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## Timing of implant placement after tooth extraction: immediate, immediate-delayed or delayed implants? A Cochrane systematic review



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This review is based on a Cochrane systematic review entitled 'Interventions for replacing missing teeth: dental implants in fresh extraction sockets (immediate, immediate-delayed and delayed implants)' published in The Cochrane Library (see <http://www.cochrane.org/> for information). Cochrane systematic reviews are regularly updated to include new research, and in response to comments and criticisms from readers. If you wish to comment on this review, please send your comments to the Cochrane website or to Marco Esposito. The Cochrane Library should be consulted for the most recent version of the review. The results of a Cochrane review can be interpreted differently, depending on people's perspectives and circumstances. Please consider the conclusions presented carefully. They are the opinions of the review authors, and are not necessarily shared by the Cochrane Collaboration.

**Purpose:** To evaluate success, complications, aesthetics and patient satisfaction among immediate, immediate-delayed and delayed implants in post-extractive sockets and whether and when augmentation procedures are necessary and which is the most effective augmentation technique.

**Materials and methods:** The Cochrane Oral Health Group's Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE were searched up to the 2nd of June 2010 for randomised controlled clinical trials (RCTs) with a follow-up of at least 1 year in function comparing immediate, immediate-delayed and delayed implants, or comparing various bone augmentation procedures around the inserted implants. Outcome measures were prosthesis and implant failures, complications, patient satisfaction and preference including aesthetics, aesthetics evaluated by a dentist, peri-implant marginal bone level changes, etc. Screening of eligible studies, assessment of the methodological quality of the trials and data extraction were conducted in duplicate and independently by two review authors. The statistical unit of the analysis was the patient. Results were expressed as fixed effects models using mean differences for continuous outcomes and risk ratios (RR) for dichotomous outcomes with 95% confidence intervals (CIs).

**Results:** Fourteen eligible RCTs were identified but only seven trials could be included. Four RCTs evaluated implant placement timing. Two RCTs compared immediate versus delayed implants in 126 patients and found no statistically significant differences. One RCT compared immediate-delayed

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versus delayed implants in 46 patients. After 2 years, patients in the immediate-delayed group perceived the time to functional loading significantly shorter, were more satisfied and an independent blinded assessor judged the level of the peri-implant marginal mucosa in relation to that of the adjacent teeth as more appropriate (RR = 1.68; 95% CI 1.04 to 2.72). These differences disappeared 5 years after loading, and significantly more complications occurred in the immediate-delayed group (RR = 4.20; 95% CI 1.01 to 17.43). One RCT compared immediate with immediately delayed implants in 16 patients for 2 years and found no differences. Three RCTs evaluated different techniques of bone grafting for implants immediately placed in extraction sockets. No statistically significant differences were observed when evaluating whether autogenous bone is needed in post-extractive sites (one trial with 26 patients) or which was the most effective augmentation technique (two trials with 56 patients).

**Conclusions:** There is insufficient evidence to determine the possible advantages or disadvantages of immediate, immediate-delayed or delayed implants, therefore these preliminary conclusions are based on few underpowered trials often judged to be at high risk of bias. There is a suggestion that immediate and immediate-delayed implants may be at a higher risk of implant failure and complications than delayed implants, on the other hand the aesthetic outcome might be better when placing implants just after tooth extraction. There is not enough reliable evidence supporting or refuting the need for augmentation procedures at immediate implants placed in fresh extraction sockets or whether any of the augmentation techniques is superior to the others.

## ■ Introduction

In many clinical situations, hopeless teeth or roots may be present in the patient's mouth. Traditionally, before placing dental implants, compromised teeth were removed and the extraction sockets were left to heal for between several months to 1 year. However, the great majority of patients are interested in shortening the treatment time between tooth extraction and implant placement, or even better, in having the implants inserted during the same session as the teeth are extracted (immediate implants). This would result in patients having fewer surgical sessions and shorter treatment periods. Another potential advantage with immediate implants is that the amount of bone loss that physiologically occurs during the remodelling phase of the extraction socket might be reduced if the implant is placed early during the healing process. Finally, it may not even be necessary to raise a flap in several situations when placing dental implants. On the other hand, there are also some potential disadvantages with immediate implants, such as i) an enhanced risk of infections and the associated failures if the socket becomes infected<sup>1,2</sup>; ii) the mismatch between the implant

surface and the socket wall, therefore gaps may be present after implantation as dental roots do not have a regular circular diameter shape; and iii) the necessity of raising a flap for covering the implants, if a two-stage implantation procedure is preferred<sup>3</sup>. It is also possible that one or more bony socket walls are partly resorbed either due to the disease processes or damaged as a result of the tooth extraction procedure.

These potential problems have been tackled in different ways. Manufacturers have designed specific implant systems to be used as immediate implants, with various tapered shapes and different diameters, in order to be used in sockets of varying dimensions<sup>4</sup>. Some clinicians wait for some time, generally 2 to 8 weeks, before placing the implants in order to achieve some soft tissue healing and decrease the risk of infections (immediate-delayed implants).

Depending on the degree and shape of damage to the extraction socket as well as the diameter of the extracted root, a portion of the implants could remain exposed and/or a residual gap between the implant and the bony wall may remain. As alveolar bone will remodel after tooth extraction, the degree of bone resorption is difficult to predict and could

leave some portion of the implants exposed, producing a poor aesthetic outcome. To prevent this problem from occurring, it has been suggested that the socket is augmented just after implant placement using various bone augmentation techniques such as autogenous bone grafts<sup>5,6</sup>, bone substitutes<sup>7,8</sup>, guided bone regeneration (GBR) with resorbable<sup>9-11</sup> or non-resorbable barriers, and various bone promoting molecules such as enamel matrix derivative<sup>12</sup>, platelet-rich plasma (PRP), growth factors and bone morphogenetic proteins (BMPs) to accelerate and increase bone formation. However, it is unclear if bone augmentation procedures are of any benefit for immediate implants, as immediate and immediate-delayed implants can be successful and heal properly without any bone graft procedures<sup>13</sup>.

A few reviews<sup>14-17</sup> evaluating the efficacy of immediate implants have been published over the years, but so far evidence has been inconclusive. It would be of great benefit to know if the number of surgical sessions, treatment time and patient discomfort may be reduced using immediate implants without compromising the success of the implant therapy, as well as if and when bone augmentation would be beneficial. This could be carried out by conducting a rigorous systematic review of randomised controlled trials (RCTs).

## ■ Materials and methods

### ■ Criteria for considering studies for the present review

All RCTs with a follow-up of at least 1 year after loading of osseointegrated dental implants comparing:

- immediate versus delayed implants
- immediate-delayed versus delayed implants
- immediate versus immediate-delayed implants
- augmentation versus no augmentation at immediate or immediate-delayed implants
- various augmentation procedures at immediate or immediate-delayed implants.

The following definitions were used:

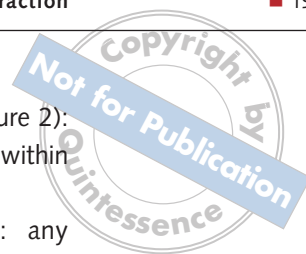
- immediate implants (test procedure 1): any implant placed in a fresh extraction socket just after tooth extraction

- immediate-delayed implants (test procedure 2): any implant placed in an extraction socket within 8 weeks after tooth extraction
- delayed implants (control procedure): any implants placed at least 2 months after tooth extraction.

Patients treated with augmentation procedures, including grafting with autogenous bone or bone substitutes, GBR, and other active agents such as BMPs or PRP at placement of immediate or immediate-delayed implants were included in the present review. Time points 1, 3 and 5 years after loading were considered. Outcome measures were as follows.

- Prosthesis failure: planned prosthesis, which could not be placed because of implant failure(s) and loss of the prosthesis secondary to implant failure(s).
- Implant failure: implant mobility and removal of stable implants dictated by progressive marginal bone loss or infection (biological failures). Biological failures were grouped as early (failure to establish osseointegration) and late failures (failure to maintain the established osseointegration). Implant mobility could be assessed manually or with instruments such as Periotest (Siemens, Bensheim, Germany) or resonance frequency (Osstell, Integration Diagnostics, Göteborg, Sweden).
- Major complications at the implant or donor site (e.g. infection, nerve injury, haemorrhage).
- Patient preference including aesthetics (only in split-mouth trials).
- Aesthetics evaluated by clinician.
- Peri-implant marginal bone level changes over time on periapical radiographs taken with the paralleling technique.
- Vertical and/or horizontal bone gain expressed in mm or percentage (only for the augmentation procedures).
- Duration of the treatment time starting from tooth extraction to functional loading of the implants.
- Difference in treatment costs.

Trials evaluating only histological outcomes were not considered in the present review.



## ■ Search strategy for identification of studies

For the identification of studies included or considered for the present review, detailed search strategies for each database searched were developed. For more details see the original Cochrane review<sup>18</sup>. The following databases were searched:

- The Cochrane Oral Health Group's Trials Register (to 2 June 2010)
- The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2010, Issue 5)
- MEDLINE (1950 to 2 June 2010)
- EMBASE (1980 to 2 June 2010).

The most recent electronic search was undertaken on the 2nd of June 2010. The following dental journals were hand searched up to December 2009: *British Journal of Oral and Maxillofacial Surgery*, *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *European Journal of Oral Implantology*, *Implant Dentistry*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Oral and Maxillofacial Surgery*, *International Journal of Periodontics and Restorative Dentistry*, *International Journal of Prosthodontics*, *Journal of Clinical Periodontology*, *Journal of Dental Research*, *Journal of Oral Implantology*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Periodontology*, and *Journal of Prosthetic Dentistry*. There were no language restrictions. All of the authors of the identified RCTs were contacted, the bibliographies of all identified RCTs and relevant review articles were checked, and personal contacts were used in an attempt to identify unpublished or ongoing RCTs. In the first version of this review, more than 55 oral implant manufacturers and an Internet discussion group (implantology@yahoogroups.com) were to be contacted. However, this was discontinued due to poor participation.

## ■ Study selection and data extraction

The titles and abstracts (when available) of all reports identified through the electronic searches were scanned independently by two review authors. For studies appearing to meet the inclusion criteria, or

for which there were insufficient data in the title and abstract to make a clear decision, the full report was obtained. The full reports obtained from all of the electronic and other methods of searching were assessed independently by two review authors to establish whether or not the studies met the inclusion criteria. Disagreements were resolved by discussion. Where resolution was not possible, a third review author 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.

Data were extracted by two review authors 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 review author was consulted where necessary. All authors were contacted for clarification or missing information. 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; details on the type of intervention; and details of the outcomes reported, including method of assessment and time intervals.

## ■ Quality assessment

This was conducted using the recommended approach for assessing risk of bias in studies included in Cochrane reviews<sup>19</sup>. It is a two-part tool, addressing the six specific domains (namely sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and 'other issues'). Each domain includes one specific entry in a 'Risk of bias' table. Within each entry, the first part of the tool involves describing what was reported to have happened in the study. The second part of the tool involves assigning a judgment relating to the risk of bias for that entry. This is achieved by answering a pre-specified question about the adequacy of the study in relation to the entry, such that a judgment of 'Yes' indicates low risk of bias, 'No' indicates high risk of bias, and 'Unclear' indicates unclear or unknown risk of bias.

The risk of bias assessment of the included trials was undertaken independently and in duplicate by two review authors as part of the data extraction process. In cases where the paper to be assessed had one or more review authors in the author list, it was independently evaluated only by those review authors not involved in the trials. After taking into account the additional information provided by the authors of the trials, studies were grouped into the categories discussed below. The present authors assumed that the risk of bias was the same for all outcomes and each study was assessed as follows:

- low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met
- unclear risk of bias (plausible bias that raises some doubt about the results) if one or more key domains were at unclear risk of bias
- high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met<sup>19</sup>.

## ■ Data synthesis

For dichotomous outcomes, the estimate of effect of an intervention was expressed as risk ratios (RR) together with 95% confidence intervals (CIs). For continuous outcomes, mean differences and standard deviations were used to summarise the data for each group using mean differences and 95% CIs. The statistical unit was the patient and not the implant(s). Meta-analyses were performed only if there were studies with similar comparisons reporting the same outcome measures. RRs and mean differences were combined using fixed-effect models if there were up to three trials, or random-effect models provided there were more than three studies in the meta-analysis. Data from split-mouth studies were to be combined with data from parallel group trials with the method outlined by Elbourne<sup>20</sup>, using the generic inverse variance method in RevMan (Cochrane Information Management System). Numbers needed to treat (NNT) were calculated for patients affected by implant failures.

The Cochrane Handbook<sup>19</sup> recommendations were followed for studies with zero-cell counts. The fixed value of 0.5 was added to all cells with zero-cell counts and RRs were calculated with the RevMan

software. If there were no events in both arms, no calculations were undertaken because in this situation the study does not provide any indication of the direction or magnitude of the relative treatment effect. For the visual analogue scores, where the median and interquartile range were presented, and the data were not skewed, the standard deviation was estimated as the width of the interquartile range/1.35.

The significance of any discrepancies in the estimates of the treatment effects from the different trials was assessed by means of Cochran's test for heterogeneity and the  $I^2$  statistic, which describes the percentage total variation across studies that is due to heterogeneity rather than chance.

## ■ Description of studies

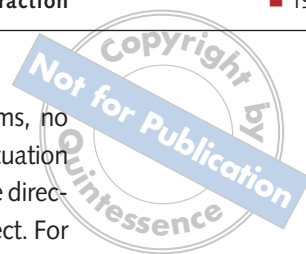
### ■ Characteristics of the trial setting and investigators

Of the 14 potentially eligible trials<sup>21-33</sup>, seven trials were included<sup>25,27,29-31,33</sup> and seven trials were excluded for the following reasons: problems with study design and/or the data,<sup>21,24</sup> reported only histological outcomes without presenting any implant-related outcomes,<sup>28</sup> described as RCT but in fact patients were not randomised<sup>23</sup>, an unknown quota of patients had immediate-delayed implant sites augmented<sup>22,32</sup> and follow-up was limited to abutment connection/implant loading<sup>26</sup>.

All trials had a parallel group study design. Data of two distinct RCTs were presented together as if it was a single RCT in one publication. However, the authors clarified this, and the present authors evaluated the trials as two separate RCTs<sup>27</sup>.

Three trials were conducted in Australia,<sup>27,30</sup> one in Denmark<sup>25</sup>, one in the Netherlands<sup>29</sup>, one in Italy<sup>31</sup> and one in the United States<sup>33</sup>. Three trials were conducted in private practices<sup>27,30</sup> and four in university dental clinics<sup>25,29,31,33</sup>.

For four trials it was declared that some sort of support was received from the industry directly involved in the product being tested, in the form of free material<sup>25,27,29</sup>. The authors of three trials declared that no support was received from commercial parties whose products were being tested in the trial<sup>30,31,33</sup>.



## ■ Characteristics of the interventions

### Immediate versus delayed implants (two trials)

One trial<sup>29</sup> compared immediate (same day) versus delayed (3 months on average) implants after extraction of periapically infected single teeth. Twenty-five patients were included in each group. Implants were placed 2 mm below the cervical junction of the adjacent teeth. Autogenous bone grafts from the trigonum retromolar or chin region were covered with a bioresorbable collagen membrane (Bio-Gide®, Geistlich, Wolhusen, Switzerland) in all patients and implants were submerged and left to heal for 6 months. Single crowns were cemented with temporary cement. All implants were Frialit®-2 Synchro (Dentsply Friadent Ceramed, Mannheim, Germany).

One trial<sup>33</sup> compared single immediate (same day) versus delayed (4 months) implants in maxillary anterior sites up to premolars. Seventy-six patients were recruited and randomised. However, it was not specified how many in each group. The implant's axis for immediate implants was directed palatal to the planned incisal edge, and at least 2 mm palatal to the emergence line angle. The implant was placed with the coronal surface of the implant 3 mm apical to the gingival margin of the planned restoration. The length of the implants was 13 mm except when the maxillary sinus limited the implant length to 11.5 mm. When a gap was present between the implant and the labial bone, a graft of human mineralised bone was used to graft the site and preserve the width of the ridge. Immediate implants were immediately provisionalised with acrylic crowns not in occlusion, whereas delayed sites were grafted with human mineralised bone (350 to 500 micron, cortical, freeze-dried, University of Miami Tissue Bank, Miami, FL, USA). After the graft had been compressed, a piece of collagen (Collaplug, Zimmer Dental, Carlsbad, CA, USA) was placed over the graft and under the margins of the labial and palatal gingiva. Chromic sutures (4-0) were placed in a horizontal mattress fashion to gently conform the gingiva to the collagen. After a healing period of 4 months, implants were placed and immediately temporised. Four

months after implant placement, final restorations were made. All implants were a straight wall design, threaded, with a roughened surface and a parallel type abutment implant interface (Certain® implant, Biomet 3i, Palm Beach Gardens, FL, USA).

### Immediate-delayed versus delayed implants (one trial)

One trial<sup>25</sup> compared immediate-delayed (10 days on average) versus delayed implants (3 months on average) after extractions of compromised single teeth. Twenty-three patients were included in each group. Implants were placed with the top of the cover screw even with the bone ridge. Autogenous bone grafting was performed when implant threads were exposed at abutment connection for immediate-delayed implants, and at both implant placement and at abutment connection for delayed implants. Implants were submerged and left to heal for approximately 3 months. Single-tooth metal-ceramic crowns were provided. All implants were Osseotite® (Biomet 3i, Palm Beach Gardens, FL, USA).

### Immediate versus immediate-delayed implants (one trial)

One trial<sup>31</sup> compared immediate implants versus immediate-delayed implants (8 weeks) after flap elevation and extractions of compromised single maxillary teeth in the aesthetic area. Eight patients (9 teeth) were included in each group. Implants were placed with an insertion torque of 35 Ncm, 2 mm apical to the cemento-enamel junction of the adjacent teeth. Implants were immediately restored within 48 hours with provisional acrylic crowns that were not in occlusal contact. All implants were tapered effect (TE) implants of the Straumann Dental Implant System (Institut Straumann, Waldenburg, Switzerland).

### Are augmentation procedures necessary? (one trial)

One trial compared particulate autogenous bone harvested from the implant site by means of a filter attached to a dedicated suction line (Osseous Coagulum Trap, Quality Aspirators, Duncanville,

TX, USA) in 14 patients versus no augmentation procedure in 12 patients, for immediate single implants placed in fresh extraction sockets at maxillary anterior or premolar sites<sup>27</sup>. Wound closure was achieved by use of a connective tissue graft taken from the palate. Implants were submerged and left to heal for 6 months. All implants were turned surface, screw-type, titanium Brånemark implants (Nobel Biocare, Göteborg, Sweden). All patients were rehabilitated with single implant supported crowns.

### Which are the most effective augmentation procedures? (two trials)

One trial compared non-resorbable expanded polytetrafluoroethylene (ePTFE) barriers (Gore-Tex®, WL Gore & Associates, Flagstaff, AZ, USA) alone in 12 patients versus resorbable barriers (Resolut®, Gore-Tex, WL Gore & Associates) alone in 11 patients, versus resorbable barrier (Resolut) supported by particulate autogenous bone harvested from the implant site by means of a filter attached to a dedicated suction line (Osseus Coagulum Trap) in 13 patients, all for immediate single implants placed in fresh extraction sockets at maxillary anterior or premolar sites<sup>27</sup>. All barriers were tucked beneath the flaps. Wound closure was achieved by use of a connective tissue graft taken from the palate. All implants were turned surface, screw-type, titanium Brånemark implants (Nobel Biocare). All patients were rehabilitated with single implant supported crowns.

Another trial compared bovine anorganic bone (Bio-Oss®, Geistlich) in 10 patients versus Bio-Oss plus resorbable porcine-derived collagen barrier (Bio-Gide) in 10 patients, both for immediate single implants placed in fresh extraction sockets at maxillary anterior or premolar sites 2 to 3 mm apical to the cemento-enamel junction of the adjacent teeth<sup>30</sup>. Barriers were trimmed as required and fixed to the implants by the healing screw. Implants were not submerged and left to heal for 6 months. All implants were ITI SLA (Institut Straumann). In the original trial, a control group that received no graft or barrier was included, but the present authors could not use the data due to the subversion of the randomisation procedure. All patients were rehabilitated with single implant supported crowns.

### ■ Characteristics of outcome measures

- Prosthesis failures: all trials.
- Implant failures: all trials.
- Major complications at implant/donor site: all trials with one exception<sup>33</sup>.
- Patient satisfaction including aesthetics<sup>25,30</sup>. This was measured by the patient's answers on a 100 mm visual analogue scale (VAS) to the following questions: i) 'How was your experience of the period between tooth extraction and insertion of the implant crown?'; ii) 'Are you in general satisfied with the appearance of the crown?'; iii) 'How was your overall experience of the treatment?' On the VAS, the most negative response corresponded to 0 and the most positive to 100<sup>25</sup>. In the other trial<sup>30</sup>, patients expressed whether or not they were dissatisfied with the aesthetic outcome.
- Patient preference including aesthetics (only in split-mouth trials): no trials.
- Aesthetics assessed by clinician: evaluated in five trials<sup>25,29-31,33</sup>. In one trial<sup>25</sup>, an experienced prosthodontist who had not been involved in the treatment and was blind to the interventions evaluated the clinical photographs of the single crowns, which included one adjacent tooth from each side. Photographs were taken 1 week after seating of the prosthetic restoration and also 16 to 18 months later. The following parameters were evaluated: i) the interproximal papilla dimensions, assessed as 0 = no papilla or negative papilla; 1 = less than half of the height of the proximal area occupied by soft tissue; 2 = at least half of the height of the proximal area occupied by soft tissue. ii) Clinical crown height, assessed as 1 = too long; 2 = too short; 3 = appropriate in relation to the level of the marginal mucosa when compared with that of the adjacent teeth (rather than the incisal/occlusal extension of the crown). The papilla score was dichotomised as good outcome (score 2) or not good outcome. The crown length was also dichotomised as appropriate (score 3) or not. In three trials,<sup>29,31,33</sup> the interproximal gingival papillae were evaluated according to the papilla score<sup>34</sup>: 0 = no papillae; 1 = less than half of the gingival embrasure; 2 = at least half of the height; 3 = complete closure of the proximal space;



4 = overgrowth. The present authors dichotomised this outcome into 0, 1 and 4 as negative outcome, and 2 to 3 as positive outcome, and evaluated the proportion for the negative outcome. The mid-buccal gingival level<sup>29</sup> was assessed by measuring the difference with the buccal gingival outline of the adjacent teeth: 0 = no difference in gingival level; 1 = less than 1 mm difference; 2 = less than 2 mm difference; 3 = less than 3 mm difference; 4 = differences in buccal gingival outline greater than 3 mm. The present authors dichotomised this outcome into 0 to 1 (positive outcome) and 2 to 4 (negative outcome) and evaluated the proportion for the negative outcome. The papilla score could not be evaluated in two trials<sup>31,33</sup> since data were presented in a way that could not be used. In one trial<sup>30</sup>, the operator assessed whether marginal mucosal recession occurred or not. In one trial<sup>31</sup>, the position of mucosal margin was measured by the operator as the distance in mm from the most apical point of the gingival margin to the implant shoulder measured with the aid of a periodontal probe. The measurements were taken to the nearest 0.5 mm at the moment of the delivery of the provisional restoration (baseline) and at the 2-year follow-up visit. In another trial<sup>33</sup>, the position of mucosal margin was measured by using a fixed reference mark on a customised stent, however data were presented in a way that could not be used in the current review.

- Peri-implant marginal bone level changes were measured in five trials<sup>25,29-31,33</sup> but data were presented in a way that could not be used in two trials<sup>30,33</sup>, whereas for another trial<sup>29</sup> the present authors randomly picked up the measurements of mesial sides since measurements at mesial and distal sides were presented separately (baseline implant placement). The preferred baseline was set at implant placement, however, in one trial<sup>25</sup>, the baseline was set at abutment connection.
- Bone gain vertically or horizontally or both expressed in mm or percentage including bone level changes over time (only for the augmentation procedures): vertical bone gain was measured in mm by direct measurements in three studies<sup>27,30</sup>.
- Treatment duration: all trials.
- Difference in treatment costs: possible to extrapolate.

## ■ Characteristics at baseline

### Main inclusion criteria

- Single post-extractive fresh sockets at anterior and premolar sites<sup>25</sup>.
- Single post-extractive fresh sockets at maxillary anterior and premolar sites<sup>27,30,31,33</sup>.
- Single post-extractive fresh sockets at maxillary anterior and premolar sites of periapically infected teeth<sup>29</sup>.

### Main exclusion criteria

- Medically compromised patients (metabolic diseases, immune deficient or under immune-suppressive therapy, irradiated, etc.)<sup>25,29,31,33</sup>.
- Smokers<sup>27,29</sup>, heavy smokers<sup>31</sup>.
- Postmenopausal women with known osteoporosis as determined by their medical internist<sup>33</sup>.
- Acute infection and suppuration at the fresh extraction socket<sup>27,30,31,33</sup>.
- 5 mm or more of buccal bone loss<sup>30</sup>.
- Insufficient bone to achieve primary stability of the implant<sup>25</sup>.
- Insufficient primary implant stability (< 25 Ncm)<sup>29</sup>.
- Loss of alveolar bone at extraction<sup>31</sup>.
- Less than 2 mm of attached or keratinised gingiva<sup>31</sup>.
- No bone present on all surfaces of the experimental tooth site within 3 mm of the gingival margin of the planned restoration<sup>33</sup>.
- Less than 1:2 crown-implant ratio<sup>33</sup>.

### Comparability of control and treatment groups at entry

They were no apparent major baseline differences for all trials, however, implants with a larger diameter were used in the immediate group in one trial<sup>29</sup>, and another trial did not present sufficient information to be able to decide<sup>33</sup>.

### Antibiotic prophylaxis at implant placement

- Amoxicillin tablets 750 mg were given 1 hour before surgery and 750 mg x 3 daily the following 5 days<sup>25</sup>.





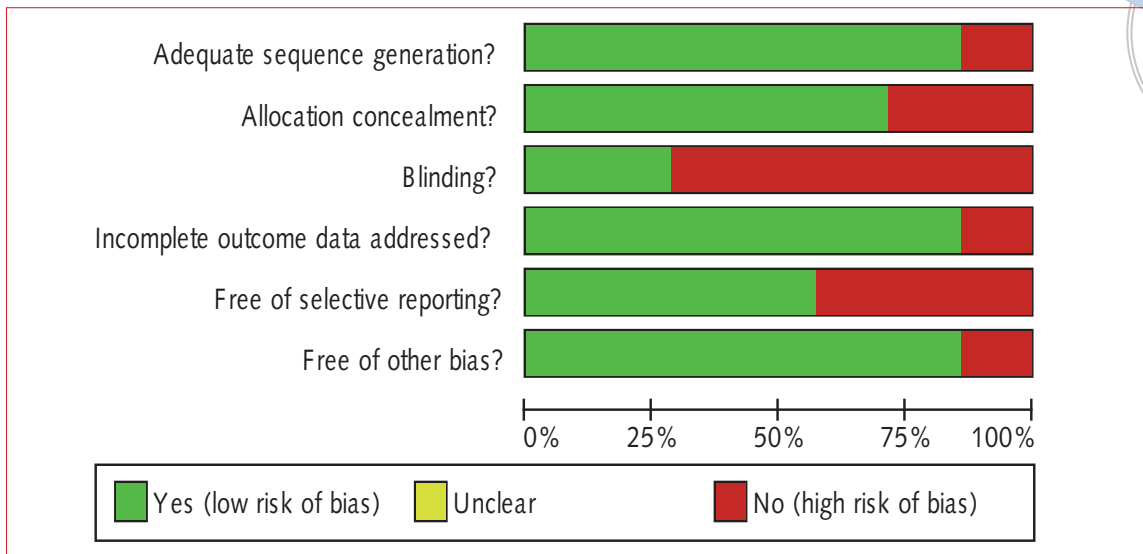


Fig 1 Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

- Clindamycin 600 mg was given 1 hour before surgery<sup>29</sup>.
- Amoxicillin 0.5 g given 3 times a day postoperatively for 7 days<sup>27</sup>.
- Amoxicillin 0.5 g given 3 times a day postoperatively for 5 days<sup>30</sup>.
- Amoxicillin with clavulanate 1 g every 12 h for 5 days<sup>31</sup>.
- Postoperative second generation cephalosporin for 7 days<sup>33</sup>.

### Type and frequency of maintenance

- Patients were referred to their own dentists for maintenance recalls every 6 months<sup>25,31,33</sup>. In one trial<sup>25</sup>, the referring dentists were contacted by letter where they were instructed in the maintenance procedure: oral hygiene instructions, scaling/cleaning with proper instruments and intra-pocket irrigation with chlorhexidine in case of suppuration. They were also invited to refer the patients back to the implant centre in case of complications that they could not handle by themselves.
- Yearly recall<sup>27,30</sup>.
- Not described<sup>29</sup>.

### Duration of the studies (after implant loading)

- One year<sup>29</sup>.
- Two years<sup>27,31,33</sup>.

- Three years<sup>30</sup>.
- Five years<sup>25</sup>.

### Sample size

Only two trials performed a sample size calculation<sup>25,29</sup>.

- The authors reported that the sample size calculations were based on a power calculation, which indicated that 26 patients in each group should be included in order to be able to find a statistically significant difference in bone defect reduction of 1 mm or more between the two groups, with  $\alpha = 0.05$  and power = 95%<sup>25</sup>. However, only 23 patients in each group were included.
- The sample size was calculated to find a difference in Implant Stability Quotient (ISQ) measured with Osstell of 10 or more, assuming a common standard deviation of 15 with a power of 80% and a type 1 error rate of 0.05. Twenty-five patients in each group would be needed to reject the null hypothesis<sup>29</sup>.

### Quality assessment

The final risk of bias assessment, after having incorporated the additional information kindly provided by the authors of the included trials, is summarised in Figures 1 and 2. For each trial, the present authors assessed whether it was at low, unclear or high risk of bias. One trial was judged to be at low<sup>29</sup> and the remaining six trials at high risk of bias.

**Fig 2** Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?
Block 2009	+	-	+	-	-	+
Chen 2005a	+	+	-	+	+	+
Chen 2005b	+	+	-	+	+	+
Chen 2007	-	+	-	+	-	+
Lindeboom 2006	+	+	+	+	+	+
Palattella 2008	+	+	-	+	+	+
Schropp 2003	+	-	-	+	-	-

■ **Results**

In total, 270 patients were enrolled in seven trials.

■ **Immediate versus delayed implant placement (two trials with 126 patients)**

One study<sup>29</sup> of parallel group design compared immediate versus delayed implants in periapical infected sites. Twenty-five patients were enrolled in each group and none dropped out. All patients were subjected to bone grafts at implant placement and regenerative therapy with resorbable membranes. Two early implant failures occurred in the immediate group, however the authors reported that no complication occurred. One year after placement, there were no statistically significant differences for prosthesis and implant failures (Fig 3), aesthetics assessed by a dentist (papilla height and the level of the peri-implant marginal mucosa in relation to that of the adjacent teeth; RR = 5.42, 95% CI 0.27 to 107.20),

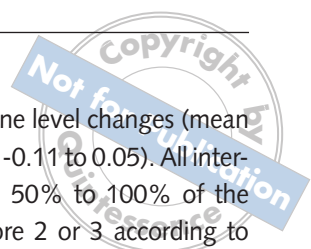
and peri-implant marginal bone level changes (mean difference -0.03 mm; 95% CI -0.11 to 0.05). All interdental papillae covered from 50% to 100% of the interdental space (papilla score 2 or 3 according to Jemt<sup>34</sup>). The trial was judged to be at low risk of bias.

One study<sup>33</sup> of parallel group design compared immediate versus delayed implants. Seventy-six patients were enrolled and 16 dropped out or were excluded, but it was not described from which group. When a gap was present at immediate implants, the site was grafted with human mineralised bone. Immediate implants were immediately provisionalised with non-occluding temporary acrylic crowns, whereas delayed sites were grafted with human mineralised bone and left to heal for 4 months before placing the implants. Two years after loading, four implants failed in the immediate group versus one in the delayed group and this was not statistically significant (Fig 3). The trial was judged to be at high risk of bias.

The meta-analysis of the two trials<sup>29,33</sup> for prosthesis and implant failures (Fig 3) did not show any statistically significant difference, though trends favoured delayed implants.

■ **Immediate-delayed versus delayed implant placement (one trial with 46 patients)**

One study<sup>25</sup> of parallel group design compared immediate-delayed versus delayed implant placement up to 5 years after loading. Twenty-three patients were enrolled in each group. Two patients withdrew, one from each group, because they did not pay for the implant crown at the 1-year follow-up. At the 5-year follow-up more dropouts/withdrawals occurred: two from the immediate-delayed group (one excluded because the implant was used to support a removable denture and one because the crown was remade) and five from the delayed group (one excluded since treatment was with a bridge and not a single crown, one because the crown was remade, and three did not want to attend the 5-year examination, though their implant-supported crowns were still in place without causing any inconvenience). At implant placement, 6 patients out of 10 of the delayed group, having bone dehiscence, had bone grafts versus none of



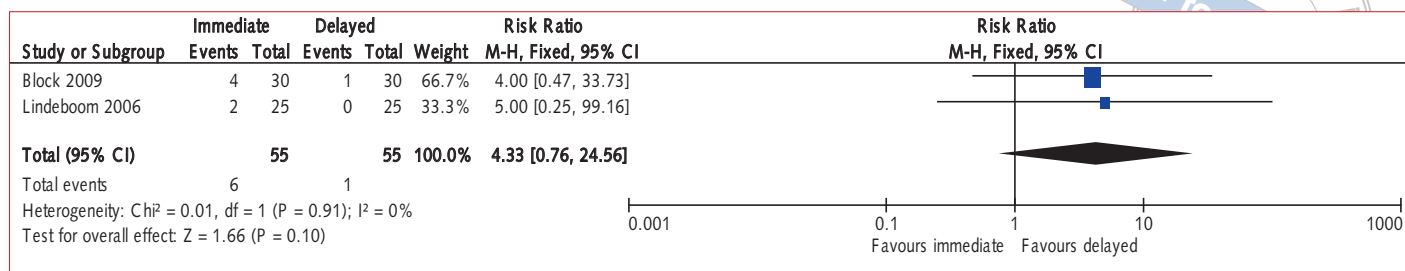


Fig 3 Meta-analysis comparing prosthesis/implant failures for immediate versus delayed implants.

the immediate-delayed group. At abutment connection 6 out of 15 patients of the immediate-delayed group with bone dehiscence and 4 out of 11 of the delayed group had bone grafts. The consequence of these bone grafting procedures on the final results are difficult to evaluate since only some patients with dehiscence were actually grafted. Three early implant failures occurred, two in the immediate-delayed group and one in the delayed group (RR = 2; 95% CI 0.19 to 20.55). Four postoperative minor complications occurred, all in the immediate-delayed group: one fistula in relation to remnants of cement at the implant-abutment joint (after meticulous scaling the fistula disappeared but the patient suffered from a bad taste originating from the peri-implant mucosa), two cases of temporary sensory disturbances which recovered within 1 month, and one minor postoperative bleeding. The following additional complications occurred up to the fifth year: five in the immediate-delayed group (one crown was remade, two crown recementations, one case with several recementations, one case with the metal margin of the implant restoration exposed) and two in the delayed group (one crown was remade and one crown was recemented). After 2 years there were no statistically significant differences for prosthesis and implant failures, complications (RR = 9; 95% CI 0.51 to 158.17), aesthetics assessed by the patient (mean difference of VAS = 7.30; 95% CI -1.99 to 16.59), papilla height assessed by the dentist (RR = 1.20; 95% CI 0.54 to 2.67) and marginal bone level changes (mean difference = 0.10; CI 95% -0.64 to 0.44). There was a statistically significant difference with patients in the delayed group perceiving the period between tooth extraction and insertion of the crown significantly longer than patients in the immediate-delayed group, mean difference of VAS -20.30 (95% CI -33.36 to -7.24). There was also statistically significantly higher patient satisfaction

in the immediate-delayed group, mean difference of VAS 6.51 (95% CI 0.39 to 12.63). An independent blinded assessor also judged the level of the peri-implant marginal mucosa in relation to that of the adjacent teeth as more appropriate in the immediate-delayed group, with RR = 1.68 (95% CI 1.04 to 2.72). After 5 years, no significant differences were observed apart from that immediate-delayed implants had significantly more complications (RR = 4.20; 95% CI 1.01 to 17.43). The trial was judged to be at high risk of bias.

#### ■ Immediate versus immediate-delayed implant placement (one trial with 16 patients)

One trial of parallel group design compared eight patients receiving nine single immediate post-extractive implants with eight patients receiving nine immediate-delayed implants 8 weeks after extraction at maxillary anterior and premolar teeth<sup>31</sup>. Implants were restored within 48 hours with provisional acrylic crowns not in occlusal contact. Two years after implant placement there were no implant failures, complications, dropouts, or statistically significant differences for the level of the peri-implant marginal mucosa in relation to the implant collar (mean difference = 0.20 mm; CI 95% -0.44 to 0.84) and peri-implant marginal bone level changes (mean difference = 0.08 mm; CI 95% -0.43 to 0.59). The trial was judged to be at high risk of bias.

#### ■ Are augmentation procedures necessary? (one trial with 26 patients)

One trial of parallel group design compared 14 patients receiving particulate autogenous bone harvested from the implant osteotomy site versus

12 patients who were not subjected to any augmentation procedure at immediate single implants placed in fresh extraction sockets at maxillary anterior and premolar sites<sup>27</sup> up to 2 years post-loading. The following bone measurements at implant placement and 6 months later at implant exposure were included in the present review: the vertical height of the defect (VDH) measured from the most apical extent of the defect to the coronal aspect of the implant collar, and the horizontal depth of the defect (HDD) measured bucco-lingually from the most buccal extent of the implant collar to the labial bone crest (at dehiscenced sites, the HDD was estimated by measuring the horizontal distance from the implant collar to a periodontal probe placed against the intact portions of the labial plate at the level of the implant collar). No patients dropped out. Two complications occurred in the group treated with autogenous bone: one abscess that determined the early failure of the implant and one wound dehiscence. In total, two implants were lost in the autogenous bone group, whereas no complications or failures occurred in the non-augmented control group (RR = 4.33; 95% CI 0.23 to 82.31). Both treatments resulted in statistically significant bone gain, however no statistically significant differences were found among the two procedures (vertical bone gain mean difference = 1.70%; 95% CI -16.09 to 19.49; horizontal bone gain mean difference = 6.40%; -9.48 to 22.28). With respect to cost and treatment time, the difference between groups may not be clinically significant. The trial was judged to be at high risk of bias.

■ **Which is the most effective augmentation technique? (two trials with 56 patients)**

One trial of parallel group design compared 12 patients receiving non-resorbable barriers versus 11 patients receiving resorbable barriers versus 13 patients receiving resorbable barriers and particulate autogenous bone harvested from the implant osteotomy site at immediate single implants placed in fresh extraction sockets at maxillary anterior or premolar sites<sup>27</sup> up to 2 years post-loading. The following bone measurements at implant placement and 6 months after implant exposure were included

in the present review: the VDH measured from the most apical extent of the defect to the coronal aspect of the implant collar, and the HDD measured bucco-lingually from the most buccal extent of the implant collar to the labial bone crest (at dehiscenced sites, the HDD was estimated by measuring the horizontal distance from the implant collar to a periodontal probe placed against the intact portions of the labial plate at the level of the implant collar). No patients dropped out. Four complications occurred, two dehiscences occurred in the resorbable group whereas one abscess (successfully treated with systemic antibiotics) and one dehiscence occurred in the group treated with resorbable barriers and autogenous bone (no statistically significant differences). All treatments resulted in statistically significant bone gain, however no statistically significant differences were found among the three procedures (Figs 4 to 6). With respect to cost and treatment time, the differences among groups may not be clinically significant. The trial was judged to be at high risk of bias.

One trial compared 10 patients receiving Bio-Oss versus 10 patients receiving Bio-Oss plus a resorbable barrier at immediate single implants placed in fresh extraction sockets at maxillary anterior or premolar sites<sup>30</sup> up to 3 years post-loading. A third control group of 10 patients who received no barrier and no graft could not be evaluated since some patients were systematically excluded from that group and included in the remaining two groups. The following bone measurements at implant placement and 6 months after implant exposure were included in the present review: the VDH measured from the most apical extent of the defect to the coronal aspect of the implant collar, and the HDD measured bucco-lingually from the most buccal extent of the implant collar to the labial bone crest (at dehiscenced sites, the HDD was estimated by measuring the horizontal distance from the implant collar to a periodontal probe placed against the intact portions of the labial plate at the level of the implant collar). After 3 years, three patients dropped out from the Bio-Oss group and five patients from the Bio-Oss plus barrier group. There were no prosthesis or implant failures. Two complications occurred in the Bio-Oss plus barrier group: one abscess developed during the healing period around one implant (the site was retreated with the same

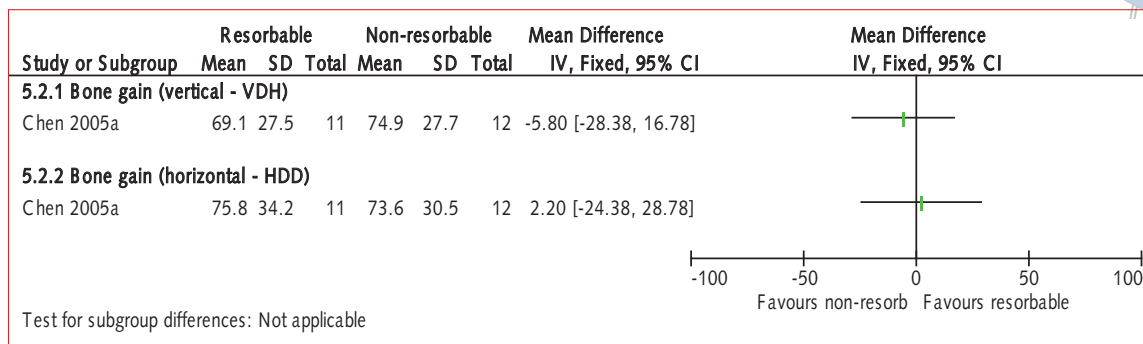


Fig 4 Forest plot comparing vertical and horizontal bone gain at immediate post-extractive implants augmented with resorbable or non-resorbable barriers.

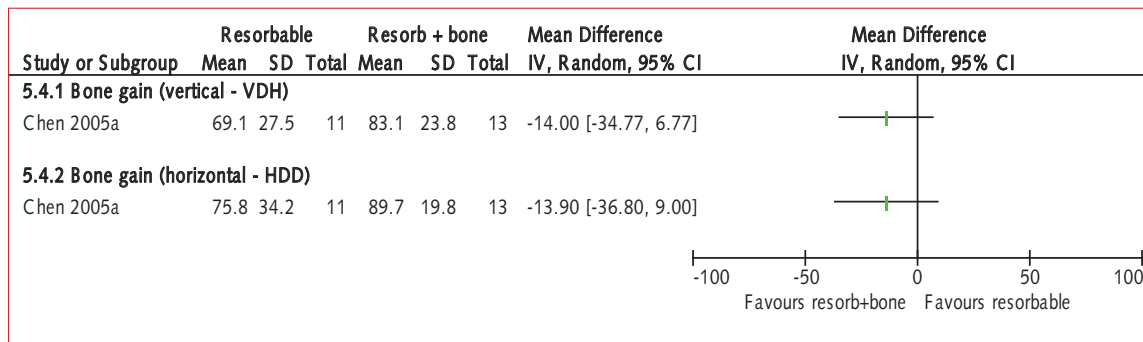


Fig 5 Forest plot comparing vertical and horizontal bone gain at immediate post-extractive implants augmented with resorbable barriers with and without autogenous bone.

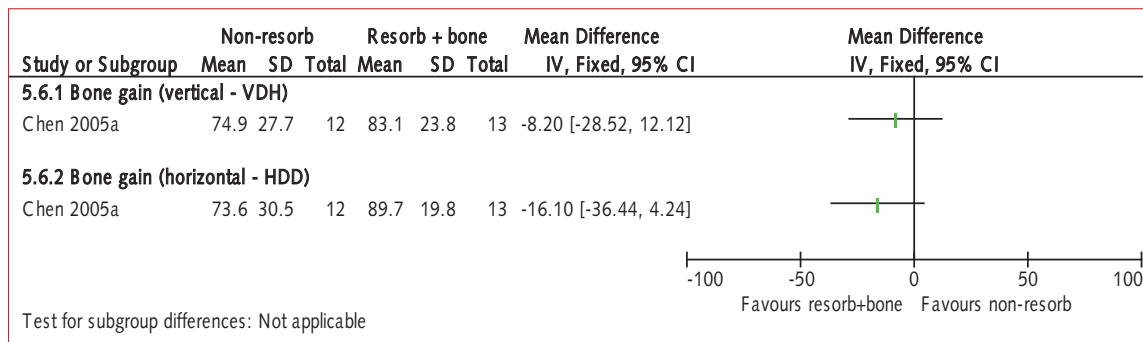
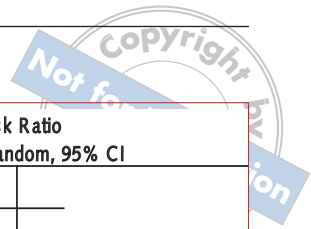


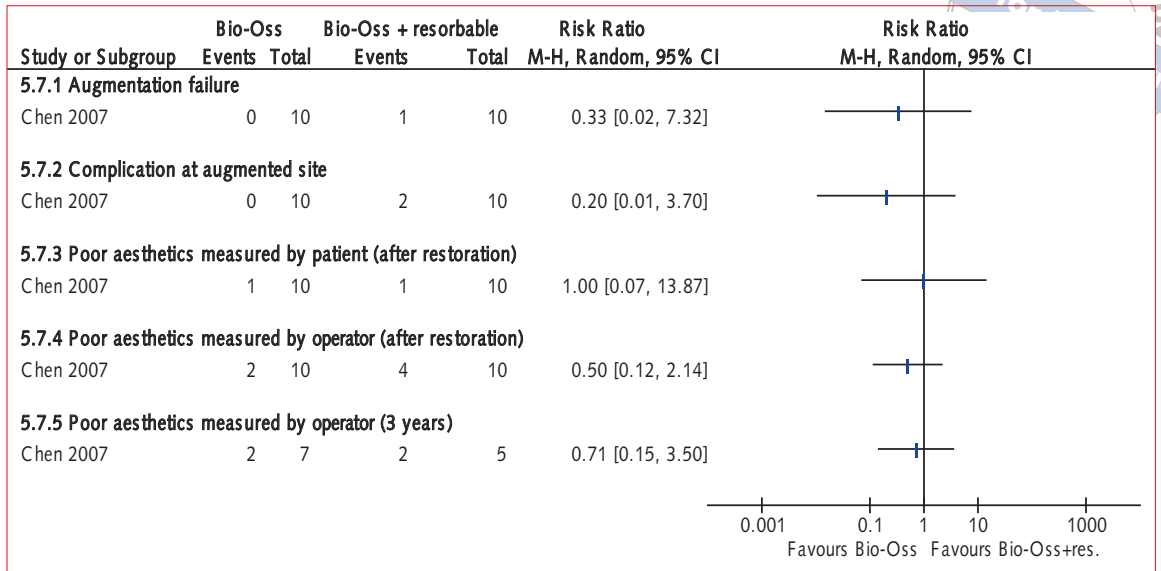
Fig 6 Forest plot comparing vertical and horizontal bone gain at immediate post-extractive implants augmented with non-resorbable barriers with autogenous bone and resorbable barriers.

procedure), and another implant displayed a chronic inflammation of the peri-implant tissues (peri-implant mucositis) for the entire study period (Fig 7). All treatments resulted in statistically significant bone gain, however, no statistically significant differences in bone gain were found between the two procedures (Fig 8). After delivery of the prostheses, one patient in each group, when asked by the operator, was dissatisfied with aesthetics due to recession of the mucosa on the buccal aspect. Both patients refused a corrective intervention with a soft tissue graft. Aesthetics (position of the soft tissue margin in relation to the adjacent teeth) were also evaluated by the operator after the 6-month healing period, at placement of the final restorations and after 3 years of loading. After healing, 3 out of 10 sites treated with Bio-Oss and 4 out of 10 sites treated with Bio-Oss plus barrier were

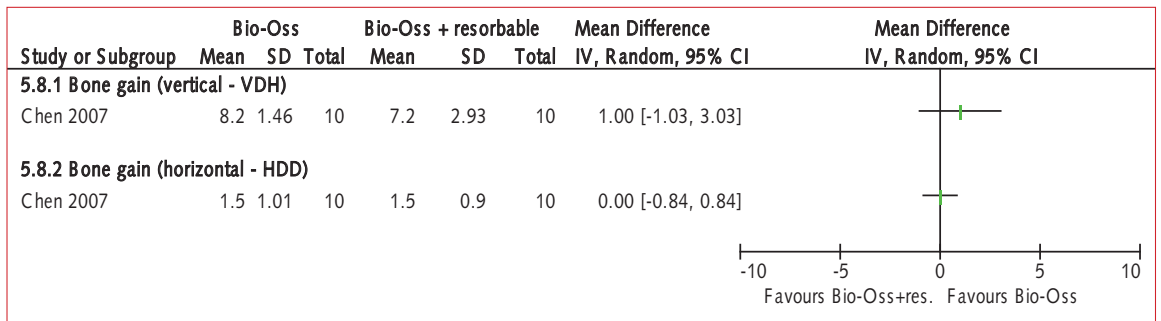
considered aesthetically unsatisfactory by the operator. The two sites which were judged as unsatisfactory by the patients were also judged unsatisfactory by the operator. The operator then treated two sites with recession in the Bio-Oss group and one patient with recession and one without recession (marginal mucosa judged to be too thin) of the Bio-Oss plus barrier group with connective tissue grafts. After placement of the final restorations (about 2 months later), the operator judged aesthetics to be poor in 2 out of 10 patients of the Bio-Oss group and in 4 out of 10 of the Bio-Oss plus barrier group. After 3 years of loading, the operator judged aesthetics to be poor in 2 out of 7 patients of the Bio-Oss group and in 2 out of 5 patients of the Bio-Oss plus barrier group. No statistically significant differences were found for any of the aesthetic outcomes (Fig 7). With respect to



**Fig 7** Forest plot comparing dichotomous outcomes at immediate post-extractive implants augmented with anorganic bovine bone with and without resorbable barriers.



**Fig 8** Forest plot comparing vertical and horizontal bone gain at immediate post-extractive implants augmented with anorganic bovine bone with and without resorbable barriers.



treatment time, the differences among groups may not be clinically significant. The only difference in cost between the two procedures was the additional cost of the barrier. The trial was judged to be at high risk of bias.

## ■ Discussion

Only four trials comparing different timing for implant placement could be included in the present review<sup>25,29,31,33</sup>. Different timings for implant placement after tooth extraction were evaluated, however all trials were underpowered, therefore only limited indications can be gained from them.

The meta-analyses of two RCTs<sup>29,33</sup> comparing immediate versus delayed implants, found no statistically significant differences for prosthesis and implant failures, though trends clearly suggested that more implant failures occurred at immediate implants (6 versus 1). No other meta-analysis could be performed, nor other outcome was signifi-

cant. According to the authors of one trial<sup>33</sup>, there was 1 mm more recession of buccal soft tissues at delayed implants. This is plausible but since data were not clearly presented in the study, the present authors were unable to evaluate this outcome as well as other outcomes that they presented. It was disappointing that limitations in data reporting in one trial<sup>33</sup> did not allow additional meta-analyses. This could have been easily obviated if the authors answered requests for information.

One study<sup>25</sup> compared immediate-delayed implants placed on average 10 days after extraction with delayed implants placed on average 3 months after extractions. After 2 years, patients in the delayed group perceived the period between tooth extraction and insertion of the crown significantly longer and were less satisfied. Moreover, an independent blinded assessor judged the level of the peri-implant marginal mucosa in relation to that of the adjacent teeth as more appropriate in the immediate-delayed group. The possible biological explanation is that the early implant placement decreased

resorption of the alveolar bone. In other words, the implants may have contributed towards maintaining the alveolar bone height with a perceived aesthetic benefit. However, after 5 years, all of these differences disappeared, and complications became statistically more common for immediate-delayed implants. These findings are difficult to interpret also because there were many dropouts that reduced the sample size. Data interpretation is further complicated by the fact that the authors withdrew several patients from the study. No patient should have been withdrawn from the study, according to the principle of the intention-to-treat analysis, which would have allowed the readers to draw their conclusions and avoided unnecessary bias.

The study comparing immediate and immediate-delayed implants<sup>31</sup>, though well conducted, included only eight patients per group. Such a small sample size does not allow for any reliable conclusion, since the probability of finding a difference is remote.

Regarding the need for bone augmentation procedures at implant placement, only one trial<sup>27</sup> evaluated whether they could be advantageous or not. The trial tested in 26 patients augmentation with autogenous bone collected from the implant site. It was underpowered to detect any difference, however all failures (two) and complications (two) occurred in the augmented group. A second trial<sup>30</sup> including a control group not subject to augmentation could not be used because the authors subverted the randomisation, allocating preferentially patients with buccal defects to the augmentation arms of the study.

Five different augmentation procedures were tested in two trials<sup>27,30</sup> including 56 patients. By dividing the few patients into five different groups, the authors eliminated the already scarce possibility of finding any possible statistically significant difference, therefore the findings were inconclusive.

The only trial<sup>26</sup> showing some statistically significant difference was excluded from the present review update because it was decided to include only trials having a follow-up of at least 1 year after loading. This trial, having a follow-up to abutment connection/implant loading, compared 10 patients with an immediate post-extractive implant covered by a resorbable barrier versus 10 patients treated with a resorbable barrier plus anorganic bovine bone

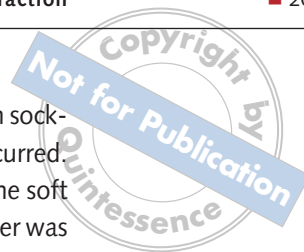
(Bio-Oss) at implants placed in fresh extraction sockets. No failures, complications or dropouts occurred. A statistically significantly higher position of the soft tissue margins in relation to the implant shoulder was found at the buccal aspects of implants treated with barrier plus Bio-Oss (2.1 mm versus 0.9 mm; mean difference = -1.2 mm; 95% CI -2.29 to -0.11)<sup>26</sup>.

With respect to generalisation of the results of the present review to general practice, failures and complications at immediate post-extractive implants were slightly higher. Caution is therefore recommended when deciding to place implants immediately after tooth extraction. The first question that clinicians should ask themselves is what are the added benefits for the patient by having immediate implants. Then the expected benefits need to be carefully weighed against the risk of complications of the chosen procedures.

## ■ Conclusions

There is insufficient evidence to determine possible advantages or disadvantages of immediate, immediate-delayed or delayed implants, therefore these preliminary conclusions are based on few underpowered trials often judged to be at high risk of bias. There is a suggestion that immediate and immediate-delayed implants may be at higher risk of implant failures and complications than delayed implants, on the other hand the aesthetic outcome might be better when placing implants just after tooth extraction. There is not enough reliable evidence supporting or refuting the need for augmentation procedures at immediate implants placed in fresh extraction sockets or whether any of the augmentation techniques is superior to the others.

There is a definite need for RCTs evaluating the best timing for placing dental implants after tooth extractions. These trials must be powered to detect a difference for primary outcomes such as prosthesis/implant success and complications, should evaluate objective aesthetic outcomes assessed by blinded outcome assessors and the patient's own perception of aesthetics, and should be reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines (<http://www.consort-statement.org/>). It is also necessary to understand when bone



augmentation procedures are indicated and which are the most effective. Trials evaluating the efficacy of non/slow resorbable bone substitutes as an alternative to autogenous bone should be prioritised.

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