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REVIEW

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Comparative evidence of different surgical techniques for the management of vertical alveolar ridge defects in terms of complications and efficacy: A systematic review and network meta-analysis

Faisal F. Alotaibi[1,2] | Isabella Rocchietta[1] | Jacopo Buti[1] | Francesco D'Aiuto[1]

[1]Unit of Periodontology, UCL Eastman Dental Institute, London, UK

[2]Department of Oral and Maxillofacial Surgery and Diagnostic Sciences, College of Dentistry, Prince Sattam bin Abdulaziz University, Alkharj, Saudi Arabia

Correspondence
Francesco D'Aiuto, Periodontology Unit, UCL Eastman Dental Institute, 21 University Street, Bloomsbury, London WC1E 6DE, UK.
Email: f.daiuto@ucl.ac.uk

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Abstract

Aim: To systematically appraise the available evidence on vertical ridge augmentation (VRA) techniques and estimate a treatment-based ranking on the incidence of complications as well as their clinical effectiveness.

Materials and Methods: Searches were conducted in six databases to identify randomized clinical trials comparing VRA techniques up to November 2022. The incidence of complications (primary) and of early, major, surgical and intra-operative complications, vertical bone gain (VBG), marginal bone loss, need for additional grafting, implant success/survival, and patient-reported outcome measures (secondary) were chosen as outcomes. Direct and indirect effects and treatment ranking were estimated using Bayesian pair-wise and network meta-analysis (NMA) models.

Results: Thirty-two trials (761 participants and 943 defects) were included. Five NMA models involving nine treatment groups were created: onlay, inlay, dense-polytetrafluoroethylene, expanded-polytetrafluoroethylene, titanium, resorbable membranes, distraction osteogenesis, tissue expansion and short implants. Compared with short implants, statistically significant higher odds ratios of healing complications were confirmed for all groups except those with resorbable membranes (odds ratio 5.4, 95% credible interval 0.92–29.14). The latter group, however, ranked last in clinical VBG.

Conclusions: VRA techniques achieving greater VBG are also associated with higher incidence of healing complications. Guided bone regeneration techniques using non-resorbable membranes yield the most favourable results in relation to VBG and complications.

KEYWORDS
complications, network meta-analysis, ridge augmentation, systematic review

Clinical Relevance

Scientific rationale for study: Several vertical ridge augmentation (VRA) techniques have been proposed and linked to different complication rates and bone gains. Network meta-analyses could inform clinicians on the best treatment choices.

Principal findings: Guided bone regeneration techniques yield the most favourable results in relation to vertical bone gain (VBG) and complications. Dense-polytetrafluoroethylene membranes performed marginally better than expanded-polytetrafluoroethylene. Resorbable membranes could be considered when minimal VBG is needed. Operator experience (>200 procedures) is directly linked to less complications.

Practical implications: VRA techniques with greater vertical bone gain are associated with greater incidence of complications. Operator experience is a deciding factor in the incidence of complications.

1 | INTRODUCTION

The demand for dental implant therapy following tooth loss has dramatically increased over the past years. Tooth loss due to trauma, infection or periodontitis results in a concomitant loss of supporting alveolar bone both in horizontal and vertical dimensions. The presence of adequate alveolar bone is a prerequisite for successful dental implant therapy. Inadequate bone height remains a challenging clinical scenario with impact on the patient's oral health and quality of life. The management of this deficiency often includes using hard and soft tissue augmentation procedures to obtain adequate support for dental implant placement. Short implants have been introduced as an alternative, but their use is not always indicated because of restorative and aesthetic considerations (Salvi et al., 2018).

Vertical ridge augmentation (VRA) procedures aiming to recreate alveolar bone before dental implant placement, although based on biologically proven concepts, are technically sensitive, operator-dependent and frequently associated with intra- and post-operative complications (Jepsen et al., 2019; Rocchietta et al., 2008; Wang & Boyapati, 2006). Evidence supporting the adoption of different VRA procedures, which has accumulated over the past three decades, includes guided bone regeneration (GBR), onlay and inlay (interpositional) bone blocks, distraction osteogenesis and others (Esposito et al., 2009). Autogenous bone blocks have been described as the 'gold standard' among these techniques (Tessier et al., 2005). Nevertheless, donor site comorbidities constitute an important challenge to clinicians and patients when considering this treatment strategy.

Although fine-tuning of techniques and biomaterials over the years have resulted in reduction of the overall incidence of complications following VRA procedures, soft-tissue dehiscence (i.e., healing complications) remains a major concern due to its higher incidence compared with other complications (Urban et al., 2019) and its significant negative impact on treatment duration and success (Tay et al., 2022).

Several systematic reviews and pair-wise meta-analyses have been conducted in an attempt to identify the best surgical technique for VRA. Owing to the large number of proposed procedures and the relatively small number of comparative studies, many treatment options have currently not been directly compared in clinical trials and hence not incorporated in traditional pair-wise meta-analyses. Bayesian network meta-analysis (NMA) approach allows the evaluation of both direct and indirect evidence, thus allowing the inclusion and comparison of all existing surgical techniques (Buti et al., 2011) as well as the estimation of ranking of the treatments. Recently, a systematic review and NMA evaluating vertical bone gains with different barrier membranes was published (Zhang et al., 2022). However, the NMA conducted in the review combined studies that investigated techniques for the management of vertical, horizontal, intra-bony and peri-implant bone defects, as well as ridge preservation techniques, thus limiting the clinical relevance of its findings. Therefore, the aims of this research were to (i) systematically review and appraise the available evidence on the incidence of complications and the clinical effectiveness of VRA techniques for the management of vertical alveolar ridge defects before dental implant placement, (ii) compare a number of reported surgical techniques and positive control and (iii) estimate a treatment-based ranking.

2 | MATERIALS AND METHODS

2.1 | Protocol and registration

The review was registered in the PROSPERO database (CRD42020189743), prepared in line with Cochrane Collaboration guidelines and reported following the PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions (PRISMA-NMA) (Hutton et al., 2015).

The following focused question was developed: 'In otherwise healthy adult patients who underwent any procedure to manage vertical alveolar ridge defects in order to place dental implants, which technique has the lowest incidence of complications and which procedure is the best in terms of clinical outcomes when compared with each other and to a positive control (no augmentation)?'

2.2 | Study eligibility criteria (in PICOS format)

(P) Population: Adult, systemically healthy patients who underwent any procedure to manage vertical alveolar ridge defects in order to place dental implants, including the use of short dental implants without augmentation.

(I) Intervention: Any VRA procedure including, but not limited to, distraction osteogenesis (DO), guided bone regeneration (GBR), onlay grafting and inlay (interpositional) grafting.

(C) Comparison: Any VRA procedure including, but not limited to, DO, GBR, onlay grafting and inlay grafting as well as no augmentation procedure using short dental implants.

(O) Outcomes:

a. *Primary outcome*:
   1. Incidence of any complications including overall healing complications (e.g., wound dehiscence, graft or membrane exposure, loss of integration and local infection), overall post-operative surgical complications (i.e., neurological and vascular complications), early healing complications (i.e., occurring within the first 2 months post procedure), major healing complications (based on the definition by Merli et al. (2007)) and/or intra-operative complications.

b. *Secondary outcomes*:
   2. Intra-surgical vertical bone gain as assessed by linear measurements at re-entry (implant placement and/or barrier removal);
   3. Radiographic or tomographic absolute and relative vertical bone gain as assessed by linear or volumetric measurements at re-entry or after the consolidation period in distraction osteogenesis;
   4. Marginal bone loss (MBL) as reported by linear measurements on intra-oral radiographs at least 1 year post loading;
   5. Implant survival rate and implant success rate in studies with minimum of 12 months follow-up post loading;
   6. Need for additional bone grafting (either partial or new complete bone grafting) at the time of dental implant placement and at re-entry procedure in staged augmentation, calculated as a percentage of the number of cases needing additional grafting of all cases;
   7. Patient-reported outcome measures including, but not limited to, quality of life, pain, discomfort and overall satisfaction with the treatment received.

(S) Studies type: Parallel or split-mouth randomised clinical trials (RCTs), of any sample size, with minimum of 6 months follow-up post augmentation/implantation.

2.3 | Information sources and search strategies

Electronic searches up to 1 November 2022 were conducted in six databases: CENTRAL (Cochrane Central Register of Controlled Trials), OVID MEDLINE, EMBASE, Web of Science, LILACS (Latin American & Caribbean Health Sciences Literature) and US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) (PRISMA flow-chart and databases' search strategies are shown in Appendix 1). Articles of any language but with English titles and/or abstracts were retrieved. Hand-searching was performed in references of identified studies and reviews as well as in the *Journal of Periodontology*, *Journal of Clinical Periodontology*, *International Journal of Oral and Maxillofacial Surgery*, *European Journal of Oral Implantology*, *Clinical Oral Implants Research*, *Clinical Implant Dentistry and Related Research*, *The International Journal of Oral and Maxillofacial Implants*, *International Journal of Oral Implantology* and the *Journal of Oral and Maxillofacial Surgery* for the period between January 2000 and November 2022.

2.4 | Study selection and data extraction

Screening of titles and abstracts was performed by one reviewer (FA). In case of uncertainty, decision on which articles whose full text had to be screened was reached by discussion with the review team (IR, JB, FD). Next, one reviewer (FA) did full-text screening of the articles for inclusion. Again, in case of uncertainty, decision was reached on inclusion or exclusion by discussion with the review team. Next, data extraction forms were developed and piloted on several papers and modified as required before use. Then, data were extracted by one reviewer (FA) followed by verification of a randomly selected sample (50%) of extracted data by two other reviewers (JB, IR). Disagreements were resolved by discussion with a fourth reviewer (FD). Authors of included studies were contacted to provide missing information about study designs or outcomes. The following data were extracted: country and setting, study design, population characteristics (age, sex, general health, smoking, history of periodontitis and location of the alveolar deficiency), interventions details, funding, conflict of interest and information about the primary and secondary outcomes of this review.

2.5 | Data synthesis

2.5.1 | Descriptive methods

Extracted data were summarized in evidence tables to detect any differences in study characteristics and to quantify the body of evidence.

2.6 | Quantitative methods

The Aggregate Data Drug Information System (ADDIS) was used for evidence synthesis based on the GeMTC package for the R statistical software. Bayesian models for meta-analysis were used via GeMTC, starting with models for pair-wise meta-analysis and then moving on to network meta-analysis (NMA) and node-splitting models (van Valkenhoef et al., 2012; van Valkenhoef et al., 2015).

2.6.1 | Measures of association

Estimates of treatment effect for direct and indirect evidence from included trials were expressed as mean differences (MDs) and 95% credible intervals (CrI) for continuous data and as odds ratios (ORs) and 95% CrI for dichotomous outcomes.

2.6.2 | Heterogeneity, inconsistency and transitivity

Heterogeneity (i.e., between-trials SD and 95% CrI) and Inconsistency (i.e., between-trial differences in the underlying treatment effects between comparisons) were estimated for NMA models. The assumption of transitivity within the network was assessed by exploring the

distribution of patient characteristics, similarity of interventions and study design across comparisons (Appendix 2).

2.6.3 | Geometry of the network

Graphical representation of evidence base was performed through network plots generated using Metainsight tool (V4.0.0 Beta) (Owen et al., 2019).

2.6.4 | Ranking of treatments

In addition to relative effects, the Bayesian analysis produced rank probabilities (i.e., the probability for each treatment to obtain each possible rank in terms of their relative effects). Cumulative ranking curves and surfaces under these curves were generated using the Metainsight tool (V4.0.0 Beta) (Owen et al., 2019). The surface under the cumulative ranking (SUCRA) curve was used as a numerical presentation of the overall ranking, which presents a single number associated with each treatment. The higher the SUCRA value (the closer to 100% if expressed in percentage), the higher the likelihood that a therapy was in the top rank, and vice versa.

2.6.5 | Sensitivity analyses

Models were generated to explore, quantify and control for sources of heterogeneity between studies based on the following covariates:

- Smoking: Excluding studies that allowed smokers to be enrolled.
- Operator experience: A questionnaire to evaluate surgical operators' experience in each included study was developed and distributed to all authors. Three main questions were included: (i) how many VRA procedures have the operator done at the time of the study? (ii) how many years of experience have the operator had at the time of the study? and (iii) whether the operator has had any formal training in VRA procedures before conducting the study. Based on the responses from the authors, regression analyses to explore the effect of experience on the outcomes were carried out.
- Risk of bias: Excluding studies that were deemed to have high risk of bias.
- Post hoc subgroup analyses: Of identified possible sources of heterogeneity in included studies and including all procedures without control (short implants with no augmentation).

2.7 | Publication bias

Presence of publication bias in the included studies was explored using funnel plots, constructed by ADDIS as part of the evidence synthesis, in which the estimate of the reported effect size is plotted against a measure of precision.

2.8 | Assessment of risk of bias and certainty in the evidence

Risk of bias was assessed at the outcome level in all included RCTs using the Cochrane risk of bias (RoB) 2.0 Tool (Sterne et al., 2019). Certainty in the evidence (CiE) was assessed at the outcome level using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach (Puhan et al., 2014).

3 | RESULTS

3.1 | Study selection

A total of 7711 records were identified, of which 7702 were by electronic searches and 9 by hand-searching. After duplicates removal, titles and/or abstracts of 6369 records were screened. Following exclusion of irrelevant titles and abstracts, full texts of 126 publications were screened, which led to the further exclusion of 79 irrelevant papers (reasons for exclusion can be found in Appendix 3) and the inclusion of 49 publications describing 32 RCTs (Table 1). Twenty-two RCTs contributed to quantitative analyses.

3.2 | Characteristics of included studies

Of the 32 RCTs included, 10 studies had a split-moth design and 22 had a parallel design. Eight studies compared short implants with long implants placed in vertically augmented area, and 24 studies compared two different vertical augmentation strategies. The included population consisted of 761 participants, with a total of 943 vertical defects. In seven studies, vertical defects without a horizontal component were included, while in eight studies the defects included were combined vertical-horizontal; lastly, in 17 studies no information was found on the type of defect. Eight studies did not limit their population to a specific area of the mouth, while the remaining studies included patients with defects only in posterior mandible ($n = 14$), anterior maxilla ($n = 3$), posterior jaws ($n = 4$), mandible ($n = 1$) or maxilla ($n = 1$). Only one study included patients with active periodontitis, while the remaining 31 studies required patients to have control of pre-existing periodontitis. Patients were enrolled in supportive care programs in nine of the included studies. Among the 32 RCTs (64 intervention arms), a variety of techniques were used for augmentation procedures, including block onlay ($n = 8$), inlay (interpositional/sandwich technique) using block ($n = 11$) or particulate ($n = 2$) bone, GBR using non-resorbable ($n = 7$) or resorbable membranes ($n = 9$, with or without titanium barriers), distraction osteogenesis ($n = 4$) and tent-pole (tenting) using cortical shells ($n = 1$) or screws or implants ($n = 1$). Bone materials used for grafting included autogenous ($n = 15$), xenogeneic ($n = 9$), allogenous ($n = 4$), alloplastic ($n = 2$) and mixture of autogenous with xenogeneic ($n = 3$) or allogenous ($n = 4$) bone. Non-resorbable barrier used across the studies were titanium mesh ($n = 6$), dense polytetrafluoroethylene (d-PTFE)

TABLE 1 Characteristics of included studies and assignment of treatment groups.

		Test			Control				
Study	• Design • Country • Setting	• Technique • Staging • Sample size	• Type of bone • Barrier	**NMA group**	• Technique • Staging • Sample size	• Type of bone • Barrier	**NMA group**	• Age • Sex • Smokers' inclusion • Area of the mouth	**Outcomes included**
Amorfini et al. (2014)	• Split-mouth • Italy • University of Genoa	• Onlay • Simultaneous • 8 participants (subgrouped by using only saline solution [A] or rhPDGF-BB [B] during grafting)	• Cortico-cancellous iliac block allografts • Collagen membrane	Onlay	• GBR • Simultaneous • 8 participants (sub-grouped by using only saline solution [A] or rhPDGF-BB [B] during grafting)	• Autologous bone chips • Double layer of collagen membrane	RM	• 59.5 years (median) • Sex NR • NR • Posterior mandible	Complications
Bernardi et al. (2018)	• Split-mouth • Italy • University of L'Aquila	• Inlay • Staged (6 months) • 36 participants	• Xenogeneic blocks • No membrane	Inlay	• Short implants (6 mm) • NA • 36 participants	NA	SI	• 43– 77 years • 50% F • NR • Posterior mandible	• Complications • Implants survival
Bianchi et al. (2008)	• Parallel • Italy • University of Bologna	• Distraction osteogenesis • 3–4 months consolidation period • 4 participants	NA	DO	• Inlay • Staged (3–4 months) • 5 participants	• Monocortical iliac crest bone • No membrane	Inlay	• 45.5 years (mean) • 54.4% F • ≤15 cig. per day • Posterior mandible	• Complications • Linear VBG on CT
Barausse et al. (2022) , Bolle et al. (2018)	• Parallel • Italy • 2 private practices and 2 hospitals	• Inlay • Staged (4 months) • 20 participants[a]	• Blocks of collagenated cancellous equine bone • Collagen membrane	Inlay	• Short implants (4 mm) • NA • 40 participants	NA	SI	• Test: 63.3 years; Control: 60 years (mean) • Test: 60% F, Control: 57.5% F • Smokers included • Posterior jaws	Complications Implants survival MBL on IORG
Byun et al. (2020)	• Parallel • Korea • 6 university hospitals	• TE + tunnelling • Staged (4 weeks from TE until grafting then 6 months until implant placement) • 23 participants	• Xenogeneic particulate bone • Collagen membrane	TE	• GBR • Staged (6 months) • 23 participants	• Xenogeneic particulate bone • d-PTFE titanium-reinforced membrane	dPTFE	• 57.6 years (mean) • 84.6% F • Non-smokers • Any area of the mouth	• Complications • Linear VBG on CBCT • MBL on CBCT
Chiapasco et al. (2004)	• Parallel • Italy • University of Milan	• GBR • Subgroup 1A: simultaneous; Subgroup 1B: staged (6–7 months) • 11 participants	• Particulate autogenous bone (from ramus and symphysis) • e-PTFE	ePTFE	• Distraction osteogenesis • 2.5–3.5 months until implant placement • 10 participants	NA	DO	• 39.9 years (mean) • 57.2% F • ≤15 cig. per day • Areas not specified	• Complications • MBL on IORG • Implants S&S

(Continues)

TABLE 1 (Continued)

Study	• Design • Country • Setting	Test • Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	Control • Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	• Age • Sex • Smokers' inclusion • Area of the mouth	Outcomes included
Chiapasco et al. (2007)	• Parallel • Italy • University of Milan	• Onlay • Staged (4–5 months) • 8 participants	• Autogenous blocks (ramus) • No Barrier	Onlay	• Distraction osteogenesis • 2.5–3.5 months until implant placement • 9 participants	NA	DO	• 41.2 years (mean) • 52.9% F • ≤15 cig. per day • Mandible	• Complications • Linear VBG on IORG • MBL on IORG • Implants S&S
Chiapasco et al. (2013)[b]	• Parallel • Italy • University of Milan	• Onlay • Staged (4–7 months) • 23 participants	• Autogenous cortical onlay • Resorbable membrane	Onlay	• Staged (4–7 months) • 21 participants	• Autogenous cortical onlay • No barrier	Onlay	• 53 years (mean) • 70.5% F • ≤20 cig. per day • Areas not specified	• Complications • Implants S&S
Cucchi, Vignudelli, Fiorino, et al. (2021), Cucchi et al. (2017)	• Parallel • Italy • Private practice	• GBR • Simultaneous • 20 participants	• 50:50 autogenous: allogeneic bone • d-PTFE	dPTFE	• GBR • Simultaneous • 20 participants	• 50:50 autogenous: allogeneic bone • Ti-Mesh	Ti	• 52 years (mean) • 67.5 F • ≤10 cig. per day • Posterior mandible	• Complications • Linear intra-surgical VBG • MBL on PA
Cucchi, Vignudelli, Franceschi, et al. (2021)[b]	• Parallel • Italy • Private practice	• Ti-mesh • Staged (6 months) • 14 participants[a]	• 50:50 autogenous: xenogeneic bone • Custom-made Ti-mesh + resorbable membrane	Ti	• Ti-mesh • Staged (6 months) • 11 participants[a]	• 50:50 autogenous: xenogeneic bone • Custom-made • Ti-mesh	Ti	• NR • 56% F • >10 cig. per day • Any area of the mouth	• Complications • Linear, volumetric and relative VBG on CBCT • Need for additional grafting
Dottore et al. (2014)[b], Kawakami et al. (2013)	• Split-mouth • Brazil • Guarulhos University	• Inlay • Staged (6 months) • 11 participants	• A mix of ncHA powder and pellets • No barrier	Inlay	• Inlay • Staged (6 months) • 11 participants	• Autogenous blocks • No barrier	Inlay	• 52.1 years (mean) • 81.8% F • Non-smokers • Posterior mandible	• Complications • VBG on DVT • MBL on IORG • Implants S&S
El Zahwy, Taha, Mounir, and Mounir et al. (2019)	• Parallel • Egypt • Cairo University	• Inlay • Simultaneous • 8 participants	• Autogenous blocks • No barrier	Inlay	• Onlay • Simultaneous • 8 participants	• Autogenous block • No barrier	Onlay	• 38.5 years (mean) • 37.5% F • NR • Anterior maxilla	• Complications • Linear VBG on CBCT
Esposito et al. (2019), Gastaldi et al. (2018), Pistilli, Felice, Piattelli, et al. (2013)	• Parallel • Italy • 8 private practices	• Inlay • Staged (4 months) • 20 participants[a]	• Xenogeneic blocks • Resorbable membrane	Inlay	• Short implants • NA • 40 participants	NA	SI	• Test: 52.8 years control: 59.9 years (mean) • 70% F • Smokers included • Posterior jaws	• Complications • MBL on IORG • Implants survival
Felice, Marchetti, et al. (2009)[b], Felice et al. (2008)	• Split-mouth • Italy • University of Bologna	• Inlay • Staged (4 months) • 10 participants	• Xenogeneic blocks • Resorbable membrane	Inlay	• Inlay • Staged (4 months) • 10 participants	• Autogenous blocks • Resorbable membrane	Inlay	• 54 years (mean) • 60% F • NR • ≤15 cig. per day • Posterior mandible	• Complications • Linear VBG on CT • MBL on IORG • PROMs

TABLE 1 (Continued)

Study	Test				Control				Outcomes included
	• Design • Country • Setting	• Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	• Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	• Age • Sex • Smokers' inclusion • Area of the mouth	
Felice, Pistilli, et al. (2009)	• Parallel • Italy • University of Bologna	• Inlay • Staged (3–4 months) • 10 participants	• Autogenous blocks • Resorbable membrane	Inlay	• Onlay • Staged (3–4 months) • 10 participants	• Autogenous blocks • Resorbable membrane	Onlay	• 53.9 years (mean) • 70% F • NR • Posterior mandible	• Complications • Linear VBG on CT • PROMs
Felice, Barausse, Pistilli, Ippolito, and Esposito (2018), Esposito, Cannizarro, et al. (2011), Felice et al. (2014), Felice et al. (2010)	• Parallel • Italy • 3 private practices	• Inlay • Staged (5 months) • 30 participants	• Xenogeneic blocks • Resorbable membrane	Inlay	• Short implants • NA • 30 participants	NA	SI	• 55.5 years (mean) • 63.3% F • Smokers included • Posterior mandible	• Complications • MBL on IORG
Felice, Barausse, et al. (2019), Esposito, Pellegrino, et al. (2011), Esposito et al. (2014), Felice, Checchi, et al. (2009), Felice, Marchetti, et al. (2009)	• Split-mouth • Italy • Different private practices and two hospitals	• Inlay • Staged (4 months) • 15 participants[a]	• Xenogeneic blocks • Resorbable membrane	Inlay	• Short implants • NA • 30 participants	NA	SI	• 56 years (mean) • 56.7% F • Smokers included • Posterior jaws	• Complications • MBL on IORG • Implants survival • PROMs
Felice, Pistilli, et al. (2019), Esposito et al. (2012), Felice, Barausse, Pistilli, Ippolito, and Esposito (2018), Felice, Barausse, Pistilli, Piattelli, et al. (2018), Pistilli, Felice, Cannizzaro, et al. (2013)	• Split-mouth • Italy • 3 hospitals and 3 private practices	• Inlay • Staged (3 months) • 20 participants[a]	• Xenogeneic blocks • Resorbable membrane	Inlay	• Short implants • NA • 40 participants	NA	SI	• 55.9 years (mean) • 72.5% F • Smokers included • Posterior jaws	• Complications • MBL on IORG • Implants survival • PROMs
Fontana et al. (2008)[b]	• Split-mouth • Italy • University of Milan	• GBR • Staged (7 months) • 5 participants	• Allogenic bone matrix • e-PTFE membrane	ePTFE	• GBR • Staged (6.5 months) • 5 participants	• Autogenous bone chips • e-PTFE membrane	ePTFE	• 55 years (mean) • 100% F • >10 cig. per day • Posterior mandible	• Complications • Linear intra-surgical VBG

(Continues)

TABLE 1 (Continued)

Study	• Design • Country • Setting	Test • Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	Control • Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	• Age • Sex • Smokers' inclusion • Area of the mouth	Outcomes included
Laino et al. (2014)[b]	• Split-mouth • Italy • University of Naples	• Inlay • Staged (6 months) • 12 participants	• Allogenic blocks • Resorbable membrane	Inlay	• Inlay • Staged (6 months) • 12 participants	• Autogenous blocks • Resorbable membrane	Inlay	• 57 years (mean) • 75% F • ≤10 cig. per day • Posterior mandible	Complications
Leong et al. (2015)	• Parallel • United States • University of Michigan	• Onlay • Staged (6 months) • 9 participants	• Block allografts • Resorbable membrane	Onlay	• Tenting • Staged (6 months) • 10 participants	• Particulate allografts • Resorbable membrane	RM	• 44–71 years • 38% F • Non-smokers • Posterior mandible	• Complications • Linear intra-surgical VBG
Maiorana et al. (2021)	• Split-mouth • Italy • University of Milan	• GBR • Staged (8 months) • 5 participants	• 50:50 autogenous: allogenic bone • d-PTFE membrane	dPTFE	• Ti-mesh • Staged (8 months) • 5 participants	• 50:50 autogenous: allogenic bone • Ti-mesh	Ti	• 54.2 years (mean) • 80% F • >10 cig. per day • Posterior mandible	• Complications • Linear intra-surgical VBG
Merli et al. (2014), Merli et al. (2007), Merli et al. (2010)	• Parallel • Italy • Private practice	• Osteosynthesis plates • Simultaneous • 11 participants	• Particulate autogenous bone • Titanium osteosynthesis plates supporting resorbable membranes	Ti	• GBR • Simultaneous • 11 participants	• Particulate autogenous bone • e-PTFE	ePTFE	• 47.3 years (mean) • 81.8% F • ≤20 cig. per day • Area not specified	• Complications • Linear intra-surgical VBG • MBL on IORG • Implants survival
Merli et al. (2020)[b]	• Parallel • Italy • Private practice	• Osteosynthesis plates • Staged (6 months) • 15 participants	• 50:50 autogenous: xenogeneic bone • Titanium osteosynthesis plates supporting resorbable membranes	Ti	• Osteosynthesis plates • Staged (6 months) • 15 participants	• Particulate autogenous bone • Titanium osteosynthesis plates supporting resorbable membranes	Ti	• 54.8 years (mean) • 50% F • >20 cig. per day • Any area of the mouth	• Complications • Linear and volumetric VBG on CBCT • PROMs
Mounir et al. (2017)	• Parallel • Egypt • Cairo University	• Inlay • Staged (duration NR) • 8 participants	• Xenogeneic bocks • No barrier	Inlay	• Ti-mesh • Staged (duration NR) • 8 participants	• Particulate xenogeneic bone • Ti-mesh	Ti	• 39 years (mean) • 37.5% F • NR • Anterior maxilla	• Complications • Linear and relative VBG on CBCT
Mounir et al. (2019)[b]	• Parallel • Egypt • Cairo University	• PEEK mesh • Staged (6 months) • 8 participants	• 50:50 autogenous: xenogeneic bone • PEEK mesh + resorbable membrane	Ti	• Ti-mesh • Staged (6 months) • 8 participants	• 50:50 autogenous: xenogeneic bone • Pre-bent Ti-mesh + resorbable membrane	Ti	• 38.5 years (mean) • 37.5% F • NR • Maxilla	• Complications • Linear and relative VBG on CBCT
Mounir et al. (2021)[b]	• Parallel • Egypt • Cairo University	• Onlay • Staged (6 months) • 7 participants	• Autogenous (symphyseal) bone • No barrier	Onlay	• Onlay • Staged (6 months) • 7 participants	• Autogenous (retromolar) bone • No barrier	Onlay	• 35–75 years • 35.7% F • NR • Anterior maxilla	• Complications • Linear VBG on CBCT

TABLE 1 (Continued)

Study	Test				Control				Outcomes included
	• Design • Country • Setting	• Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	• Technique • Staging • Sample size	• Type of bone • Barrier	NMA group	• Age • Sex • Smokers' inclusion • Area of the mouth	
Roccuzzo et al. (2007)	• Parallel • Italy • Private practice	• Ti-mesh • Staged (4–6 months) • 12 participants	• Autogenous blocks • Ti-mesh	Ti	• Onaly • Staged (4–6 months) • 12 participants	• Autogenous blocks • No barrier	Onlay	• 48.6 years (mean) • 66.7% F • NR • Any area of the mouth	• Complications • Linear intra-surgical VBG • Need for additional grafting
Rokn et al. (2018)	• Split-mouth • Iran • Tehran University	• GBR • Staged (6 months) • 11 participants	• Mix of particulate autogenous and allogenic bone • Resorbable membrane	RM	• Short implants • NA • 11 participants	NA	SI	• 50.3 years (mean) • 81.8% F • NR • Posterior mandible	• Complications • Linear intra-surgical VBG • MBL on IORG • Implants survival
Ronda et al. (2014)	• Parallel • Italy • Private practice	• d-PTFE • staged and simultaneous • 13 participants	• 50:50 autogenous: allogenic bone granules • d-PTFE membrane	dPTFE	• e-PTFE • staged and simultaneous • 13 participants	• 50:50 autogenous: allogenic bone granules • d-PTFE membrane	ePTFE	• 49.6 years (mean) • 95.7% F • ≤10 cig./day • Posterior mandible	• Complications • Linear intra-surgical VBG
Schortinghuis et al. (2008)[b]	• Parallel • The Netherlands • Groningen University Hospital	• Distraction osteogenesis + ultrasound • NA • 5 participants	NA	DO	• Distraction osteogenesis + placebo • NA • 4 participants	NA	DO	• 56 years (mean) • NR • NR • Mandible	• Complications • Ultrasonographic VBG
Shah et al. (2018)	• Parallel • United States • Harvard University	• GBR • NR • 25 participants	• Alloplastic bone • Resorbable membrane	RM	• Short implants • NA • 25 participants	NA	SI	• 58.4 years (mean) • 62% F • Smokers included • Any area of the mouth	• Complications • Implant survival

Abbreviations: BVC, bone volume change; CT/CBCT, computed tomography/cone beam computed tomography; d-PTFE, dense polytetrafluoroethylene; e-PTFE, expanded polytetrafluoroethylene; F, female; GBR, guided bone regeneration; IORG, intra-oral radiograph; MBL, marginal bone loss; NA, not applicable; NMA, network meta-analysis; NR, not reported; OPG, orthopantomogram; PA, periapical radiograph; PEEK, polyetheretherketone; PROM, patient-reported outcome measure; rhPDGF-BB, recombinant human platelets-derived growth factor-BB; S&S, success and survival; SI, short implant; TE, tissue expansion; Ti, titanium; VBG, vertical bone gain.

[a]Accounting for participants included in this review only.

[b]Compared two interventions within the same NMA group.

($n = 4$), expanded PTFE (e-PTFE) ($n = 4$), titanium osteosynthesis plates ($n = 2$) and polyetheretherketone (PEEK) mesh ($n = 1$). Staged dental implant placement approach was used in 24 studies and simultaneous approach in 4 studies, while 2 studies used both approaches. Lastly, tissue expander was used in one study for a period of 4 weeks before bone graft augmentation (Tables 1–3, Appendix 4).

3.3 | Risk of bias within studies and certainty in the evidence

The majority of the studies were judged to have some concerns in relation to risk of bias ($n = 29$). Three studies were judged to be at high risk, while none of the studies was judged to be at low risk of bias. The domain 'selection of reported results' was the most serious methodological issue (Appendix 5).

Certainty in the evidence ranged from moderate to very low, with 'study limitations' and 'imprecision' being the two main reasons for downgrading. No serious issues were observed in relation to inconsistency, indirectness, publication bias, intransitivity or incoherence (Table 4).

3.4 | Treatment grouping

The following treatment groups were created:

- *ONLAY*: onlay blocks with any type of bone.
- *INLAY*: inlay (interpositional or sandwich) with any type of bone.
- *e-PTFE*: GBR with e-PTFE non-resorbable membranes with any type of bone.
- *d-PTFE*: GBR with d-PTFE non-resorbable membranes with any type of bone.
- *Ti*: use of titanium meshes or plates as barriers; PEEK meshes are included in this group.
- *RM*: GBR using any resorbable membranes with any type of bone. Tent-pole technique using screws or implants with resorbable membrane is included in this group.
- *TE*: techniques that use tissue expanders before bone grafting.
- *DO*: distraction osteogenesis.
- *SI*: short implants of any length.

3.5 | Data synthesis

3.5.1 | Healing complications

Incidence of healing complications was obtained for all included studies (from published articles and/or correspondence with authors). Across all studies, 155 incidents of healing complications occurred in the management of 943 defects (16.4%). Ten RCTs could not be included in the quantitative analysis because they compared two techniques within one treatment group (Table 2).

Network meta-analysis

All treatment groups ($n = 9$) were analysed for healing complications with a total of 36 possible comparisons (13 direct comparisons based on data from 22 RCTs and 23 indirect comparisons) (Figure 1).

When compared with short dental implants (positive control), all treatment groups, except RM (OR 5.3, 95% CrI 0.92, 29), had statistically significant higher chance of having healing complications, with DO being the highest (OR 95, 95% CrI 12, 960) and INLAY the lowest (OR 13, 95% CrI 4.5, 41) (Table 4).

Treatment ranking

SI was the best performing group in ranking (Pr = 0.95, SUCRA = 99.26), followed by RM (Pr = 0.72, SUCRA = 82.8), INLAY (Pr = 0.57, SUCRA = 69.68) and d-PTFE (Pr = 0.36, SUCRA = 55.69) (Figure 2).

Pair-wise single meta-analysis

Five possible pair-wise single meta-analyses (SMAs) resulted in a statistically significant difference for SI when compared with INLAY (OR 0.09, 95% CrI 0.04, 0.02) (Appendix 6).

Heterogeneity and inconsistency

Insubstantial heterogeneity between studies was observed based on the inter-studies SD 95% CrI (1.13–6.89) not containing 1. The node-splitting models included 12 observations with no statistically significant difference between direct and indirect comparisons ($p > .05$) (Appendix 7).

Publication bias

No evidence of publication bias was observed when examining funnel plots (Appendix 8). With the exclusion of the positive controls (short implants), intervention effect centred at comparison-specific pooled effect for NMAs plotted against the SE showed relatively symmetrical distribution with little skewness of treatment effects.

Alternative treatments grouping

When groups using GBR techniques (i.e., d-PTFE. e-PTFE and RM) were combined into one group, the results showed that this group ranked second (alongside INLAY) after SI with regard to healing complications (Appendix 9).

Sensitivity analyses

The following sensitivity analyses were performed:

i. Smoking: Because of the limited number of RCTs reporting sensitivity analysis based on smoking status, an analysis at the participant level could not be conducted. Instead, studies that allowed smokers to be enrolled ($n = 19$) were excluded from the analysis (Appendix 10). No substantial differences from the main analysis were observed.
ii. Operator experience: A total of 17 operators involved in 15 RCTs provided information on the number of VRA surgeries they completed before conducting the study. Most of the operators were

TABLE 2 Incidence, description and classification of complications in the included studies.

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Amorfini et al. (2014)	Allogenic onlay blocks (8)	GBR [RM] (8)	HC: 100% (8) SC: Zero IC: NR	HC: 37.5% (3) SC: Zero IC: NR	HC could not be classified due to lack of details.	HC could not be classified due to lack of details.	Published manuscripts and authors' correspondence
Bernardi et al. (2018)	Xenogeneic inlay blocks (36)	Short implants (36)	HC: 55.6% (20) SC: 52.8% (19) IC: NR	HC: 11.1% (4) SC: 11.1% (4) IC: NR	HC: Four early infections which did not lead to major complications (classified as early and minor); Ten late infection onset which led to implant loss/removal (classified as late and major); Six complications which could not be classified due to lack of details. SC: All cases of temporary paraesthesia.	HC: All were late infection onset which led to implant removal (classified as late and major). SC: All cases of temporary paraesthesia.	Published manuscripts and authors' correspondence
Bianchi et al. (2008)	Distraction osteogenesis (4)	Autogenous inlay blocks (5)	HC: 27.3% (3) SC: Zero IC: NR	HC: 16.7% (1) SC: Zero IC: NR	HC: Two cases of progressive lingual inclination of the distracted segment during the distraction period which was managed by orthodontic traction (classified as early and minor); One case of local infection at time of implant placement which was resolved by local debridement (classified as late and minor).	HC: One case of early wound dehiscence, inflammation, and partial resorption of the cranial segment which resolved with local debridement and did not preclude subsequent implant placement (classified as early and minor).	Published manuscripts
Barausse et al. (2022)	Xenogeneic inlay blocks (20)	Short implants (40)	HC: 31.6% (6) SC: 15.8% (3) IC: Zero	HC: 2.5% (1) SC: Zero IC: 2.5% (1)	HC: One case of wound dehiscence at 10 days post-augmentation which resulted in graft removal (classified as early and major); One case of swelling and exudate at 3 months post-augmentation which resulted in graft removal (classified as late and major); Four cases of partial loss of augmented height at second surgery, 4 months post-augmentation (classified as late and minor). SC: Three cases of temporary paraesthesia.	HC: One case of implant mobility and discomfort at site 2 weeks post-implantation which led to implant removal (classified as early and major). IC: One implant migrated into the sinus 4 months post-implantation.	Published manuscripts

(Continues)

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Byun et al. (2020)	Tissue expansion + tunnelling (23)	GBR [d-PTFE] (23)	HC: 13% (3) SC: Zero IC: NR	HC: 8.7% (2) SC: Zero IC: NR	HC: All in expansion period. Two cases of over expansion due to silicon envelope tearing which healed without dehiscence and one case of mucosal perforation managed by immediate expander removal and grafting. Healing course was observed (classified as early and minor).	HC: Two cases of minor wound dehiscence during the first 2 months of augmentation (classified as early and minor).	Published manuscripts and authors' correspondence
Chiapasco et al. (2004)	GBR [e-PTFE] (11)	Distraction osteogenesis (10)	HC: 27.3% (3) SC: 18.2% (2) IC: NR	HC: 20% (2) SC: Zero IC: NR	HC: One membrane exposure at 4 weeks post-augmentation which resulted in early membrane removal and compromised regeneration (classified as early and major); One membrane exposure at 8 weeks which was managed by with application of chlorhexidine gel until membrane removal (classified as early and minor); One membrane exposure with suppuration at 10 weeks which resulted in immediate removal of the membrane (classified as late and major). SC: Two cases of transient paraesthesia of the lower lip occurred in two patients who underwent bone harvesting from the chin, lasting 2 and 4 weeks, respectively. A paraesthesia to the frontal mandibular teeth was also present in both cases, but in one of case this was permanent.	HC: Two cases of progressive lingual inclination of the distracted segment occurring during distraction. Managed by orthodontic traction. Desired position was reached (classified as early and minor).	Published manuscripts

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Chiapasco et al. (2007)	Autogenous onlay blocks (8)	Distraction osteogenesis (9)	HC: 12.5% (1) SC: 37.5% (3) IC: NR	HC: 33.3% (3) SC: Zero IC: NR	HC: One case of graft exposure at 2 months post-augmentation, resulting in partial loss of the graft. Treatment completed using short implants (classified as early and major). SC: Two cases of paraesthesia of inferior dental nerve following surgery at donor site, one temporary and one permanent.	HC: Two cases of progressive lingual inclination of the distracted segment occurred during distraction. Managed by orthodontic traction. Desired position was reached (classified as early and minor); One case of distraction interruption before completion due to the impossibility of the distracted segment to be moved further (classified as early and major).	Published manuscripts
Chiapasco et al. (2013)[a]	Autogenous onlay blocks with pericranium coverage (23)	Autogenous onlay blocks (21)	HC: 8.7% (2) SC: 4.3% (1) IC: NR	HC: 19.1% (4) SC: 4.8% (1) IC: NR	HC: Two cases of dehiscence during the first two months post-augmentation. Managed by surgical curettage, freshening of the dehiscence margins and chlorhexidine mouthwash and gel. In both cases a complete healing of the dehiscence was observed (classified as early and minor). SC: One case of temporary paraesthesia.	HC: Four cases of dehiscence during the first two months post-augmentation. Managed by surgical curettage, freshening of the dehiscence margins and chlorhexidine mouthwash and gel. In two of the 4 cases, dehiscence healed with only a negligible graft resorption (classified as early and minor); In the other two cases, dehiscence persisted and caused complete resorption of the grafted bone (classified as early and major). SC: One case of temporary paraesthesia.	Published manuscripts and authors' correspondence
Cucchi, Vignudelli, Fiorino, et al. (2021)	GBR [d-PTFE] (20)	Titanium mesh (20)	HC: 15% (3) SC: 5% (1) IC: Zero	HC: 21% (4) SC: 15.8% (3) IC: Zero	HC: One case of abscess without exposition and one membrane exposure with infection which happened during the first 2 months post-augmentation and affected the amount of newly formed bone (classified as early and major); One membrane exposure without infection during the period 3–6 months post-augmentation which did not affect the amount of newly formed bone (classified as late and minor). SC: One case of temporary paraesthesia of the mental nerve.	HC: Two cases of exposure with infection and one case of abscess without exposition which happened during the first 2 months and affected amount of newly formed bone (classified as early and major); One membrane exposure without infection during the period 3–6 months post-augmentation which did not affect the amount of newly formed bone (classified as late and minor). SC: Three cases of temporary paraesthesia of the mental nerve.	Published manuscripts and authors' correspondence

(Continues)

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Cucchi, Vignudelli, Franceschi, et al. (2021)[a]	Titanium mesh + RM (14)	Titanium mesh (11)	HC: 7.1% (1) SC: 14.3% (2) IC: 14.3% (2)	HC: 36.4% (4) SC: 9.1% (1) IC: 9.1% (1)	HC: One case of exposure before 2 months post-augmentation (classified as early). SC: Two cases of paraesthesia (not clear whether temporary or permanent). IC: Two cases of mesh fracture.	HC: One case of abscess and one case of exposure before 2 months post-augmentation (classified as early); Two cases of exposure after 2 months post-augmentation (classified as late). SC: One case of paraesthesia (not clear whether temporary or permanent). IC: One case of mesh misfitting.	Published manuscripts and authors' correspondence
Dottore et al. (2014)[a]	Alloplastic inlay (11)	Autogenous inlay blocks (11)	HC: 18.2% (2) SC: 36.4% (4) IC: NR	HC: 9.1% (1) SC: 54.6% (6) IC: NR	HC: One case of titanium miniplates exposure after a period of 4–5 months post-augmentation, treated with chlorhexidine mouth rinse and mechanical cleaning (classified as late and minor); One case of complete graft failure (classified as major). SC: Four cases of paraesthesia (not clear whether temporary or permanent).	HC: One case of titanium miniplates exposure after a period of 4–5 months post-augmentation, treated with chlorhexidine mouth rinse and mechanical cleaning (classified as late and minor). SC: Six cases of paraesthesia (not clear whether temporary or permanent).	Published manuscripts and authors' correspondence
El Zahwy et al. (2019)	Autogenous inlay blocks (8)	Autogenous onlay blocks (8)	HC: Zero SC: Zero IC: 12.5% (1)	HC: 75% (6) SC: Zero IC: Zero	IC: In one case, a crack occurred in the autograft during implant placement, which was simultaneous with grafting, and was fixed with a screw.	HC: Five cases of dehiscence and graft exposure during the first month post-augmentation which were persistent and led to mobility of the graft in three cases and complete loss of the graft in the two other cases (classified as early and major); One case of thread exposure (classified as late and minor).	Published manuscripts and authors' correspondence

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Esposito et al. (2019)	Xenogeneic inlay blocks (20)	Short implants (40)	HC: 5% (1) SC: 70% (14) IC: 10% (2)	HC: Zero SC: 20% (8) IC: Zero	HC: One case of graft exposure during the first month post-augmentation. A bone fragment was removed and the exposed bone was cleaned with ultrasound. At the second month, the miniplate was also exposed and the major portion of the osteotomised bone segment was lost (classified as early and major). SC: All cases of temporary paraesthesia. IC: In one case, a small intra-surgical haemorrhage occurred and the osteotomised portion of the mandibular graft fractured when placing the plate, a miniplate was placed. In a second case, the tip of the piezo device perforated the lingual side while preparing the graft bed.	SC: All cases of temporary paraesthesia.	Published manuscripts
Felice, Marchetti, et al. (2009)[a]	Xenogeneic inlay blocks (10)	Autogenous inlay blocks (10)	HC: 10% (1) SC: 100% (10) IC: 10% (1)	HC: 20% (2) SC: 100% (10) IC: 10% (1)	HC: One case of lingual dehiscence. The exposed bone was ground with a round bur and the site healed completely after 10 days (classified as early and minor) SC: All cases of temporary paraesthesia. IC: In one case, the tip of the piezo device perforated the lingual side while preparing the graft bed.	HC: One case of buccal dehiscence at 2 weeks post-augmentation which improved with increased use of chlorohexidine (classified as early and minor); One case of a large dehiscence resulting in graft removal (classified as early and major). SC: All cases of temporary paraesthesia. IC: One case of fracture of the osteotomised bone.	Published manuscripts

(Continues)

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Felice, Pistilli, et al. (2009)	Autogenous inlay blocks (10)	Autogenous onlay blocks (10)	HC: 30% (3) SC: 40% (4) IC: NR	HC: 30% (3) SC: 20% (2) IC: NR	HC: Two cases of buccal dehiscence 2 weeks post-augmentation which improved with increased use of chlorohexidine (classified as early and minor); One case of buccal dehiscence 1-week post-augmentation which resulted in inflammation and resorption of the cranial segment (classified as early and major). SC: All cases of temporary hypoesthesia.	HC: One cases of dehiscence 2 weeks post-augmentation. The exposed bone was ground with a round bur and the site healed completely after 20 days (classified as early and minor); One case of dehiscence which required surgical re-entry to remove inflammatory tissue, mobilise a new mucoperiosteal flap, and completely cover the bone graft (classified as early and major); One case of acute inflammation 2 weeks post-augmentation which required surgical re-entry for screw removal and resulted in considerable loss of the graft (classified as early and major). SC: One case of permanent hypoesthesia; One case of temporary hypoesthesia.	Published manuscripts
Felice, Barausse, Pistilli, Ippolito, and Esposito (2018), Felice, Barausse, Pistilli, Piattelli, et al. (2018)	Xenogeneic inlay blocks (30)	Short implants (30)	HC: 13.3% (4) SC: 53.3% (16) IC: 10% (3)	HC: Zero SC: 6.7% (2) IC: Zero	HC: Three cases of dehiscence during the first month post-augmentation which healed in 4 months (classified as early and minor); One cases of dehiscence during the first month post-augmentation which was persistent and led to implant loss (classified as early and major). SC: All cases of temporary paraesthesia. IC: Three cases of disintegration of the bone block during grafting procedure.	SC: All cases of temporary paraesthesia.	Published manuscripts
Felice, Barausse, et al. (2019)	Xenogeneic inlay blocks (15)	Short implants (30)	HC: 6.7% (1) SC: 66.7% (10) IC: Zero	HC: Zero SC: 3 (10%) IC: 3 (10%)	HC: One case of dehiscence during the first 2 weeks which was managed with chlorohexidine mouthwash and gel (classified as early and minor). SC: All cases of temporary paraesthesia.	SC: All cases of temporary paraesthesia. IC: All cases of perforation of the sinus lining at implant placement.	Published manuscripts

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Felice, Pistilli, et al. (2019)	Xenogeneic inlay blocks (20)	Short implants (40)	HC: 15% (3) SC: 23.3% (7) IC: 5% (1)	HC: Zero SC: Zero IC: Zero	HC: One case of graft exposure 2 weeks post-augmentation resulting in graft infection; One case had 2 fistulas which resulted in complete replacement of the graft by fibrotic tissue; One case of dehiscence and graft mobility 10 days post-augmentation resulting in graft removal (all classified as early and major). SC: All cases of temporary paraesthesia. IC: In one case, the mobilised bone segment fractured during fixation.		Published manuscripts
Fontana et al. (2008)[a]	GBR [e-PTFE + Allogenic bone] (5)	GBR [e-PTFE + autogenous bone] (5)	HC: Zero SC: 20% (1) IC: NR	HC: 20% (1) SC: 20% (1) IC: NR	SC: One case of temporary paraesthesia.	HC: One case of infection without membrane exposure 2 months post-augmentation resulting in membrane removal and after 6 months the second surgery was performed following the standard protocol and without any further complications (classified as early and minor). SC: One case of temporary paraesthesia.	Published manuscripts
Laino et al. (2014)[a]	Allogenic inlay blocks (12)	Autogenous inlay blocks (12)	HC: 8.3% (1) SC: Zero IC: NR	HC: Zero SC: 16.6% (2) IC: NR	HC: One case of exposure of a titanium plate 2 months post-augmentation managed by plaque removal (classified as early and minor).	SC: All cases of temporary paraesthesia.	Published manuscripts
Leong et al. (2015)	Allogenic onlay blocks (9)	Tenting [RM] (10)	HC: 77.8% (7) SC: NR IC: NR	HC: 30% (3) SC: NR IC: NR	HC: All cases of dehiscence (could not be classified due to lack of details).	HC: All cases of dehiscence (could not be classified due to lack of details).	Published manuscripts
Maiorana et al. (2021)	GBR [d-PTFE] (5)	Titanium mesh (5)	HC: Zero SC: Zero IC: NR	HC: 40% (2) SC: Zero IC: NR		HC: Two cases of premature exposure during the first 2 months post-augmentation which was left to heal spontaneously and did not affect the outcome (classified as early and minor).	Published manuscripts

(Continues)

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Merli et al. (2014)	Titanium osteo-synthesis plates + RM (11)	GBR [e-PTFE] (11)	HC: 36.4% (4) SC: NR IC: NR	HC: 45.5% (5) SC: NR IC: NR	HC: Two cases of abscess resulting in barrier removal (classified as major); One case of dehiscence managed by chlorohexidine and one case of early infection, in both cases augmentation was successful (classified as minor).	HC: One case of dehiscence/ infection 3 weeks post-augmentation which resulted in barrier removal (classified as early and major); Two cases had fistulas during the first 2 months post-augmentation managed by barrier removal and antibiotics, in both cases augmentation procedure was successful (classified as early and minor); One case had lymph node swelling 1 month post augmentation which was managed by antibiotics (classified as early and minor); One case had a fistula at abutment connection which disappeared after cleaning (classified as late and minor).	Published manuscripts and authors' correspondence
Merli et al. (2020)[a]	Titanium osteo-synthesis plates + RM [xenogeneic and autogenous bone] (15)	Titanium osteo-synthesis plates + RM [autogenous bone] (15)	HC: Zero SC: 6.7% (1) IC: NR	HC: 13.3% (2) SC: Zero IC: NR	SC: One case of temporary paraesthesia.	HC: All cases of plates exposition during the first 2 months post-augmentation which was managed by chlorohexidine gel (classified as early and minor).	Published manuscripts and authors' correspondence
Mounir et al. (2017)	Xenogeneic inlay blocks (8)	Titanium mesh (18)	HC: Zero SC: Zero IC: NR	HC: 12.5% (1) SC: Zero IC: NR		HC: One case of dehiscence 10 days post-augmentation which was managed by daily saline irrigation and healed with secondary intention (classified as early and minor)	Published manuscripts and authors' correspondence
Mounir et al. (2019)[a]	PEEK mesh (8)	Titanium mesh (8)	HC: 12.5% (1) SC: Zero IC: NR	HC: 12.5% (1) SC: Zero IC: NR	HC: One case of mesh exposure 2 weeks post-augmentation which was managed by daily saline irrigation and healed with secondary intention (classified as early and minor).	HC: One case of mesh exposure 2 weeks post-augmentation which was managed by daily saline irrigation and healed with secondary intention (classified as early and minor)	Published manuscripts and authors' correspondence
Mounir et al. (2021)[a]	Autogenous onlay blocks [symphyseal bone] (7)	Autogenous onlay blocks [retromolar bone] (7)	HC: Zero SC: Zero IC: Zero	HC: Zero SC: 14.3% (1) IC: Zero		SC: One case of temporary paraesthesia.	Published manuscripts and authors' correspondence

TABLE 2 (Continued)

Study	Intervention (*n* of participants)		Complications % (*n*)		Description and classification of complications		Source of findings
	Test	Control	Test	Control	Test	Control	
Roccuzzo et al. (2007)	Autogenous onlay blocks + titanium mesh (12)	Autogenous onlay blocks (12)	HC: 33.3% (4) SC: Zero IC: NR	HC: 50% (6) SC: 8.3% (1) IC: NR	HC: Three minimal mesh exposures during the first 2 months post-augmentation (classified as early and minor); One case of extensive mesh exposure during the first 2 months post-augmentation which resulted in early mesh removal (classified as early and major).	HC: Three cases of graft discoloration (necrosis) at second stage surgery which required removal necrotic portion and additional bone grafting; Two cases of significant graft resorption; One case of complete graft dislodgment at second stage surgery (all classified as late and major). SC: One case of temporary paraesthesia.	Published manuscripts and authors' correspondence
Rokn et al. (2018)	GBR [RM] (11)	Short implants (11)	HC: 50% (5) SC: 30% (3) IC: NR	HC: Zero SC: Zero IC: NR		HC: All cases of membrane exposure which was managed by chlorohexidine application (classified as minor). SC: All cases of temporary paraesthesia.	Published manuscripts
Ronda et al. (2014)	GBR [d-PTFE] (13)	GBR [e-PTFE] (13)	HC: Zero SC: NR IC: NR	HC: Zero SC: NR IC: NR	SC (did not specify to which group): Three cases of temporary paraesthesia; Minor vascular complications leading to various grades of local oedema or hematoma.		Published manuscripts
Schortinghuis et al. (2008)[a]	Distraction osteogenesis + ultrasound (5)	Distraction osteogenesis (4)	HC: Zero SC: Zero IC: NR	HC: Zero SC: Zero IC: NR			Published manuscripts
Shah et al. (2018)	GBR [RM] (25)	Short implants (25)	HC: Zero SC: Zero IC: NR	HC: Zero SC: Zero IC: NR			Authors' correspondence

Abbreviations: CT/CBCT, computed tomography/cone beam computed tomography; d-PTFE, dense-polytetrafluoroethylene; e-PTFE, expanded-polytetrafluoroethylene; GBR, guided bone regeneration; HC, healing complications; IC, intra-operative complications; NR, not reported; PEEK, polyetheretherketone; RM, resorbable membrane; SC, surgical complications.

[a]Compared two interventions within the same NMA group.

TABLE 3 Results of individual studies for secondary outcomes.

	Intervention (*n* of participants)		Vertical bone gain mean (SD) [measuring method]		Marginal bone loss mean (SD) [at-year]		Success and survival rate[a] [at-year]		Incidence of need for additional grafting %	
Study	**Test**	**Control**	**Test**	**Control**	**Test**	**Control**	**Test**	**Control**	**Test**	**Control**
Bernardi et al. (2018)	Xenogeneic inlay blocks (36)	Short implants (36)					Survival at [1]: 84.5% At implant level	Survival at [1]: 94.2% At implant level		
Bianchi et al. (2008)	Distraction osteogenesis (4)	Autogenous inlay blocks (5)	10.36 mm (±2.96) [CT]	5.9 mm (±0.76) [CT]						
Barausse et al. (2022)	Xenogeneic inlay blocks (20)	Short implants (40)			[1]: 0.77 mm (±0.04) [3]: 0.71 mm (±0.52) [5]: 1.03 mm (±0.61)	[1]: 0.57 mm (±0.03) [3]: 0.87 mm (±0.66) [5]: 0.58 mm (±0.4)	Survival at [1]: 97.8% at implant level 94.7% at patient level	Survival at [1]: 97.5% at implant level 95% at patient level		
Byun et al. (2020)	Tissue expansion + tunnelling (23)	GBR [d-PTFE] (23)	3.55 mm (±1.56) [CBCT]	1.9 mm (±1.58) [CBCT]	[1]: 0.52 mm (±0.21)	[1]: 0.41 mm (±0.22)				
Chiapasco et al. (2004)	GBR [e-PTFE] (11)	Distraction osteogenesis (10)	3.73 mm (±1.38) [IORG]	5.59 mm (±1.3) [IORG]	[1]: 1.29 mm (±0.4)	[1]: 1.13 mm (±0.3)	Success at [1]: 84% [2]: 80% [3]: 68% Survival at [1, 2, 3]: 100% At implant level	Success at [1]: 84% [2]: 80% [3]: 68% Survival at [1, 2, 3]: 100% At implant level		
Chiapasco et al. (2007)	Autogenous onlay blocks (8)	Distraction osteogenesis (9)	5 mm (±1.07) [IORG]	5.3 mm (±1.58) [IORG]	[1]: 0.9 mm (±0.4)	[1]: 0.9 mm (±0.4)	Success at [1, 2, 3, 4, 5]: 89.5% Survival at [1, 2, 3, 4, 5]: 100% At implant level	Success at [1]: 100% [2, 3, 4, 5]: 94.7% Survival at [1, 2, 3, 4, 5]: 100% At implant level		
Chiapasco et al. (2013)[a]	Autogenous onlay blocks with pericranium coverage (23)	Autogenous onlay blocks (21)					Survival at [1, 2, 3, 4]: 99.1% At implant level	Survival at [1, 2, 3, 4]: 100% At implant level		
Cucchi, Vignudelli, Fiorino, et al. (2021)	GBR [d-PTFE] (20)	Titanium mesh (20)	4.2 mm (±1) [I.S.]	4.1 mm (±1) [I.S.]	[1]: 0.67 mm (±0.3)	[1]: 0.61 mm (±0.28)				
Cucchi, Vignudelli, Franceschi, et al. (2021)[a]	Titanium mesh + RM (14)	Titanium mesh (11)	6.36 mm (±2.22) 843.13 mm^3 (±389.52) 82.3% (±17.98) [CBCT]	4.47 mm (±2.45) 803.07 mm^3 (±553.78) 74.32% (±22.1) [CBCT]					8% among tests and controls	
Dottore et al. (2014)[a]	Alloplastic inlay (11)	Autogenous inlay blocks (11)	7 mm (±1.76) [DVT]	6.5 mm (±2.4) [DVT]	[1]: 0.78 mm (±0.82)	[1]: 1.02 mm (±0.93)	For test and controls Survival at [1]: 95.45%	Success at [1]: 90.9% At implant level		
El Zahwy et al. (2019)	Autogenous inlay blocks (8)	Autogenous onlay blocks (8)	3.34 mm (±1.2) [CBCT]	0.02 mm (±1.86) [CBCT]						

TABLE 3 (Continued)

Study	Intervention (*n* of participants)		Vertical bone gain mean (SD) [measuring method]		Marginal bone loss mean (SD) [at-year]		Success and survival rate[a] [at-year]		Incidence of need for additional grafting %	
	Test	Control	Test	Control	Test	Control	Test	Control	Test	Control
Marco Esposito et al. (2019)	Xenogeneic inlay blocks (20)	Short implants (40)			[1]: 1.03 mm (±0.31) [3]: 1.39 mm (±0.4) [5]: 1.7 mm (±0.46)	[1]: 1.91 mm (±0.26) [3]: 1.07 mm (±0.3) [5]: 1.24 mm (±0.34)	Survival at [1]: 95% [3]: 94.7% [5]: 94.4% At patient level	Survival at [1]: 97.5% [3]: 94.7% [5]: 94.1% At patient level		
Felice, Marchetti, et al. (2009)[a]	Xenogeneic inlay blocks (10)	Autogenous inlay blocks (10)	4 mm (±1) [CT]	5.6 mm (±1) [CT]	[1]: 0.59 mm (±0.4)	[1]: 0.82 mm (±0.59)				
Felice, Pistilli, et al. (2009)	Autogenous inlay blocks (10)	Autogenous onlay blocks (10)	4.52 mm (±1.1) [CT]	3.64 mm (±1.1) [CT]						
Felice, Barausse, Pistilli, Ippolito, and Esposito (2018), Felice, Barausse, Pistilli, Piattelli, et al. (2018)	Xenogeneic inlay blocks (30)	Short implants (30)			[1]: 1 mm (±0.31) [3]: 1.76 mm (±0.72) [5]: 2.34 mm (±0.75)	[1]: 1 mm (±0.36) [3]: 1.24 mm (±0.36) [5]: 1.49 mm (±0.4)				
Felice, Barausse, et al. (2019)	Xenogeneic inlay blocks (15)	Short implants (30)			[1]: 1.2 mm (±0.47) [3]: 1.68 mm (±0.5) [5]: 2.1 mm (±0.61)	[1]: 0.97 mm (±0.56) [3]: 1.23 mm (±0.49) [5]: 1.49 mm (±0.59)	Survival at [1]: 93.4% [3]: 92.9% [5]: 90.9% At patient level	Survival at [1]: 96.7% [3]: 89.3% [5]: 88.5% At patient level		
Felice, Pistilli, et al. (2019)	Xenogeneic inlay blocks (20)	Short implants (40)			[1]: 1.07 mm (±0.06) [3]: 1.54 mm (±0.14) [5]: 2.11 mm (±0.59)	[1]: 1.03 mm (±0.25) [3]: 1.27 mm (±0.25) [5]: 1.44 mm (±0.33)	Survival at [1]: 95% [3]: 94.1% [5]: 93.7% At patient level	Survival at [1]: 96.7% [3]: 89.3% [5]: 88.5% At patient level		
Fontana et al. (2008)[a]	GBR [e-PTFE + Allogenic bone] (5)	GBR [e-PTFE + autogenous bone] (5)	4.2 mm (±0.88) [I.S.]	4.7 mm (±0.48) [I.S.]						
Leong et al. (2015)	Allogenic onlay blocks (9)	Tenting [RM] (10)	1.78 mm (±2.06) [I.S.]	1 mm (±2.13) [I.S.]						
Maiorana et al. (2021)	GBR [d-PTFE] (5)	Titanium mesh (5)	4.2 mm (±2.2) [I.S.]	1.5 mm (±2.6) [I.S.]						
Merli et al. (2014)	Titanium osteo-synthesis plates + RM (11)	GBR [e-PTFE] (11)	1.5 mm (±2.6) [I.S.]	2.48 mm (±1.13) [I.S.]	[1]: 0.51 mm (±0.34)	[1]: 0.59 mm (±0.58)	Survival at [6]: 100%	Survival at [6]: 100%		

(Continues)

TABLE 3 (Continued)

Study	Intervention (*n* of participants)		Vertical bone gain mean (SD) [measuring method]		Marginal bone loss mean (SD) [at-year]		Success and survival rate[a] [at-year]		Incidence of need for additional grafting %	
	Test	Control	Test	Control	Test	Control	Test	Control	Test	Control
Merli et al. (2020)[a]	Titanium osteo-synthesis plates + RM [xenogeneic and autogenous bone] (15)	Titanium osteo-synthesis plates + RM [autogenous bone] (15)	3.7 mm (±1.9) 869 mm^3 (±881) [CBCT]	2.2 mm (±1.4) 648 mm^3 (±439) [CBCT]						
Mounir et al. (2017)	Xenogeneic inlay blocks (8)	Titanium mesh (18)	4.7 mm (±1.3) 31.6% (±22.5) [CBCT]	3.7 mm (±0.8) 20.7% (±13.3) [CBCT]						
Mounir et al. (2019)[a]	PEEK mesh (8)	Titanium mesh (8)	4.4 mm (±1.5) 31.8% (±22.7) [CBCT]	3.1 mm (±1) 20.9% (±13.3) [CBCT]						
Mounir et al. (2021)[a]	Autogenous onlay blocks [symphyseal bone] (7)	Autogenous onlay blocks [retromolar bone] (7)	2.8 mm (±1.3) [CBCT]	5 mm (±1.8) [CBCT]						
Roccuzzo et al. (2007)	Autogenous onlay blocks + titanium mesh (12)	Autogenous onlay blocks (12)	4.8 mm (±1.5) [I.S.]	3.6 mm (±1.4) [I.S.]					16.67%	41.67%
Rokn et al. (2018)	GBR [RM] (11)	Short implants (11)	2.2 mm (±1.1) [I.S.]		[1]: 0.47 mm (±0.34)	[1]: 0.3 mm (±0.54)	Survival at [1]: 100%	Survival at [1]: 100%		
Ronda et al. (2014)	GBR [d-PTFE] (13)	GBR [e-PTFE] (13)	5.49 mm (±1.58) [I.S.]	4.91 mm (±1.78) [I.S.]						
Schortinghuis et al. (2008)[a]	Distraction osteogenesis + ultrasound (5)	Distraction osteogenesis (4)	4.6 mm (±0.9) [US]	5.8 mm (±1.3) [US]						
Shah et al. (2018)	GBR [RM] (25)	Short implants (25)					Survival at [6]: 96% At implant and patient levels	Survival at [1]: 84% At implant and patient levels		

Abbreviations: CBCT, cone bean computed tomography; CT, computed tomography; DVT, dental volume tomography; empty cells, not reported; IORG, intraoral radiograph; US, ultrasonography.
[a]Compared two interventions within the same NMA group.

TABLE 4 Incidence of healing complications; odds ratios (ORs) (95% CrI) and certainty in the evidence.

		Direct		Indirect		NMA	
Comparison		**OR (95% CrI)**	**CiE**	**OR (95% CrI)**	**CiE**	**OR (95% CrI)**	**CiE**
d-PTFE vs.	TE	0.68 (0.2, 2.32)	Low[a,b]	NE	NE	0.66 (0.06, 8.14)	Low
	Ti	0.35 (0.05, 2.20)	Low[a,b]	1.24 (0.01, 160.77)	Very low[a,c]	0.42 (0.07, 2.31)	Low
	INLAY			2.25 (0.18, 31.67)	Low[a,b]	2.25 (0.18, 31.67)	Low
	SI			28.73 (2.04, 477.38)	Moderate[a]	28.73 (2.04, 477.38)	Moderate
	DO			0.31 (0.02, 3.80)	Low[a,b]	0.31 (0.02, 3.80)	Low
	RM			5.23 (0.31, 107.62)	Low[a,b]	5.23 (0.31, 107.62)	Low
	e-PTFE	1.00 (0.06, 16.85)	Low[a,b]	0.29 (0.01, 4.76)	Low[a,b]	0.43 (0.04, 3.88)	Low
	ONLAY			0.35 (0.03, 4.08)	Low[a,b]	0.35 (0.03, 4.08)	Low
TE vs.	Ti			0.65 (0.03, 12.21)	Low[a,b]	0.65 (0.03, 12.21)	Low
	INLAY			3.50 (0.10, 128.14)	Very low[a,c]	3.50 (0.10, 128.14)	Very low
	SI			42.77 (1.20, 1917.14)	Moderate[a]	42.76 (1.20, 1917.14)	Moderate
	DO			0.46 (0.01, 16.59)	Low[a,b]	0.46 (0.01, 16.59)	Low
	RM			7.97 (0.20, 409.17)	Very low[a,c]	7.97 (0.20, 409.17)	Very low
	e-PTFE			0.66 (0.02, 18.26)	Low[a,b]	0.66 (0.02, 18.26)	Low
	ONLAY			0.55 (0.02, 16.12)	Low[a,b]	0.55 (0.02, 16.12)	Low
Ti vs.	INLAY	4.53 (0.16, 270.43)	Very low[a,b]	6.23 (0.48, 107.77)	Low[a,b]	5.34 (0.84, 43.45)	Low
	SI			68.49 (8.72, 739.29)	Moderate[a]	68.49 (8.72, 739.29)	Moderate
	DO			0.73 (0.09, 5.76)	Low[a,b]	0.73 (0.09, 5.76)	Low
	RM			12.24 (1.36, 173.68)	Moderate[a]	12.24 (1.36, 173.68)	Moderate
	e-PTFE	1.45 (0.11, 21.11)	Low[a,b]	0.58 (0.34, 13.60)	Low[a,b]	1.01 (0.16, 6.70)	Low
	ONLAY	0.5 (0.04, 7.39)	Low[a,b]	1.84 (0.1, 34.47)	Low[a,b]	0.83 (0.14, 5.22)	Low
INALY vs.	SI	11.24 (3.74, 41.26)	Moderate[a]	43.38 (1.21, 2143.00)	Moderate[a]	12.63 (4.50, 40.87)	Moderate
	DO	0.14 (0.01, 2.72)	Low[a,b]	0.17 (0.01, 1.62)	Low[a,b]	0.13 (0.02, 0.83)	Moderate[d]
	RM			2.35 (0.40, 16.14)	Low[a,b]	2.35 (0.40, 16.14)	Low
	e-PTFE			0.19 (0.02, 1.89)	Low[a,b]	0.19 (0.02, 1.89)	Low
	ONLAY	0.18 (0.02, 1.12)	Low[a,b]	0.12 (0.01, 1.16)	Low[a,b]	0.16 (0.04, 0.59)	Moderate[d]
SI vs.	DO			0.01 (0.001, 0.08)	Moderate[a]	0.011 (0.001, 0.08)	Moderate
	RM	0.11 (0.01, 1.21)	Low[a,b]	0.38 (0.20, 9.58)	Low[a,b]	0.19 (0.03, 1.10)	Low
	e-PTFE			0.02 (0.001, 0.17)	Moderate[a]	0.02 (0.001, 0.17)	Moderate
	ONLAY			0.01 (0.002, 0.06)	Moderate[a]	0.012 (0.002, 0.06)	Moderate
DO vs.	RM			17.20 (1.95, 228.65)	Moderate[a]	17.20 (1.95, 228.65)	Moderate
	e-PTFE	0.72 (0.06, 8.5)	Low[a,b]	5.7 (0.18. 200.34)	Very low[a,c]	1.43 (0.19, 11.95)	Low
	ONLAY	2.95 (0.20, 47.47)	Low[a,b]	0.51 (0.04, 6.89)	Low[a,b]	1.15 (0.19, 7.29)	Low
RM vs.	e-PTFE			0.08 (0.004, 1.08)	Low[a,b]	0.08 (0.004, 1.08)	Low
	ONLAY	0.04 (0.01, 0.30)	Moderate[a]	0.16 (0.01, 0.28)	Moderate[a]	0.07 (0.01, 0.31)	Moderate
e-PTFE vs.	ONLAY			0.81 (0.09, 7.28)	Low[a,b]	0.81 (0.09, 7.28)	Low

Abbreviations: CiE, certainty in the evidence; CrI, credible intervals; NE, not estimable (cannot be estimated because the treatment group was not connected in a loop in the evidence network); NMA, network meta-analysis.

[a]Downgraded by one due to risk of bias.

[b]Downgraded by one due to imprecision.

[c]Downgraded by two due to imprecision.

[d]Imprecision of direct and indirect estimates disregarded due to precision of NMA estimate.

experienced (mean of 482 procedures and a median of 200), with only four (23.5%) having carried out less than 50 procedures. A regression analysis, aiming to investigate whether the number of previous surgeries can predict incidence of healing complications, showed a statistically significant negative correlation between operator experience and incidence of healing complications ($R^2 = 0.25$, $p = .04$) (Figure 3). Additionally, similar analyses were conducted to explore the effect of the number of years in practice as well as

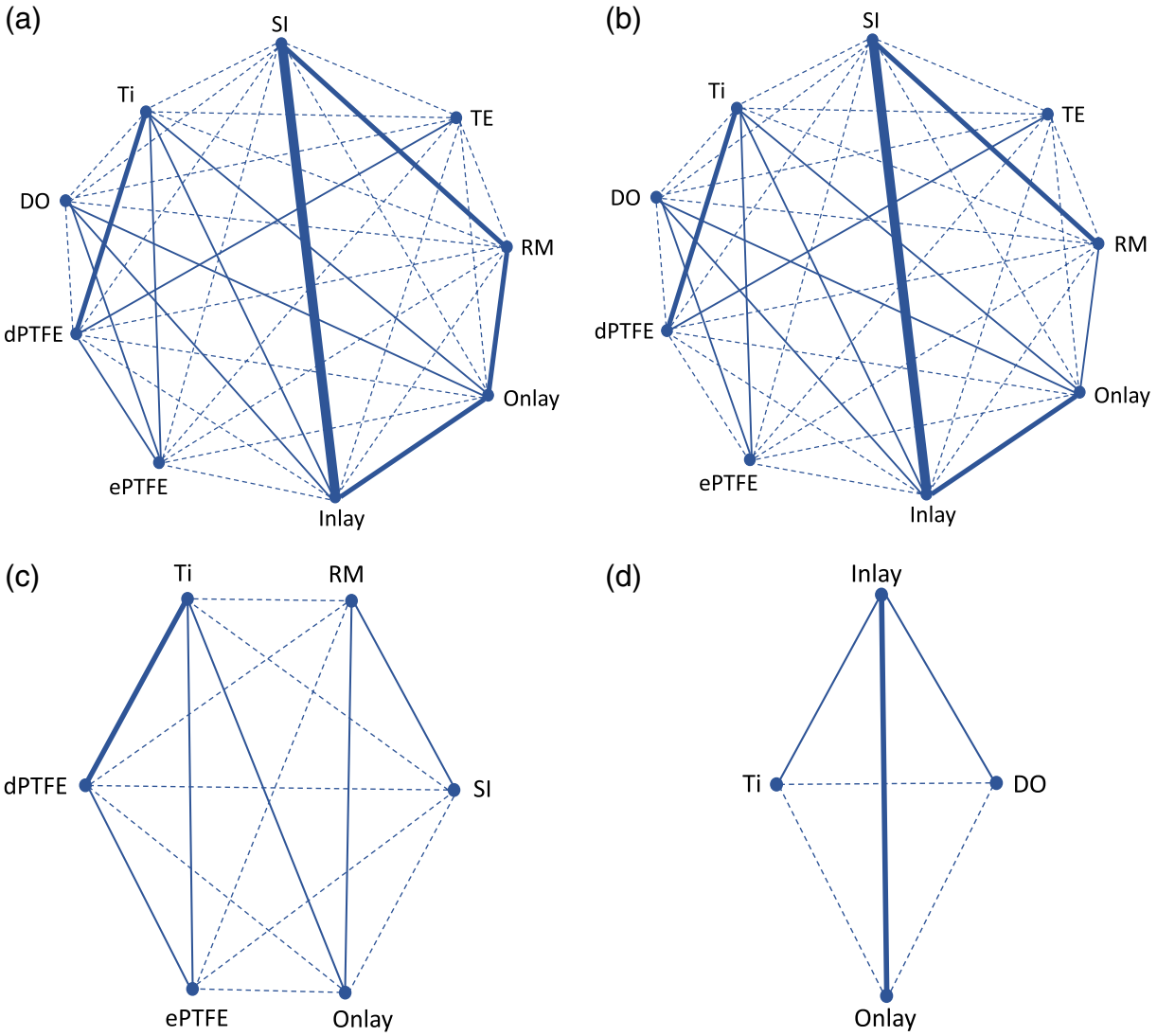

FIGURE 1 Network diagrams of (a) incidence of healing complications, (b) incidence of surgical complications, (c) vertical bone gain measured intra-surgically, (d) vertical bone gain measured on computed tomography/cone beam computed tomography. Solid lines refer to direct comparisons while dotted lines refer to indirect comparisons. Width of solid lines is proportional to number of studies included for each comparison.

having formal training in VRA on incidence of healing complications. The results did not show any correlation between these two parameters and incidence of healing complications.

iii. Risk of bias: Results of NMA with the exclusion of RCTs that were deemed at high risk of bias ($n = 4$) were confirmed (Appendix 10).

iv. Post hoc subgroup analyses: Three sub-analyses were conducted as follows (the resulting network plots, treatment effects and ranking tables, SUCRA and node-splitting models for each sub-analysis are shown in Appendix 10):

   a. Excluding the short implants group: Eight studies were excluded from the main NMA. Direct ($n = 11$, based on 14 RCTs) and indirect ($n = 19$) comparisons of all remaining groups confirmed that ranking of VRA techniques remained the same as in the main analysis.

   b. Excluding split-mouth design studies: Six studies were excluded from the main NMA. Direct ($n = 13$, based on 16 RCTs) and indirect ($n = 23$) comparison of all groups confirmed that ranking of all techniques remained the same as in the main analysis except for TE (which was ranked fifth but moved to sixth) and Ti (was ranked sixth but moved to fifth) groups.

   c. Excluding studies that used simultaneous implant placement approach: Eight studies were excluded from the main NMA. Direct ($n = 10$, based on 15 RCTs) and indirect ($n = 18$) comparisons of all groups except e-PTFE (which did not contribute to the analysis) showed that the d-PTFE group was the best preforming among the VRA groups, followed by TE, RM and INLAY.

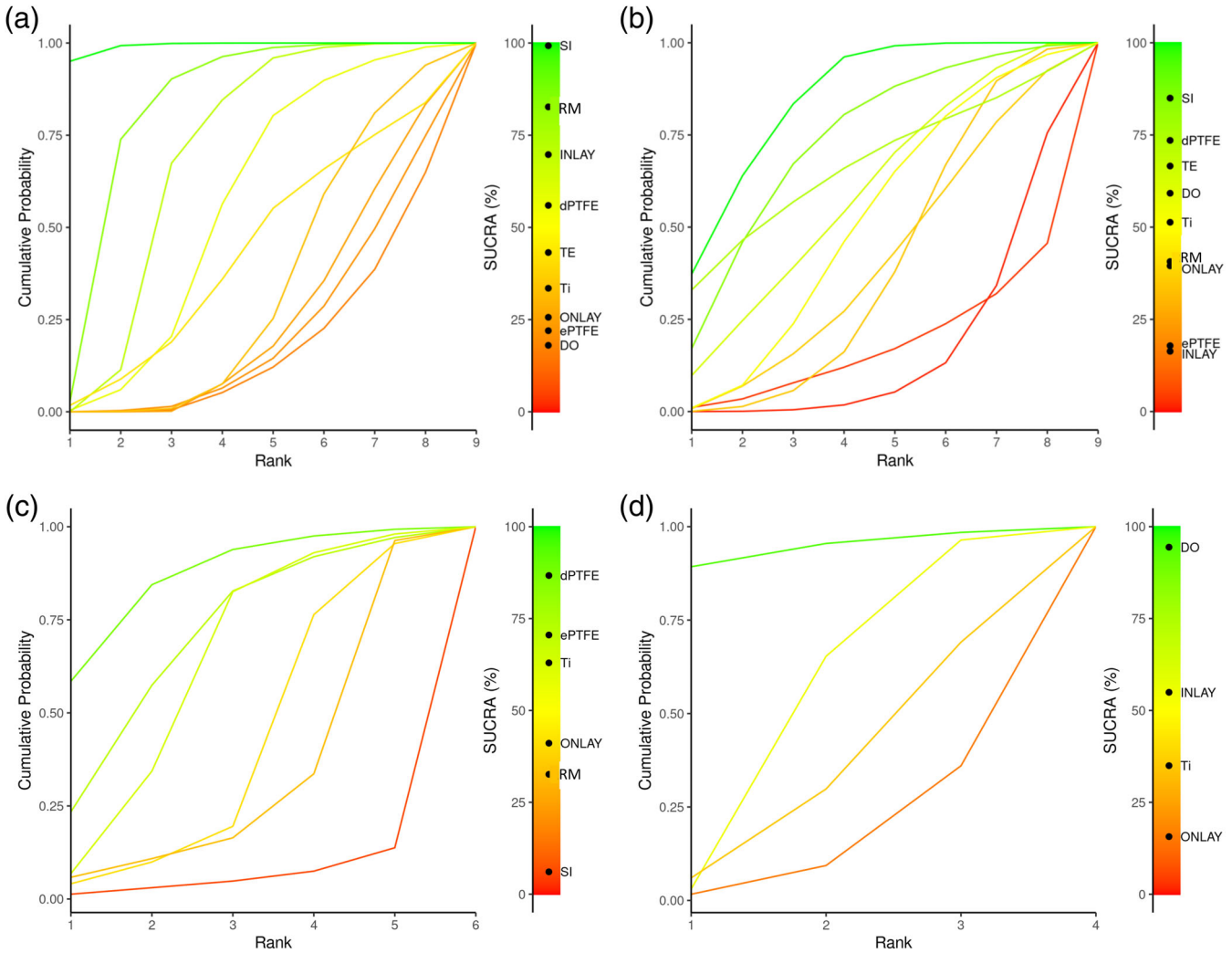

FIGURE 2 The surface under the cumulative ranking curve (SUCRA) for (a) incidence of healing complications, (b) incidence of surgical complications, (c) vertical bone gain measured intra-surgically, (d) vertical bone gain measured on computed tomography/cone beam computed tomography. Higher SUCRA values and cumulative ranking curves nearer the top left indicate better performance.

3.5.2 | Surgical complications

Incidence of post-operative surgical complications was obtained from 29 RCTs; 146 incidents occurred in the management of 867 defects (16.8%). Permanent paraesthesia accounted for 2% ($n = 3$) of all surgical complications. Thirteen RCTs could not be included in the quantitative analysis (3 studies did not report the incidence and 10 studies compared two techniques within the same treatment group) (Table 2).

Network meta-analysis

All treatment groups were analysed for surgical complications with a total of 36 possible comparisons (11 direct comparisons based on data from 19 RCTs and 25 indirect comparisons) (Figure 1). When compared with the short dental implant group, three treatment groups had significantly higher chance of having surgical complications; INLAY (OR 13.3, 95% CrI 7.29, 28.4), ONLAY (OR 5.68, 95% CrI 1.35, 28.2) and RM (OR 5.5, 95% CrI 1.05, 36.6) (Appendix 11).

Treatment ranking

The treatment group that had the highest probability to be rank 1 was SI (Pr = 0.35, SUCRA = 83.61), with d-PTFE reported as the second-best treatment (Figure 2).

Pair-wise single meta-analysis

Out of four possible pair-wise SMAs, a statistically significant difference between SI compared with INLAY was observed (OR 0.07, 95% CrI 0.04–0.15) (Appendix 11).

Heterogeneity and inconsistency

Insubstantial heterogeneity between studies was observed based on the inter-studies SD 95% CrI (1.01–3.82). The node-splitting models in this NMA included eight observations and suggested that there was

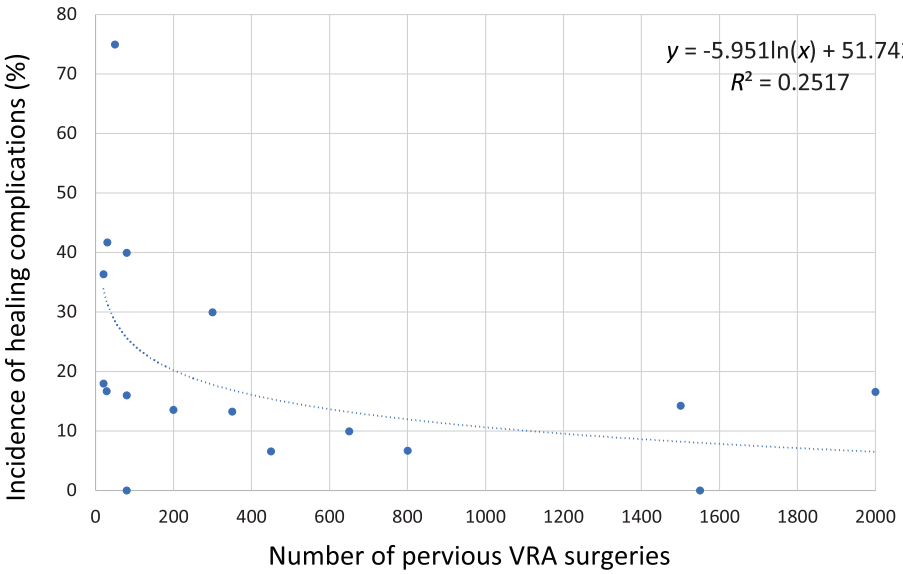

FIGURE 3 Regression analysis exploring correlation between surgical experience (expressed in number of previous vertical ridge augmentation [VRA] surgeries) and incidence of healing complications.

no statistical difference between direct and indirect comparisons ($p > .05$).

Publication bias

Publication bias was examined using funnel plots. Intervention effect centred at comparison-specific pooled effect for network meta-analyses plotted against the SE showed symmetrical distribution with no obvious skewness of treatment effects.

3.5.3 | Early healing complications

One-hundred and fifty-five incidents of healing complications were reported across all studies. Of those, 33 could not be categorized as early or late due to inapplicability ($n = 3$, TE group) or lack of reporting or response from the authors ($n = 30$). Of the remaining 122 incidents, 75 (61.4%) were categorized as early healing complications, while 47 (38.6%) were categorized as late (Table 2).

3.5.4 | Major healing complications

Of the 155 incidents of healing complications reported across all studies, 26 could not be categorized as major or minor due to lack of reporting or response from the authors. Of the remaining 126 incidents, 58 (46%) were categorized as major healing complications, while 68 (54%) were categorized as minor (Table 2).

3.5.5 | Intra-operative complications

Ten RCTs reported intra-operative complications with an incidence of 4.9% across those studies (Table 2). INLAY was the treatment group that had the highest incidence (9.3%), most of which were attributed to fracture of the coronal segment of the split.

3.5.6 | Vertical bone gain

- Linear vertical bone gain (VBG) measured intra-surgically

Seven RCTs reported this outcome. One of these could not be included in the NMA as it compared two techniques within the same treatment group (Table 3).

Network meta-analysis

Six treatment groups were analysed with a total of 15 possible comparisons (6 direct comparisons based on data from seven RCTs and 9 indirect comparisons) (Figure 1, Appendix 12).

Treatments ranking

d-PTFE (Pr = 0.58, SUCRA = 86.46) ranked first in terms of VBG, followed by e-PTFE (Pr = 0.33, SUCRA = 70.28), Ti (Pr = 0.48, SUCRA = 62.81), ONLAY (Pr = 0.56, SUCRA = 40.76), RM (Pr = 0.61, SUCRA = 32.52) and SI (Pr = 0.84, SUCRA = 7.17) (Figure 2).

Pair-wise single meta-analysis

Only one possible pair-wise SMA was possible (Ti vs. d-PTFE) with a mean difference of −0.89 (95% CrI −3.86, 1.45) favouring d-PTFE (Appendix 12).

Heterogeneity and inconsistency

No substantial heterogeneity between studies was observed based on the inter-studies SD 95% CrI (1.07–13.07). The node-splitting models in this NMA included eight observations. It suggested that there was no statistical difference between direct and indirect comparisons ($p > .05$).

Alternative treatment grouping

When GBR techniques (i.e., d-PTFE, e-PTFE and RM) where combined into one group, the results showed that the group ranked first in intra-surgical VBG (Appendix 12).

- Linear VBG measured on CT/CBCT

Twelve RCTs reported this outcome, eight of which could not be included in the NMA as they were comparing techniques within the same treatment group (Table 3).

Network meta-analysis

Four treatment groups were analysed for this outcome with a total of six possible comparisons (three direct comparisons based on data from four RCTs, and three indirect comparisons) (Figure 1). When compared with INLAY (the most connected group in the network), one treatment group had a higher mean difference (DO [MD = 4.54, 95% CrI −1.54, 10.4]), while the other two groups had lower mean differences (ONLAY [MD = −2.06, 95% CrI −6.09, 1.86] and Ti [MD = −1.01, 95% CrI −6.5, 4.59]). None of the differences was statistically significant (Appendix 13).

Treatment ranking

The treatment group that had the highest probability to be ranked 1 was DO (Pr = 0.89, SUCRA = 94.44) followed by INLAY (Pr = 0.62, SUCRA = 54.86), Ti (Pr = 0.39, SUCRA = 34.9) and ONLAY (Pr = 0.64, SUCRA = 15.79) (Figure 2).

Pair-wise single meta-analysis

Only one possible pair-wise SMA was carried out (ONLAY vs. INLAY). Two studies contributed to the comparison and yielded a mean difference of −2.1 (95% CrI −5.28, 0.99) favouring INLAY (Appendix 13).

Heterogeneity and inconsistency

No substantial heterogeneity between studies was observed based on the inter-studies SD 95% CrI (1.41–75.19). Owing to the inapplicability of node-splitting, inconsistency could not be evaluated.

- Relative bone gain
  Three studies reported the relative bone gain three dimensionally; Cucchi, Vignudelli, Franceschi, et al. (2021) compared two different strategies of Ti; Mounir et al. (2017) compared Ti and INLAY; and Mounir et al. (2019) compared two different strategies within Ti (Table 3). NMA was not possible owing to the limited number of studies.
- Volumetric bone gain
  Three studies reported this outcome. Amorfini et al. (2014) compared INLAY with RM; Merli et al. (2020) compared two strategies within Ti; and Cucchi, Vignudelli, Franceschi, et al. (2021) compared d-PTFE with Ti (Table 3).

3.5.7 | Marginal bone loss (MBL)

Data on MBL at 1, 3 and 5 years post loading were obtained and analysed. At 1 year, 12 RCTs reported the outcome but 2 of them did not contribute to the NMA, as they compared techniques within the same treatment group (Table 3). The remaining 10 studies formed two networks, one comparing five treatment groups, and the other comparing three treatment groups. NMA was not possible at 3 and 5 years.

Network meta-analysis

For the first network, five treatment groups were analysed for this outcome at 1 year with a total of 10 possible comparisons (four direct comparisons based on data from four RCTs and six indirect comparisons). For the second network, three treatments groups were analysed for the same outcome with a total of four possible comparisons (three direct comparisons based on six RCTs and one indirect comparison). None of the differences was statistically significant (Appendix 14).

Treatment ranking

The treatment group that had the highest probability to be ranked one was Ti followed by DO (Appendix 14).

Pair-wise single meta-analysis

Three possible pair-wise SMAs were carried out comparing SI and INLAY at 1, 3 and 5 years:

- At 1 year: Five RCTs contributed to the analysis and resulted in a mean difference of −0.12 (95% CrI −0.25, 0.01) favouring SI.
- At 3 years: Four RCTs contributed to the analysis and resulted in a mean difference of −0.36 (95% CrI −0.57, −0.15) favouring SI.
- At 5 years: Four RCTs contributed to the analysis and resulted in a mean difference of −0.65 (95% CrI −0.97, −0.32) favouring SI (Appendix 14).

Heterogeneity and inconsistency

Substantial heterogeneity between studies was observed with inter-studies SD 95% CrI (1.00–1.08) containing 1. Owing to the inapplicability of node-splitting, inconsistency could not be evaluated.

3.5.8 | Implant success, survival and failure

Twelve RCTs reported success and/or survival at the patient and/or implant level (Table 3). Owing to heterogeneity in definitions and measurements, no analysis was attempted for this outcome.

3.5.9 | Need for additional grafting

Only two RCTs reported this outcome. Roccuzzo et al. (2007) compared Ti with ONLAY, and the results showed an OR of 0.28 (95% CrI 0.04, 1.88) favouring Ti. The second RCT (Cucchi, Vignudelli, Franceschi, et al., 2021) reported an incidence of 8% (two incidents in 25 cases) with Ti mesh use (Table 3).

3.5.10 | Patient-reported outcome measures

Only one RCT (Merli et al., 2020) used a validated tool to measure patient-reported outcome measures (PROMs). A visual analogue scale

(VAS) was used to assess pain at surgery and 1 week post surgery, and functional limitation 1 week post surgery when comparing the use of 100% autogenous bone (AB) or 50% deproteinized bovine bone matrix and 50% autogenous bone, both with 'the fence technique'. The difference was statistically significant for the pain experienced at surgery ($p = .04$, favouring AB) but not statistically significant for pain and functional limitation 1 week post surgery ($p = .11$ and .89, respectively). Three other RCTs used non-validated questionnaires to report PROMs (Felice et al., 2008; Felice, Barausse, et al., 2019; Felice, Pistilli, et al., 2009).

4 | DISCUSSION

This NMA suggested that GBR performed best among the VRA techniques when considering clinical VBG and incidence of complications. An average of 16% complications was reported across 32 studies and 761 participants/943 defects. Operator experience is directly linked to the incidence of complications.

In particular, d-PTFE performed marginally better than e-PTFE when comparing both clinical outcomes and incidence of complications. This could be attributed to the higher cell occlusivity in the former, rendering this technique less prone to bacterial colonization and penetration (Tay et al., 2022).

Resorbable membranes were ranked superior to PTFE membranes in relation to the incidence of healing complications (RM ranked second, d-PTFE fourth and e-PTFE eighth) but inferior in relation to VBG (d-PTFE ranked first, e-PTFE second and RM fifth). It could be that resorbable membranes, because of their lack of physical stiffness, are adopted in cases where less vertical bone augmentation and flap advancement are needed, thus resulting in less flap tension, a major cause of premature membrane exposure (Burkhardt & Lang, 2010).

These results are consistent with those of a recent review, which found GBR to be effective in managing cases with vertical defects and d-PTFE preforming better than e-PTFE, but they are in contradiction to the findings that resorbable membranes result in higher incidence of healing complications (Urban et al., 2019).

Inlay techniques ranked second in the incidence of healing complications (alongside GBR) and in VBG on CT/CBCT (after distraction osteogenesis). However, it ranked last in the incidence of surgical complications and had the highest incidence of intra-operative complications. Most of intra-operative complications were attributed to fracture of the coronal segment of the split ridge during the surgery. Additional limitations of the technique include the need for a minimum of 5 mm of vertical bone to start with, to allow for ridge splitting, and the constraint of the amount of bone gain that can be achieved in vertical dimension by the extent to which the lingually attached periosteum can be stretched, while no bone gain can be achieved in the horizontal dimensions. Nevertheless, the use of the technique in selected cases could result in low incidence of healing complications.

Onlay techniques were used in six of the studies that contributed to the NMA, five of those using autogenous blocks. The network-analysis (with and without the one study that did not use autogenous blocks) found the technique to have a significantly higher chance of healing complications and to yield significantly lower VBG when compared with GBR and Inlay. These findings support the statement of a previous Cochrane review, which reported that 'regarding autogenous blocks as the gold standard is a generally accepted paradigm that has not been confirmed' (Esposito et al., 2009).

This systematic review was conducted to evaluate and compare the effectiveness of the various techniques used for VRA and to rank them using Bayesian NMA. Incidence of healing complications was chosen as the primary outcome. Nevertheless, a holistic approach, considering all relevant secondary outcomes (e.g., VBG, surgical and intra-operative complications and implants success and survival), should be taken when comparing the effectiveness of the various techniques. Short implant technique was included as a positive control rather than an alternative. The use of short implants as an alternative for VRA has been investigated and discussed extensively in previous reviews (Nisand et al., 2015; Pauletto et al., 2021). Our choice to include short implant technique was based on the lack of a gold standard treatment in the field. This is obviously a surgical technique and treatment option associated with quicker and better healing patterns. However, we could argue it might not be the best comparison to use when addressing vertical bone gains and associated healing complications. The rationale of this choice was mostly based on the clinical decision process each clinician will have to adopt when dealing with cases with important vertical bone deficiencies. More long-term studies should consider using a negative control, especially when evaluating PROMs.

Cigarette smoking has been linked to negative outcomes on soft and hard tissue wound healing, with the chances of treatment failure largely increased in smokers (37%) as opposed to non-smokers (5%) (Li & Wang, 2008; Lindfors et al., 2010). It was not possible to fully investigate the correlation between smoking and the incidence of complications at the patient level in the current review owing to the limited number of studies reporting the data. However, when studies that allowed smokers to be enrolled ($n = 19$) were excluded from the analyses, no substantial differences from the main analysis were observed. Investigators should aim to report patient-level data about known confounders to help inform future reviews.

Primary wound closure is necessary for the success of VRA procedures (Burkhardt & Lang, 2010). Features also known to be linked to VRA outcomes include (i) width of keratinized mucosa, (ii) flap thickness, (iii) flap flexibility (tension) and (iv) vestibular depth. Factors affecting flexibility and vestibular depth include previous surgery at the site and inflammation of tissues (Chao et al., 2015). Investigation of the correlation of these factors with the incidence of complication and amount of VBG was not within the scope of this review, although we recognize their importance. Future research and systematic reviews can explore these associations.

The need for additional bone grafting at re-entry was reported in two RCTs. Cucchi, Vignudelli, Franceschi, et al. (2021) reported an incidence of 8% with the use of titanium mesh and a 50–50 mix of particulate autogenous and xenogeneic bone. Roccuzzo et al. (2007) reported an incidence of 16% with the use of titanium mesh and

autogenous blocks and an incidence of 41.6% with the use of autogenous blocks alone. A previous systematic review by Naenni et al. (2019) found a similarly wide range of incidences (1%–34%) with lateral bone augmentation procedures. Findings from this review suggest that the presence of a barrier membrane and/or xenograft material is likely to decrease the incidence and amount of graft resorption. Further studies are needed to fully investigate this question.

Data on dental implant's success and survival in the included studies suffered from high heterogeneity arising from (i) difference in or lack of reporting of criteria for success/survival and (ii) difference in the level of data reporting (patient level vs. implant level). It was, therefore, not possible to conduct a meta-analysis. However, the NMA of bone stability around implants placed in augmented bone as compared with implants placed in pristine bone or in implants placed in augmented bone using different techniques did not show any statistical differences, which is in line with the findings of previous reviews (Bitinas & Bardijevskyt, 2021; Urban et al., 2019).

PROMs provide valuable information to patients and clinicians when choosing between different interventions and are increasingly being used as endpoints in clinical trials (Vodicka et al., 2015). Only one trial (3% off all trials) in the current review reported the use of a validated PROM (Merli et al., 2020). However, the two intervention arms in this study were very similar, as both groups underwent VRA using the fence technique with autogenous bone (100% vs. 50%–50% mixed with xenogeneic bone) harvested in a similar manner. Studies comparing different VRA techniques would be more beneficial in informing patient and clinician choices. Three other RCTs (Felice et al., 2008; Felice, Barausse, et al., 2019; Felice, Pistilli, et al., 2009) reported the use of non-validated questionnaires to measure patient-reported outcomes. Information acquired via non-validated measures are more prone to biases and methodological variations and cannot therefore be used to draw meaningful conclusions. More emphasis should be placed on gathering PROMs using validated tools in future trials.

It is well recognized that VRA procedures are challenging and operator-dependent. To our knowledge, this the first review that attempts to systematically investigate the correlation between operator experience and the rate of complications in VRA techniques. The results confirmed that VRA techniques are to be performed by experienced operators with a steep learning curve. Reasonable operator experience (>200 procedures) was directly linked to less incidence of complications. The influence of surgical experience on outcomes related to implant therapy has been previously reported (Lambert et al., 1997; Preiskel & Tsolka, 1995; Zoghbi et al., 2011). Experience is one of many intercorrelated 'human factors' known to affect surgical competence and performance (Renouard et al., 2017; 2023). Lessons learned from aviation sector and other high-risk industries, as well as from research in medical teaching, stress the importance of recognizing those human factors as potential causes of surgical complications (Aerden et al., 2014; Fabri & Zayas-Castro, 2008; Helmreich, 2000). These lessons include having solid theoretical knowledge about the procedure at hand, the implementation of appropriate checklists, the systematic use of feedback (reporting and analysis of errors by a grouping of professionals) as well as human resources management and threat and error management.

Limitations of the present work include, despite our wide inclusion criteria, the relatively small number of studies available for the different techniques and hence in the treatment groups. Additionally, based on the available data it was not possible to fully evaluate the influence of smoking and other patient factors associated with successful or unsuccessful outcomes. Furthermore, it is recognized that the difficulty of performing VRA varies greatly depending on the location and three-dimensional extent of the vertical defect as well as on the classification of edentulism (Kennedy I-IV). Sub-analyses to explore the effects of these factors were not possible based on the available data, so we urge the readers to interpret the results with caution. Likewise, pre- and post-operative care regimens (e.g., corticosteroid and antibiotics intake) have been suggested to impact the incidence of post-operative complications and patients' perception of dental implant therapy (Payer et al., 2020; Wagner et al., 2022). However, data on regimens used in the included studies suffered from a high level of heterogeneity and there was a general lack of reporting of this information, hindering the systematic evaluation of their effect in this review. Further, we decided to use and include short dental implants as the comparison group against the other augmentation procedures. Although we believe that this is an appropriate comparison when discussing and evaluating the incidence of complications of surgical procedures, this might not be the same when evaluating the long-term success of dental implants. This is why we urge caution when inferring and comparing survival of short dental implants versus conventional dental implants, as it was not the aim of this review.

On the other hand, our systematic review methodology was based on a pre-registered protocol, with a strict analytical methodology including all possible VRA techniques reported, possible confounding factors and indirect comparisons, giving greater confidence when interpreting the quantitative analyses. Additionally, sub-group analyses exploring the effects of known, important sources of heterogeneity were conducted when possible and compared with the main analysis, thus further improving confidence in the presented results.

5 | CONCLUSIONS

When evaluating VRA techniques, those with greater VBG are associated with more incident complications. GBR techniques using non-resorbable membranes yielded the most favourable results in terms of VBG and complications. Resorbable membranes could be considered when minimal VBG is needed. The use of inlay technique in selected cases can result in low incidence of healing complications. Operator experience (>200 procedures) is directly linked to fewer VRA complications. Further well-designed RCTs are needed to evaluate the efficacy and cost effectiveness of VRA strategies.

6 | IMPLICATIONS FOR FUTURE RESEARCH

Considerable variability in the choice and definitions of reported outcomes was observed during this review. Use of the recently established

core outcome sets (Tonetti et al., 2023), with the aim of informing benefits, harms and outcome definitions of bone augmentation procedures, may be helpful for clinical trials, and subsequently to those conducting systematic reviews, in the future. Additionally, the two main reasons for downgrading certainty in the evidence in the present review were risk of bias and imprecision. Future researchers should aim to improve the quality of VRA clinical studies by adopting meticulous design approaches, taking into consideration correct sample size calculations and including all possible sources of bias.

AUTHOR CONTRIBUTIONS

Faisal F. Alotaibi and Francesco D'Aiuto developed the original idea for the project. Faisal F. Alotaibi wrote the first draft of the research protocol, which was edited and revised by Isabella Rocchietta, Jacopo Buti and Francesco D'Aiuto. All authors discussed and formulated the final research design. Faisal F. Alotaibi identified research reports and extracted data in agreement with Isabella Rocchietta, Jacopo Buti and Francesco D'Aiuto. Faisal F. Alotaibi and Jacopo Buti carried out the statistical analyses, which were discussed and interpreted by all authors. Faisal F. Alotaibi drafted the final report, which was edited and revised by all authors.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Ethics approval was not required for this systematic review. Nonetheless, all research steps were conducted in line with principles of research ethics.

ORCID

Faisal F. Alotaibi https://orcid.org/0000-0002-8790-5632
Jacopo Buti https://orcid.org/0000-0001-9945-0666
Francesco D'Aiuto https://orcid.org/0000-0001-8654-935X

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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