CLINICAL ORAL IMPLANTS RESEARCH

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Surgical protocols for ridge preservation after tooth extraction. A systematic review

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Abstract

Objective: This systematic review aims to evaluate the scientific evidence on the efficacy in the surgical protocols designed for preserving the alveolar ridge after tooth extraction and to evaluate how these techniques affect the placement of dental implants and the final implant supported restoration.

Material and methods: A thorough search in MEDLINE-PubMed, Embase and the Cochrane Central Register of controlled trials (CENTRAL) was conducted up to February 2011. Randomized clinical trials and prospective cohort studies with a follow-up of at least 3 months reporting changes on both the hard and soft tissues (height and/or width) of the alveolar process (mm or %) after tooth extraction were considered for inclusion.

Results: The screening of titles and abstracts resulted in 14 publications meeting the eligibility criteria. Data from nine of these 14 studies could be grouped in the meta-analyses. Results from the meta-analyses showed a statistically significant greater ridge reduction in bone height for control groups as compared to test groups (weighted mean differences, WMD = −1.47 mm; 95% CI [−1.982, −0.953]; $P < 0.001$; heterogeneity: $I^2 = 13.1\%$; χ^2 P-value = 0.314) and a significant greater reduction in bone width for control groups compared to the test groups (WMD = −1.830 mm; 95% CI [−2.947, −0.732]; $P = 0.001$; heterogeneity: $I^2 = 0\%$; χ^2 P-value = 0.837). Subgroup analysis was based on the surgical protocol used for the socket preservation (flapless/flapped, barrier membrane/no membrane, primary intention healing/no primary healing) and on the measurement method utilized to evaluate morphological changes. Meta-regression analyses demonstrated a statistically significant difference favoring the flapped subgroup in terms of bone width (meta-regression; slope = 2.26; 95% IC [1.01; 3.51]; $P = 0.003$).

Conclusions: The potential benefit of socket preservation therapies was demonstrated resulting in significantly less vertical and horizontal contraction of the alveolar bone crest. The scientific evidence does not provide clear guidelines in regards to the type of biomaterial, or surgical procedure, although a significant positive effect of the flapped surgery was observed. There are no data available to draw conclusions on the consequences of such benefits on the long-term outcomes of implant therapy.

The alveolar processes in the jaws are tooth-dependent structures that will undergo significant structural changes whenever the teeth are lost. The dynamics and magnitude of these changes have been investigated in the dog model (Kuboki et al. 1988; Devlin et al. 1997; Cardaropoli et al. 2003; Araujo & Lindhe 2005; van Kesteren et al. 2010) as well as in humans (Amler et al. 1960; Evian et al. 1982; Devlin & Sloan 2002; Trombelli et al. 2008). These investigations have identified the key processes of tissue modelling and remodelling after tooth extraction that eventually lead to a reduction on the overall ridge dimensions with significant changes in both the buccal and lingual bone crests.

The amount of vertical and horizontal resorption of the socket walls has been investigated with different methods, ranging from studying and measuring cast models (Pietrokovski & Massler 1967; Johnson 1969; Schropp et al. 2003), to radiographic analysis

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(Schropp et al. 2003), clinical assessment with individually pre-fabricated acrylic stents during re-entry surgeries (Lekovic et al. 1998; Camargo et al. 2000) and histological studies in experimental animal models (Cardaropoli et al. 2003; Araujo & Lindhe 2005). These studies have evidenced that most of the resorption occurs during the first 3 months of healing, although dimensional changes can be observed up to 1 year after tooth extraction, resulting in approximately 50% reduction of the bucco-lingual dimension of the alveolar ridge (Schropp et al. 2003), mainly due to the resorption of the buccal bone plate (Araujo & Lindhe 2005).

The clinical consequences of these physiological hard and soft tissue changes may affect the outcome of the ensuing therapies aimed to restore the lost dentition, either by limiting the bone availability for ideal implant placement or by compromising the aesthetic result of the prosthetic restorations. To counteract these early tissue changes after tooth extraction, different socket preservation therapies have been proposed, ranging from a careful flapless tooth extraction aiming for an undisturbed socket healing (Fickl et al. 2008a, 2008b), to the immediate placement of dental implants (Paolantonio et al. 2001), to filling the resulting alveolar socket with different grafting materials, with and without barrier membranes (Fickl et al. 2008a, 2008b).

The possible beneficial effect of a flapless surgery during tooth extraction for limiting the resorptive process of the alveolar crest has been investigated in pre-clinical models by comparing the outcomes with a flapped conventional surgery. Although some studies have shown slightly less pronounced bone remodelling of the alveolar ridge after flapless tooth extraction (Fickl et al. 2008a, 2008b), other studies have failed to encounter significant differences between flapped and flapless tooth extractions (Araujo & Lindhe 2009).

Similarly, the possible beneficial effect of using grafting procedures or guided bone regeneration (GBR) to preserve the ridge after tooth extraction has been tested in both animal and human studies. Using the dog experimental model (Araujo & Lindhe 2009; Araujo et al. 2008) filled the socket immediately after tooth extraction with bovine-derived hydroxyapatite or with an autogenous bone graft (Araujo & Lindhe 2011). While the placement of the xenograft counteracted the ridge contraction in the buco-lingual dimension, grafting with autogenous bone did not significantly alter the ridge resorptive process. In humans, the application of regenerative bio-materials, such as bone autografts, allografts, guided tissue regeneration procedures, xenografts and most recently, growth factors, has also been evaluated with varying degrees of success to maintain the anatomical dimensions of the alveolar ridge after tooth extraction. A recent systematic review (Ten Heggeler et al. 2010) evaluated the efficacy of these therapies in non-molar alveolar regions suggesting that these techniques may not prevent the physiological resorptive bone processes after tooth extraction, although they may aid in reducing the resulting bone dimensional changes. This investigation, however, could not draw firm conclusions due to the limitations in the existing clinical research.

In terms of histological outcomes in humans (Becker et al. 1999), used different biomaterials, such as demineralized freeze-dried bone, autologous bone, human morphogenetic proteins in a carrier to graft human extraction sockets, reporting that the graft materials were, 3–7 months later, mainly surrounded by connective tissue. In contrast (Artzi et al. 2000), using the same xenogeneic graft material found the graft particles in direct contact with bone, although in a similar study, using the same grafting material (Carmagnola et al. 2003) found the graft particles remained within the socket more than 6 months after the extraction and only 40% of the particles were in direct contact with bone. It is, therefore, uncertain whether these socket preservation therapies improve the outcomes of the different rehabilitation approaches after tooth loss.

The objective of the present study was to systematically review all the scientific evidence regarding these therapeutic interventions for socket preservation after tooth extraction and to assess systematically the potential benefit of such techniques/materials when compared with what occurs when the socket is left to heal spontaneously.

The specific objectives were: (1) to describe the surgical techniques and biomaterials most commonly used to preserve the socket architecture after tooth extraction; (2) to evaluate their expected outcome on the alveolar ridge dimension and (3) to assess their impact on the bone availability for ideal implant placement or on the resulting prosthetic restoration.

Material and methods

Development of a protocol

A protocol covering all aspects of the systematic review methodology was developed before the start of the review, including the following definitions (Needleman 2002):

- Focused question.
- Study population.
- Types of intervention.
- Types of comparisons.
- Search strategy.
- Eligibility criteria for study inclusion.
- Outcome measures.
- Screening methods and data extraction.
- Quality assessment and data synthesis.
- Assessment of heterogeneity and drawing of conclusions.

Focused question

"Which are the effects of the different socket preservation approaches used immediately after tooth extraction, compared to the spontaneous healing of the socket, in terms of the alveolar ridge hard and soft tissue dimensional changes and in terms of providing sufficient bone availability for implant placement and/or a restorative final successful outcome?"

Population of study, type of intervention and type of comparison

The population of interest for this review was represented by humans with at least one tooth to be extracted, older than 18 years and in good general health. A minimum sample size (10 subjects per group) was established in an attempt to minimize the publication bias. The definition used for extraction socket preservation therapy was: "Any therapeutic approach carried out immediately after tooth extraction aimed to preserve the alveolar socket architecture and to provide the maximum bone availability for implant placement."

The specific therapeutic interventions evaluated in this study were:

- filling the socket with autologous bone grafts or bone substitutes (allogenic, xenogenic and synthetic grafts);
- isolating the socket with the use of barrier membranes, soft tissue autografts or soft tissue substitutes (allogenic and others) and,
- promoting the healing process of the socket by the addition of growth factors or bone morphogenetic proteins.

These interventions were compared to the spontaneous healing of the socket.

Search strategy

Three electronic databases were used as sources in the search for studies satisfying the

inclusion criteria: (1) The National Library of Medicine (MEDLINE via Pubmed); (2) Embase and (3) Cochrane Central Register of Controlled Trials. These databases were searched for studies published until February 2011. The search was limited to human subjects.

The following search terms were used:

Population

(<[text words] Tooth> OR <[MeSH terms/all subheadings] "Tooth">) AND

([text words] Extraction)

OR

(<[Text words] Tooth extraction OR Extraction socket* OR Alveolar socket* OR dental extraction* OR tooth removal OR socket* OR ridge-socket* OR post-extraction socket* OR fresh extraction socket* OR alveolar crest> OR <[MeSH terms/all subheadings] "Tooth Extraction*" OR "Tooth socket*">)

Intervention

[text words] Socket*preservation OR Ridge preservation OR bone preservation OR socket* seal OR Site* preservation OR Bone filler* OR Autologous bone graft* OR autologous bone OR autogenous bone graft* OR Autogenous bone OR bone substitute* OR growth factor* OR rhBMP OR bone morphogenetic protein* OR allogenic graft* or Allograft* OR xenogenic graft* OR OR xenogeneic graft* OR xenograft* OR synthetic graft* OR Barrier membrane* OR membrane* OR resorbable membrane* or non-resorbable membrane OR guided bone regeneration OR GBR OR freeze dried bone allograft* OR demineralized freeze dried bone allograft* OR DFDBA OR FDBA OR Bio-Oss OR Bio-Oss Collagen OR Alloplast* OR tricalciumphosphate OR cerasorb OR Bioglass OR polymeric OR collagen sponge OR Collagen OR collagen fleece OR collagen plug* OR Bioguide OR Ossix OR Gore tex OR ePTFE OR soft tissue* autograft* OR connective tissue graft* OR punch OR free gingival graft* OR soft tissue* substitute* OR allogenic soft tissue* OR alloderm OR acellular dermal matrix OR collagen matrix.

There were no language restrictions. All reference lists of the selected studies were checked for cross-references. The following journals were hand-searched: *Journal of Clinical Periodontology, Journal of Periodontology, Journal of Periodontal Research; Clinical Oral Implants Research, International Journal of Oral & Maxillofacial Implants* and *Clinical Implant Dentistry and Related Research*.

Eligibility criteria for study inclusion

Randomized clinical trials (RCT) or prospective cohort studies with a follow-up of at least 3 months after tooth extraction were considered for inclusion in this review.

Outcome measures

The primary outcome variable chosen was the bone dimensional changes occurring in the socket wall after the tooth extraction and the socket preservation therapy, measured as the changes in the height and width of the alveolar process (mm or %).

As secondary outcome variables, we considered the soft tissue dimensional changes (in mm or %), the presence and amount of keratinized tissue at time of implant placement (yes/no or mm), the changes in clinical attachment levels (CAL) evaluated at the mesial and distal adjacent teeth, the availability of bone for implant placement (yes or no), the need for soft and/or hard tissue augmentation techniques at the time of implant placement (number and type), the outcome of the final implant supported restoration evaluated in terms of the prosthetic and/or aesthetic result and assessed by the dentist or the patient using different parameters or indexes (Jemt index, VAS scale, etc.), and the peri-implant health status evaluated radiographically or clinically by means of probing pocket depths, CAL, bleeding on probing and the plaque index.

Screening methods and data extraction

First, two reviewers (PM and DR) screened independently the titles and abstracts and did the primary search. Subsequently, the studies appearing to meet the inclusion criteria, or those with insufficient data in the title and abstract to make a clear decision, were selected for evaluation of the full manuscript, which was carried out independently by the same two reviewers who determined their eligibility. Any disagreement was resolved by discussion with a third reviewer (FV). To prevent selection bias, the reviewers were blind to the name of the authors, institutions and journal titles. All studies that met the inclusion criteria underwent a validity assessment. The reasons for rejecting studies at this or at subsequent stages were recorded. Special attention was paid to duplicate publications to avoid a likely bigger impact of the same data on the overall result.

Data extraction

Two reviewers (PM and DR) independently extracted the data using specially designed data extraction forms. Any disagreement was discussed and a third reviewer (EF or FV) was consulted when necessary. The inter-reviewer reliability of the data extraction was calculated by determining the percentage of agreement and the correlation coefficients with Kappa analysis. Authors of studies were contacted for clarification when data were incomplete or missing. Data were excluded until further clarification could be available if agreement could not be reached. When the results of a study were published more than once or if the results were presented in a number of publications, the most complete dataset was included only once.

Quality assessment

The quality assessment of the included studies was undertaken independently and in duplicate by one reviewer (PM) who was blind to the name of the authors, institutions and journal titles. This assessment was based on the study design utilized according to the following criteria for *Randomized controlled trials:* Quality assessment was carried out following the recommendations by Cochrane for assessing risk of bias (Higgins et al. 2009) and also based on criteria proposed by Ten Heggeler et al. (2010), which are based on the RCT-checklist of the Dutch Cochrane Center (2009), the CONSORT-statements (Schulz et al. 2010), MOOSE-statement (Stroup et al. 2000), STROBE statements (von Elm et al. 2007) and the recommendations by Needleman (2002) and Esposito et al. (2001). Studies were defined as low risk of bias if these six criteria were clearly met in the study: random allocation, definition of inclusion/exclusion criteria for selecting the population, measures to blind the patient and examiner, selection of a representative population group, use of identical treatment between groups except for the intervention and detailed reporting of the follow-up. When missing one of these criteria, the study was classified as moderate potential risk of bias. Missing two or more of these criteria resulted in a high potential risk of bias (Ten Heggeler et al. 2010).

The statistical heterogeneity among studies was assessed using the Q test according to Dersimonian and Laird, as well as the I^2 index (Higgins et al. 2003) to know the percentage of variation in the global estimate that was attributable to heterogeneity (I^2 = 25%: low; I^2 = 50%: moderate; I^2 = 75%: high heterogeneity). When the heterogeneity values were high, a subgroup analysis was carried out using the following explanatory variables: (1) use of membrane (Yes/No); (2) surgical technique (flap Yes/No); (3) primary wound closure and (4) measurement tool used to assess the morphological changes. This subgroup analysis was performed using meta-regression.

Data analysis

To summarize and to compare the selected studies, the data on the primary outcome (mean bone dimensional changes) were pooled and analysed using means and 95% confidence intervals. The data on secondary outcomes were analysed depending on the type of variable. For dichotomous variables (e.g. successful implant placement), the estimates of the effect were expressed as risk ratio and 95% confidence intervals. For continuous variables (bone level changes, soft tissue changes), weighted mean differences (WMD) and 95% confidence intervals were used.

The study-specific estimates were pooled using both the fixed effect model (Mantel-Haenzel-Peto test) and the random effect model (Dersimonian-Laird test). If a significant heterogeneity was found, the random effect model results were presented.

A Forest Plot was created to illustrate the effects on the meta-analysis of the different studies and the global estimation. The publication bias was evaluated using a Funnel plot and the Egger's linear regression method. A sensitivity analysis of the meta-analysis results was also performed (Tobias 1999). STATA® (StataCorp LP, Lakeway Drive, College Station, TX, USA) intercooled software was used to perform all analyses. Statistical significance was defined as a P-value <0.05.

Results

Screening

The search strategy resulted in 296 articles. After an initial phase of screening (agreement between reviewers of 89.53%; kappa = 0.46), 17 potentially relevant articles were identified. After reading the complete manuscripts, three studies were excluded due to inadequate study design (Block & Jackson 2006); inadequate control group (Yilmaz et al. 1998) and due to only reporting secondary outcomes (Norton et al. 2003). Hand-search or cross-reference did not result in any additional article. Therefore, 14 studies were finally included (Fig. 1).

Study design and study population

Twelve studies were RCTs with two to five study groups and with a follow-up period between 3 and 7 months (Hoad-Reddick et al. 1994; Lekovic et al. 1997; Lekovic et al. 1998; Bolouri et al. 2001; Froum et al. 2002; Iasella et al. 2003; Fiorellini et al. 2005; Barone et al. 2008; Aimetti et al. 2009; Crespi et al. 2009; Casado et al. 2010; Oghli & Steveling 2010) (Table 1). Two studies were controlled clinical studies, one with two study groups and a 6-month follow-up period (Serino et al. 2003) and the other with three study groups and a 3-month follow-up (Serino et al. 2008). Six studies presented a split-mouth design, whereas eight studies presented a parallel design.

The study population ranged from 10 individuals to 125. Smoking habit was reported in four studies (Hoad-Reddick et al. 1994; Lekovic et al. 1997; Lekovic et al. 1998; Bolouri et al. 2001; Froum et al. 2002; Iasella et al. 2003; Fiorellini et al. 2005; Barone et al. 2008; Aimetti et al. 2009; Crespi et al. 2009; Casado et al. 2010; Oghli & Steveling 2010) ranging from 0% to 12%. The periodontal status of the extracted teeth was defined in three studies (Serino et al. 2003; Serino et al. 2008). The localization of extracted teeth in the mouth was reported in nine studies (Hoad-Reddick et al. 1994; Lekovic et al. 1997; Lekovic et al. 1998; Bolouri et al. 2001; Froum et al. 2002; Iasella et al. 2003; Fiorellini et al. 2005; Barone et al. 2008; Aimetti et al. 2009; Crespi et al. 2009; Casado et al. 2010; Oghli & Steveling 2010) in which most, studied non-molar sites (Hoad-Reddick et al. 1994; Lekovic et al. 1997; Lekovic et al. 1998; Bolouri et al. 2001; Froum et al. 2002; Iasella et al. 2003; Fiorellini et al. 2005; Barone et al. 2008; Aimetti et al. 2009; Crespi et al. 2009; Casado et al. 2010; Oghli & Steveling 2010), although some were very specific to mandibular (Hoad-Reddick et al. 1994) or maxillary anterior teeth (Aimetti et al. 2009), whereas others included any teeth (Bolouri et al. 2001; Crespi et al. 2009).

Type of intervention and type of biomaterials

Most of the studies (Hoad-Reddick et al. 1994; Lekovic et al. 1997; Lekovic et al. 1998; Bolouri et al. 2001; Froum et al. 2002; Iasella et al. 2003; Fiorellini et al. 2005; Ba-

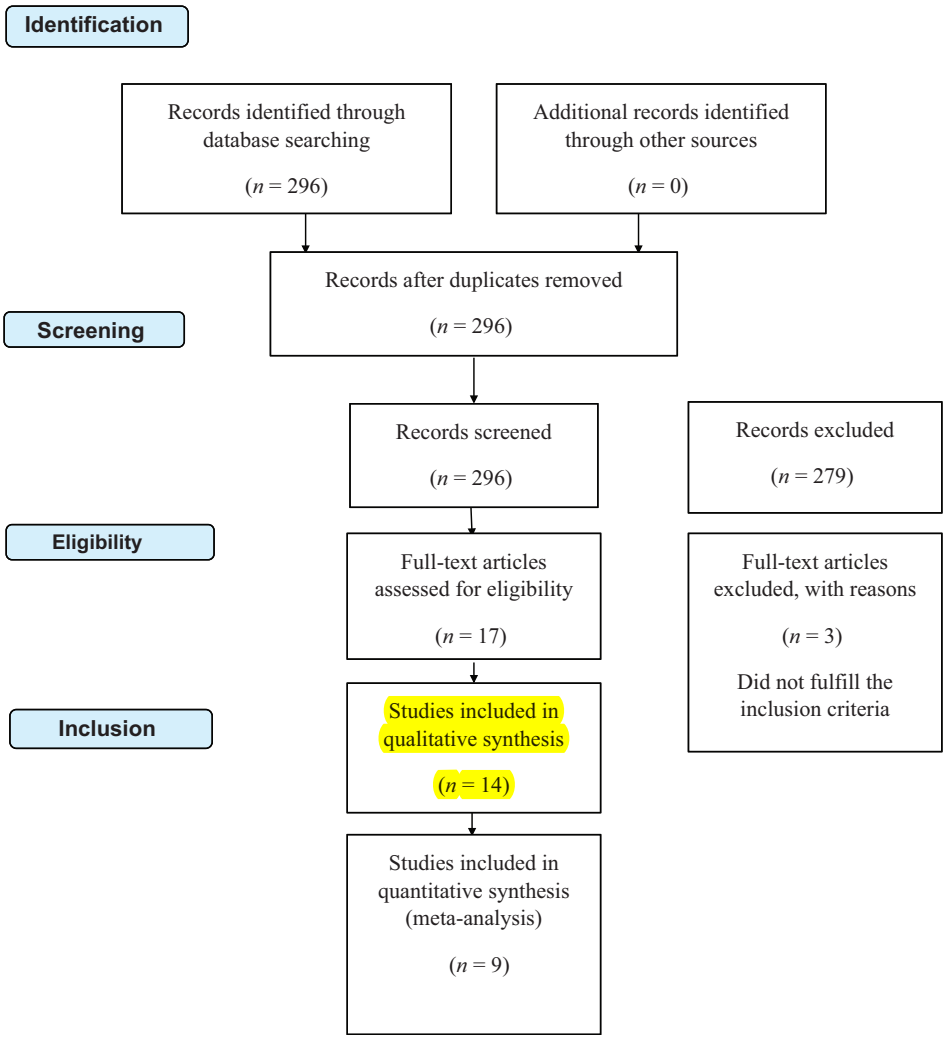

Fig. 1. Flow diagram (PRISMA format) of the screening and selection process.

Table 1. **Methods, participants, interventions, outcomes, site and funding of the selected studies**

Study (#)	Method	Participants	Surgical considerations	Intervention	Measurement method	Outcome	Site and funding
Hoad-Reddick et al. (1994) (1)	RCT Two study groups Parallel groups 6 months follow-up	18 individuals (-na) Aged 54.4 years Smoking habit: na Periodontal status: na	Flapless Primary closure: na Type of socket: na	Test: Hydroxyapatite granules Control: No socket filling	Lateral cephalographs and dental pantomograms	Hard tissue dimensions: defect height (mm)	Not explained Not available
Lekovic et al. (1997) (2)	RCT Two study groups Split mouth 6 months follow-up	10 individuals (-3) Aged 49.8 years Smoking habit: na Periodontal status: na	Flap Primary closure: YES Type of socket: na	Test: ePTFE® membrane Control: No socket filling	Reentry surgery	Hard tissue dimensions: defect height (mm), defect width (mm)	Yugoslavia Not available
Lekovic et al. (1998) (3)	RCT Two study groups Split mouth 6 months follow-up	16 individuals (-0) Aged 52.6 years Smoking habit: na Periodontal status: na	Flap Primary closure: YES Type of socket: na	Test: membrane of glycolide and lactide polimers Control: No socket filling	Reentry surgery	Hard tissue dimensions: defect height (mm), defect width (mm)	Yugoslavia Not available
Bolouri et al. (2001) (4)	RCT Two study groups Split mouth 24 months follow-up	18 individuals (-14) Aged 54.4 years Smoking habit: na Periodontal status: na	Flap Primary closure: YES Type of socket: na	Test: Bioplant HTR® Control: No socket filling		Hard tissue dimensions: optical density	USA Bioplant Inc. South Norwalk, CT
Froum et al. (2002) (5)	RCT Three study groups Split mouth 6–8 months follow-up	19 individuals (-na) Aged na Smoking habit: 0% Periodontal status: na	Flap Primary closure: YES Type of socket: 4-wall	Test 1: Bioactive glass Test 2: DFDBA Control: No socket filling	Histological analysis	Histological analysis	USA Orthovita
Serino et al. (2003) (6)	CT Two study groups Parallel groups 6 month follow-up	45 individuals (-na) Aged na Smoking habit: na Periodontal status: periodontitis	Flap Primary closure: YES Type of socket: na	Test: Sponge of polylactide-polyglycolide acid Control: No socket filling	Reentry surgery + stent	Hard tissue dimensions: defect height (mm) Histological analysis	Italy Not available
Iasella et al. (2003) (7)	RCT Two study groups Parallel groups 4–6 months follow-up	24 individuals (-na) Aged 51.5 Smoking habit: na Periodontal status: periodontitis	Flap Primary closure: NO Type of socket: na	Test: FDBA + tetracycline + collagen \ mombrane Control: No socket filling	Clinical + stent	Hard tissue dimensions: defect height (mm), defect width (mm) Soft tissue dimensions Histological analysis	USA Not available
Fiorellini et al. (2005) (8)	RCT Five study groups Parallel groups 6 months follow-up	80 individuals (-0) Aged 47.4 Smoking habit: na Periodontal status: na	Flap Primary closure: YES Type of socket: 3-wall(no buccal wall)	Test 1: 0.75 mg/ml rhBMP/ACS Test 2: 1.50 mg/ml rhBMP/ACS Control 1: No socket filling Control 2: placebo	CT scan	Defect height and width (mm CTscan) Need for augmentation technique Histological analysis	USA Wyeth/Genetics Institute, Cambridge, MA
Barone et al. (2008) (9)	RCT Two study groups Parallel groups 7 months follow-up	40 individuals (-0) Aged: na Smoking habit: 12.5% Periodontal status: na	Flap Primary closure: YES Type of socket: 4-wall	Test: Corticocancellous porcine bone + collagen membrane Control: No socket filling	Reentry + stent	Hard tissue dimensions: defect height (mm), defect width (mm) Histological analysis	Italy Not available

Table 1. (continued)

Study (#)	Method	Participants	Surgical considerations	Intervention	Measurement method	Outcome	Site and funding
Serino et al. (2008) (10)	CT Two study groups Parallel groups 3 months follow-up	20 individuals (-0) Aged: na Smoking habit: na Periodontal status: Periodontitis	Flap Primary closure: NO Type of socket: na	Test: Sponge of polylactide-polyglycolide acid Control: No socket filling	Histological analysis	Histological analysis	Italy Not available
Aimetti et al. (2009) (11)	RCT Two study groups Parallel groups 3 months follow-up	40 individuals (na) Aged: 51.27 Smoking habit: 0% Periodontal status: na	Flapless Primary closure: NO Type of socket: na	Test: Medical-grade calcium sulphate hemihydrate Control: No socket filling	Reentry + stent	Dimensions changes: defect height (mm), defect width (mm) Histological analysis	Italy Not available
Crespi et al. (2009) (12)	RCT Three study groups Split mouth 3 months follow-up	15 individuals (na) Aged: 51.3 Smoking habit: 0% Periodontal status: na	Flapless Primary closure: YES (tissue graft) Type of socket: 3-wall (no buccal wall)	Test 1: Magnesium-enriched hydroxyapatite Test 2: Calcium sulphate Control: No socket filling	Periapical X rays	Dimensions changes: defect height (mm). Radiological outcomes Histological analysis	Italy Not available
Casado et al. (2010) (13)	RCT Four study groups Split mouth 4 months follow-up	19 individuals (na) Aged: na Smoking habit: na Periodontal status: na	Flap Primary closure: YES Type of socket: na	Test 1: bovine BMP + bOM Test 2: bovine BMP + bOM + absorbable membrane Test 3: absorbable membrane Control: No socket filling	Clinical + stent	Dimensions: defect width (mm) Histological analysis	Brazil Not available
Oghli & Steveling (2010) (14)	RCT Three study groups Parallel groups 3 months follow-up	125 individuals (-14) Aged: na Smoking habit: na Periodontal status: na	Flapless Primary closure: YES (soft tissue graft) Type of socket: na	Test 1: Autogenous soft tissue graft + collagen plug2 Test 2: Autogenous soft tissue graft + collagen matrix with gentamicin Control: No socket filling	Cast	Dimensions changes: defect height (mm)	Saudi Arabia + Germany Not available

Abbreviations of the interventions: NA, data not available; RCT, randomized clinical trial; ACS, absorbable collagen sponge; e-PTFE, expanded polytetrafluoroethylene; BMP, bone morphogenetic protein; bOM, bovine organic matrix; CT scan, computerized tomography scanner; RhBMP, recombinant human BMP-2; FDBA, freeze-dried bone allograft; DFDBA, demineralized freeze-dried bone allograft.

Table 2. **Quality assessment of the articles included**

#	Author (year)	Quality criteria: Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?	Risk of bias
1	Hoad-Reddick et al. (1994)	c	c	0	c	a	a	High
2	Lekovic et al. (1997)	c	c	0	a	a	a	High
3	Lekovic et al. (1998)	a	c	1	a	a	a	High
4	Bolouri et al. (2001)	b	c	1	c	a	a	High
5	Froum et al. (2002)	c	a	1	c	a	a	High
6	Serino et al. (2003)	b	b	b	a	a	a	Moderate
7	Iasella et al. (2003)	b	c	0	c	a	a	High
8	Fiorellini et al. (2005)	b	b	2	a	a	a	High
9	Barone et al. (2008)	a	c	1	a	a	a	Moderate
10	Serino et al. (2008)	b	b	b	a	a	a	Moderate
11	Aimetti et al. (2009)	b	c	1	c	a	a	High
12	Crespi et al. (2009)	b	c	1	c	a	a	High
13	Casado et al. (2010)	c	c	0	c	a	a	High
14	Oghli & Steveling (2010)	b	c	0	a	a	a	High

Abbreviations of the interventions: a: adequate explanation in the text; b: inadequate explanation in the text; c: not listed; 0: not blinded; 1: single-blinded; 2: double-blinded.

rone et al. 2008; Aimetti et al. 2009; Crespi et al. 2009; Casado et al. 2010; Oghli & Steveling 2010) elevated buccal and lingual mucoperiosteal flaps to perform the tooth extraction and achieved primary closure, except two studies that did not aim for primary closure (Iasella et al. 2003; Serino et al. 2003; Serino et al. 2008) (Table 1). Flapless extraction of the teeth was performed in four studies (Hoad-Reddick et al. 1994; Aimetti et al. 2009; Crespi et al. 2009; Oghli & Steveling 2010) with two studies aiming to primary closure through a soft tissue autograft (Crespi et al. 2009; Oghli & Steveling 2010). Four studies reported on the socket status after the extraction, with two studies reporting full integrity of the socket walls (Barone et al. 2008) or minimum buccal bone loss (Froum et al. 2002) (≤2 mm), whereas two studies (Fiorellini et al. 2005; Crespi et al. 2009) reported the absence of the buccal bone wall.

Different biomaterials were used in the test groups of the studies included in the review. Test treatment could be either graft alone (Hoad-Reddick et al. 1994; Lekovic et al. 1997; Lekovic et al. 1998; Bolouri et al. 2001; Froum et al. 2002; Iasella et al. 2003; Fiorellini et al. 2005; Barone et al. 2008; Aimetti et al. 2009; Crespi et al. 2009; Casado et al. 2010; Oghli & Steveling 2010) or membrane alone (Lekovic et al. 1997; Lekovic et al. 1998; Casado et al. 2010), a combination of both (Iasella et al. 2003; Barone et al. 2008; Casado et al. 2010) or a combination of graft and autogenous soft tissue graft (Crespi et al. 2009 and Oghli & Steveling 2010).

Methods of measurement

The changes in the primary outcomes were assessed by clinical and radiographical examinations, as well as, by evaluation of cast models. Hoad-Reddick et al. (1994), Fiorellini et al. (2005) and Crespi et al. (2009) used radiographs (orto-pantomography, CT scans, and periapical X-rays respectively). Lekovic et al. (1998), Lekovic et al. (1997), Serino et al. (2003), Barone et al. (2008), Serino et al. (2008) and Aimetti et al. (2009) assessed directly the bone changes at a re-entry surgery. Within this group, four studies (Serino et al. 2003; Serino et al. 2008; Barone et al. 2008; Aimetti et al. 2009) used an acrylic stent to allow for reproducible measurements, whereas two studies (Lekovic et al. 1997; Lekovic et al. 1998) utilized titanium pins (Table 1). Two studies used clinical measurements combined with acrylic stents (Iasella et al. 2003; Casado et al. 2010), whereas other two (Lekovic et al. 1997; Oghli & Steveling 2010) used cast models to evaluate the dimensional changes between baseline and the end of the investigation. The most frequent method was the mid-buccal measurement.

Quality assessment

Data from the quality assessment are reported in Table 2. All studies except one randomized controlled trial (Barone et al. 2008) and two controlled trials (Serino et al. 2003; Serino et al. 2008) were considered to have a high risk of bias.

Study outcomes. Descriptive analyses of the changes in the hard tissue dimensions

Table 3a depicts the differences in the bone crest height between baseline and the end of the investigations reported for test and control groups. Eleven of 14 studies evaluated the changes in the height of the bone crest comparing the socket preservation therapy with sockets left to heal spontaneously (Hoad-Reddick et al. 1994; Lekovic et al. 1997; Lekovic et al. 1998; Iasella et al. 2003; Barone et al. 2008; Aimetti et al. 2009; Crespi et al. 2009). Overall, the control groups demonstrated a mean vertical bone loss that ranged from −0.3 to −3.75 mm, whereas in the test groups, results were more heterogeneous demonstrating mean vertical bone changes ranging from −2.48 to 1.3 mm.

Differences between test and control groups, as reported by the authors, were statistically significant in four studies included in the systematic review (Lekovic et al. 1997; Lekovic et al. 1998; Iasella et al. 2003; Fiorellini et al. 2005). Lekovic et al. (1997) evaluated the ridge bone dimensional changes at re-entry using titanium pins after GBR with e-PTFE membranes covering the socket walls in submerged healing or an untreated socket control. The same research group used a similar experimental design to assess GBR with a biabsorbable membrane (Lekovic et al. 1998). Results from both studies demonstrated statistically significant differences ($P < 0.0005$) in favour of the GBR approach demonstrating a greater vertical resorption in the control group.

Iasella et al. (2003) with a similar design, although evaluating the bone dimensional changes at re-entry using an acrylic stent, assessed the efficacy of filling the sockets with freeze-dried bone allografts + tetracycline and a collagen membrane in semi-submerged healing. Differences with the untreated control group were statistically significant for the mid-buccal as well as mesial and distal locations ($P < 0.05$), but not for the mid-lingual locations.

Fiorellini et al. (2005) evaluated the ridge height changes after therapy by computed tomography reporting statistically significant differences ($P = 0.007$) when comparing the use of an absorbable collagen sponge (ACS) soaked with 1.50 mg/ml rhBMP-2 with the untreated control group.

Table 3b depicts the differences in the width of the bone crest between baseline and the end of the evaluation period reported for test and control groups in eight of the 14 studies (Lekovic et al. 1997; Lekovic et al. 1998; Iasella et al. 2003; Fiorellini et al. 2005; Barone et al. 2008; Aimetti et al. 2009; Casado et al. 2010; Oghli & Steveling 2010). Overall, the control groups demonstrated a mean horizontal bone loss that ranged from −0.16 to −4.50 mm, whereas in the test groups, results were more homogeneous demonstrating mean horizontal bone changes ranging from 3.25 to −2.50 mm. The differences between test and control groups were statistically significant in five studies.

Changes in soft tissue dimensions

Mean dimensional changes of soft tissues are presented in Table 4. Two studies evaluated the dimensional changes of the overall alveolar ridge contour combining the changes of hard and soft tissues (Lekovic et al. 1997; Oghli & Steveling 2010). Whereas Iasella et al. (2003) evaluated the changes in gingival thickness at different locations of the crest, Lekovic et al. (1997) measured these changes on cast models, both reporting significantly less vertical and horizontal resorption in the test group ($P = 0.001$). Oghli & Steveling (2010), however, could not demonstrate differences between using a collagen sponge with/without gentamicine plus a circular soft tissue graft to protect the wound, with the untreated control socket ($P = 0.07$). Iasella et al. (2003) also evaluated the gingival thickness with an ultrasonic device at buccal and lingual/palatal locations. Differences between the ridge preservation therapy and the untreated control were only statistically significant for buccal sites.

Implant-related outcomes

Table 5 shows the studies with reported outcomes on implant placement after tooth extraction (Hoad-Reddick et al. 1994; Bolouri et al. 2001; Froum et al. 2002; Iasella et al. 2003; Serino et al. 2003; Fiorellini et al. 2005; Serino et al. 2008; Crespi et al. 2009; Aimetti et al. 2009; Casado et al. 2010). Two studies (Barone et al. 2008; Aimetti et al. 2009) reported the placement of implants after 3 and ≥7 months without providing any details on further soft or hard tissues augmentation procedures. Two studies (Serino et al. 2003; Serino et al. 2008) reported the placement of dental implants after 6 and 3 months of healing respectively, specifying that all implants achieved good primary stability in both test and control groups. In one study (Fiorellini et al. 2005), implants were inserted after 4 months of healing and statistically significant differences were reported in favour of the test group 1 (ACS+ 1.50 mg/ml rhBMP-2) when compared to test group 2 (ACS+ 0.75 mg/ml rhBMP-2) and the control treatment, in regards to the number of secondary augmentation surgeries needed, although no further details were provided in regards to the number and type of these procedures. In the test 1 sites, 56.25% demonstrated adequate bone volume for implant placement, whereas the corresponding figures in test 2 and control groups were 25% and 12.5% respectively.

Histological outcomes

Nine studies evaluated histologically, the type of bone healing after 3 to ≥7 months from the tooth extraction. Biopsies were taken using a trephine before the osteotomy preparation for implants insertion. Serial decalcified sections were analysed under light microscopy for qualitative and quantitative histo-morphometrical analysis. Fiorellini et al. (2005) and Casado et al. (2010) provided descriptive histological observations, whereas Froum et al. (2002), Barone et al. (2008), Serino et al. (2008), Aimetti et al. (2009) and Crespi et al. (2009) calculated fractions of bone mineral, connective tissue and residual graft material at different apico-coronal levels of the socket. Serino et al. (2003) described the fraction of bone mineral, whereas Iasella et al. (2003) evaluated fractions of cellular/acellular and trabecular bone.

Meta-analysis

Nine of the 14 included studies reported similar comparisons and could be grouped in the meta-analyses (Figs 2 and 3). The primary outcome variables, defined as bone dimensional changes (height and width of alveolar process) were analysed and compared between the test (socket preservation therapy) and control group (spontaneous socket healing). None of the other secondary outcome variables could be grouped in meta-analysis.

Seven studies were grouped in the meta-analysis for bone height as the outcome variable (Fig. 2). Two studies Fiorellini et al. (2005), Crespi et al. (2009) evaluated two different preservation procedures, consequently, each test socket preservation procedure vs. the control group was considered as an independent study in the meta-analysis. As there was a high heterogeneity among the studies ($I^2 = 95.2\%$; $\text{Tau}^2 = 0.639$; χ^2 P-value <0.001), we selected the random effect model for the statistical evaluation. A statistically significant greater reduction in bone height for control groups was demonstrated when compared to the test groups (WMD = −1.47 mm; 95% CI [−1.982, −0.953]; $P < 0.001$; heterogeneity: $I^2 = 13.1\%$; χ^2 P-value = 0.314). Due to this high heterogeneity, several subgroup analyses were performed based on the surgical protocol used for the socket preservation (flapless/flapped, barrier membrane/no membrane, primary intention healing/no primary healing) and on the measurement method utilized to evaluate the morphological changes.

None of the subgroup analyses achieved a non-significant heterogeneity value. A tendency towards greater weighted mean differences in favour of the test groups was observed with flapless surgical protocol, no membrane, primary intention healing and with use of X-rays as measurement method (Table 6). The meta-regression analysis failed to encounter statistically significant differences among subgroups (data not shown).

Seven studies were grouped in the meta-analysis on bone width as outcome variable (Fig. 3). In two studies, more than one test group were evaluated in comparison with the control, and therefore they were considered as independent (Serino et al. 2008; Oghli & Steveling 2010). Also one study presented data measured with two different outcome measurements (cast models and re-entry surgery) and they were also included independently in the analyses (Lekovic et al. 1997). As there was a high heterogeneity detected among studies ($I^2 = 99.0\%$; $\text{Tau}^2 = 2.997$; χ^2 P-value <0.001), the random effect model was selected for the analysis. The results showed a statistically significant greater reduction in bone width for control groups when compared to the socket preservation thera-

Table 3a. **Outcome variables: changes in bone height, expressed as mean (mm)**

	Vertical changes of the alveolar crest						
Publication (#)	Interventions/groups	Measurement method	Surgical considerations	Control	Test	Diff.	*P*-value
Hoad-Reddick et al. (1994) (1)	Test: Hydroxyapatite granules Control: No socket filling	Lateral cephalographs and dental pantomograms	Flapless Primary closure: NO Type of socket: NA	2.42	0.65	ND:1.77	NA
Lekovic et al. (1997); _1 (2)	Test: ePTFE® membrane Control: No socket filling	Reentry surgery	Flap Primary closure: YES Type of socket: NA	−1.2	−0.5	Mb: −0.7	0.001
Lekovic et al. (1998) (3)	Test: membrane of glycolide and lactide polimers Control: No socket filling	Reentry surgery	Flap Primary closure: YES Type of socket: NA	−1.5	−0.38	Mb: −1.12	≤0.0005
Serino et al. (2003) (6)	Test: Sponge of polylactide–polyglycolide acid Control: No socket filling	Reentry surgery + stent	Flap Primary closure: YES Type of socket: NA	−0.8	1.3	Mb: −2.1	NA
Iasella et al. (2003) (7)	Test: FDBA + tetracycline + collagen mombrane Control: No socket filling	Clinical + stent	Flap Primary closure: NO Type of socket: NA	−0.9	1.3	Mb: −2.2	<0.05
Fiorellini et al. (2005)_1 (8)	Test 1: 0.75 mg/ml rhBMP/ACS Control: No socket filling	CT scan	Flap Primary closure: YES Type of socket: 3-wall (no buccal wall)	−1.17	−0.62	ND: −0.55	NS
Fiorellini et al. (2005)_2 (8)	Test 2: 1.50 mg/ml rhBMP/ACS Control: No socket filling	CT scan	Flap Primary closure: YES Type of socket: 3-wall (no buccal wall)	−1.17	−0.02	ND: −1.15	0.007
Barone et al. (2008) (9)	Test: Corticocancellous porcine bone + collagen membrane Control: No socket filling	Reentry + stent	Flap Primary closure: YES Type of socket: 4-wall	−3.6	−0.7	Mb: −2.9	NA
Barone et al. (2008) (9)	Test: Corticocancellous porcine bone + collagen membrane Control: No socket filling	Reentry + stent	Flap Primary closure: YES Type of socket: 4-wall	−3.6	−0.7	Mb: −2.9	NA
Aimetti et al. (2009) (11)	Test: Medical-grade calcium sulphate hemihydrate Control: No socket filling	Reentry + stent	Flapless Primary closure: NO Type of socket: NA	−1.2	−0.5	Mb: −0.7	NA
Crespi et al. (2009)_1 (12)	Test 1: Magnesium-enriched hydroxyapatite Control: No socket filling	Periapical X-rays	Flapless Primary closure: YES (tissue graft) Type of socket: 3-wall(no buccal wall)	−3.75	−0.48	ND: −3.27	NA
Crespi et al. (2009)_2 (12)	Test 2: Calcium sulphate Control: No socket filling	Periapical X-rays	Flapless Primary closure: YES (tissue graft) Type of socket: 3-wall(no buccal wall)	−3.75	−2.48	ND: −1.27	NA

Abbreviations of the interventions: *P*-values of the statistical analysis of the intergroup differences in the changes between baseline and end of the study. SD of the means of the intergroup differences in the changes between baseline and end of the study. NS, not statistically significant; NA, data not available; Mb, midbuccal; ND, not defined site; ACS, absorbable collagen sponge; RhBMP, recombinant human BMP-2; e-PTFE, expanded polytetrafluoroethylene; FDBA, freeze-dried bone allograft.

Table 3b. **Outcome variables: changes in bone width, expressed as mean (mm)**

	Horizontal changes of the alveolar crest						
Publication (#)	Interventions/groups	Measurement method	Surgical considerations	Control	Test	Diff.	*P*-value
Lekovic et al. (1997)_2 (2)	Test: ePTFE® membrane Control: No socket filling	Reentry surgery	Flap Primary closure: YES Type of socket: NA	−4.4	−1.8	−2.6	0.002
Lekovic et al. (1998) (3)	Test: membrane of glycolide and lactide polimers Control: No socket filling	Reentry surgery	Flap Primary closure: YES Type of socket: NA	−4.56	−1.31	−3.25	<0.00001
Iasella et al. (2003) (7)	Test: FDBA + tetracycline + collagen mombrane Control: No socket filling	Clinical + stent	Flap Primary closure: NO Type of socket: NA	−2.6	−1.2	−1.4	<0.05
Fiorellini et al. (2005)_1 (8)	Test 1: 0.75 mg/ml rhBMP/ACS Control: No socket filling	CT scan	Flap Primary closure: YES Type of socket: 3-wall(no buccal wall)	0.57	1.76	−1.19	NS
Fiorellini et al. (2005)_2 (8)	Test 2: 1.50 mg/ml rhBMP/ACS Control: No socket filling	CT scan	Flap Primary closure: YES Type of socket: 3-wall (no buccal wall)	0.57	3.27	−2.7	0.000
Barone et al. (2008) (9)	Test: Corticocancellous porcine bone + collagen membrane Control: No socket filling	Reentry + stent	Flap Primary closure: YES Type of socket: 4-wall	−4.5	−2.5	−2	NA
Aimetti et al. (2009) (11)	Test: Medical-grade calcium sulphate hemihydrate Control: No socket filling	Reentry + stent	Flapless Primary closure: NO Type of socket: NA	−3.2	−2	−1.2	NA
Casado et al. (2010)_1 (13)	Test 1: bovineBMP + bOM Control: No socket filling	Clinical + stent	Flap Primary closure: YES Type of socket: NA	−0.16	3.05	−3.21	NA
Casado et al. (2010)_2 (13)	Test 2: bovineBMP+bOM+resorbable membrane Control: No socket filling	Clinical + stent	Flap Primary closure: YES Type of socket: NA	−0.16	2.42	−2.58	NA
Casado et al. (2010)_3 (13)	Test 3: resorbable membrane Control: No socket filling	Clinical + stent	Flap Primary closure: YES Type of socket: NA	−0.16	2.9	−3.06	NA
Oghli & Steveling (2010)_1 (14)	Test 1: Autogenous soft tissue graft + collagen plug2 Control: No socket filling	Cast	Flapless Primary closure: YES (soft tissue graft) Type of socket: NA	−0.3	−0.8	0.5	0.001
Oghli & Steveling (2010)_2 (14)	Test 2: Autogenous soft tissue graft + collagen matrix with gentamicin Control: No socket filling	Cast	Flapless Primary closure: YES (soft tissue graft) Type of socket: NA	−0.3	−0.1	−0.2	0.07

Abbreviations of the interventions: *P*-values of the statistical analysis of the intergroup differences in the changes between baseline and end of the study. NS, not statistically significant; NA, data not available; bOM, bovine organic matrix.

Table 4. **Outcome variables. Soft tissue changes**

	Soft tissue changes						
Publication (#)	Interventions/groups	Measurement method	Surgical considerations	Control	Test	Diff.	*P*-value
Lekovic et al. (1997)_1 (2)	Test: ePTFE® membrane Control: No socket filling	Cast	Flap; primary closure: YES Type of socket: NA Vertical measurements	−1	−0.2	Mb: −0.8	0.001
			Flap; Primary closure: YES Type of socket: NA Horizontal measurements	−4.2	−1.8	−2.4	0.001
Iasella et al. (2003) (7)	Test: FDBA + tetracycline + collagen mombrane Control: No socket filling	Ultrasonic metre	Flap Primary closure: NO Type of socket: NA	0.4	−0.1	0.5	<0.05
Oghli & Steveling (2010)_1 (14)	Test 1: Autogenous soft tissue graft + collagen plug2 Control: No socket filling	Cast	Flapless Primary closure: YES (soft tissue graft) Type of socket: NA Horizontal measurements	−0.3	−0.8	0.5	0.001
Oghli & Steveling (2010)_2 (14)	Test 2: Autogenous soft tissue graft + collagen matrix with gentamicin Control: No socket filling	Cast	Flapless Primary closure: YES (soft tissue graft) Type of socket: NA Horizontal measurements	−0.3	−0.1	−0.2	0.07

P-values of the statistical analysis of the intergroup differences in the changes between baseline and end of the study.

pies (WMD = −1.830 mm; 95% CI [−2.947, −0.732]; $P = 0.001$; heterogeneity: $I^2 = 0\%$; χ^2 *P*-value = 0.837). Due to the high heterogeneity initially detected among the studies, several subgroup analyses were performed. None of the subgroup analyses achieved a non-significant heterogeneity value for all groups. A tendency towards greater weighted mean differences in favour of test groups was observed with the use of membranes, a flapped surgical protocol, primary intention healing and with CT as outcome measurement (Table 7). The meta-regression analyses demonstrated a statistically significant difference only in the flapless/flapped subgroup (meta-regression; slope = 2.26; 95% CI [1.01; 3.51]; $P = 0.003$).

Publication bias and sensitivity analyses

No publication bias was detected for changes in bone height ($P = 0.352$; Egger's test), nor in bone width ($P = 0.357$; Egger's test). The sensitivity analysis to assess the effect of individual studies on the summary estimates of the meta-analysis showed that the exclusion of single studies did not substantially alter any estimates. In terms of bone height changes, the greater change in WMD could be attributed to Crespi et al. (2009) (−23.25%) (Table 8). In regards to bone width, the sensitivity analyses identified three potential studies as responsible for most of the heterogeneity (Fiorellini et al. [2005] [−10.49%], Lekovic et al. [1998] [−11.46%] and Oghli & Steveling [2010] [15.15% and 10.79%]) (Table 9).

Discussion

Socket preservation therapies have been proposed with the aim of maintaining the hard and soft tissue dimensions of the alveolar ridge that are partially lost after tooth extraction as part of the natural physiological healing process. This objective is particularly pursued in preparation for dental implant installation to have the best bone availability for successful implant prosthesis (Tarnow & Eskow 1996). Unfortunately, there are very few well-designed clinical studies evaluating the efficacy of these therapeutic procedures and the potential benefit of the different techniques/materials used is still debatable.

The present systematic review seeks to provide scientific evidence on the existing RCTs and CTs evaluating different surgical protocols aimed for preserving the bone of the alveolar ridge after tooth extraction. The primary outcome variables selected were the vertical and horizontal hard and soft tissue dimensional changes of the bone crest at least 3 months after the tooth extraction. Overall, the results from the meta-analysis demonstrated statistically significant higher alveolar bone crest preservation in both height and width in the test groups (interventions for ridge preservation) when compared with the healing of the untreated control socket. In regards to the changes in bone height, the overall WMD difference between test and control groups amounted to 1.47 mm. Hence, the results from the meta-analysis suggest that the use of socket preservation therapies limits the dimensional changes (vertical and horizontal) of the alveolar ridge after tooth extraction. These data are in agreement with a recent similar systematic review also assessing the influence and potential benefit of socket preservation procedures after tooth extraction in non-molar regions of the mouth (Ten Heggeler et al. 2010). These authors concluded, however, that although a benefit of such techniques could be observed, vertical and horizontal bone loss can be expected.

These results must be evaluated with caution as the quality assessment of the selected studies demonstrated that all but two studies (Barone et al. 2008; Serino et al. 2008) had a high potential risk of bias. Furthermore, the use of different biomaterials and surgical techniques has been combined in this meta-analysis, as well as the use of different types of sockets (single/multiple, position in the mouth and number of residual bony walls), different reason of tooth extraction and different methods of evaluation. This lack of con-

Table 5. **Implant-related outcomes**

	Implant-related outcomes							
Publication	Interventions/groups	Implant placement	Time after extraction	Control	Test	Secondary augmentation surgery	Histology	Restoration
Hoad-Reddick et al. (1994) (1)	Test: Hydroxyapatite granules Control: No socket filling	No	–	–	–	–	No	NA
Bolouri et al. (2001) (4)	Test: Bioplant HTR Control: No socket filling	No	–	–	–	–	No	NA
Froum et al. (2002) (5)	Test 1: Bioactive glass Test 2: DFDBA Control: No socket filling	No	–	–	–	–	Yes	NA
Serino et al. (2003) (6)	Test: Sponge of polylactide–polyglycolide acid Control: No socket filling	Yes	6 months	All sites	All sites	NA	Yes	NA
Iasella et al. (2003) (7)	Test: FDBA + tetracycline + collagen mombrane Control: No socket filling	Yes	4–6 months	–	–	–	Yes	NA
Fiorellini et al. (2005) _1 (8)	Test 1: 0.75 mg/ml rhBMP/ACS Control: No socket filling	Yes	4 months	Yes 12.5% adequate bone volume	Yes 25% adequate bone volume	10	Yes	NA
Fiorellini et al. (2005) _2 (8)	Test 2: 1.50 mg/ml rhBMP/ACS Control: No socket filling	Yes	4 months	Yes 12.5% adequate bone volume	Yes 56.25% adequate bone volume	3 $P < 0.05$ test 1 vs. test 2 and control (11)		NA
Barone et al. (2008) (9)	Test: Corticocancellous porcine bone + collagen membrane Control: No socket filling	Yes	≥7 months	NA	NA	NA	Yes	NA
Serino et al. (2008) (10)	Test: Sponge of polylactide–polyglycolide acid Control: No socket filling	Yes	3 months	All sites	All sites	NA	Yes	NA
Aimetti et al. (2009) (11)	Test: Medical-grade calcium sulphate hemihydrate Control: No socket filling	Yes	3 months	NA	NA	NA	Yes	NA
Crespi et al. (2009) (12)	Test 1: Magnesium-enriched hydroxyapatite Test 2: Calcium sulphate Control: No socket filling	Yes	3 months	–	–		Yes	NA
Casado et al. (2010) (13)	Test 1: bovineBMP + bOM Test 2: bovineBMP + bOM + resorbable membrane Test 3: resorbable membrane Control: No socket filling	No	–	–	–	–	Yes	NA

Abbreviations of the interventions: NA, data not available; RCT, randomized clinical trial; ACS, absorbable collagen sponge; e-PTFE, expanded polytetrafluoroethylene; BMP, bone morphogenetic protein; bOM, bovine organic matrix; CT scan, computerized tomography scanner; RhBMP, recombinant human BMP-2; FDBA, freeze-dried bone allograft; DFDBA, demineralized freeze-dried bone allograft.

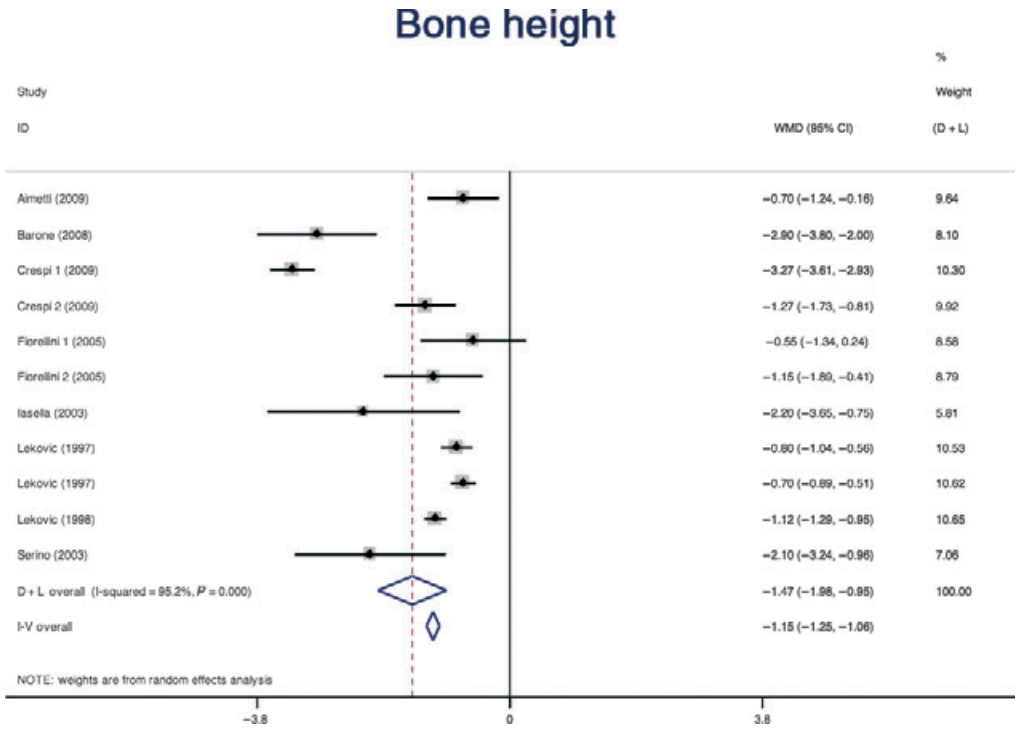

Fig. 2. Meta-analysis: changes in bone height.

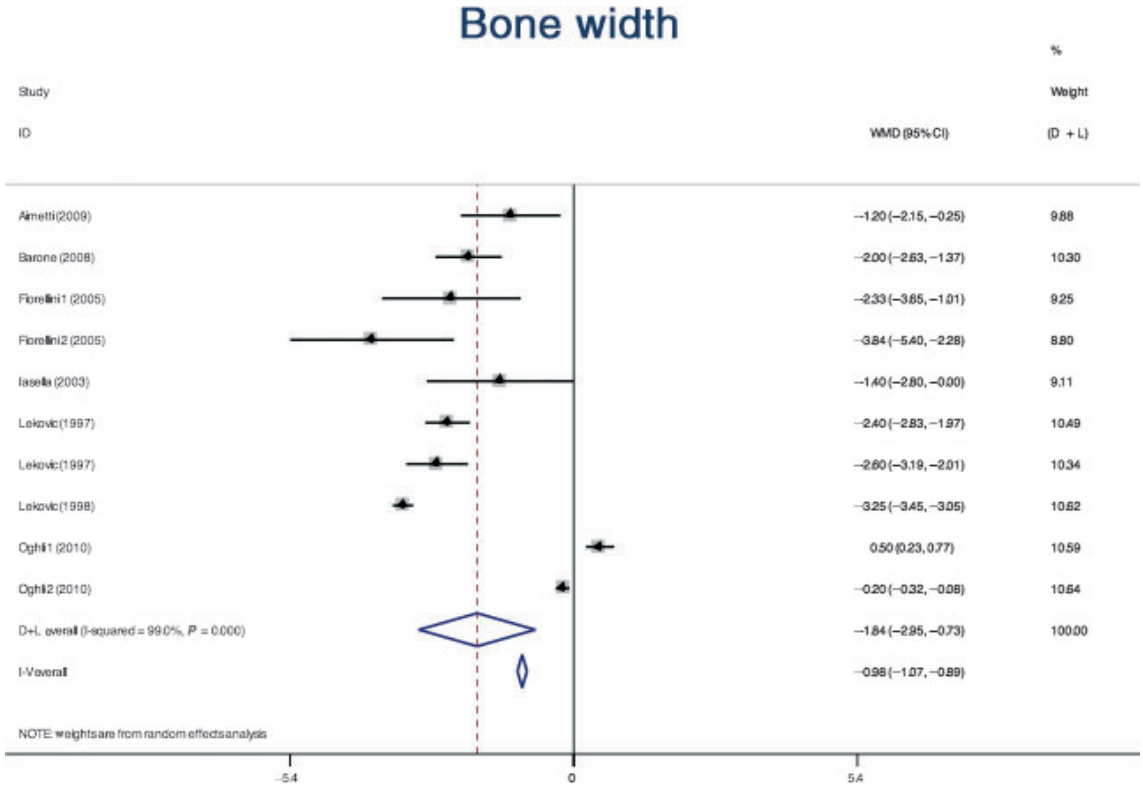

Fig. 3. Meta-analysis: changes in bone width.

sistency and standardization, in spite of the lack of publication bias, may have contributed to the high heterogeneity of the results. In fact, in terms of vertical bone height changes, 23.25% of this effect was attributed to the study by Crespi et al. (2009) utilizing magnesium-enriched hydroxyapatite combined with the closing of the socket with a soft tissue autograft. This individual study,

Table 6. **Meta-analyses by subgroups for changes in bone height**

	WMD	95% CI	*P*-value	*I*-squared
Membrane				
(a) No	−1.511	−2.583; −0.440	0.006	95.2%
(b) Yes	−1.192	−1.589; −0.834	0.000	87.9%
Flap				
(a) No	−1.756	−3.400; −0.112	0.036	97.6%
(b)Yes	−1.179	−1.516; −0.842	0.000	81.7%
Primary closure				
(a) No	−1.293	−2.730; 0.145	0.078	72.4%*
(b) Yes	−1.506	−2.077; −0.935	0.000	96.1%
Outcome variable				
(a) Reentry + stent	−1.861	−3.606; −0.386	0.013	89.3%
(b) X-rays	−2.276	−4.236; −0.316	0.023	97.9%
(c) CT	−0.866	−1.453; −0.279	0.004	14.5%
(d) Clinical (stent)	−2.200	−3.649; −0.751	0.003	NA
(e) Cast	−0.800	−1.039; −0.561	0.000	NA
(f) Reentry surgery	−0.912	−1.324; −0.501	0.000	90.6

NA, not applicable, as only one study was included in the subgroup.
*Non-statistically significant differences.

Table 7. **Meta-analyses by subgroups for changes in bone width**

	WMD	95% CI	*P*-value	*I*-squared
Membrane				
(a) No	−0.982	−1.738; −0.227	0.011	93.3%
(b) Yes	−2.465	−3.074; −1.856	0.000	86.6%
Flap				
(a) No	−0.148	−0.788; 0.492	0.650	92.6%
(b)Yes	−2.563	−3.101; −2.795	0.000	81.2%
Primary closure				
(a) No	−1.263	−2.049; −0.478	0.002	0%
(b) Yes	−1.968	−3.217; −0.732	0.002	99.2%
Outcome variable				
(a) Reentry + stent	−1.682	−2.449; −0.914	0.000	47.0%*
(b) CT	−3.026	−4.501; −1.551	0.000	52.3%*
(c) Clinical (stent)	−1.400	−2.797; −0.003	0.050	NA
(d) Cast	−0.682	−1.841; 0.476	0.248	98.4%
(e) Reentry surgery	−2.986	−3.612; −2.361	0.000	76.2%

CT, computerized tomography; NA, not applicable, as only one study was included in the subgroup.
*Non-statistically significant differences.

Table 8. **Sensitivity analyses of the outcome variable bone heigth changes made with random effect model**

	Random estimation			Heterogeneity	
Study omitted	WMD	95% CI	WMD change (%)	*I*-squared (%)	*P*-value
Aimetti (2009)	−1.55	−2.10; −1.00	5.70	12.44	0.328
Barone (2008)	−1.34	−1.86; −0.82	−8.70	4.85	0.396
Crespi_1 (2009)	−1.13	−1.41; −0.84	−23.25	49.25	0.038
Crespi_2 (2009)	−1.49	−2.05; −0.93	1.69	16.14	0.295
Fiorellini_1 (2005)	−1.55	−2.10; −1.01	5.93	12.6	0.327
Fiorellini_2 (2005)	−1.50	−2.05; −0.95	2.18	19.07	0.268
Iasella (2003)	−1.42	−1.95; −0.89	−3.07	18.87	0.269
Lekovic_1 (1997)	−1.55	−2.15; −0.96	5.83	0	0.447
Lekovic_2 (1997)	−1.57	−2.17; −0.96	6.69	0	0.465
Lekovic (1998)	−1.52	−2.19; −0.86	3.89	0	0.561
Serino (2003)	−1.42	−1.95; −0.89	−3.27	19.07	0.268
None	−1.47	−1.98; −0.95	0	13.71	0.314

Crespi_1: Magnesium-enriched hydroxyapatite vs. no socket filling.
Crespi_2: Calcium sulphate vs. no socket filling.
Fiorellini_1: 0.75 mg/ml rhBMP/ACS vs. no socket filling.
Fiorellini_2: 1.5 mg/ml rhBMP/ACS vs. no socket filling.
Lekovic_1: outcome measured in cast model.
Lekovic_2: outcome measured in reentry surgery.

reporting mean differences between test and control groups of 3.27 mm, however, only selected sockets without full integrity of their bone walls, usually lacking the buccal cortical bone. This negative prognostic factor for bone regeneration during undisturbed socket healing may in part, have contributed to the bigger effect of the socket preservation therapy, compared with the other studies included in the meta-analysis. Likewise, in regards to the changes in bone width, three studies provided the bigger heterogeneity in the meta-analysis, contributing to 15.15%, 11.46% and 10.49% of the overall change respectively (Lekovic et al. 1998; Fiorellini et al. 2005; Oghli & Steveling 2010). In particular, on the negative effect side, Oghli & Steveling (2010) that utilized a collagen sponge as socket filler reported a higher bone horizontal resorption in the test group. Apart from the null efficacy of the filler used, the fact that cast models were used to measure these horizontal changes may have prevented an accurate evaluation of the true dimensions of the alveolar crest. In contrast, Fiorellini et al. (2005) observed a difference of 3.85 mm in bone width when comparing the use of 1.50 mg/ml rhBMP/ACS vs. the control socket.

The factors that may have contributed to the obtained outcomes may be categorized as: (1) the clinical conditions of the socket site, i.e. integrity/non-integrity of the socket bone walls, dimension and presence/absence of adjacent teeth; (2) the surgical protocol utilized, i.e. flapped/flapless surgery or primary flap closure/secondary intention healing; (3) the biomaterial used, i.e. membrane/no membrane, type of graft material and (4) the type of evaluation method utilized. In an attempt to assess the influence of each of these factors, a subgroup analysis was performed, as well as meta-regression. The subgroup analysis of flapped/flapless surgery demonstrated a minor influence in the vertical resorption process, although it showed a significant difference in favour of the flapped group in regards to the ridge horizontal dimensional changes. When comparing the relative efficacy of using barrier membranes and/or grafts, while the use of membranes alone reported more vertical bone change than the use of grafts alone, membranes obtained better results than grafts (either alone or the combination of membrane and graft) in terms of horizontal bone changes. The subgroup analysis to assess the influence of flap closure demonstrated a slight tendency towards less bone loss in the horizontal direction when the sockets healed by

Table 9. **Sensitivity analyses of the outcome variable bone width made with random effect model**

Study omitted	Random estimation		WMD change (%)	Heterogeneity	
	WMD	95% CI		*I*-squared (%)	*P*-value
Aimetti (2009)	−1.91	−3.09; −0.73	3.84	0	0.785
Barone (2008)	−1.82	−3.01; −0.63	−0.94	0	0.780
Fiorellini_1 (2005)	−1.79	−2.96; −0.62	−2.71	0	0.773
Fiorellini_2 (2005)	−1.65	−2.80; −0.49	−10.49	0	0.875
Iasella (2003)	−1.88	−3.05; −0.72	−2.41	0	0.772
Lekovic_1 (1997)	−1.77	−2.97; −0.58	−3.47	0	0.797
Lekovic_2 (1997)	−1.75	−2.93; −0.57	−4.73	0	0.792
Lekovic (1998)	−1.63	−2.46; −0.80	−11.46	0	0.381
Oghli_1 (2010)	−2.12	−3.35; −0.88	15.15	0	0.953
Oghli_2 (2010)	−2.04	−3.31; 0.77	10.79	0	0.903
None	−1.84	−2.95; −0.73	0	0	0.837

WMD, weighted mean differences; CI, confidence interval.
Fiorellini_1: 0.75 mg/ml rhBMP/ACS vs. no socket filling.
Fiorellini_2: 1.5 mg/ml rhBMP/ACS vs. no socket filling.
Lekovic_1: outcome measured in cast model.
Lekovic_2: outcome measured in reentry surgery.
Oghli_1: autogenous soft tissue graft + collagen plug vs. no socket filling.
Oghli_2: autogenous soft tissue graft + collagen matriz with gentamicin vs. no socket filling.

primary intention. In terms of the evaluation methods used, only the radiographic evaluation demonstrated significant vertical (X-ray) and horizontal (CT) changes when comparing test and control groups. The use of cast models and re-entry procedures was not able to demonstrate such significant differences.

The results of the meta-regression analysis showed that the surgical procedure (flapped/flapless) was the most important factor influencing the results. Flapped surgical procedures demonstrated a significantly lesser horizontal resorption of the socket, when compared to flapless surgeries (meta-regression; slope = 2.26; 95% CI [1.01; 3.51]; $P = 0.003$). These results may be due to the importance of achieving full closure and first intention healing, mainly when the socket is filled with a biomaterial or covered with a barrier membrane. The effect of raising a flap on the healing process of the socket after tooth extraction is still controversial with results from experimental models reporting less pronounced bone remodelling of the alveolar ridge after tooth extraction with a flapless approach (Fickl et al. 2008a, 2008b) or when using socket preservation procedures (Fickl et al. 2008a, 2008b; Blanco et al. 2010) and when placing implants immediately after the tooth extraction (Blanco et al. 2010). Other studies with a similar experimental design, however, have failed to encounter significant bone dimensional differences between flapped and flapless tooth extractions (Araujo & Lindhe 2009).

The changes in the horizontal dimension have been the ones benefited most by the socket preservation techniques evaluated in this systematic review. Precisely bone loss in a horizontal dimension is the most important consequence of tooth extraction during the first 3–6 months of healing (Schropp et al. 2003). In this meta-analysis, the bone horizontal changes in the control group were heterogeneous, ranging from −0.16 to −4.50 mm. These differences may be due to different factors, such as the socket location and the thickness of the socket walls. Recent studies in humans have shown the influence of the location and the thickness of the socket walls in the ensuing modelling and remodelling processes after tooth extraction (Ferrus et al. 2010; Januario et al. 2011).

One major limitation of this systematic review is that no meta-analyses could be performed on implant-related outcomes, due to the lack of sufficient data. This fact is important as there is no clear evidence that the occurrence of bone resorption after tooth extraction may significantly limit the placement of dental implants. In fact, one study (Serino et al. 2008) reported that implants could be placed in all patients independently of the group of treatment. The positive influence of the socket preservation therapy may be attributed more to achieving enhanced restorative and aesthetic outcomes, as well as better maintenance of healthy peri-implant soft tissues. These possible influences were not evaluated in the reviewed studies. Only one study assessed the possible influence of the socket preservation therapy on the need of further augmentation therapies and in fact, the test group reported reduced needs of bone augmentation (Fiorellini et al. 2005).

In conclusion, the results from this systematic review and meta-analysis have shown that although some degree of bone modelling and remodelling will occur after tooth extraction, different ridge preservation procedures resulted in significantly less vertical and horizontal contraction of the alveolar bone crest. The obtained results, however, could not indicate which is the type of surgical procedure or biomaterial most suitable for this clinical indication, although the use of barrier membranes, a flap surgical procedure and full flap closure demonstrated better results. There are limited data, however, on the possible influence of these therapies on the long-term outcomes of implant therapy.

References

Aimetti, M., Romano, F., Griga, F.B. & Godio, L. (2009) Clinical and histologic healing of human extraction sockets filled with calcium sulfate *The International Journal of Oral & Maxillofacial Implants* **24**: 902–909.

Amler, M.H., Johnson, P.L. & Salman, I. (1960) Histological and histochemical investigation of human alveolar socket healing in undisturbed extraction wounds. *Journal of the American Dental Association* **61**: 32–44.

Araujo, M.G. & Lindhe, J. (2005) Dimensional ridge alterations following tooth extraction: an experimental study in the dog. *Journal of Clinical Periodontology* **32**: 212–218.

Araujo, M., Linder, E., Wennstrom, J. & Lindhe, J. (2008) The influence of Bio-Oss Collagen on healing of an extraction socket: an experimental study in the dog. *The International journal of periodontics & restorative dentistry* **28**: 123–135.

Araujo, M.G. & Lindhe, J. (2009) Ridge alterations following tooth extraction with and without flap elevation: an experimental study in the dog. *Clinical oral implants research* **20**: 545–549.

Araujo, M.G. & Lindhe, J. (2011) Socket grafting with the use of autologous bone: an experimental study in the dog. *Clinical oral implants research* **22**: 9–13.

Artzi, Z., Tal, H. & Dayan, D. (2000) Porous bovine bone mineral in healing of human extraction sockets. Part 1: Histomorphometric evaluations at 9 months. *Journal of Periodontology* **71**: 1015–1023.

Barone, A., Aldini, N.N., Fini, M., Giardino, R., Calvo Guirado, J.L. & Covani, U. (2008) Xenograft versus extraction alone for ridge preservation

after tooth removal: a clinical and histomorphometric study *Journal of Periodontology* **79**: 1370–1377.

Becker, W., Dahlin, C., Lekholm, U., Bergstrom, C., van Steenberghe, D., Higuchi, K. & Becker, B. E. (1999) Five-year evaluation of implants placed at extraction and with dehiscences and fenestration defects augmented with eptfe membranes: results from a prospective multicenter study. *Clinical Implant Dentistry & Related Research* **1**: 27–32.

Blanco, J., Alves, C.C., Nunez, V., Aracil, L., Munoz, F. & Ramos, I. (2010) Biological width following immediate implant placement in the dog: Flap vs. Flapless surgery. *Clinical Oral Implants Research* **21**: 624–631.

Block, M.S. & Jackson, W.C. (2006) Techniques for grafting the extraction site in preparation for dental implant placement. *Atlas of the Oral and Maxillofacial Surgery Clinics of North America* **14**: 1–25.

Bolouri, A., Haghighat, N. & Frederiksen, N. (2001) Evaluation of the effect of immediate grafting of mandibular postextraction sockets with synthetic bone *Compendium of Continuing Education in Dentistry (Jamesburg, N.J.: 1995)* **22**: 955–958, 960, 962 passim; quiz 966.

Camargo, P.M., Lekovic, V., Weinlaender, M., Klokkevold, P.R., Kenney, E.B., Dimitrijevic, B., Nedic, M., Jancovic, S. & Orsini, M. (2000) Influence of bioactive glass on changes in alveolar process dimensions after exodontia. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics* **90**: 581–586.

Cardaropoli, G., Araujo, M. & Lindhe, J. (2003) Dynamics of bone tissue formation in tooth extraction sites. An experimental study in dogs. *Journal of Clinical Periodontology* **30**: 809–818.

Carmagnola, D., Adriaens, P. & Berglundh, T. (2003) Healing of human extraction sockets filled with bio-oss. *Clinical Oral Implants Research* **14**: 137–143.

Casado, P.L., Duarte, M.E., Carvalho, W., Esmeraldo da Silva, L. & Barboza, E.P. (2010) Ridge bone maintenance in human after extraction. *Implant Dentistry* **19**: 314–322.

Crespi, R., CapparË, P. & Gherlone, E. (2009) Magnesium-enriched hydroxyapatite compared to calcium sulfate in the healing of human extraction sockets: radiographic and histomorphometric evaluation at 3 months. *Journal of Periodontology* **80**: 210–218.

Devlin, H., Hoyland, J., Newall, J.F. & Ayad, S. (1997) Trabecular bone formation in the healing of the rodent molar tooth extraction socket. *Journal of Bone and Mineral Research* **12**: 2061–2067.

Devlin, H. & Sloan, P. (2002) Early bone healing events in the human extraction socket. *The International Journal of Oral and Maxillofacial Surgery* **31**: 641–645.

Esposito, M., Coulthard, P., Worthington, H.V. & Jokstad, A. (2001) Quality assessment of randomized controlled trials of oral implants. *The International Journal of Oral & Maxillofacial Implants* **16**: 783–792.

Evian, C.I., Rosenberg, E.S., Coslet, J.G. & Corn, H. (1982) The osteogenic activity of bone removed from healing extraction sockets in humans. *Journal of Periodontology* **53**: 81–85.

Ferrus, J., Cecchinato, D., Pjetursson, E.B., Lang, N. P., Sanz, M. & Lindhe, J. (2010) Factors influencing ridge alterations following immediate implant placement into extraction sockets. *Clinical Oral Implants Research* **21**: 22–29.

Fickl, S., Zuhr, O., Wachtel, H., Bolz, W. & Huerzeler, M. (2008a) Tissue alterations after tooth extraction with and without surgical trauma: a volumetric study in the beagle dog. *Journal of Clinical Periodontology* **35**: 356–363.

Fickl, S., Zuhr, O., Wachtel, H., Stappert, C.F., Stein, J.M. & Hurzeler, M.B. (2008b) Dimensional changes of the alveolar ridge contour after different socket preservation techniques. *Journal of Clinical Periodontology* **35**: 906–913.

Fiorellini, J.P., Howell, T.H., Cochran, D., Malmquist, J., Lilly, L.C., Spagnoli, D., Toljanic, J., Jones, A. & Nevins, M. (2005) Randomized study evaluating recombinant human bone morphogenetic protein-2 for extraction socket augmentation. *Journal of Periodontology* **76**: 605–613.

Froum, S., Cho, S.C., Rosenberg, E., Rohrer, M. & Tarnow, D. (2002) Histological comparison of healing extraction sockets implanted with bioactive glass or demineralized freeze-dried bone allograft: a pilot study. *Journal of Periodontology* **73**: 94–102.

Higgins, J.P., Thompson, S.G., Deeks, J.J. & Altman, D.G. (2003) Measuring inconsistency in meta-analyses. *BMJ* **327**: 557–560.

Higgins, J.P.T. & Green, S. (eds) *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org (accessed on 31 May 2010).

Hoad-Reddick, G., Grant, A.A. & McCord, J.F. (1994) Osseoretention? Comparative assessment of particulate hydroxyapatite inserted beneath immediate dentures. *The European Journal of Prosthodontics and Restorative Dentistry* **3**: 61–65.

Iasella, J.M., Greenwell, H., Miller, R.L., Hill, M., Drisko, C., Bohra, A.A. & Scheetz, J.P. (2003) Ridge preservation with freeze-dried bone allograft and a collagen membrane compared to extraction alone for implant site development: a clinical and histologic study in humans. *Journal of Periodontology* **74**: 990–999.

Januario, A.L., Duarte, W.R., Barriviera, M., Mesti, J.C., Araujo, M.G. & Lindhe, J. (2011) Dimension of the facial bone wall in the anterior maxilla: a cone-beam computed tomography study. *Clinical Oral Implants Research* **22**: 1168–1171.

Johnson, K. (1969) A study of the dimensional changes occurring in the maxilla following tooth extraction. *Australian Dental Journal* **14**: 241–244.

van Kesteren, C.J., Schoolfield, J., West, J. & Oates, T. (2010) A prospective randomized clinical study of changes in soft tissue position following immediate and delayed implant placement. *The International Journal of Oral & Maxillofacial Implants* **25**: 562–570.

von Elm, E., Altman, D.G., Egger, M., Pocock, S.J., Gotzsche, P.C. & Vandenbroucke, J.P. (2007) The strengthening the reporting of observational studies in epidemiology (strobe) statement: guidelines for reporting observational studies. *Lancet* **370**: 1453–1457.

Kuboki, Y., Hashimoto, F. & Ishibashi, K. (1988) Time-dependent changes of collagen crosslinks in the socket after tooth extraction in rabbits. *Journal of Dental Research* **67**: 944–948.

Lekovic, V., Camargo, P.M., Klokkevold, P.R., Weinlaender, M., Kenney, E.B., Dimitrijevic, B. & Nedic, M. (1998) Preservation of alveolar bone in extraction sockets using bioabsorbable membranes. *Journal of Periodontology* **69**: 1044–1049.

Lekovic, V., Kenney, E.B., Weinlaender, M., Han, T., Klokkevold, P., Nedic, M. & Orsini, M. (1997) A bone regenerative approach to alveolar ridge maintenance following tooth extraction. Report of 10 cases. *Journal of Periodontology* **68**: 563–570.

Needleman, I.G. (2002) A guide to systematic reviews. *Journal of clinical periodontology* **29**: [Suppl. 3]: 6–9; discussion 37–38.

Norton, M.R., Odell, E.W., Thompson, I.D. & Cook, R.J. (2003) Efficacy of bovine bone mineral for alveolar augmentation: a human histologic study. *Clinical Oral Implants Research* **14**: 775–783.

Oghli, A.A. & Steveling, H. (2010) Ridge preservation following tooth extraction: a comparison between atraumatic extraction and socket seal surgery. *Quintessence International* **41**: 605–609.

Paolantonio, M., Dolci, M., Scarano, A., d'Archivio, D., di Placido, G., Tumini, V. & Piattelli, A. (2001) Immediate implantation in fresh extraction sockets: A controlled clinical and histological study in man. *J Periodontol* **72**: 1560–1571.

Pietrokovski, J. & Massler, M. (1967) Alveolar ridge resorption following tooth extraction. *Journal of Prosthetic Dentistry* **17**: 21–27.

Schulz, K.F., Altman, D.G. & Moher, D. (2010) Consort 2010 statement: updated guidelines for reporting parallel group randomized trials. *Obstetrics and Gynecology* **115**: 1063–1070.

Schropp, L., Wenzel, A., Kostopoulos, L. & Karring, T. (2003) Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study. *The International Journal of Periodontics & Restorative Dentistry* **23**: 313–323.

Serino, G., Biancu, S., Iezzi, G. & Piattelli, A. (2003) Ridge preservation following tooth extraction using a polylactide and polyglycolide sponge as space filler: a clinical and histological study in humans. *Clinical Oral Implants Research* **14**: 651–658.

Serino, G., Rao, W., Iezzi, G. & Piattelli, A. (2008) Polylactide and polyglycolide sponge used in human extraction sockets: bone formation following 3 months after its application. *Clinical Oral Implants Research* **19**: 26–31.

Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., Rennie, D., Moher, D., Becker, B.J., Sipe, T.A. & Thacker, S.B. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of observational studies in epidemiology (moose) group. *Journal of the American Medical Association.* **283**: 2008–2012.

Tarnow, D.P. & Eskow, R.N. (1996) Preservation of implant esthetics: soft tissue and restorative considerations. *Journal of Esthetic Dentistry* **8**: 12–19.

Ten Heggeler, J.M., Slot, D.E. & Van der Weijden, G.A. (2010) Effect of socket preservation therapies following tooth extraction in non-molar regions in humans: a systematic review. *Clinical Oral Implants Research* **22**: 779–788.

Tobías, A. (2008) Preferred reporting items for systematic reviews and meta-analyses: the prisma statement. *Stata Techical Bulletin* **47**: 15–17.

Trombelli, L., Farina, R., Marzola, A., Bozzi, L., Liljenberg, B. & Lindhe, J. (2008) Modeling and remodeling of human extraction sockets. *Journal of Clinical Periodontology* **35**: 630–639.

Yilmaz, S., Efeoglu, E.& Kilic, A.R. (1998) Alveolar ridge reconstruction and/or preservation using root form bioglass cones. *Journal of Clinical Periodontology* **25**: 832–839.