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Effectiveness of sinus lift procedures for dental implant rehabilitation: a Cochrane systematic review

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Key words *bone augmentation, dental implant, randomised controlled clinical trial, sinus lift, systematic review*

Conflict-of-interest statement: Marco Esposito, Pietro Felice and Paul Coulthard are among the authors of four of the included trials, however, they were not involved in the quality assessment of these trials.

This review is based on a Cochrane systematic review entitled 'Interventions for replacing missing teeth: augmentation procedures of the maxillary sinus' 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.

Background: Insufficient bone volume is a common problem encountered in the rehabilitation of the edentulous posterior maxillae with implant supported prostheses. Bone volume is limited by the presence of the maxillary sinus together with loss of alveolar bone height. Sinus lift procedures increase bone volume by augmenting the sinus cavity with autogenous bone and/or commercially available biomaterials.
Objectives: To test whether and when augmentation of the maxillary sinus is necessary and which are the most effective augmentation techniques for rehabilitating patients with implant-supported prostheses.
Search methods: The Cochrane Oral Health Group's Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE were searched. Several dental journals were hand searched. The bibliographies of review articles were checked, and personal references were searched. More than 55 implant manufacturing companies were also contacted. The last electronic search was conducted on 7th January 2010.
Selection criteria: Randomised controlled trials (RCTs) of different techniques and materials for augmenting the maxillary sinus for rehabilitation with dental implants reporting the outcome of implant therapy at least to abutment connection.

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Data collection and analysis: Screening of eligible studies, assessment of the methodological quality of the trials and data extraction were conducted independently and in duplicate. Authors were contacted for any missing information. Results were expressed as random-effects models using mean differences for continuous outcomes and odds ratios for dichotomous outcomes with 95% confidence intervals. The statistical unit of the analysis was the patient.

Results: Ten RCTs out of 29 potentially eligible trials were suitable for inclusion. One trial including 15 patients, evaluated whether 5-mm-long implants with a diameter of 6 mm could be an alternative to sinus lift in bone having a residual height of 4 to 6 mm. Nine trials with 235 patients compared different sinus lift techniques and, of these, four trials (114 patients) evaluated the efficacy of platelet-rich plasma (PRP). Since different techniques were evaluated in different trials, only two meta-analyses evaluating the efficacy of PRP could be performed for implant failures (two trials) and complications (three trials). No statistically significant difference was observed for any of the evaluated interventions.

Conclusions: Conclusions are based on few trials, usually underpowered, having short follow-ups, and often judged to be at high risk of bias, therefore they should be viewed as preliminary and interpreted with great caution. It is still unclear when sinus lift procedures are needed. Short implants (5 mm) can be successfully loaded in maxillary bone with a residual height of 4 to 6 mm, but their long-term prognosis is unknown. Elevating the sinus lining in the presence of 1 to 5 mm of residual bone height without the addition of a bone graft may be sufficient to regenerate new bone to allow rehabilitation with implant-supported prostheses. Bone substitutes might be successfully used as replacements for autogenous bone. If the residual alveolar bone height is 3 to 6 mm, a crestal approach to lifting the sinus lining and placing 8 mm implants may lead to less complications than a lateral window approach and placing implants at least 10 mm long. PRP treatment does not seem to improve the clinical outcome of sinus lift procedures with autogenous bone or bone substitutes.

■ Introduction

Missing teeth may result in a functional and cosmetic deficit and have traditionally been replaced with dentures or bridges. Dental implants offer an alternative, they are inserted into the jawbones and used to support dental prostheses. Dental implants rely on the maintenance of a direct structural and functional connection between living bone and the implant surface, this is termed osseointegration and was first described by Brånemark[1]. Osseointegration has undoubtedly been one of the most significant scientific breakthroughs in dentistry over the past 40 years.

Insufficient bone volume is a common problem encountered in the rehabilitation of the edentulous posterior maxilla with implant-supported prostheses. The bone available for implant placement may be limited by the presence of the maxillary sinus together with loss of alveolar bone height. Bone volume may be increased by augmentation, and the sinus cavity is commonly augmented with autogenous bone and/or biomaterials.

Implant placement may be combined with sinus augmentation as a 'one-stage' technique. Alternatively, sinus augmentation may be carried out at some time prior to implant placement, as a 'two-stage' technique which requires an additional surgical episode.

■ Techniques of sinus augmentation (sinus lift)

Boyne described the pre-prosthetic surgical technique of retrograde sinus augmentation, and in some cases blade implants were placed[2]. The technique required a window to be prepared in the lateral wall of the sinus via a buccal sulcus incision. The mucosal lining was elevated to create a cavity into which

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particulate bone from the iliac crest was placed and allowed to heal for about 6 months or more before placing the implants.

Tatum described five tissue incisions (crestal, palatal, split-thickness palatal, vertical and horizontal vestibular), three types of bone access (crestal, buccal wall and Le Forte I) and the use of autogenous bone, allografts and alloplasts. In addition, Tatum described sinus augmentation and implant placement as a one-stage and a two-stage technique[3].

The technique known as a lateral window sinus lift is widely used today and is considered reliable particularly when autogenous bone is used[4,5]. Summers described a less invasive one-stage technique for sinus floor elevation with simultaneous implant placement called the osteotome sinus floor elevation. Summers considered it necessary to have at least 6 mm of residual bone to ensure primary stability of the implant. Concave-tipped osteotomes of increasing diameter applied via a crestal approach advanced a mass of bone beyond the level of the original sinus floor, elevating the mucosal lining. Summers combined this procedure with the addition of a bone graft material[6]. For cases of less than 6 mm of residual bone height, Summers proposed a two-stage approach. A bone plug is defined with a trephine and displaced superiorly with the use of a broad osteotome. Hydrostatic pressure elevates the mucosal lining of the sinus. The resultant osteotomy is filled with a bone graft material and the implant placed after a period of healing[7].

Cosci modified the crestal approach technique utilising an atraumatic lifting drill to reduce the risk of perforation of the mucosa lining the sinus using a one-stage technique with as little as 3 mm of residual bone[8]. Bone can be collected with a trephine directly from the osteotomy site to be used as grafting material, a bone substitute can be used or the implant tip can hold up the sinus membrane that will work as a natural barrier for bone regeneration. While the crestal approach is less invasive and is a one-stage technique, there are some disadvantages associated with it. The amount of bone which can be gained using a crestal approach is usually less than what can be obtained with the lateral window technique, and a minimal amount of crestal bone height of about 3 mm is generally recommended to stabilise the implant at placement[8].

In order to obtain simultaneous vertical bone augmentation with a sinus lift procedure, Cannizzaro proposed a technique that is a combination of a sinus lift and an onlay graft. Implants are placed in the ulna, bone blocks containing the implants are retrieved with a trephine, inserted into the sinus via a crestal approach and left protruding occlusally for some mm in order to obtain simultaneous vertical bone gain[9].

Materials used in sinus lift procedures

Autogenous bone has long been considered the gold standard. Intra-oral donor sites (chin and ramus) are convenient but yield limited volume. Extra-oral donor sites (iliac crest, tibia, ulna, rib and calvarium) increase surgical complexity and are associated with significant (and under-reported) morbidity and scarring, therefore alternative grafting materials (bone substitutes) are used.

Allografts consist of 'same species' tissue. Cadaveric bone is harvested and various techniques (freeze drying and irradiation) reduce antigenicity. The grafts are then sterilised and supplied by specially licensed tissue banks.

Xenografts consist of 'different species' tissue. Anorganic bovine and equine bone predominate. Chemical removal of the organic component creates a mineral scaffold.

Alloplasts are synthetic bone substitutes. There are many types classified in terms of porosity as dense, macro-porous, micro-porous, and either crystalline or amorphous. The structure influences performance. Some examples are beta-tricalcium phosphate, bio-active glass and calcium sulphate.

All of these grafts can be delivered in various convenient ways such as bone particles or large blocks, can be mixed with autogenous bone and can be very stable over time or highly resorbable, depending on their chemical characteristics.

Bone formation may be promoted by the use of biologically active molecules such as bone morphogenic proteins (BMPs), growth factors, platelet rich plasma (PRP) and other molecules.

Urist found that cell-free, decalcified bone implanted into extra-skeletal sites stimulated new bone formation[10]. The molecules responsible belong to the growth factor B family and are called BMP's[11].

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A number have been discovered, and their use requires a delivery system that mimics the physical properties and release kinetics of bone.

Some authors have proposed sinus augmentation without the use of a graft material, with coagulated blood acting as a scaffold for bone formation. Lundgren proposed maintaining a space by suturing the sinus lining to the lateral wall[12]. The implant apex may be used to support the sinus membrane[13-18]. Some bone regeneration does occur though the actual clinical benefit remains in doubt since this method has not been compared to appropriate control procedures.

Alternative techniques to sinus lift

When anatomical conditions permit, there are a few alternative techniques to sinus augmentation. Onlay bone grafts may be used for horizontal or vertical augmentation. These procedures are evaluated in another Cochrane systematic review[19].

Implants can also be placed with an angulated direction in order to avoid the maxillary sinus[20]. These implants are called 'tilted' or 'angulated' implants and they can only be used when anatomical conditions permit.

Zygomatic implants offer an alternative to sinus augmentation. Long implants pass through the sinus[21] or laterally from the sinus into the zygomatic process. Zygomatic implants are evaluated in another Cochrane review[22]. In some situations, angled implants may be placed into the pterygomaxilla[23].

Another alternative to sinus lift procedures is the use of short implants. Current research is focused on evaluating short implants placed without augmentation, offering the option of a less complex, cheaper and faster alternative to augmentation. There are few comparative studies evaluating the efficacy of short implants[19]. Implants with lengths of 5 to 8 mm are currently used and may be defined as short implants[24], though this is controversial as some authors consider implants of 7 to 10 mm to be short[25]. A review of the literature suggested a failure rate of around 10% for implants 7 mm long[25]. The design of the included studies requires this figure to be viewed with caution, it may represent a gross underestimation. Nevertheless, these figures suggest that shorter implants may have a poorer prognosis than longer ones. Since it is commonly believed that shorter implants (8 mm or less) have a poorer prognosis than longer implants, clinicians place longer implants if bone allows. When bone height is 5 to 8 mm clinicians must decide whether to augment or place short implants. New and possibly improved implant surface modifications and designs, with thus far no reliable evidence of their superiority having been documented[26], together with improved surgical techniques may shift the balance in favour of short implants when the alternative is a more complex augmentation procedure.

Several 'systematic' reviews have been published on the outcome of sinus-lift procedures[4,5,27-32], however, since those findings were not based on the most reliable clinical studies, a systematic review based on the most reliable evidence would be useful to summarise the current scientific knowledge.

Objectives

The objectives of the present review were to test the null hypothesis of no difference in the success, function, complications and patient satisfaction of augmenting or not and between different maxillary sinus lift techniques for dental implant treatment against the alternative hypothesis of a difference. This included, in particular, testing (a) whether and when sinus lift procedures are necessary and (b) which is the most effective augmentation technique for sinus lift.

Materials and methods

Criteria for considering studies in the present review

Randomised controlled clinical trials (RCTs) including patients with missing teeth and an atrophic posterior maxilla who may require augmentation of the maxillary sinus prior or at placement of dental implants were included in the present review.

The following interventions/comparisons were considered: any bone augmentation technique, active agent (such as BMPs, PRP) or biomaterials used in relation with osseointegrated, root-formed dental implants. For trials to be considered in the

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present review, implants had to be placed and the outcome of the implant therapy had to be reported at least at the endpoint of the abutment connection procedure. The following time points were considered: abutment connection, prosthetic loading, up to 1 year, 3 and 5 years after loading.

The following outcome measures were considered:

- Prosthesis failure: planned prosthesis which could not be placed due to 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). Failures that occurred before prosthesis placement were considered early failures. Implant mobility could be assessed manually or with instruments such as Periotest (Siemens AG, Benshein, Germany) or resonance frequency (Osstell, Integration Diagnostics, Göteborg, Sweden).
- Augmentation procedure failure: failure of the augmentation procedure not affecting the success of the implant.
- Major complications at treated sites (e.g. sinusitis, infection, haemorrhage, etc.).
- Major complications at bone donor sites (e.g. nerve injury, gait disturbance, infection, etc.).
- Patient satisfaction.
- Patient preference (only in split-mouth trials).
- Bone gain expressed in mm or percentage.
- Duration of the treatment time starting from the first intervention to the functional loading of the implants.
- Treatment costs.

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

Search strategies for identification of studies

For the identification of studies included or considered for this review, detailed search strategies were developed for each database searched. For more details see the original Cochrane review[33]. The following databases were searched:

- The Cochrane Oral Health Group's Trials Register (to 7th January 2010)
- The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2009, Issue 4)
- MEDLINE via OVID (1950 to 7th January 2010)
- EMBASE via OVID (1980 to 7th January 2010).

The most recent electronic search was undertaken on 7th January 2010 and there were no language restrictions.

The *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* were hand searched up to January 2010.

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 were written to through an Internet discussion group (implantology@yahoogroups.com) for information on trials, however it was discontinued due to poor yield.

Study selection

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 the studies met the inclusion criteria or not. Disagreements were resolved by

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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 were recorded.

Quality assessment

The quality 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 authors list, it was independently evaluated only by those review authors not involved in the trials.

Three main quality criteria were examined:

- allocation concealment, recorded as (a) adequate, (b) unclear or (c) inadequate
- treatment blind to outcome assessors, recorded as (a) yes, (b) no, (c) unclear or (d) not possible
- completeness of follow up (is there a clear explanation for withdrawals and dropouts in each treatment group?) assessed as (a) yes or (b) no. In cases where clear explanations for dropouts were given, a further subjective evaluation of the risk of bias assessing the reasons for the dropout was made.

After taking into account the additional information provided by the authors of the trials, studies were grouped into the following categories:

- low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met
- high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met.

Further quality assessment was carried out to assess sample size calculations, definition of exclusion/inclusion criteria, and comparability of control and test groups at entry. The quality assessment criteria were pilot tested using several articles.

Data extraction

Data were extracted independently by two review authors 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 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, source of recruitment and criteria for inclusion; details of the type of intervention and details of the outcomes reported, including method of assessment and time intervals.

For dichotomous outcomes, the estimate of the effect of an intervention was expressed as odds ratios (OR) 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. Appropriate data were extracted from the split-mouth studies[34]. The statistical unit was the patient and not the augmentation procedure or the implants. In split-mouth studies the augmentation procedures or the prostheses within each pair were the unit of analysis[34].

The significance of any discrepancies in the estimates of the treatment effects from the different trials was to be assessed by means of Cochran's test for heterogeneity, and heterogeneity would have been considered significant if $P < 0.1$. The I^2 statistic, which describes the percentage total variation across studies that is due to heterogeneity rather than chance, was used to quantify heterogeneity, with I^2 over 50% being considered moderate to high heterogeneity.

A meta-analysis was conducted only if there were studies of similar comparisons reporting the same outcome measures. Odds ratios were combined for dichotomous data, and mean differences for continuous data, using 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[35], using the generic inverse variance method in RevMan.

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Results

Of the 29 potentially eligible trials[36-63], 19 had to be excluded for various reasons such as: reported only histological outcomes without presenting any implant related outcomes[37-48]; problems with study design and data reporting[49-52]; too short of a follow-up[53], data of only 4 out of 16 patients treated were presented[36]; and not an RCT[54].

Of the 10 included trials, three were conducted in Italy[55-57], two in Sweden[58,59], one in Spain[60], one in Germany[61], one in France[62], one in The Netherlands[63] and one was a multicentre trial conducted in four European centres (Belgium, Hungary, UK and Italy)[64].

Two trials had a parallel group study design[55,58], six had a split-mouth design[56,57,59,62-64] and two had a mixed split-mouth/parallel group design[60,61], but only data from their split-mouth portion could be used in the present review.

For six trials, it was declared that support was received from industry directly involved in producing the product being tested in the form of free material[56-59,63,64], but for one study[57] the discounted implants were not under evaluation. The authors of four trials declared that no support was received from commercial parties whose products were being tested in the trials[55,60-62].

Seven trials were conducted at universities or specialist dental clinics and three trials in private practices[55,56,65]. One of the centres (Brugge, Belgium) of the multicentre trial[64] was also a private practice. The interventions that follow were tested.

Is sinus lift necessary? (1 trial with 15 patients)

This trial examined one to three 5-mm-long implants of 6 mm in diameter versus one to three 10 mm or longer implants of 4 mm in diameter placed in sinuses augmented with 100% bovine anorganic bone (Bio-Oss®, Geistlich Pharmaceutical, Wolhusen, Switzerland) with lateral windows sealed using a resorbable collagen membrane (OsseoGuard®, Biomet 3i, Palm Beach, FL, USA) 4 months before[56]. All augmentation procedures were performed under local anaesthesia. All implants were left to heal submerged for 4 months. Rescue™ implants (MegaGen, Gyeongbuk, South Korea) as short implants and EZ Plus (MegaGen) as long implants, with internal connection, were used. Implant site preparation was also different since a 5 mm diameter trephine was used initially to prepare the osteotomy sites for Rescue implants. Provisional screw-retained reinforced resin prostheses were replaced after 4 months by definitive screw-retained metal-ceramic prostheses.

Which is the most effective sinus lift procedure? (9 trials with 235 patients)

One trial examined one-stage lateral sinus lift with monocortical iliac bone blocks fixed in most cases with two implants and left to heal for 6 months versus two-stage lateral sinus lift with particulate bone from the iliac crest left to heal for 6 months with two implants (in most cases) inserted into the healed graft and left to heal for an additional 6 months[58]. All of the augmentation procedures were performed under general anaesthesia. All implants were turned titanium self tapping (Nobel Biocare, Göteborg, Sweden) and were rehabilitated with screw-retained cross-arch implant supported prostheses.

A study was conducted on two-stage lateral sinus lift with autogenous particulate bone from the mandibular ramus versus two-stage lateral sinus lift with a mixture of 80% Bio-Oss and 20% particulate bone from the mandibular ramus, left to heal for 6 months in a split-mouth trial[59]. A fibrin glue (Tisseel® Duo Quick, Immuno, Wien, Austria) was added to the grafts after thrombin (Immuno) for both interventions. A third treatment group was composed of patients who refused to provide autogenous bone but accepted the treatment with a two-stage sinus lift with 100% Bio-Oss. For the latter group, a resorbable porcine-derived collagen barrier (Bio-Gide, Geistlich Pharmaceutical) was used to cover the sinus defect and the healing time was prolonged to an average of 8.5 months (range 8 to 9.5). Procedures were performed under local anaesthesia and oral sedation. All implants were turned titanium self tapping (Nobel Biocare): the Mark II implant type was used in the former two groups and Mark III in the latter. All patients were rehabilitated with screw-retained metal-ceramic fixed prostheses.

Another study examined a two-stage lateral sinus lift with autogenous particulate bone from the

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iliac crest versus a two-stage sinus lift with 1.5 to 2 g of beta-tricalcium phosphate (Cerasorb®, Curasan AG, Kleinostheim, Germany) and left to heal for 6 months[64]. In 10 of the 20 patients, the alveolar crest was also widened with cortical bone blocks fixed with microscrews. No membranes were used to cover the bone. All of the augmentation procedures were performed under general anaesthesia. Patients were instructed not to wear their upper dentures for 30 days. In 16 patients, Ankylos® (Dentsply Friadent, Mannheim, Germany) implants were used, whereas in four patients Protetim (Hódmezővásárhely, Hungary) implants were used. The authors did not provide any explanation for using two different implant systems. Two implants were placed in each augmented sinus.

One trial studied one-stage sinus lift using one to three 8-mm-long implants placed in simultaneously crestally augmented sinus with autogenous particulate bone, harvested from the implant site, versus one to three 10 mm or longer implants placed in simultaneously augmented sinuses using the lateral approach with a mixture of 50% particulate autogenous bone from the tuberosity area and 50% Bio-Oss[55]. A modified 'Cosci technique' was used to crestally augment the sinus. In brief, implant sites were prepared with a 2.5 mm trephine drill up to about 1 mm of the sinus cortical wall, to collect autogenous bone, and with a 3.1 mm diameter atraumatic lifting drill. Resorbable barriers (Biomend® Extend, Sulzer Dental, Carlsbad, CA, USA) were used to seal the lateral windows. All augmentation procedures were performed under local anaesthesia. All implants were left to heal submerged for 45 days and were functionally loaded within 1 week after abutment connection. All implants were tapered Screw-Vent® MP-1 HA Dual Transition Selective Surface Implants (Zimmer Dental) inserted in underprepared osteotomy sites with a torque of at least 35 Ncm.

A study analysed two-stage sinus lift with lateral window approach using either a synthetic resorbable barrier (GTR™ Biodegradable Membrane System, Inion, Tampere, Finland) to keep the sinus membrane or 100% granular Bio-Oss[57]. Inion barriers were used to seal the lateral windows. Inion barriers are made of a synthetic co-polymer (trimethylene carbonate l-lactide polyglycolide) that needs to be softened in a plasticising solution, allowing the membrane to be cut and moulded to exactly fit the space. The barrier then hardens in the new position maintaining the new shape and the space. This material should biodegrade *in situ* after 8 to 12 weeks. All augmentation procedures were performed under local anaesthesia. After 6 months, one to 3 implants were placed per side and submerged for 4 months. All implants were Way® (Geass, Pozzuolo del Friuli, Italy) with a laser-treated surface and internal connection. Provisional screw-retained reinforced resin prostheses were replaced after 4 months by definitive screw-retained metal-ceramic prostheses.

Trials evaluating the efficacy of PRP with grafts (4 trials with 114 patients)

One trial examined two-stage lateral sinus lift with autogenous blocks and particulate bone together with buccal onlays and monocortico-cancellous bone grafts, to reconstruct the width of the maxilla, fixed with titanium screws harvested from the iliac crest with or without PRP and left to heal for 3 months in a split-mouth trial[63]. Barriers were not used. PRP was made using the Platelet Concentration Collection System kit (PCCS® kit, 3i Implant Innovations, Palm Beach Gardens, FL, USA). A total of 54 ml of blood was mixed with 6 ml of anticoagulant (citrate dextrose) and processed with the platelet concentration system. To promote the release of growth factors from the platelets, a 10% calcium chloride ($CaCl_2$) solution and the patient's serum, as a source of autologous thrombin, were added before actual reconstruction of the defect with the bone graft. The resulting gel was mixed with the bone graft and some gel was applied at the closure of the wound at the side treated with PRP. Three implants were inserted into the healed graft of each side and were left to heal for an additional 6 months. All of the augmentation procedures were performed under general anaesthesia. Surgical templates were used to optimise implant insertion. All implants were turned titanium self tapping (Nobel Biocare) and were rehabilitated with two implant-supported prostheses.

A study analysed two-stage sinus lift with lateral window approach using either autogenous particulate bone from the iliac crest alone or the same graft plus PRP[61]. All sites were also horizontally augmented with cortico-spongeous blocks from the

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iliac crest fixed with screws. PRP was produced at a university institute of clinical immunology and transfusion medicine under transfusion medical standards. Autologous platelet concentrate from PRP was derived from 450 ml of citrate phosphate dextrose-anticoagulated blood. The PRP was concentrated using differential centrifugation, then stored for 24 h and adjusted up to 10^{10} platelets/ml. The concentrations obtained were 11 to 12 times above the baseline level of whole blood. All augmentation procedures were performed under general anaesthesia. After 4 months of healing, different implant systems (no details provided) were inserted and left to heal submerged for 6 months.

Another trial examined two-stage lateral sinus lift with autogenous cortico-cancellous blocks from the iliac crest versus granules of bone with platelet concentrates (APCs) and a biological glue (Tissucol, Baxter, Maurepas, France), left to heal for 6 months in a split-mouth trial[62]. Plateletphoresis was conducted at least 3 days before surgery on a plateletpheresis collection system (Trima Accel, Version 5.1, Gambro BCT, Lakewood, CO), a single-needle continuous-flow separation system. The targeted concentration was a post-donation platelet count of more than 100×10^6 per ml. Citrate (ACD-A) was used for anticoagulation. APCs were delivered by the cell-processing laboratory in a 20 ml transfer bag that was centrifuged for 15 minutes. The plasma was removed with a plasma extraction device to reach the target volume of 8 to 15 ml. Two ml of cancellous bone was mixed with half of the APC volume and 1 ml of Tissucol. The remaining APCs were mixed with 0.5 ml Tissucol to obtain a membrane for covering the grafted area. Sites treated with bone blocks were covered by 1 ml of Tissucol. Implants were placed 6 months after the augmentation procedure.

One trial compared one or two-stage sinus lift procedures using a lateral window technique and 100% granular Bio-Oss with or without PRP, left to heal for 6 months with a hybrid split-mouth parallel design trial[60]. Patients having up to 4 mm of residual bone height were augmented first and implants were placed after 6 months, whereas patients with residual bone more than 4 mm and up to 7 mm received implants during the sinus lift procedures. Implants were left to heal unloaded for 6 months. Ten to 20 ml of venous blood were collected 30 minutes prior to the surgery and mixed with a 3.8% sodium citrate solution at a 5:1 ratio, achieving anticoagulation through calcium binding. The blood was then centrifuged and separated into 3 layers: red blood cells (RBCs), PRP and poor plasma. Flow cytometry was used for platelet counting. Platelet counts were 2.97 ± 0.7-fold greater than peripheral blood. PRP was activated with a 30% $CaCl_2$ solution and a PRP gel was obtained and mixed with Bio-Oss. The entire bone of the buccal window was removed, and, after the sinus was filled with the bone substitute, no barrier was used to seal the window. Patients were instructed not to wear their upper dentures for 2 to 3 weeks after surgery. Osseotite® (Biomet 3i) implants were used.

Characteristics of outcome measures

- Prosthesis failure[55-60,63,64].
- Implant failure by individual implant stability assessment with removed prostheses (with the exception for single implants)[55-64].
- Augmentation procedure failure[55-64].
- Major complications at treated sites: perforation of the sinus membrane only (though not a major complication)[57], various complications[55-57,59-64].
- Major complications at bone donor site[55,59,63,64]. In the present review, complications at treated and donor sites were combined when appropriate.
- Patient satisfaction: no trial.
- Patient preference (only in split-mouth trials)[56,57]. Data for one trial[56] were reported, however they might be biased because of the study design. All augmentation procedures were performed first and, after 4 months, test and control implants were placed bilaterally in the same surgical session. The potential advantage of having the prostheses on the short implants loaded 4 months earlier was lost with this study design.
- Bone gain expressed in mm or percentage: vertical bone gain was measured in mm by direct measurement in three trials[57,61,62], however, for two trials[61,62] data were presented in a way that could not be used.
- Duration of the treatment period starting from the first intervention to the functional loading of the implants: all trials.

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Table 1 Risk of bias assessment after having included additional explanations provided by the authors of the examined trials.

Study	Allocation concealment	Outcome assessor blind	Withdrawals	Risk of bias
Wannfors 2000[58]	Unclear	No	None	High
Hallman 2002[59]	Adequate	No	None	High
Raghoebar 2005[63]	Unclear	Yes	None	High
Szabó 2005[64]	Unclear	No	None	High
Schaaf 2008[61]	Inadequate	Yes	None	High
Bettega 2009[62]	Unclear	Unclear	Yes, explanations given	High
Cannizzaro 2009[55]	Adequate	Yes	None	Low
Felice 2009a[56]	Adequate	Not possible, but independent assessor	None	Low
Felice 2009b[57]	Adequate	Yes	None	Low
Torres 2009[60]	Adequate	Yes	None	Low

- Treatment costs: no trials. However, this outcome measure was indirectly extrapolated in the present review for all trials.
- Duration of follow-up (including unpublished data kindly provided by the investigators):
  – to the abutment connection[61,62,64]
  – 4-month post-loading[56,57]
  – 1-year post-loading[55,59]
  – 2-year post-loading[57,63]
  – 3-year post-loading[58].

Risk of bias in included studies

The final quality scoring after having incorporated the additional information kindly provided by the authors of the trials is summarised in Table 1. It was assessed whether each trial was at low or high risk of bias. Six studies were judged to be at high risk of bias, and four at low risk of bias.

Main inclusion criteria

- Severely resorbed maxillae (classes V and VI)[66] with maxillary sinuses having <5 mm in height of residual alveolar bone with reduced stability and retention of upper dentures[63].
- 1 to 5 mm in height of residual alveolar bone in the floor of the edentulous sinus[57].
- 2 to 7 mm in height of residual alveolar bone in the floor of the edentulous sinus[58].
- 3 to 6 mm in height of residual alveolar bone in the floor of the edentulous sinus[55].
- 4 to 6 mm in height of residual alveolar bone in the floor of the edentulous sinus[56].
- Less than 5 mm in height of residual alveolar bone in the floor of the edentulous sinus[59,64].
- Less than 8 mm in height of residual alveolar bone in the floor of the edentulous sinus[62].
- Severe atrophy of the edentulous or partially edentulous posterior maxilla, and intention to treat with onlay bone blocks and sinus floor augmentation[61]. Residual bone height values appeared to be in the range of 1 to 12 mm according to the measurements kindly provided by the authors.
- 1 to 7 mm in height of residual alveolar bone in the floor of the edentulous sinus[69].

Main exclusion criteria

- Smokers[62].
- Bone metabolic diseases[58].
- Medication interfering with bone metabolism (i.e. corticosteroids, bisphosphonates, etc.)[55-58].
- Sinusitis[55-58,62].
- History of maxillary sinusitis or sinus surgery[60,62].
- History of reconstructive, pre-prosthetic surgery or previous oral implantology[63].
- Edentulous period less than 1 year[63].
- Severe systemic disease (ASA III and IV)[60].
- None specified[59,64].

An *a priori* calculation for the sample size was undertaken in only two trials[55,56], however in one trial[55] the number of included patients did not reach the calculated sample size.

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Baseline comparability between treatment groups

- No apparent major baseline differences[57,58,60,63].
- Unclear whether major baseline differences existed[59,61,62,64].

The following major baseline differences existed: more large diameter implants were placed in the sites treated with 8-mm-long implants and crestal sinus lift[55], and short 6 mm diameter implants were compared to longer implants with a 4 mm diameter[56].

Effects of interventions

Is sinus lift necessary? (1 trial with 15 patients)

One trial compared 5-mm-long implants of 6 mm diameter versus different implants at least 10 mm long with a diameter of 4 mm placed in laterally augmented sinuses with 100% Bio-Oss[56]. The original trial included a second group of 15 patients treated according to a split-mouth design in the mandible that was of no interest for the present review. Only patients having 4 to 6 mm of residual alveolar bone height with a thickness of 8 mm or more below the sinus were included. Fifteen patients were treated according to a split-mouth design. All patients were followed up to 4 months after loading, therefore there were no dropouts. One prosthesis could not be placed when planned in the short implant side because one implant was found to be mobile at abutment connection. This was not statistically significant (McNemar $P = 1.00$, exact odds ratio [Stata 'epitab' procedure] was 0 [95% CI 0 to 39]; unable to calculate SE to display data in RevMan). The implant was successfully replaced by an implant placed more distally and loaded. Four perforations of the sinus lining occurred: one in the augmented group versus 3 in the 5-mm-long implant group. The difference was not statistically significant (McNemar $P = 0.50$, exact odds ratio [Stata] was 0 [95% CI 0 to 5.3]; unable to calculate SE to display data in RevMan). All patients expressed no preference for either of the two procedures, judging both of them as acceptable. However, this measurement was considered to be biased as previously described in 'Characteristics of outcome measures'. With respect to cost and treatment time, the long implant group required one additional surgical intervention for placing the implants (two-stage procedure) plus the cost of the bone substitute with the barrier and 4 additional months to complete the treatment. The trial was judged to be at low risk of bias.

Which is the most effective sinus lift procedure? (9 trials with 235 patients)

One trial compared two techniques for augmenting atrophic maxillary sinuses[58] (Fig 1). Only patients having 2 to 7 mm of residual alveolar bone in the floor of the edentulous sinus were included. Twenty patients were treated with a one-stage sinus lift with monocortical iliac bone blocks, and the other 20 patients were treated with a two-stage sinus lift with particulate bone from the iliac crest. All patients were followed up to 3 years after loading, therefore there were no dropouts. However, data were presented in a way which could not be used for all of the time points intended for evaluation. Three patients refused to have their prostheses removed and x-ray examination at the 3-year follow up. The only complications reported were 11 perforations of the sinus membrane in nine patients of the one-stage group versus 11 perforations in 10 patients of the two-stage group. At the time of abutment connection, 11 implants in eight patients were found to not be osseointegrated in the one-stage group versus seven implants in six patients of the two-stage group. At 1 year, an additional five implants were lost in the one-stage group versus one in the two-stage group. At 3 years, one additional implant was lost in the one-stage group versus two in the two-stage group. Two patients of the one-stage group had problems with the fixed prostheses at 1 year. In one patient, the prosthesis was lost due to four implant failures whereas in another patient the prosthesis had to be redesigned due to lack of space for the tongue (the present review did not consider this as a prosthesis failure in the calculations, since it was independent of the bone grafting technique). One prosthesis was lost due to the failure of a strategically positioned implant at 1 year in the two-stage group. There was no statistically significant difference for any of the outcomes considered in the review. With respect to

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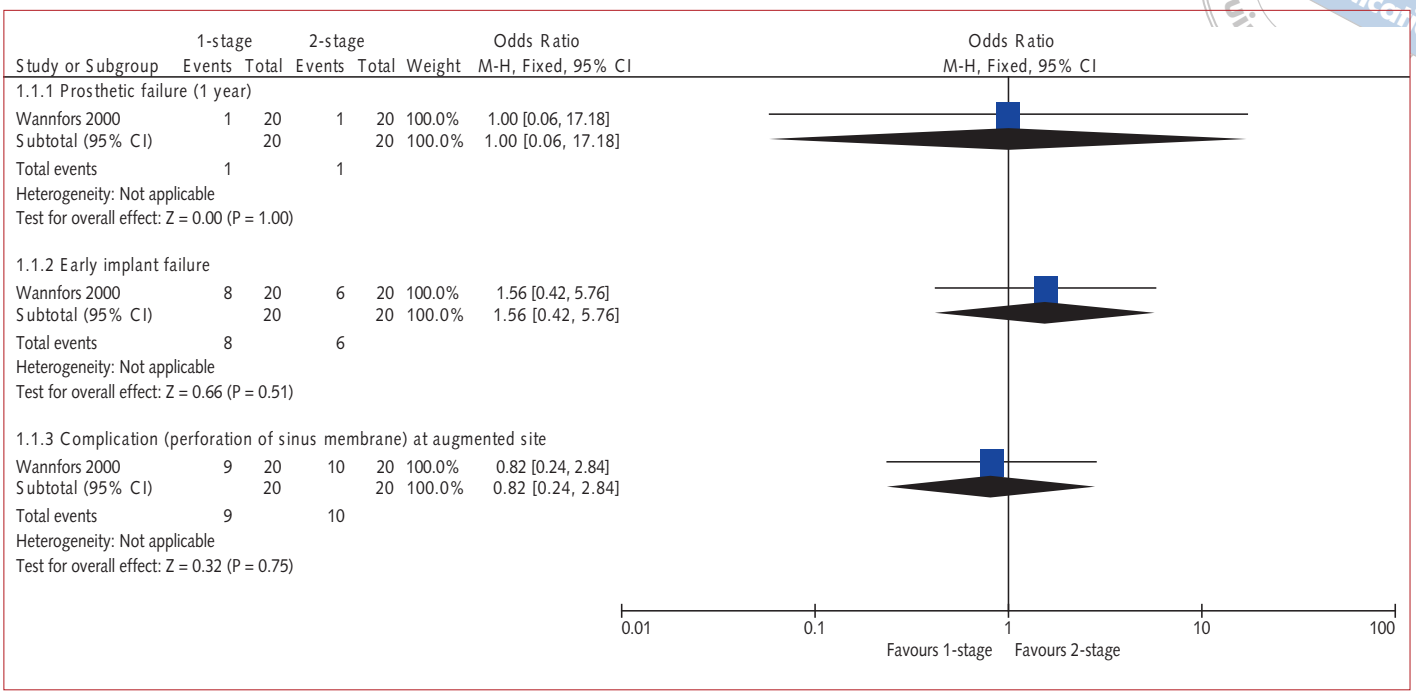
Fig 1 Forest plot comparing one-stage sinus lift with monocortical iliac bone blocks versus two-stage sinus lift with particulate bone from the iliac crest. No statistically significant differences were observed.



cost and treatment time, all of the procedures were performed under general anaesthesia. However, the two-stage group required one additional surgical intervention for placing the implants whereas implants were placed simultaneously with the augmentation procedure in the one-stage group. The healing period was 6 months longer in the two-stage group. The trial was judged to be at high risk of bias.

One trial compared three two-stage techniques for augmenting atrophic maxillary sinuses[59] (Fig 2). Only patients with less than 5 mm of alveolar bone height in the sinus floor and fixed dentition on the opposite jaw were included. The trial was designed as a sort of split-mouth/parallel-preference trial. Eleven patients willing to provide autogenous bone from the mandibular ramus were treated with a split-mouth approach (autogenous bone versus 80% Bio-Oss and 20% autogenous bone), whereas 10 patients who refused to have their bone harvested from the mandible were treated with 100% Bio-Oss. All patients were followed up to 1 year after loading, therefore there were no dropouts. During the post-operative phase, no complications occurred either in the augmented sites or in the donor sites. However, a severe resorption of the autogenous bone graft occurred in two patients. At abutment connection, six implants failed in five patients in the group treated with autogenous bone only and two implants failed in two patients in the group treated with 80% Bio-Oss. No implants or prostheses were lost at the 1-year evaluation. The author confirmed that additional implants were lost at the 2-year follow up in two patients, causing the failure of the fixed prostheses. The complete information should be published in a future 5-year follow-up report. There was no statistically significant difference for any of the outcomes considered in the review. With respect to cost and treatment time, the only difference in cost was the use of the bone substitute. The healing period was 6 months. The trial was judged to be at high risk of bias.

One trial compared two techniques for augmenting atrophic maxillary sinuses[64]. Only patients with less than 5 mm of alveolar bone height in the sinus floor were included. Twenty patients were treated with a split-mouth approach with a two-stage sinus lift and particulate bone from the iliac crest on one side and and a two-stage sinus lift with 100% Cerasorb (a beta-tricalcium phosphate bone substitute) on the contralateral sinus. In 10 patients, an additional autogenous onlay bone block was placed to widen the alveolar crest. All patients were followed

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Fig 2 Forest plot comparing autogenous bone from the mandibular ramus versus 80% Bio-Oss and 20% autogenous bone. No statistically significant differences were observed though trends for implant failures favoured 80% Bio-Oss and 20% autogenous bone.

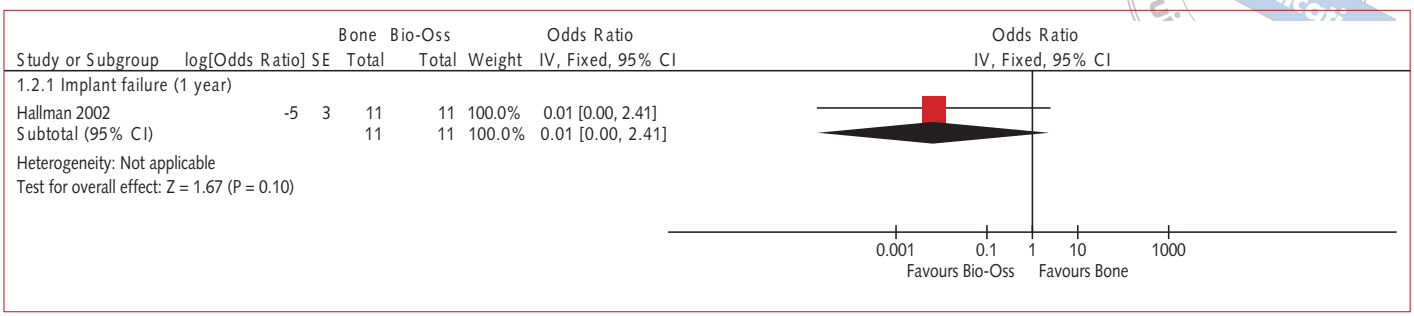
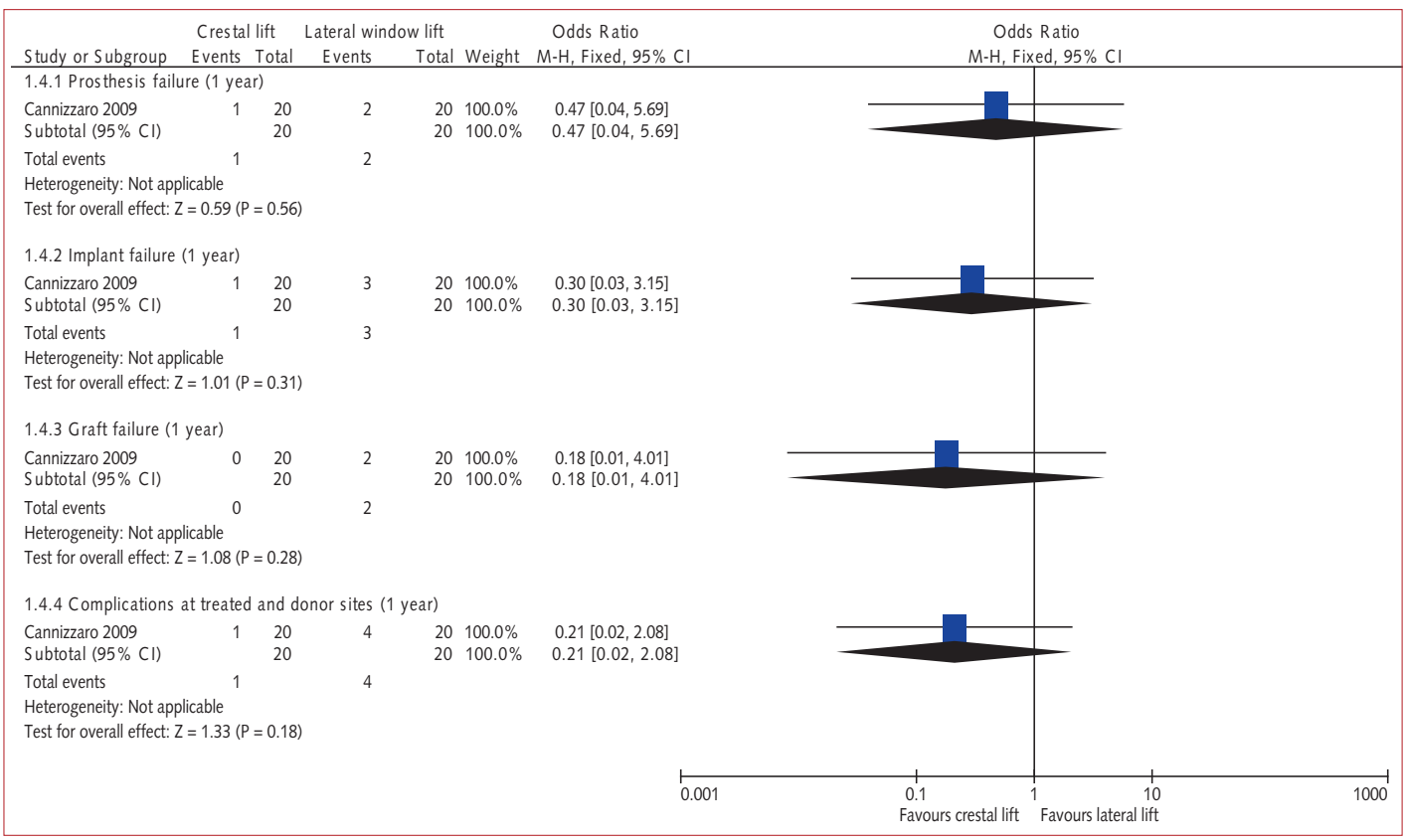


Fig 3 Forest plot comparing sinus lift through a crestal approach with autogenous bone and 8-mm-long implants versus sinus lift through a lateral window approach with a mixture of 50% particulate autogenous bone from the tuberosity area and 50% Bio-Oss and at least 10-mm-long implants. One year after loading, no statistically significant differences were observed though trends favoured the less invasive procedure, i.e. crestal sinus lift with 8-mm-long implants.



up to implant loading and there were no dropouts. No serious post-operative complications occurred at the implant sites. Three complications occurred at the bone graft donor sites: one permanent sensory loss of the lateral femoral cutaneous nerve and two had prolonged wound drainage (2 to 3 weeks). At abutment connection two implants failed, one in each group. They both had to be replaced in order to place the prosthesis and this caused a delay of 3 to 6 months (these were not considered prosthesis failures in the calculations). There was no statistically significant difference for any of the outcomes considered in the review. With respect to cost and treatment time, the only difference was the cost of the bone substitute. The trial was judged to be at high risk of bias.

One trial compared two one-stage techniques for augmenting maxillary sinuses[55] (Fig 3). Only patients having 3 to 6 mm of bone height at the sinus floor were included. Twenty patients were treated with

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Fig 4a Forest plot comparing two two-stage lateral window sinus lift procedures: granular bone substitute (Bio-Oss) versus a resorbable rigid barrier (Inion) to maintain space for bone regeneration. No statistically significant differences in complications were observed.

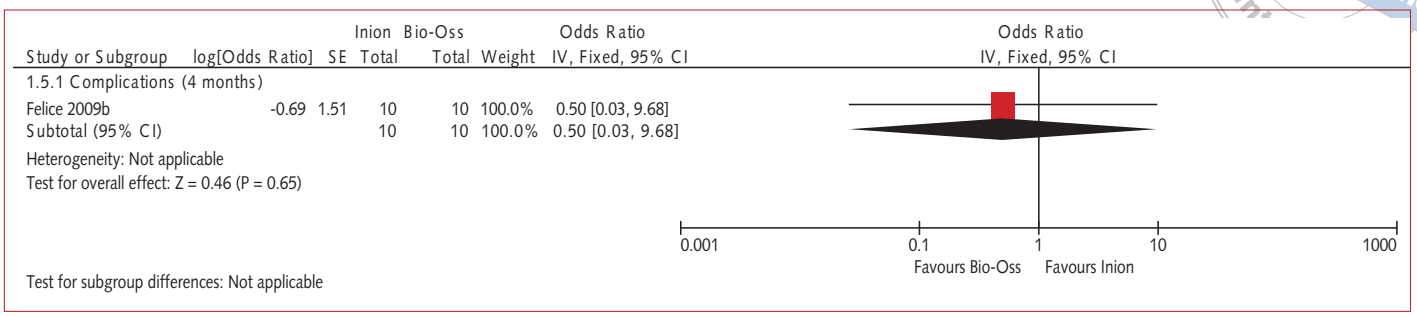
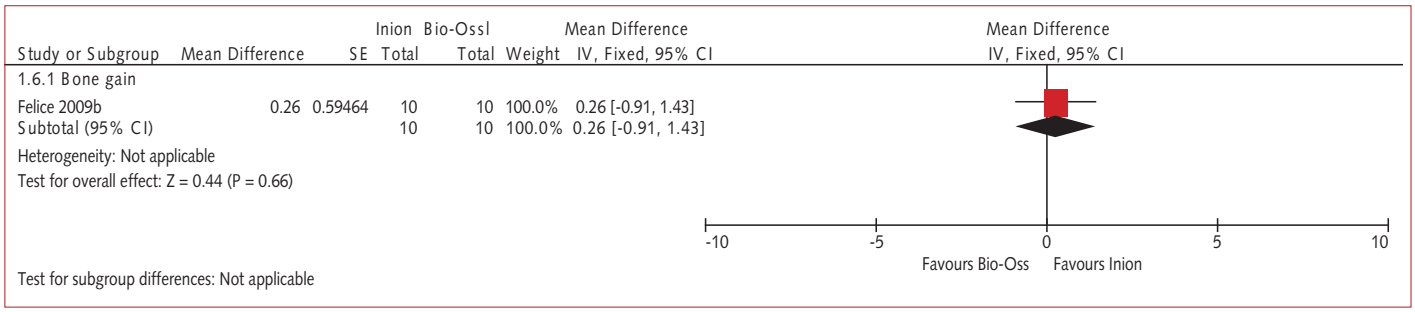


Fig 4b Forest plot comparing two two-stage lateral window sinus lift procedures: granular bone substitute (Bio-Oss) versus a resorbable rigid barrier (Inion) to maintain space for bone regeneration. No statistically significant differences in vertical bone gain were observed.



a sinus lift through a crestal approach, autogenous bone and 8-mm-long implants, and 20 patients were treated with a sinus lift through a lateral window approach with a mixture of 50% particulate autogenous bone from the tuberosity area and 50% Bio-Oss and implants at least 10 mm long. All patients were followed up to 1 year after loading, therefore there were no dropouts. Four complications occurred in four sinuses laterally augmented (one abscess and one sinusitis, both determining the failure of the graft and the implants), versus one peri-implant infection in the short implant group. One implant failed in the short implant group at abutment connection and five implants (four in the immediate post-operative phase and one at abutment connection) in three patients in the long implant group. Two prostheses could not be placed in the long implant group versus one in the short implant group because of implant failures. There was no statistically significant difference for any of the outcomes considered in the review. The additional cost of the bone substitute in the group with the lateral approach should be considered. All implants were loaded 7 weeks after sinus lift. The trial was judged to be at low risk of bias.

One trial compared two two-stage techniques for augmenting maxillary sinuses using a lateral window approach[57] (Fig 4a and b). Only patients having 1 to 5 mm of bilateral bone height at the sinus floor were included. Ten patients were treated with a split-mouth approach. After elevation of the sinus lining, one side was filled with granular Bio-Oss whereas an Inion resorbable rigid barrier was used to maintain space to allow bone regeneration in the contralateral site. All patients were followed up to 4 months after loading, therefore there were no dropouts. After 6 months, both interventions gained bone (14.4 mm for Inion versus 14.1 mm for Bio-Oss) with no significant differences between the procedures. There were no differences in complications between groups (two perforations of the maxillary lining at the Inion treated sites versus one at Bio-Oss site). However, in one of the patients where a perforation occurred at the Inion site, at implant placement, the sinus was two-thirds filled with soft tissue. Implants were placed anyway and the site was successfully retreated with Bio-Oss. No implant failed. The clinician preferred Bio-Oss because it was simpler to handle. There were no statistically significant differ-

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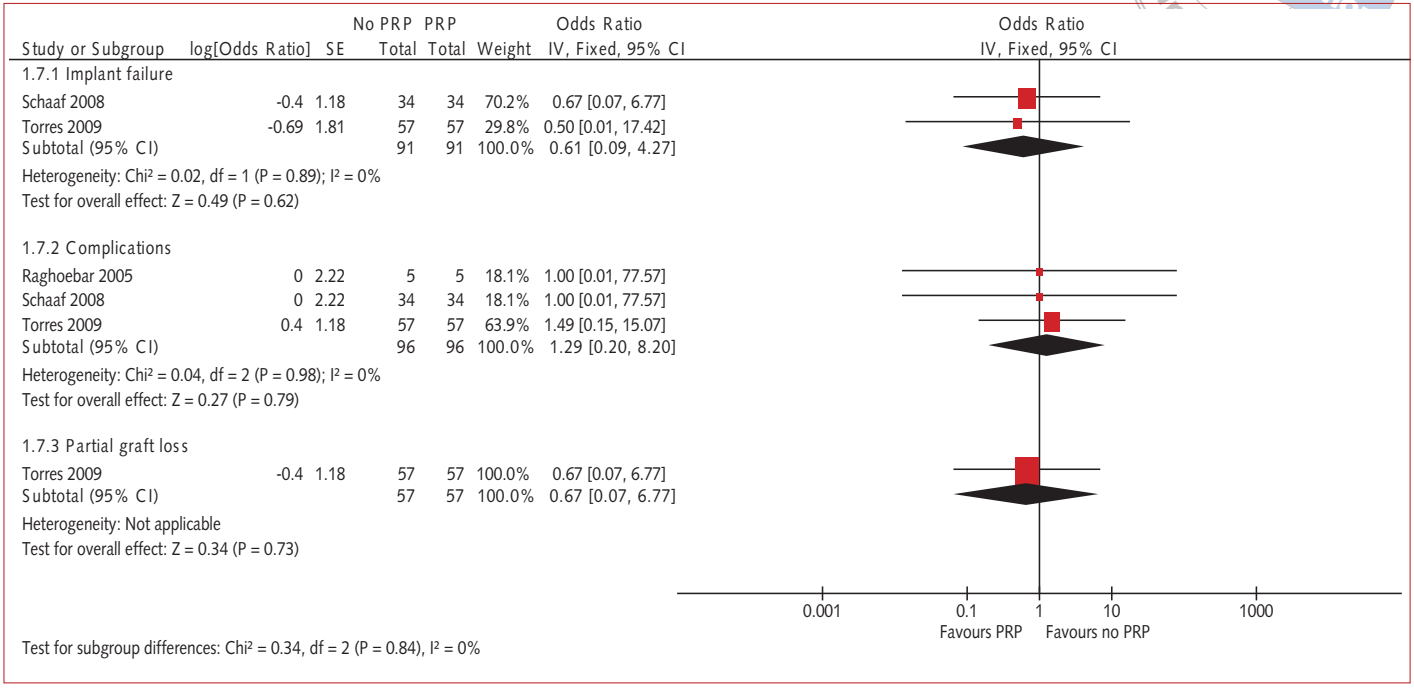
Fig 5 Forest plot illustrating meta-analyses of trials evaluating the efficacy of platelet rich plasma (PRP) in conjunction with sinus lift procedures. No statistically significant differences were observed.



ences in patient preference 1 month after surgery and 1 month after delivery of definitive prostheses: eight patients had no preference while two preferred the Bio-Oss treated side. With respect to cost, the bone substitutes and the barrier in one group and the cost of the barrier alone in the other should be considered. There was no significant difference in time to complete the augmentation procedure (19.8 minutes for Inion versus 20.5 for Bio-Oss) and all implants were loaded 11 months after sinus lift. The trial was judged to be at low risk of bias.

Trials evaluating the efficacy of PRP with grafts (4 trials with 114 patients)

One trial compared two techniques for augmenting resorbed maxillae including atrophic maxillary sinuses[63]. Only patients with less than 5 mm of alveolar bone height in the sinus floor were included. Five patients were treated with a split-mouth approach with a two-stage sinus lift and autogenous bone together with buccal onlay grafts, harvested from the iliac crest. One side was treated with platelet-rich plasma (PRP) and the other without. All patients were followed for 2 years after implant loading and there were no dropouts. No serious complications occurred at the grafted sites: one sinus membrane was perforated during surgery but healing was uneventful. A small incision breakdown occurred in the first week at the non-PRP side of one patient. A seroma which healed uneventfully was the only complication that occurred at the donor sites. During the prosthetic phase, one implant failed in the PRP side, but no prosthesis failed. There was no statistically significant difference for any of the outcomes considered in the review (Fig 5). The difference in cost and treatment time was the use of PRP. Prostheses were inserted about 10 months after augmentation. The trial was judged to be at high risk of bias.

One trial compared a two-stage sinus lift with a lateral window approach using either autogenous particulate bone from the iliac crest alone or the same graft with PRP in fully edentulous patients[61] (Fig 5). All sites were also horizontally augmented with cortico-spongeous blocks and left to heal for 4 months. A total of 34 patients treated according to a split-mouth design and 19 patients treated according to parallel group design were included in the first publication but no clinical data were provided[67]. In the second publication, the clinical data of the 34 patients treated with a split-mouth approach were presented, and only the data of those patients is

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used in the present review[61]. All patients were followed up to abutment connection (6 months after implant insertion) and there were no dropouts. Only complications at augmented sites were reported: one sinusitis in two patients, one from each group. Six patients experienced implant failures at abutment connection: one patient lost one implant at both sites, three patients lost one implant each at the non-PRP treated sites only, and two patients lost one and three implants at the PRP side. There was no statistically significant difference for any of the outcomes considered in the review. The difference in cost and treatment time was the use of PRP. The trial was judged to be at high risk of bias.

One trial compared two two-stage techniques for augmenting maxillary sinuses[62] (data not shown). Only patients with less than 8 mm of alveolar bone height in the sinus floor were included. Eighteen patients were treated with a split-mouth approach with a two-stage sinus lift with autogenous bone blocks from the iliac crest and Tissucol on one side, and autologous granular bone and platelet concentrations (APCs) with Tissucol on the other. Patients were followed up to 1 year after implant placement and there were two dropouts before implant placement for financial reasons. There was no complication due to cytapheresis or surgery. All implants were stable 1 year after placement. There was no statistically significant difference for any of the outcomes considered in the review. The difference in cost and treatment time was the use of APCs. The trial was judged to be at high risk of bias.

One trial compared one or two-stage sinus lift procedures using a lateral window technique and 100% granular Bio-Oss with or without PRP and left to heal for 6 months with a hybrid split-mouth parallel design[60]. In the original publication, 87 patients were included. Only the data of the 57 patients treated according to a split-mouth procedure are presented in the present review (Fig 5). Twenty-five patients having up to 4 mm of residual bone height were augmented first and 98 implants were placed after 6 months, whereas in 32 patients with residual bone ranging between 4 mm to 7 mm, 128 implants were placed simultaneously with the sinus augmentation procedure. Implants were left to heal unloaded for 6 months. Two years after loading, no drop-out occurred. Five perforations of the maxillary membrane occurred in five patients: three patients belonged to the PRP group and two to the non-PRP group. Partial loss of the graft occurred in five patients treated with the two-stage procedure: two patients belonged to the PRP group and three to the non-PRP group. According to the authors, no prosthesis failed. Four implants failed in three patients treated according a two-stage procedure. Three implants failed in two patients at sides which were not treated with PRP. There was no statistically significant difference for any of the outcomes considered in the review. The difference in cost and treatment time was the use of PRP. The trial was judged to be at low risk of bias.

The only meta-analysis possible was with three trials that compared particulate bone from the iliac crest[61,63] or Bio-Oss[60] with and without PRP in split-mouth trials. In two studies[61,63], sites were also augmented with onlay blocks of autogenous bone. There were no statistically significant differences between groups for implant failures and complications (Fig 5).

■ Discussion

Twenty-nine potentially eligible trials were identified, but data from only 10 investigations were able to be used. Twelve trials had to be excluded because they presented only histological data. The observation that the majority of randomised clinical trials evaluating sinus lift procedures report only histological findings without providing any useful information on the actual clinical outcome of the sinus lift procedure and implant rehabilitation is rather disappointing and alarming. This is not to say that histological information is not useful, but if not backed up by meaningful clinical outcomes it would appear that human beings are used instead of animals as histological experimental models and this is difficult to justify.

Sample sizes were relatively small, with only two trials[55,56] undertaking a sample size calculation. It is therefore possible that many of these trials were underpowered to demonstrate any significant difference between groups. Nevertheless, the included trials did provide limited but indeed useful insight into possible avenues for future clinical research and some clinical indications which should be carefully evaluated by clinicians when deciding whether

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to perform an augmentation procedure or not, or which augmentation procedure to select.

The present study first evaluated whether and when it may be necessary to augment the maxillary sinus and then which are the most effective augmentation procedures. This distinction is relevant since it is possible that ineffective procedures which could be even potentially dangerous are widely performed, despite no improvements of treatment prognosis or patients' quality of life.

Only one trial evaluated whether sinus lift procedures are indicated in patients having a residual crestal height between 4 and 6 mm[56]. The findings of this study are inconclusive due to the small sample size and the short follow-up (4 months after loading), however, they suggest that 5-mm-long implants with a diameter of 6 mm can be successfully loaded 4 months after placement without the need for any augmentation procedure. Though the only implant failure occurred in the short implant group, the implant was successfully replaced with another short implant placed more distally. There is a need for more trials to understand in which clinical situations sinus lift procedures are beneficial for patients. When evaluating which are the most effective augmentation procedures, there were eight trials providing some indications[55,57-59,61-64]. Studies were grouped as follows.

When trying to answer the question whether grafting is necessary to obtain bone regeneration, even in a case of a severely atrophic sinus, the findings from the only trial (pilot) investigating this hypothesis[57] clearly indicated that no graft is needed to obtain new bone in the sinus cavity, if it is possible to keep sufficient space using a resorbable rigid barrier. On the other hand, the operator found it technically simpler to use a bone substitute rather than to mould a space-maintaining barrier. The same study also suggested that there is no clear correlation between the amount of newly formed bone, evaluated with histomorphometry, and the clinical success of the implants. In fact, all implants became successfully osseointegrated even in the presence of an average of 24% of newly formed bone. In general, authors using surrogate outcomes, such as histomorphometry, as the only outcome to predict implant success in cases of sinus augmentations with various materials should be more careful when drawing conclusions. More clinically relevant primary outcomes such as implant failure and complications should be used in conjunction with surrogate outcomes.

The question whether autogenous bone could be replaced by bone substitutes to reduce patient morbidity was addressed in two trials[59,64]. One trial[64] is of little use because the follow-up was limited to abutment connection and onlay bone blocks were used in half of the patients. The findings of the other trial[59] suggest that 80% or even 100% Bio-Oss can be used as bone substitutes. Autogenous bone grafting might be replaced by bone substitutes by this indication, however larger trials with longer follow-up should be conducted to validate these preliminary findings.

One trial compared a one-stage crestal sinus lift procedure with autogenous bone and 8-mm-long implants with a lateral window sinus lift with a mix of autogenous bone and 50% Bio-Oss to place longer implants[55]. Though no statistically significant differences were found, there were more complications and failures with the lateral window augmentation procedure. It is interesting to observe that all implants were placed in bone with a residual height of 3 to 6 mm and were loaded less than 2 months after the sinus lift. It is generally accepted that 2 months in humans is insufficient to allow for new bone formation. Therefore, the original bone must have been sufficient to hold the implants with both lifting procedures adding little or even no benefit.

When comparing a one-stage monocortical bone block versus a two-stage technique with particulate bone harvested from the iliac crest for maxillary sinus lifting, no statistically or clinically significant differences were observed[58]. However, the use of autogenous bone blocks from the iliac crest in a one-stage procedure is a technique that is nowadays seldom used and most of the sinus lifting procedures are now performed under local anaesthesia.

Four trials[60-63] evaluated the possible advantage of using PRP to accelerate bone healing for sinus augmentation. No clinical benefit could be observed in any of the trials when using PRP, therefore there appear to be no reasons to justify its use in this application.

With respect to generalisation of the results of the present review to general practice, most of the augmentation procedures evaluated were performed by experienced clinicians, therefore caution is recommended when extrapolating the results to other clinical settings. The first clinical question that a clinician

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should ask is what are the potential added benefits for a patient by augmenting the maxillary sinus. Then, the more effective procedure associated with less risks of complication/discomfort for the patient should be selected.

■ Conclusions

The conclusions are based on few trials with few patients, sometimes having a short follow-up, and often being judged to be at high risk of bias. Therefore, the conclusions have to interpreted with great caution and should be viewed as very preliminary and to be confirmed by large multicentre trials.

One trial investigated whether and when it is necessary to augment the maxillary sinus:

- It is still unclear when sinus lift procedures are needed.
- Implants 5 mm long and 6 mm wide can be successfully loaded in maxillary bone with a residual height of 4 to 6 mm below the sinus without any augmentation procedure, though the long-term prognosis is unclear.

Nine trials investigated which are the most effective sinus lift techniques, four of which evaluated the efficacy of PRP:

- If the residual alveolar bone height is 3 to 6 mm, a crestal approach to lift the sinus lining and place 8 mm implants may possibly lead to fewer complications than a lateral window approach placing, at the same time, implants at least 10 mm long.
- Keeping the sinus lining elevated with a rigid resorbable barrier in the presence of 1 to 5 mm of residual bone height without the addition of a graft is sufficient to regenerate new bone to allow rehabilitation with implant-supported prostheses. However, it is technically simpler to fill the sinus with a granular bone substitute.
- Bone substitutes such Bio-Oss and Cerasorb might be as effective as autogenous bone grafts for augmenting atrophic maxillary sinuses, therefore they might be used as a replacement to autogenous bone grafting.
- PRP treatment with autogenous bone grafts or bone substitutes may not improve the outcome of sinus lift procedures for implant rehabilitation.

In order to understand when sinus lift procedures are needed and which are the most effective sinus lift techniques, larger and well-designed trials are needed. Such trials should be reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines[68] (http://www.consort-statement.org/). It is difficult to provide clear indications with respect to which sinus lift procedures should be evaluated first. However, once it has been established in which clinical situations these procedures are actually needed, priority could be given to those interventions that are simpler, less invasive, involve less risk of complications, and reach their goals within the shortest time frame. Research efforts should be concentrated on a few important clinical questions using larger sample sizes, which might be obtained through collaborative efforts among various research groups. One of the the identified research priorities is to evaluate whether and when one-stage lifting via a crestal approach can replace the more invasive lateral window procedures. Another priority is to evaluate whether bone substitutes can be used for replacing autogenous bone in augmenting severely atrophic maxillary sinuses.

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