RCTs identified were written to in order to obtain further information about the trials and to attempt to identify unpublished studies. In addition we wrote to 55 producers of implant systems.

LANGUAGE
There were no language restrictions.

METHODS OF THE REVIEW
STUDY SELECTION
The titles and abstracts (when available) of all reports identified through the electronic searches were scanned independently by two reviewers. For studies appearing to meet the inclusion criteria, or for which there is insufficient data in the title and abstract to
make a clear decision, the full report was obtained. The full reports obtained from all the electronic and other methods of searching were assessed independently by two reviewers to establish whether the studies met the inclusion criteria or not. Disagreements were resolved by discussion. Where resolution was not possible, a third reviewer was consulted. All studies meeting the inclusion criteria then underwent validity assessment and data extraction. Studies rejected at this or subsequent stages were recorded in the table of excluded studies, and reasons for exclusion recorded.

QUALITY ASSESSMENT
The quality assessment of the included trials was undertaken independently and in duplicate by two reviewers as part of the data extraction process. Three main quality criteria were examined: allocation concealment (recorded as adequate, unclear, inadequate and not used); blind outcome assessment (recorded as yes, no, unclear and not possible); and completeness of follow up (is there a clear explanation for withdrawals and drop outs in each treatment group?). The agreement between the quality assessments was measured using the kappa statistic. Further quality assessment was carried out to assess baseline comparability between treatment groups.

After taking into account the additional information provided by the authors of the trials, studies were grouped into the following categories:
(A) Low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met.
(B) Moderate risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were partly met.
(C) High risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met as described in the Cochrane Reviewers' Handbook 6.7.

DATA EXTRACTION
Data were extracted by two reviewers independently using specially designed data extraction forms. The data extraction forms were piloted on several papers and modified as required before use. Any disagreement was discussed and a third reviewer consulted where necessary. Authors were contacted for clarification or missing information whenever possible. Data were excluded until further clarification was available if agreement could not be reached. For each trial the following data were recorded: Year of publication, country of origin and source of study funding. Details of the participants including demographic characteristics, source of recruitment and criteria for inclusion. Details of the type of intervention Details of the outcomes reported, including method of assessment, and time intervals.

DATA SYNTHESIS
For dichotomous outcomes, the estimate of effect of an intervention was expressed as relative risks together with 95% confidence intervals (CIs). For continuous outcomes, means and standard deviations were used to summarise the data for each group using mean differences and 95% CIs.

Clinical heterogeneity was to be assessed by examining the types of participants and interventions for all outcomes in each study. Only if there were studies of similar comparisons reporting the same outcome measures was meta-analysis to be attempted. As there were no studies comparing similar interventions, none of the meta-analysis procedures described above or below were conducted. It was planned that relative risks would be combined for binary data, and standardised mean differences for continuous data, using a random effects model. The significance of any discrepancies in the estimates of the treatment effects from the different trials were to be assessed by means of Cochran's test for heterogeneity and any heterogeneity investigated.

Sensitivity analyses were to be undertaken to examine the effect of randomisation, allocation concealment and blind outcome assessment on the overall estimates of effect. In addition, the effect of including unpublished literature on the review's findings was also to be examined.

It was planned to undertake subgroup analyses where possible with respect to time of outcome measures and time from augmentation procedure to implant placement and time from implant placement to implant restoration.

DESCRIPTION OF STUDIES
See 'Characteristics of included studies table'. See 'Characteristics of excluded studies table'.

CHARACTERISTICS OF THE TRIAL SETTING AND INVESTIGATORS
Of the ten eligible trials (Antoun 2001; Carpio 2000; Dahlin 1991; Friedmann 2002; Gher 1994; Majzoub 1999; Schlegel 1998; Tawil 2001; Wannfors 2000; Zitzmann 1997), four were excluded because of problems with study design (Gher 1994; Schlegel 1998; Tawil 2001; Zitzmann 1997) and two because we were unable to use any of the data presented (Majzoub 1999; Wannfors 2000). Of the four included trials, one was conducted in France (Antoun 2001), one in the USA (Carpio 2000), one in Sweden (Dahlin 1991), and one in Germany (Friedmann 2002). Three trials had a parallel group study design and one a split mouth design (Dahlin 1991). Three trials received support from industry (Antoun 2001; Carpio 2000; Friedmann 2002). All four studies were conducted at university dental clinics and included adults.

CHARACTERISTICS OF THE INTERVENTIONS
One of the included studies compared onlay bone grafting with and without a barrier membrane (Antoun 2001). Another compared resorbable and non-resorbable barrier membranes over a xenograft (Friedmann 2002). The other two studies compared guided bone regeneration (GBR) (Carpio 2000; Dahlin 1991).
One of these compared resorbable versus non-resorbable barriers for augmentation around implants showing fenestration at placement (Carpio 2000) and the other compared a non-resorbable barrier membrane with no membrane, also around implants showing fenestration at placement (Dahlin 1991).

The onlay bone grafting study (Antoun 2001) used non-resorbable expanded polytetrafluoroethylene (ePTFE) barrier membrane (WL Gore and Associates, Inc., Flagstone, USA) versus no membrane. The membranes were stabilised with minititanium screws and the wound closed with Gore-Tex sutures in the membrane group or vicryl sutures in the group without a membrane. The onlay bone graft was harvested from the symphyseal region of the mandible, re-contoured to fit the defect and immobilised with titanium screws. Cancellous bone was also harvested from the donor site to fill discrepancies. Implants (Bränemark, Nobel Biocare, Gothenburg, Sweden) were placed 6 months after bone grafting.

The study comparing membranes over a xenograft (Friedmann 2002) used a resorbable collagen membrane (Ossix) and a non-resorbable ePTFE membrane (Gore-Tex). Patients were randomised to one of these barrier membranes which was placed over a deproteinized bovine bone mineral graft to augment the lateral alveolus 7 months prior to implant placement.

The earlier GBR study (Dahlin 1991) compared non-resorbable ePTFE barrier membrane (Gore-Tex, WL Gore and Associates, Inc., Flagstone, USA) versus no barrier. A slight space was maintained over the exposed titanium surface by manual convex shaping of the membrane but no bone or other space maintainer was used. The barrier was allowed to extend 3 to 4 mm around the defect and stabilised by tucking one edge under the periosteum. All implants were titanium self tapping (Nobel Biocare, Goteborg, Sweden).

The other GBR study (Carpio 2000) compared resorbable porcine-derived collagen barrier (BioGide, OsteoHealth, Inc., Shirley, USA) versus non-resorbable ePTFE barrier (Gore-Tex, WL Gore and Associates, Inc., Flagstone, USA). Both groups had a 1:1 mixture of bovine anorganic bone (Bio-Oss, OsteoHealth, Inc.) and autogenous bone derived from the osteotomy site placed beneath the barrier. The barrier was stabilised with either two polylactic acid bioabsorbable pins (Osseofix, Implant Innovations Inc., or Resorpin, OsteoHealth Inc.), or the implant cover screw or the mucogingival flap only. All implants were machined surface, screw-type, titanium (Implant Innovations Inc., West Palm Beach, Florida, USA).

CHARACTERISTICS OF OUTCOME MEASURES
Implant failure at second stage surgery, 6 months after implant placement was recorded in both studies comparing GBR techniques (Carpio 2000; Dahlin 1991). The size of the bone graft was measured by direct measurement in one study (Carpio 2000) and as the difference in surface area on digitized photographic images taken at implant placement and 6 months later at the implant exposure surgery in another (Dahlin 1991). The study comparing onlay bone grafting techniques used direct measurement of the graft with callipers and also computerized tomography (CT) scan analysis (Antoun 2001). Morbidity measures included wound dehiscence, graft or implant exposure, and membrane exposure during the 6 month period after bone augmentation surgery in all three studies. We have interpreted graft or implant exposure and membrane exposure as dehiscence. Implants were followed up to abutment connection and no data on implants carrying functional loads were presented. The study comparing different barrier membranes with a xenograft reported graft failure, wound dehiscence and wound infection (Friedmann 2002). In this study, no implant outcomes were presented.

METHODOLOGICAL QUALITY

See ‘Additional Table 01’.

RANDOMISATION AND ALLOCATION CONCEALMENT
The description of the method of randomisation and allocation concealment was unclear in three studies despite writing to the authors for clarification. One of these three authors responded. The description was adequate in one included study.

BLINDING
It is not possible to blind the outcome assessor to some outcome measures such as direct bone graft measurement when evaluating the effect of a barrier membrane because the membrane may be obvious. However, it may be possible to blind other outcome measures such as graft size measured by computerized tomography (CT). We wrote to the study authors to ask if any blinding was attempted but did not receive a reply about this aspect of the study. Any attempt at patient blinding was unclear in the articles.

COMPLETENESS OF FOLLOW UP
There were no withdrawals in the four studies.

SAMPLE SIZE
None of the studies included in this review reported that they had undertaken a priori calculation for the sample size.

BASELINE COMPARABILITY BETWEEN TREATMENT GROUPS
There were no baseline differences between groups regarding bone defect size around implants in one trial (Carpio 2000). The other three studies did not provide information about baseline comparability.

AGREEMENT OF QUALITY ASSESSMENT
The percentage agreement and kappa scores between the two raters was: 100% agreement (kappa 1.0) for allocation concealment and 100% agreement (kappa 1.0) for outcome assessor blinding. Kappa could not be calculated for patient blinding and reporting.
of attrition as this was constant for one reviewer but the agreement was 75% for both. The agreement for outcome assessor blinding was perfect as this was not possible in all the studies. The agreement for allocation concealment was perfect as this was unclear in all studies.

**RESULTS**

In total 95 patients were enrolled in the four trials.

- Onlay bone graft with or without barrier ("Comparison 01", "Outcomes 01-02")

Twelve patients were enrolled in the parallel group study comparing onlay bone grafts with a non-resorbable barrier membrane versus onlay bone grafts alone (Antoun 2001) with seven in the bone graft group without barrier and five in the bone graft with barrier group. There was no infection or bone graft exposure in either group but one patient had a membrane exposure in the membrane group over 6 months. Implants (Brånemark, Nobel Biocare, Göteborg, Sweden) were placed at this re-entry surgery but no implant related outcomes were reported.

- Guided bone regeneration

Seven patients were enrolled in the split mouth designed study that compared a non-resorbable barrier with no barrier in patients requiring bone regeneration procedures at implant placement fenestrations at two contralateral sites (Dahlín 1991). There was no infection, implant or barrier exposure in either group. There was a significant increase in percent bone gain for the test group when compared with the control, mean difference = 70 (95% confidence interval (CI): 36 to 104, p = 0.002). No outcomes related to the implant in function were reported.

Forty-eight patients were enrolled in the resorbable collagen membrane versus non-resorbable barrier study (Carpio 2000) with 23 in the collagen group and 25 in the expanded polytetrafluoroethylene (ePTFE) group. Implant failure by mobility testing was assessed at 6 months after implant placement. There was no significant difference in failures with five failures in the resorbable membrane group and four in the non-resorbable group ("Comparison 02", "Outcomes 01"). There was no statistically significant difference in dehiscence over 6 months ("Comparison 02", "Outcome 02"). The length, width and circumference of the bone defect around the implant was measured at implant placement and 6 months later at the implant exposure surgery. The presentation of reduction in the defect size data was not clear in the article but the authors confirmed the standard error had been presented so we were able to use the data in this review. There were no significant differences in reduction in length or width of defect ("Comparison 02", "03"). No outcomes related to the implant in function were reported.

- Xenograft with resorbable and non-resorbable barrier membrane ("Comparison 03", "Outcomes 01-03")

Twenty-eight patients were enrolled in the resorbable versus non-resorbable barrier over bovine graft study (Friedmann 2002). There was a statistically significant difference with more infections in the non-resorbable group compared to the resorbable group, relative risk 0.05 (95% CI: 0.00 to 0.74). One graft in the non-resorbable group failed completely and required re-augmentation at the 7 month re-entry surgery. Implants were placed at the re-entry surgery but no implant related outcomes were reported.

**DISCUSSION**

We were only able to include four of ten eligible studies investigating bone augmentation techniques for implant treatment because of problems with study design or data presentation. Two of the excluded studies had unclear study designs, and the unit of randomisation was the implant rather than the patient in three studies, but the analysis failed to reflect this. These methodological problems are not uncommon in the dental implant literature (Esposito 2001) and it is recommended that clinicians seek advice from clinical research methodologists and statisticians when designing and analysing studies. None of the studies, included or excluded, had undertaken a priori calculation for the sample size and all of the studies were small. It is likely that the studies were therefore underpowered to demonstrate any significant difference in outcome measures between groups. In addition, no data on functionally loaded implants were presented.

This review includes studies investigating only three aspects of bone augmentation surgery of the many various techniques in practice and therefore presents a rather limited view of the clinical area. One study investigated only grafting, and another different types of membrane over xenograft, and the other two studies investigated guided bone regeneration. The bone in the onlay graft study was harvested from the mandibular symphysis. It would be of interest for future studies to further investigate this popular technique and also other intraoral harvest sites and iliac crest grafting from the hip. The comparison of a resorbable and non-resorbable membrane with a xenograft reported morbidity but it would be of interest to know about implant outcomes.

The purpose of bone augmentation is to enable implant treatment to go ahead, hence our interest in prosthesis failure and implant failure, and yet only one of the studies investigated any implant outcome. There is a need for studies to have a longer follow up to report on implant outcomes. While we included the morbidity outcome measure of premature implant exposure, the clinical significance of this complication is uncertain. It may be that the implant is more at risk of failure if it is not protected by overlying mucosa. Wound dehiscence is regarded as a negative outcome as one may anticipate contamination with oral microorganisms.
and an increased risk of infection of the underlying graft material, and similarly exposure of a barrier membrane an increased risk of infection of the membrane, although there is little evidence to support this view. Wound dehiscence has been reported to have a deleterious effect on implant survival (Tolman 1995).

There are a multitude of alloplastic, allograft and xenograft graft materials available. It is very difficult for clinicians to make a decision about which material to use without studies comparing their effectiveness. Unfortunately we found no studies comparing materials for bone augmentation. We do know of two ongoing studies. One study is comparing beta-tricalcium phosphate (Ceresorb, Curasan AG., Germany) with autogenous bone harvested from the iliac crest for bilateral sinus augmentation in a split mouth design (Szabo G). We also know of another ongoing study in Sweden that is comparing one-stage and two-stage sinus inlay bone grafting techniques (Johansson B).

A U T H O R S’ C O N C L U S I O N S

Implications for practice

This review included randomised controlled clinical trials (RCTs) evaluating bone augmentation techniques of onlay grafting with and without a non-resorbable expanded polytetrafluoroethylene (ePTFE) barrier, a xenograft with a resorbable collagen membrane and with a non-resorbable ePTFE barrier, and guided bone regeneration. Based on the available results of RCTs, there is no evidence supporting superior success with one or other of the alternative techniques for either of these three aspects of bone augmentation technique. There was weak evidence that a non-resorbable membrane was better than no membrane for permitting bone growth about dental implants, and that a resorbable membrane over a bone graft may allow healing with fewer infections than a non-resorbable membrane. These conclusions are based on only one RCT for onlay grafting technique, one RCT for the xenograft technique, and two RCTs for guided bone regeneration, all with implants that were not functionally loaded and very few patients.

Implications for research

In order to understand if there is a bone augmentation technique that is significantly more effective than another for oral implant treatment, more well designed long term trials are needed. Such trials should be reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (Moher 2001) (http://www.consort-statement.org/). It would be of interest for future studies to investigate alternative surgical techniques such as onlay grafting with different sites of bone harvest, onlay grafting versus alveolar distraction, and alternative alloplastic, allograft and xenograft graft materials as well as the effectiveness of bone promoting molecules.

P O T E N T I A L C O N F L I C T O F I N T E R E S T

None known.

A C K N O W L E D G E M E N T S

We wish to thank Sylvia Bickley (Cochrane Oral Health Group) for her assistance with literature searching, Emma Tavender and Luisa Fernandez (Cochrane Oral Health Group) for their help with the preparation of this review, Lillian Carpio and Bjorn Johansson for providing us with information on their trials. We would also like to thank the following referees: Jayne Harrison, Jan Hirsch and Ian Needleman.

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Internal sources of support

- University Dental Hospital of Manchester UK
- The Sahlgrenska Academy at Goteborg University SWEDEN
- University of Oslo NORWAY
References to studies included in this review

Antoun 2001 (published data only)

Carpio 2000 (published data only)

Dahlin 1991 (published data only)

Friedmann 2002 (published data only)

References to studies excluded from this review

Gher 1994

Majzoub 1999

Schlegel 1998

Tawil 2001

Wannfors 2000

Zitzmann 1997

References to ongoing studies

Johansson B
A prospective randomised study of 1- and 2-stage sinus inlay bone grafts... Ongoing study Starting date of trial not provided. Contact author for more information.

Szabo G
Histological and clinical evaluation of the bone substitute Ceresorb and autogenous bone for maxillary augmentation by sinus lift: an international multicentre randomised controlled trial.. Ongoing study 2001..

Additional references

Brånemark 1977

Chin 1999

Coulthard 2002

Esposito 2001

Esposito 2003

Higuchi 1992

Kahnberg 1989

Keller 1992
Moher 2001

Obwegeser 1969

Palmer 2000

Tatum 1986

Tolman 1995

Tong 1998

Valentin-Opran 2002

Wenz 2001

*Indicates the major publication for the study

**TABLES**

Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Antoun 2001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>6-month follow-up randomised, parallel group study. There were no withdrawals.</td>
</tr>
<tr>
<td>Participants</td>
<td>Patients requiring maxillary or mandibular ridge augmentation prior to implant placement 6 months later. The edentulous span had to be large enough for placement of at least one implant but not exceeding a 4 tooth span. Adults treated at School of Dentistry, Paris, France. All patients had no known contraindications to intraoral surgery. 12 patients enrolled (7 in the bone graft group and 5 in the bone graft with barrier membrane group).</td>
</tr>
<tr>
<td>Interventions</td>
<td>Onlay bone graft versus onlay bone graft with non-resorbable expanded polytetrafluoroethylene (ePTFE) barrier (WL Gore and Associates, Inc., Flagstone, USA). Membrane stabilised with minititanium screws. Wound closure with Gore-Tex sutures in membrane group or vicryl sutures in no membrane group.</td>
</tr>
</tbody>
</table>
Characteristics of included studies (Continued)

onlay bone graft was harvested from the symphyseal region of the mandible and re-contoured to fit the defect and immobilised with titanium screws. Cancellous bone was harvested from the donor site to fill discrepancies.

| Outcomes | Morbidity measures as infection, bone graft exposure, barrier exposure at 2 weeks, 1, 2, 3, 4, 5 and 6 months after bone graft surgery. The bone graft size was measured with calliper and sent on computer tomography (CT) scan at graft surgery (baseline) and at 6 months. At re-entry surgery at 6 months the following two bone quality evaluations were made: clinical evaluation of bone density by probing on a 1-5 scale; histological evaluation of a trephined bone biopsy. Implants (Brånemark, Nobel Biocare, Goteborg, Sweden) were placed at this re-entry surgery but no implant related outcomes were reported. |

Notes

Allocation concealment B

Study | Carpio 2000

| Methods | 6-month follow-up randomised, parallel group study. There were no withdrawals. |
| Participants | Patients requiring bone regeneration procedures at implant placement. Adults treated at the University of Buffalo, New York, USA. Patients were excluded if they were heavy smokers, had required lateral ridge or sinus augmentation prior to implant placement, or suffered from diabetes, hyperparathyroidism, osteoporosis, severe liver or kidney condition, active sinusitis, cancer or using immunosuppressive or corticosteroids, were or could have been pregnant, or had any addiction to drugs or alcohol. 48 patients enrolled (23 in the collagen group and 25 in the ePTFE group). |
| Interventions | Resorbable porcine-derived collagen barrier membrane (BioGide, OsteoHealth, Inc., Shirley, USA) versus non-resorbable ePTFE barrier (Gore-Tex, WL Gore and Associates, Inc., Flagstone, USA). Both groups had a 50%-50% mixture of bovine anorganic bone (Bio-Oss, OsteoHealth, Inc.) and autogenous bone derived from the osteotomy site placed beneath the barrier. All implants were machined surface, screw-type, titanium (Implant Innovations Inc., West Palm Beach, Florida, USA). The barrier was stabilised with either two polylactic acid bioabsorbable pins (Osseofix, Implant Innovations Inc., or Resorpin, OsteoHealth Inc.), the implant cover screw or the mucogingival flap. |
| Outcomes | Implant failure by mobility testing at 6 months. Morbidity measures as implant exposure, wound dehiscence, and barrier exposure. These were undertaken at 2, 5, 7, 10, 15, 21, 28 days postoperatively and then monthly up to 6 months. The bone graft size was calculated as the difference in length, width and circumference of the bone defect around the implant measured at implant placement and 6 months later at the implant exposure surgery. |

Notes

Allocation concealment B

Study | Dahlin 1991

| Methods | 6-month follow-up randomised, split mouth study. There were no withdrawals. |
| Participants | Patients requiring bone regeneration procedures at implant placement at two contralateral sites. Adults treated at the University of Goteborg, Sweden. Patients were included if they were edentulous and had a vertical height of alveolar bone of not less than 13 mm, with horizontal resorption and buccal concavities (causing potential risk for fenestration at implant placement) on computer tomography (CT) scan. 7 patients enrolled. |
| Interventions | Non-resorbable ePTFE barrier (Gore-Tex, WL Gore and Associates, Inc., Flagstone, USA) versus no barrier. A slight space was maintained over the exposed titanium surface by manual convex shaping of the membrane but no bone or other space maintainer was used. All implants were titanium self tapping (Brånemark, Nobel Biocare, Goteborg, Sweden). The barrier was allowed to extend 3-4 mm around the defect and stabilised by tucking one edge under the periosteum. |
| Outcomes | Implant failure at 6 months. Morbidity measures as implant exposure, barrier exposure and inflammation during the 6-month period. The bone graft size was calculated as the difference in surface area on digitised... |
Characteristics of included studies (Continued)

Photographic images, measured using computer image analysis software, taken at implant placement and 6 months later at the implant exposure surgery.

Notes
Allocation concealment B

Study Friedmann 2002
Methods 7-month follow-up randomised, parallel group study. There were no withdrawals.
Participants Patients requiring lateral alveolus bone augmentation either in the maxilla or mandible prior to implant placement 7 months later. Adults treated at the School of Dentistry, Berlin, Germany. 28 patients enrolled (14 in the deproteinized bovine bone mineral and collagen membrane group and 14 in the deproteinised bovine bone mineral and ePTFE membrane group).
Interventions Deproteinized bovine bone mineral and collagen membrane (Ossix) versus deproteinized bovine bone mineral and ePTFE membrane (Gore-Tex).
Outcomes Morbidity measured as wound dehiscence, wound infection and graft failure over 7 months. Wound infection was defined as presence of pus.

Notes
Allocation concealment A

Characteristics of excluded studies

Gher 1994 Problems with design and analysis. The unit of randomisation was both the patient and the implant and it was not possible to use the data without further information from authors. The authors did not reply to our letter.
Majzoub 1999 Unable to use data as presented on a site not patient basis. Conflicting reporting of infection and dehiscence data.
Schlegel 1998 Inappropriate study design, neither parallel group nor split mouth.
Tawil 2001 Inappropriate study design, neither parallel group nor split mouth.
Wannfors 2000 Unable to use data as not presented at level of patient. Sinus inlay autogenous bone graft: 1-stage versus 2-stage.
Zitzmann 1997 Unclear study design.

Characteristics of ongoing studies

Study Johansson B
Trial name or title A prospective randomised study of 1- and 2-stage sinus inlay bone grafts.
Participants
Interventions
Outcomes
Starting date
Contact information Dr Bjorn Johansson, Department of Oral and Maxillofacial Surgery, Soder Hospital, S-183 85 Stockholm, Sweden.
Notes This is a continuation of the excluded study by Wannfors 2000.

Study Szabo G
Trial name or title Histological and clinical evaluation of the bone substitute Ceresorb and autogenous bone for maxillary augmentation by sinus lift: an international multicentre randomised controlled trial.
Characteristics of ongoing studies (Continued)

Participants
Patients requiring bilateral maxillary augmentation by iliac crest grafting prior to implant placement.

Interventions
Ceresorb versus autogenous iliac crest bone for bilateral sinus lift in split mouth designed study.

Outcomes
Implant failure at 1, 2 and 3 years of function.

Starting date

Contact information
Prof. G Szabo, Semmelweis Orvostudományi Egyetem Szájsebészeti és Fogászati Klinika, Budapest VIII, Maria utca 52, Hungary.

Notes

ADDITIONAL TABLES

Table 01. Quality assessment

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<thead>
<tr>
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<th>outcome assessor blind</th>
<th>withdrawals</th>
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<td>none</td>
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</tr>
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<td>no</td>
<td>none</td>
<td>c</td>
</tr>
<tr>
<td>Dahlin 1991</td>
<td>unclear</td>
<td>no</td>
<td>none</td>
<td>c</td>
</tr>
<tr>
<td>Friedmann 2002</td>
<td>adequate</td>
<td>no</td>
<td>none</td>
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GRAPHS

Comparison 01. Onlay graft: with versus without barriers

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
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<tbody>
<tr>
<td>01 Morbidity: infection</td>
<td></td>
<td></td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>Totals not selected</td>
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<tr>
<td>02 Morbidity: dehiscence over 6 months</td>
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<td>12</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>4.00 [0.20, 82.01]</td>
</tr>
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Comparison 02. Implants with bone defects at placement: resorbable versus non-resorbable barriers

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
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</thead>
<tbody>
<tr>
<td>01 Failure</td>
<td>1</td>
<td>48</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>1.36 [0.41, 4.45]</td>
</tr>
<tr>
<td>02 Morbidity: dehiscence over 6 months</td>
<td>1</td>
<td>48</td>
<td>Relative Risk (Fixed) 95% CI</td>
<td>0.93 [0.37, 2.37]</td>
</tr>
<tr>
<td>03 Augmentation size</td>
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<td></td>
<td>Weighted Mean Difference (Fixed) 95% CI</td>
<td>Totals not selected</td>
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Comparison 03. Xenografts with resorbable or non-resorbable

<table>
<thead>
<tr>
<th>Outcome title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Graft failure</td>
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<td></td>
<td>Relative Risk (Random) 95% CI</td>
<td>Totals not selected</td>
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<tr>
<td>02 Morbidity: infection</td>
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<td>Relative Risk (Random) 95% CI</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>03 Morbidity: dehiscence over 7 months</td>
<td>1</td>
<td>28</td>
<td>Relative Risk (Random) 95% CI</td>
<td>0.90 [0.54, 1.50]</td>
</tr>
</tbody>
</table>
### Fig. 1. Comparison 01. Onlay graft: with versus without barriers

#### 01.01 Morbidity: infection

Review:  Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment  
Comparison: 01 Onlay graft: with versus without barriers  
Outcome: 01 Morbidity: infection

<table>
<thead>
<tr>
<th>Study</th>
<th>graft with membrane</th>
<th>graft alone</th>
<th>Relative Risk (Fixed)</th>
<th>Weight</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
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<td>Antoun 2001</td>
<td>0/5</td>
<td>0/7</td>
<td>Not estimable</td>
<td></td>
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</tr>
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</table>

Total (95% CI): 5 7  
Total events: 1 (graft with membrane), 0 (graft alone)  
Test for heterogeneity: not applicable  
Test for overall effect $z=0.90$  $p=0.4$

### Fig. 2. Comparison 01. Onlay graft: with versus without barriers

#### 01.02 Morbidity: dehiscence over 6 months

Review:  Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment  
Comparison: 01 Onlay graft: with versus without barriers  
Outcome: 02 Morbidity: dehiscence over 6 months

<table>
<thead>
<tr>
<th>Study</th>
<th>graft with membrane</th>
<th>graft alone</th>
<th>Relative Risk (Fixed)</th>
<th>Weight</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antoun 2001</td>
<td>1/5</td>
<td>0/7</td>
<td></td>
<td>100.0</td>
<td>4.00 [0.20, 82.01]</td>
</tr>
</tbody>
</table>

Total (95% CI): 5 7  
Total events: 1 (graft with membrane), 0 (graft alone)  
Test for heterogeneity: not applicable  
Test for overall effect $z=0.90$  $p=0.4$
### Fig. 3. Comparison 02. Implants with bone defects at placement: resorbable versus non-resorbable barriers

#### 02.01 Failure

**Review**: Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment  
**Comparison**: 02 Implants with bone defects at placement: resorbable versus non-resorbable barriers  
**Outcome**: 01 Failure

<table>
<thead>
<tr>
<th>Study</th>
<th>resorbable</th>
<th>non-resorbable</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpio 2000</td>
<td>5/23</td>
<td>4/25</td>
<td>1.36 [0.41, 4.45]</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>23</td>
<td>25</td>
<td>1.36 [0.41, 4.45]</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 5 (resorbable), 4 (non-resorbable)  
Test for heterogeneity: not applicable  
Test for overall effect $z=0.51$ $p=0.6$

### Fig. 4. Comparison 02. Implants with bone defects at placement: resorbable versus non-resorbable barriers

#### 02.02 Morbidity: dehiscence over 6 months

**Review**: Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment  
**Comparison**: 02 Implants with bone defects at placement: resorbable versus non-resorbable barriers  
**Outcome**: 02 Morbidity: dehiscence over 6 months

<table>
<thead>
<tr>
<th>Study</th>
<th>resorbable</th>
<th>non-resorbable</th>
<th>Relative Risk (Fixed)</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpio 2000</td>
<td>6/23</td>
<td>7/25</td>
<td>0.93 [0.37, 2.37]</td>
<td>100.0</td>
<td></td>
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<tr>
<td>Total (95% CI)</td>
<td>23</td>
<td>25</td>
<td>0.93 [0.37, 2.37]</td>
<td>100.0</td>
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</tbody>
</table>

Total events: 6 (resorbable), 7 (non-resorbable)  
Test for heterogeneity: not applicable  
Test for overall effect $z=0.15$ $p=0.9$
Fig. 5. Comparison 02. Implants with bone defects at placement: resorbable versus non-resorbable barriers

02.03 Augmentation size

Review: Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment
Comparison: 02 Implants with bone defects at placement: resorbable versus non-resorbable barriers
Outcome: 03 Augmentation size

<table>
<thead>
<tr>
<th>Study</th>
<th>resorbable</th>
<th>non-resorbable</th>
<th>Weighted Mean Difference (Fixed)</th>
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<tr>
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<td>N</td>
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<tr>
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<td>01 reduction in length of defect</td>
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<tr>
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<td>23</td>
<td>2.65 (2.93)</td>
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<td></td>
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<tr>
<td>02 reduction in width of defect</td>
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<td></td>
<td></td>
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<td>Carpio 2000</td>
<td>23</td>
<td>1.95 (2.88)</td>
<td>25</td>
<td>2.65 (2.80)</td>
</tr>
</tbody>
</table>

Fig. 6. Comparison 03. Xenografts with resorbable or non-resorbable

03.01 Graft failure

Review: Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment
Comparison: 03 Xenografts with resorbable or non-resorbable
Outcome: 01 Graft failure

<table>
<thead>
<tr>
<th>Study</th>
<th>resorbable</th>
<th>non-resorbable</th>
<th>Relative Risk (Random)</th>
<th>Relative Risk (Random)</th>
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<tr>
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<tr>
<td>Friedmann 2002</td>
<td>0/14</td>
<td>1/14</td>
<td>0.33 [ 0.01, 7.55]</td>
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</table>

Fig. 7. Comparison 03. Xenografts with resorbable or non-resorbable

03.02 Morbidity: infection

Review: Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment
Comparison: 03 Xenografts with resorbable or non-resorbable
Outcome: 02 Morbidity: infection

<table>
<thead>
<tr>
<th>Study</th>
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<th>Relative Risk (Random)</th>
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<td>0/14</td>
<td>10/14</td>
<td>0.05 [ 0.00, 0.74]</td>
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</table>
**Fig. 8. Comparison 03. Xenografts with resorbable or non-resorbable**

**03.03 Morbidity: dehiscence over 7 months**

Review: Interventions for replacing missing teeth: bone augmentation techniques for dental implant treatment

Comparison: 03 Xenografts with resorbable or non-resorbable

Outcome: 03 Morbidity: dehiscence over 7 months

<table>
<thead>
<tr>
<th>Study</th>
<th>resorbable n/N</th>
<th>non-resorbable n/N</th>
<th>Relative Risk (Random) 95% CI (%)</th>
<th>Weight (%)</th>
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<td>Total (95% CI)</td>
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<td>14</td>
<td>100.0</td>
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<td>0.90 [0.54, 1.50]</td>
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Total events: 9 (resorbable), 10 (non-resorbable)

Test for heterogeneity: not applicable

Test for overall effect z=0.40  p=0.7