Received: 16 February 2020 | Revised: 9 October 2020 | Accepted: 16 November 2020

DOI: 10.1111/clr.13690

REVIEW ARTICLE

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Relative performance of various biomaterials used for maxillary sinus augmentation: A Bayesian network meta-analysis

Bálint Trimmel[1] | Noémi Gede[2] | Péter Hegyi[2,3] | Zsolt Szakács[2,3] | Gyöngyi Anna Mezey[4] | Eszter Varga[5] | Márton Kivovics[6] | Lilla Hanák[2] | Zoltán Rumbus[2] | György Szabó[7]

[1]Department of Oral Diagnostics, Faculty of Dentistry, Semmelweis University, Budapest, Hungary

[2]Institute for Translational Medicine, Medical School, University of Pécs, Pécs, Hungary

[3]Szentágothai Research Centre, University of Pécs, Pécs, Hungary

[4]Department of Public Health, Faculty of Medicine, University of Szeged, Szeged, Hungary

[5]Department of Pediatrics, Medical School, University of Pécs, Pécs, Hungary

[6]Department of Community Dentistry, Faculty of Dentistry, Semmelweis University, Budapest, Hungary

[7]Department of Oro-Maxillofacial Surgery and Stomatology, Faculty of Dentistry, Semmelweis University, Budapest, Hungary

Correspondence
Bálint Trimmel, D.M.D., Department of Oral Diagnostics, Semmelweis University, 47. Szentkirályi Street, Budapest, H-1088, Hungary.
Email: trimmel.balint@dent.semmelweis-univ.hu

Funding information
Human Resources Development Operational Programme Grant, Grant/Award Number: EFOP-3.6.2-16-2017-0006; Economic Development and Innovation Operative Program, Grant/Award Number: GINOP-2.3.2-15-2016-00048

Abstract

Objectives: To assess the histomorphometric outcomes obtained in randomized clinical trials (RCTs) with different biomaterials used for maxillary sinus augmentation (MSA).

Materials and Methods: A search of the existing medical literature until October 1, 2019, was performed. Inclusion criteria were (a) RCTs assessing a two-stage MSA from the lateral approach using autologous bone or biomaterials for grafting and (b) reported histomorphometric outcomes based on crestal bone core biopsy samples. The Bayesian method was used to perform pairwise meta-analyses and network meta-analysis (NMA). The primary outcome, the new bone percentage (NB %), was calculated as mean differences with 95% credible intervals. The interventions were ranked by their posterior probability by calculating the surface under the cumulative ranking curve values.

Results: Thirty-four RCTs (842 MSAs) were included in the analysis with a normal healing period (5–8 months). All comparisons were presented in a league table. On the basis of the ranking probability, the most effective bone grafting material for NB% was bovine xenograft + bone marrow concentrate (BMC) (81%), followed by bovine xenograft + platelet-rich plasma (PRP) (77%), bioactive glass ceramic + autologous bone 1:1 (70%), nanocrystalline hydroxyapatite in silica gel (70%), and bioactive glass ceramic (70%). Autologous bone graft alone took the twelfth position with 57%.

Conclusion: Within the limitations of the present NMA, the analysis did not confirm autologous bone alone as the gold standard for MSA and showed superiority of composite grafts such as bovine xenograft + BMC after 5–8 months of healing.

KEYWORDS

bayesian method, biomaterials, bone grafting, bone substitutes, morphometric analysis, network meta-analysis, sinus floor elevation

1 | INTRODUCTION

To facilitate implant placement in the areas of the posterior maxilla with insufficient alveolar height, a maxillary sinus augmentation (MSA) technique using a lateral approach was invented (Boyne & James, 1980). Over the last 40 years, a variety of modifications to this technique has been published and clinical trials have confirmed its predictability and long-term efficacy (Antonoglou et al., 2018; Chanavaz et al., 1995; Pjetursson et al., 2008; Raghoebar et al., 2019; Tatum et al., 1993). The first and one of the best grafting materials for this intervention is the autologous bone (AB), which was considered by many authors as the "gold standard." It possesses osteoinductive, osteoconductive, and osteogenic capabilities, but also involves donor-site morbidity. This is the main reason for the search for biomaterials to substitute AB grafts. In the last few decades, biomaterials such as xenografts, allografts, synthetic grafts, growth factors, platelet concentrates, and a variety of composite grafts have been investigated to identify an optimal solution for MSA (Lutz, 2018; Schlegel et al., 2016).

For evaluation of grafted areas, histomorphometric analysis from bone core biopsy samples is used to assess the following parameters: the proportions of newly formed bone (NB), residual graft (RG) particles, and non-mineralized tissue (NMT) (Moy et al., 1993; Price et al., 1998). A greater percentage of NB indicates a successful integration of the bone graft, and this vital bone is one of the most important factors for dental implant osseointegration.

Previous systematic reviews on histomorphometric outcomes tried to synthesize the evidence to identify the most predictable grafting material for MSA (Corbella et al., 2016; Danesh – Sani et al., 2017; Ting et al., 2017). However, in order to pool data for a meta-analysis, similar trials with same comparisons are needed. Further, the variety of biomaterials used, the differences in healing times, and comparators across different studies are the major limitations for a quantitative synthesis. In contrast, a network meta-analysis (NMA) can handle multiple interventions if the assumption of transitivity is met.

Thus, the purpose of the present systematic review was to perform a Bayesian NMA on the dataset of previously published RCTs and rank the biomaterials used for two-stage MSA by NB formation capacity. The null hypothesis was that the highest amount of NB formation after MSA is associated with the use of AB alone as grafting material.

2 | MATERIALS AND METHODS

2.1 | Protocol and registration

This network meta-analysis is reported in accordance with the PRISMA-NMA Statement. The protocol has been registered in PROSPERO (International Prospective Register of Systematic Reviews) a priori under registration number CRD42019137740.

2.2 | PICO and eligibility

The PICOTS (patient characteristics, intervention, comparison and outcome, timing and study design) format was applied to the clinical question (Table 1).

2.3 | Search strategy

A systematic search without applied filters or restrictions was performed in Cochrane Library (CENTRAL), EBSCO, Embase, MEDLINE (via PubMed), and WOS (WOS core Collection) electronic databases with records published up to October 1, 2019.

The search key was as follows: *("sinus membrane elevation" OR "sinus lift" OR "sinus augmentation" OR "sinus floor augmentation" OR "sinus floor elevation" OR "msfe" OR "sinus graft" OR "maxillary augmentation") AND (graft OR material OR bone).*

Besides electronic databases, a hand search of cited and citing papers was performed.

2.4 | Study selection and data collection

All the relevant articles were combined in a reference manager software (EndNote X9; Clarivate Analytics). After removing duplicates, the remaining records were screened in the following three steps: screening by titles (a), screening by abstracts (b), and finally, screening of the full text (c). Study selection was performed by two authors independently (B.T and M.K.). Disagreements between reviewers were resolved by discussion and consultations with a third author (G. Sz.) Data extraction was performed independently by two reviewers (B.T and M.K.) using a standardized preconstructed data extraction sheet. The following information was extracted: first authors' names, year of publication, study design, number of participants, average age of the participants, sex distribution, number of surgical sites, number of biopsy samples, applied healing time, the residual ridge height, maxillary sinus width, and the percentage of NB based on histomorphometric records.

2.5 | Risk of bias assessment

Potential sources of bias in the included studies were explored using the Cochrane Handbook. Review Manager 5.3 software and the Cochrane Risk of Bias Tool were applied to evaluate seven domains. For the final judgment of the overall risk assessment, only six domains were considered. More details are shown in Appendix S1.

2.6 | Data processing and statistical analysis

Subgrouping for the meta-analysis may result in loss of information from the original studies. To reduce the clinical heterogeneity

TABLE 1 PICOTS criteria

PICOTS criteria	
Patient characteristics (P)	Patients treated with maxillary sinus augmentation (MSA) via the lateral approach were included. Patients treated with (1) one stage or non-lateral access MSA or (2) MSA combined with vertical or horizontal augmentation were excluded.
Intervention (I)	Biomaterials including: (1) allograft, (2) bovine xenograft, (3) porcine xenograft, (4) equine xenograft, (5) biphasic calcium phosphate, (6) beta-tricalcium-phosphate, (7) bioactive glass ceramic, (8) nanocrystalline hydroxyapatite, (9) magnesium-enriched hydroxyapatite, (10) rigid biodegradable (L-lactic, D-lactic, and glycolic acid)copolymer membrane, (11) bovine xenograft mixed with autologous bone 1:1, (12) bovine xenograft mixed with autologous bone 1:1 followed by laser stimulation, (13) bovine xenograft mixed with autologous bone 4:1, (14) bovine xenograft mixed with autologous bone 7:3, (15) bovine xenograft mixed with platelet-rich fibrin, (16) bovine xenograft mixed with platelet-rich plasma, (17) bovine xenograft mixed with bone marrow aspirates, (18) bovine xenograft mixed with bone marrow concentrate, (19) bioactive glass ceramic mixed with autologous bone 1:1, (20) beta-tricalcium-phosphate mixed with autologous bone 1:1, (21) beta-tricalcium-phosphate mixed with platelet-rich plasma, (22) beta-tricalcium-phosphate mixed with platelet-rich fibrin, (23) autologous bone mixed with platelet-rich plasma, (24) autologous bone mixed with autologous platelet concentrate, (25) biphasic calcium phosphate mixed with fibrin sealant, (26) poly(lactic-co-glycolic acid)-based polymer (PLGA)-coated biphasic calcium phosphate, (27) biphasic calcium phosphate mixed with enamel matrix proteins (EMD), (28) nanocrystalline hydroxyapatite in silica gel, (29) nanocrystalline hydroxyapatite in silica gel mixed with plasma rich in growth factors, (30) titan granules mixed with platelet-rich fibrin, (31) allograft mixed with autologous bone 1:1, (32) beta-tricalcium-phosphate mixed with autologous bone, (33) beta-tricalcium-phosphate mixed with autologous bone 10:1, (34) equine xenograft mixed with hyaluronic acid matrix, (35) equine xenograft mixed with porous titanium granules, (36) collagen-stabilized bovine xenograft, (37) biphasic calcium sulfate mixed with bovine xenograft 2:1, (38) biphasic calcium sulfate mixed with biphasic calcium phosphate 2:1, (39) porcine xenograft mixed with autologous bone 1:1, (40) bovine xenograft mixed with synthetic peptide in sodium hyaluronate, and (41) beta-tricalcium-phosphate mixed with recombinant human growth and differentiation factor-5.
Comparison (C)	Autologous bone
Outcome (O)	New bone formation determined based on histomorphometric analysis from crestal bone core biopsy samples were included. Histomorphometric data based on lateral bone core biopsy samples were excluded.
Timing (T)	(T1) early healing (bone core biopsy harvesting occurred 2–5 months after MSA), (T2) normal healing (bone core biopsy harvesting occurred 5–8 months after MSA), and (T3) late healing group (bone core biopsy harvesting occurred more than 8 months after MSA).
Study design (S)	Randomized controlled trials.

associated with the differences in healing periods applied in the studies, the extracted data were classified into three subgroups: early (bone core biopsy harvesting occurred more than 2 but a maximum of 5 months after MSA), normal (bone core biopsy harvesting occurred more than 5 but a maximum of 8 months after MSA), and late (bone core biopsy harvesting occurred more than 8 months after MSA) healing groups.

The commonly used categories for biomaterials, such as xenografts or alloplasts, are too general and cover a wide variety of biomaterials with different properties. During data processing, in order to overcome this disadvantage and preserve the information for the types and nature of biomaterials, 42 subgroups were created.

For visualization of the connections between biomaterial subgroups, a spider web-like graph was created based on the predefined healing periods. If a connected network was identified, the Bayesian method was used to perform pairwise meta-analyses and NMA. The Bayesian approach for NMAs describes the range and probability of the parameter of interest (e.g., treatment effect). The posterior distribution produced by this method predicts the new range and probability of plausible values for these parameters with the representation of uncertainty. These properties make the model suitable for drawing direct probability statements (Dias & Caldwell, 2019; Spiegelhalter et al., 2004).

All the analyses were carried out under a random effect model. The primary outcome, the NB percentage (continuous), was calculated as mean difference (MD) with 95% credible intervals (95% CrI). Node-splitting analysis was performed for examination of consistency. The model was optimized, and posterior samples were generated using Markov Chain Monte Carlo methods running in four chains. At least 20,000 adaptation iterations were set to determine convergence and 10,000 simulation iterations.

The network estimates (pooled estimates of direct and indirect data) of each intervention were presented in comparison with placebo and with each other in a forest plot. The interventions were ranked by their posterior probability by calculating the surface under the cumulative ranking (SUCRA) curve values, and the cumulative probabilities of each treatment were characterized by a single value between 0% and 100%. Ranking probabilities have the advantage of allowing easy-to-interpret conclusions with their application ("Treatment A has a 55% chance of being the best"). The higher the percentage or SUCRA value, the higher the likelihood of the treatment being in the top rank, or being one of the top ranks (Dias & Caldwell, 2019; Salanti et al., 2011).

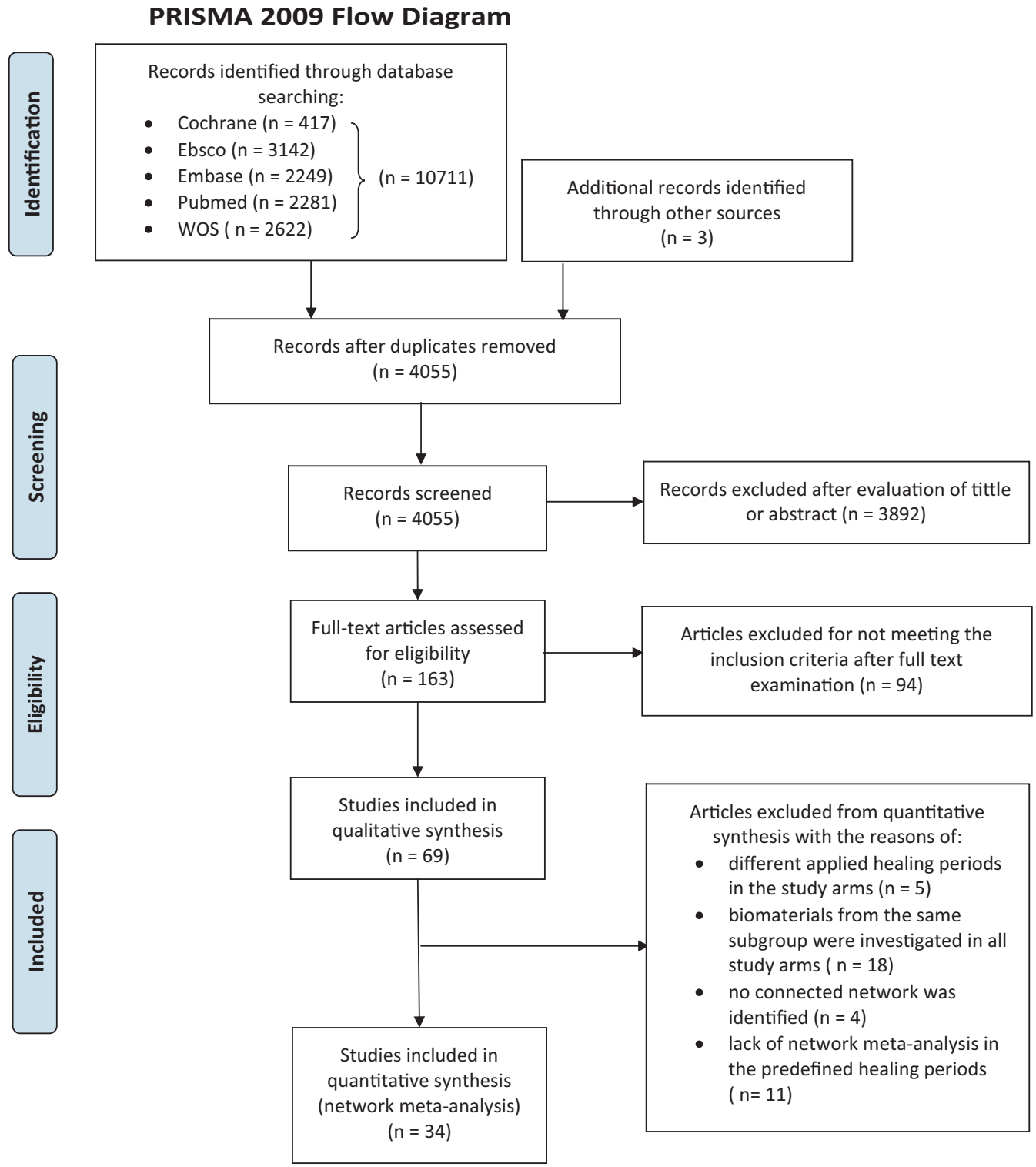


FIGURE 1 PRISMA flow diagram. From: Moher et al. (2009).

To check for publication bias, a visual inspection of funnel plots and Egger's test was performed. All computations were performed using the R (V. 3.5.2) package gemtc (V. 0.8–2) along with the Markov Chain Monte Carlo engine JAGS (V. 3.4.0), package netmeta (V. 1.1–0), and STATA 16.0 (StataCorp LLC).

2.7 | Quality of evidence

There is no widely accepted and applied method for grading the evidence of NMA. The limitations of the existing rating methods did not allow their use in the present NMA (Chaimani et al., 2019).

Nevertheless, elements of the GRADE rating system were used to assess the certainty of confidence derived from the results and describe the limitations and strengths of the findings.

3 | RESULTS

3.1 | Study selection and characteristics

Figure 1 shows the flowchart of this meta-analysis. All inclusion criteria were fulfilled by 69 studies. Data extraction was performed as described previously. In a total of 34 studies that used a normal healing period (5–8 months), a connected network was identified, which provided an opportunity for NMA.

The trials excluded from quantitative synthesis are summarized in Appendix S2. Characteristics of the studies included in the NMA, including patient and biomaterial characteristics, are summarized in Table 2.

3.2 | Risk of bias within the studies included

The overall assessment for risk of bias showed low risk in 5 studies, unclear risk in 20 studies, and high risk in 9 studies.

More details are shown in Figure 2 and Appendix S3.

3.3 | Summary of the network (5–8 months)

The total sample consisted of 842 MSAs from 34 RCTs (Batas et al., 2019; Bettega et al., 2009; Cordaro et al., 2008; Felice et al., 2009; Flichy-Fernández et al., 2019; Galindo-Moreno et al., 2008, 2011; Jelusic et al., 2017; Khairy et al., 2013; Kılıç et al., 2017; Kurkcu et al., 2012; Lee et al., 2017; Lindgren et al., 2009; Kivovics et al., 2018; Meimandi et al., 2017; Menezes et al., 2018; Meymandi et al., 2017; Nery et al., 2017; Nizam et al., 2018; Oh et al., 2019; de Oliveira et al., 2016; Pasquali et al., 2015; Payer et al., 2014; Pereira, Gorla, et al., 2017; Pereira, Menezes, et al., 2017; Stacchi et al., 2017; Szabó et al., 2005; Theodoro et al., 2018; Torres et al., 2009; Wagner et al., 2012; Wildburger et al., 2014; Wiltfang et al., 2003; Zerbo et al., 2004; Zhang et al., 2012).

There was one triple-arm RCT (de Oliveira et al., 2016) that investigated bone marrow concentrates (BMC) with different centrifugation protocols. Based on our subgroup formation, both interventions were pooled in the bovine xenograft + bone marrow concentrate (bovine + BMC) subgroup. Meta-analyses cannot handle experiments comparing the same material. Therefore, the study arm containing BMC with a double centrifugation protocol was excluded from the analysis. In the present NMA, the bovine + BMC subgroup contains the results of three clinical trials using single centrifugation protocols to produce the bone marrow concentrate (de Oliveira et al., 2016; Pasquali et al., 2015; Wildburger et al., 2014).

The connections between biomaterial subgroups are presented as a spider web-like graph in *Figure 3*, and the biomaterials of the network are summarized in Table 3.

3.4 | Results of NMA

Significant differences were detected between the bovine + BMC composite graft and the biodegradable copolymer and between the bovine + BMC composite graft and the allograft, with the composite graft being favored in both comparisons. The other 376 comparisons did not show significant differences between the applied biomaterials. Based on these findings, the hypothesis that AB alone is the most favorable material for MSA was rejected. The results of all comparisons are presented in Table 4.

The ranking probabilities for all of the biomaterials were estimated at each possible rank associated with any material. Then, their hierarchy was calculated using the SUCRA curve, as well as the mean ranks. According to the SUCRA ranking, the most effective biomaterials for the outcome NB% over a healing period of 5 to 8 months after MSA were bovine + BMC (81%), followed by bovine + platelet-rich plasma (PRP) (77%), bioactive glass ceramic + AB 1:1 (70%), nanocrystalline hydroxyapatite in silica gel (70%), and bioactive glass ceramic (70%). AB alone as grafting material took the twelfth position (57%). More details are shown in Figure 4 and Appendix S4.

4 | DISCUSSION

The present Bayesian NMA synthesizes the findings for the performance of different biomaterials in a two-stage MSA based on their NB formation capabilities and compare them to AB. This advanced statistical model is suitable for making probability statements even for comparisons that were not directly investigated in a head-to-head trial. The results of this quantitative synthesis are based on a dataset of 34 RCTs that used healing periods of 5–8 months, and 28 biomaterial subgroups have been compared in this study. The analyses showed significant differences in two comparisons—(a) between bovine + BMC composite graft and biodegradable copolymer and (b) between bovine + BMC composite graft and allograft—but there were no significant differences in the other 376 comparisons. In the two comparisons with significant differences, the composite graft was superior. The better performance with AB alone as grafting material compared to other biomaterials with respect to NB% hypothesis was not confirmed if a healing period of 5–8 months was applied before dental implant placement. For the other two predefined healing periods (graft healing time less than 5 months and more than 8 months), a quantitative synthesis could not be performed for the following reasons: (a) the low number of available RCTs and (b) the

TABLE 2 Characteristics of the studies included in the NMA are presented in the data extraction sheet: first authors' names, year of publication, sample size (number of maxillary sinus augmentation (MSA)), applied grafting materials, subgroup categories of grafting materials, the percentage of NB, the region of interest (ROI) of the histomorphometry, the residual ridge height, the sinus widths, and the applied healing time

Data extraction sheet				
Publication data		**Sample size**	**Intervention**	
First Author	**Year of publication**	**Number of MSA**	**Applied biomaterial**	**Subgroup category**
Batas	2019	6	Bovine xenograft mixed with platelet-rich fibrin (PRF)	Bovine + PRGF
		6	Bovine xenograft	Bovine
Flichy-Fernández	2019	16	Poly(lactic-co-glycolic acid)-coated (PLGA-coated) biphasic calcium phosphate (HA/β-TCP = 60/40)	BCP + PLGA
		20	Biphasic calcium phosphate (HA/β-TCP = 60/40)	BCP
Oh	2019	27	Biphasic calcium phosphate (HA/β-TCP = 60/40)	BCP
		25	Bovine xenograft	Bovine
Kivovics	2018	12	Albumin impregnated demineralized freeze-dried bone allograft	Allo
		11	Bovine xenograft	Bovine
Menezes	2018	9	Bioactive glass ceramic mixed with autologous bone (1:1)	Bioglass + AB 1:1
		12	Autologous bone	AB
Nizam	2018	13	Bovine xenograft mixed with leukocyte- and platelet-rich fibrin (L-PRF)	Bovine + PRF
		13	Bovine xenograft	Bovine
Theodoro	2018	6	Bovine xenograft mineral mixed with autologous bone (1:1)	Bovine + AB 1:1
		6	Bovine xenograft mixed with autologous bone (1:1) for sinus grafting, followed by LLLT.	Bovine + AB 1:1 + laser stimulation
Jelusic	2017	30	Nanoporous biphasic calcium phosphate (HA/β-TCP = 60/40)	BCP
		30	Beta-tricalcium phosphate (β-TCP)	β-TCP
Kilic	2017	9	Beta-tricalcium phosphate (β-TCP)	β-TCP
		9	Beta-tricalcium phosphate (β-TCP) mixed with platelet-rich plasma (PRP)	β-TCP + PRP
		8	Beta-tricalcium phosphate (β-TCP) mixed with platelet-rich fibrin (PRF)	β-TCP + PRF
Lee	2017	7	Bovine xenograft	Bovine
		8	Porcine xenograft	Porcine
Meimandi	2017	10	Nanocrystalline hydroxyapatite in a silica gel mixed with plasma rich in growth factors (PRGF)	HA + silica gel + PRGF
		10	Nanocrystalline hydroxyapatite in a silica gel	HA + silica gel
Meymandi	2017	9	Nanocrystalline hydroxyapatite in a silica gel	HA + silica gel
		9	Biphasic calcium phosphate (HA/β-TCP = 60/40)	BCP
Nery	2017	10	Biphasic calcium phosphate (HA/β-TCP = 60/40)	BCP
		10	Biphasic calcium phosphate (HA/β-TCP = 60/40) mixed with enamel matrix proteins (EMD)	BCP + EMD
Pereira	2017	11	Beta-tricalcium phosphate (β-TCP)	β-TCP
		9	Beta-tricalcium phosphate (β-TCP) mixed with autologous bone (1:1)	β-TCP + AB (1:1)
		12	Autologous bone	AB
Pereira	2017	10	Bioactive glass ceramic	Bioglass
		10	Bioactive glass ceramic mixed with autologous bone (1:1)	Bioglass + AB 1:1
		10	Autologous bone	AB
Stacchi	2017	26	Sintered nanocrystalline hydroxyapatite (HA)	HA (nano)
		26	Bovine xenograft	Bovine

Histomorphometry outcome				Surgical sites anatomy		Graft healing time
New bone (%)						
Mean	*SD*	*p*	ROI of the histomorphometry	Residual ridge height	Sinus widths	Month
35.6	8.26	n.s.	Augmented area above the residual ridge	Less than 3 mm	Not reported	6
37.8	3.15					6
31.25	13.82	n.s.	Not reported	2.5 +- 1.58 mm	6.8 +- 1.48 mm	6
34.09	14.11			3.46 +- 0.87 mm	7.38 +−1.32 mm	6
28.84	7.94	0.286	Augmented area above the residual ridge	Mean 3.8 mm (2.2–5.8 mm)	Not reported	6
25.13	9.56					6
36.28	8.00	<0.05	Augmented area above the residual ridge	1–5 mm	Not reported	6
50.23	10.79					6
45.8	13.8	n.s.	Apical 1/3 of the sample	Less than 5 mm	Not reported	6
42	16.6					6
21.38	8.78	0.96	Augmented area above the residual ridge	2.45+−0.79 mm	Not reported	6
21.25	5.59			2.53+−0.61 mm		6
35.5	3.95	0.64	Total sample	4 mm	Not reported	6
32	13.75					6
38.42	12.61	0.379	Not reported	2.73+−1.06 mm	Not reported	6
36.16	19.37			2.78+−1.31 mm		6
33.4	10.43	n.s.	Not reported	Less than 7 mm	Not reported	6
34.83	10.12	n.s.				6
32.03	6.34	n.s.				6
26.15	7.11	n.s.	Total sample	2.06+−0.43 mm	Not reported	6
29.77	9.38			1.90+−0.80 mm		6
30.29	8.45	0.85	Total sample	2–4 mm	Not reported	6
30.84	6.76					6
25.29	7.29	0.0001	Total sample	Not reported	Not reported	6
18.69	5.63					6
43.4	6.1	0.94	Apical 6mm	3–5 mm	Not reported	6
43	9					6
44.8	22.1	0.03	Apical 1/3 of the sample	Less than 5 mm	Not reported	6
32.8	16	n.s				6
46.1	16.3	n.s				6
45.6	13.5	n.s.	Apical 1/3 of the sample	Less than 5 mm	Not reported	6
45.8	13.9	n.s.				6
39.9	15.8	n.s.				6
34.9	15	0.428	Total sample	2.03+−0.75 mm	Not reported	6
38.5	17					6

(Continues)

TABLE 2 (Continued)

Data extraction sheet				
Publication data		**Sample size**	**Intervention**	
First Author	**Year of publication**	**Number of MSA**	**Applied biomaterial**	**Subgroup category**
de Oliveira	2016	7	Bovine xenograft	Bovine
		7	Bovine xenograft mixed with bone marrow concentrate (BMC)	Bovine + BMC
Pasquali,	2015	8	Bovine xenograft	Bovine
		8	Bovine xenograft mixed with bone marrow concentrate (BMC)	Bovine + BMC
Wildburger	2014	6	Bovine xenograft mixed with bone marrow concentrate (BMC)	Bovine + BMC
		7	Bovine xenograft	Bovine
Khairy	2013	5	Autologous bone	AB
		5	Autologous bone mixed with platelet-rich plasma (PRP)	AB + PRP
Payer	2013	5	Bovine xenograft	Bovine
		6	Bovine xenograft mixed with bone marrow aspirates (BMA)	Bovine + BMA
Kurkcu	2012	10	Bovine xenograft	Bovine
		13	Beta-tricalcium phosphate (β-TCP)	ß-TCP
Wagner	2012	29	Biphasic calcium phosphate (HA/β-TCP = 60/40) mixed with fibrin sealant (FS)	BCP + FS
		29	Autologous bone graft mixed with bovine xenograft	Bovine + AB 1:1
Zhang	2012	6	Bovine xenograft mixed with platelet-rich fibrin (PRF)	Bovine + PRF
		5	Bovine xenograft	Bovine
Galindo-Moreno	2011	14	Bovine xenograft mixed with autologous bone (50/50)	Bovine + AB 1:1
		14	Bovine xenograft mixed with autologous bone (80/20)	Bovine + AB 4:1
Bettega	2009	12	Autologous bone	AB
		12	Autologous bone mixed with autologous platelet concentrate (APC)	AB + APC
Lindgren	2009	11	Biphasic calcium phosphate (HA/β-TCP = 60/40) + 1 micro-implant 2x10mm	BCP
		11	Bovine xenograft + 1 micro-implant 2x10mm	Bovine
Felice	2009	10	Rigid biodegradable copolymer membrane (L-lactic, D-Lactic, and glycolic acid)	Biodegradable copolyn
		10	Bovine xenograft	Bovine
Torres	2009	5	Bovine xenograft mixed with platelet-rich plasma (PRP)	Bovine + PRP
		5	Bovine xenograft	Bovine
Cordaro	2008	14	Biphasic calcium phosphate (HA/β-TCP = 60/40)	BCP
		18	Bovine xenograft	Bovine
Galindo-Moreno	2008	5	Bovine xenograft with autologous bone (1:1)	Bovine + AB 1:1
		5	Bioactive glass ceramic mixed with autologous bone (1:1)	Bioglass + AB 1:1
Szabó	2005	20	Beta-tricalcium phosphate (β-TCP)	β-TCP
		20	Autologous bone	AB
Zerbo	2004	5	Autologous bone	AB
		5	Beta-tricalcium phosphate (β-TCP)	β-TCP
Wiltfang	2003	17	Beta-tricalcium phosphate (β-TCP) mixed with platelet-rich plasma (PRP)	β-TCP + PRP
		18	Beta-tricalcium phosphate (β-TCP)	β-TCP

Histomorphometry outcome				Surgical sites anatomy		Graft healing time
New bone (%)						
Mean	*SD*	*p*	ROI of the histomorphometry	Residual ridge height	Sinus widths	Month
27.3	5.55	n.s.	Augmented area above the residual ridge	2.2+−1.2 mm	Not reported	6
38.44	12.34					6
27.3	5.55	0.002	Augmented area above the residual ridge	less than 4 mm	Not reported	6
55.15	20.91					6
13.5	5.4	n.s.	Augmented area above the residual ridge	Less than 3 mm	Not reported	6
13.9	8.5					6
39.5	7.4	0.003	Not reported	Less than 5 mm	Not reported	6
28	4.1					6
10.41	5.25	n.s.	Augmented area above the residual ridge	Less than 3 mm	Not reported	6
14.17	3.59					6
30.13	3.45	0.001	Augmented area above the residual ridge	Less than 5 mm	Not reported	6.38
21.09	2.86					6.6
20	7.70	n.s.	Augmented area above the residual ridge	2–5 mm	Not reported	6 ± 1
24.5	7.1					6 ± 1
18.35	5.62	0.138	Augmented area above the residual ridge	Less than 5 mm	Not reported	6
12.95	5.33					6
36	9.44	0.114	Total sample	Less than 5 mm	Not reported	6
37.38	17.46					6
42.5	28.25–51.15%	0.625	Not reported	3.0 (1.75–6.0) mm	Not reported	6
37.1	31.15–48.7%			3.0 (1.75–4.0) mm		6
41.1	9.8	n.s.	Augmented area above the residual ridge	Less than 5 mm	Not reported	8
41.6	14					8
24.2	6.5	0.002	Total sample	1–5 mm	Not reported	6
36.1	4.6					6
31	5	<0.05	Total sample	1–3 mm	Not reported	6
21.3	4.5					6
21.6	10	0.53	Augmented area above the residual ridge	5.1 +−1.1 mm	Not reported	6.73
19.8	7.9			4.9 +- 0.8 mm		6.8
31.02	7.33	0.68	Central portion of the sample	Less than 5 mm	Not reported	6
33.08	8.18		(alveolar crest + apical 1.5 mm excluded)			6
36.47	6.9	0.25	Augmented area above the residual ridge	Less than 5 mm	Not reported	6
38.34	7.4					6
41	10	0.009	Augmented area above the residual ridge	4–8 mm	Not reported	6
19	5					6
38	32%–43%	<0.05	4 mm apical section of the sample	2–7 mm	Not reported	6
29	25%–37%					6

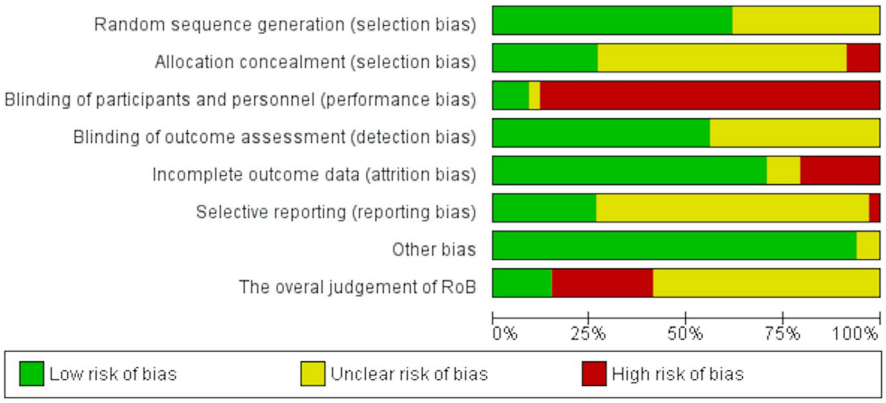


FIGURE 2 Risk of bias graph reviews the authors' overall judgements about each risk of bias item as a percent of the total number of studies

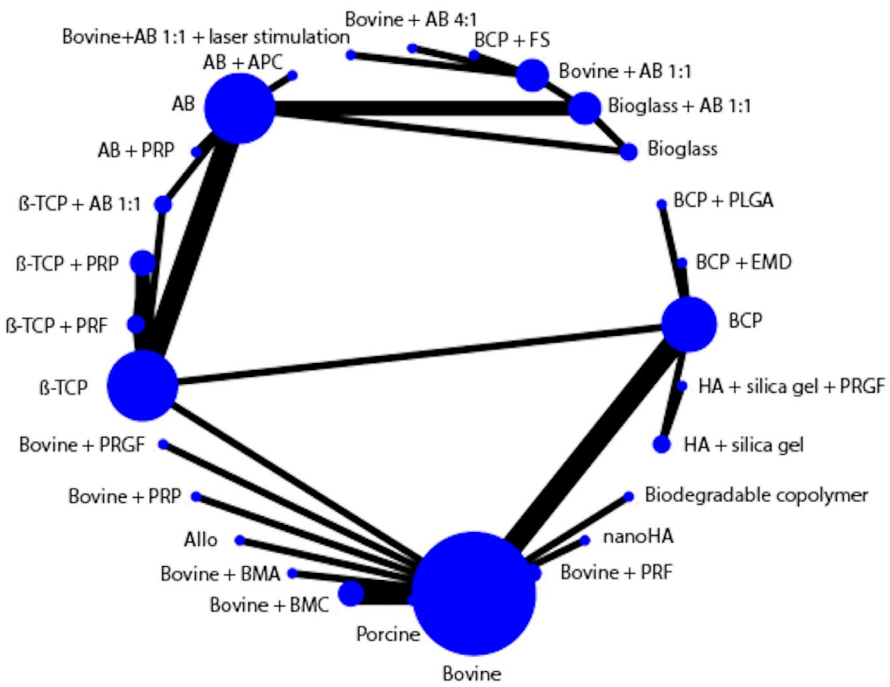


FIGURE 3 On the spider web-like graph, the network of biomaterial subgroups for 5–8 months of healing is presented. Blue nodes represent the interventions. The size of the node is proportional to the number of studies included. Black lines represent the direct comparisons in randomized trials, and the line thickness is directly proportional to the number of comparisons. Abbreviations: autologous bone (AB), allograft (Allo), bovine xenograft (Bovine), porcine xenograft (Porcine), biphasic calcium phosphate (BCP), beta-tricalcium-phosphate (ß-TCP), bioactive glass ceramic (Bioglass), nanocrystalline hydroxyapatite (nanoHA), rigid biodegradable (L-lactic, D-Lactic and glycolic acid)copolymer membrane (Biodegradable copolymer), bovine xenograft + autologous bone 1:1 (Bovine + AB 1:1), bovine xenograft + autologous bone 1:1 composite graft followed by laser stimulation (Bovine + AB 1:1 + laser stimulation), bovine xenograft + autologous bone 4:1 (Bovine + AB 4:1), bovine xenograft + platelet-rich fibrin (Bovine + PRF), bovine xenograft + platelet-rich plasma (Bovine + PRP), bovine xenograft + bone marrow aspirates (Bovine + BMA), bovine xenograft + bone marrow concentrate (Bovine + BMC), bioactive glass ceramic + autologous bone 1:1 (Bioglass + AB 1:1), beta-tricalcium-phosphate + autologous bone 1:1 (ß-TCP + AB 1:1), beta-tricalcium-phosphate + platelet-rich plasma (ß-TCP + PRP), beta-tricalcium-phosphate + platelet-rich fibrin (ß-TCP + PRF), autologous bone + platelet-rich plasma (AB + PRP), autologous bone + autologous platelet concentrate (AB + APC), biphasic calcium phosphate + fibrin sealant (BCP + FS), poly(lactic-co-glycolic acid)-based polymer (PLGA)-coated biphasic calcium phosphate (BCP + PLGA), biphasic calcium phosphate + enamel matrix proteins (EMD) (BCP + EMD), nanocrystalline hydroxyapatite in silica gel + plasma rich in growth factors (HA + silica gel + PRGF)

low or no connection rate between these studies with the applied subgroup categories for biomaterials.

In a previous systematic review (Danesh-Sani et al., 2017), the histomorphometric findings of 136 comparative and non-comparative prospective clinical trials using crestal or lateral bone core biopsy harvesting and immediate or delayed dental implant placement protocols were pooled together and the following conclusions were made: (a) The use of AB is associated with the highest amount of NB and the

TABLE 3 The grafting materials of the network are presented in the data extraction sheet: grafting materials used for maxillary sinus augmentation (MSA) regarding to the applied subgroup category, number of trials, the number that used the grafting material for MSA, and the number of MSA (sample size)

Summary of network (5–8 months)		
Grafting material	**Number of trials**	**Number of MSA**
autologous bone (AB) (Bettega et al., 2009; Khairy et al., 2013; Menezes et al., 2018; Pereira, Gorla, et al., 2017; Pereira, Gorla, et al., 2017; Szabó et al., 2005; Zerbo et al., 2004)	7	76
allograft (Allo) (Kivovics et al., 2018)	1	12
bovine xenograft (Bovine) (Batas et al., 2019; Cordaro et al., 2008; Felice et al., 2009; Kurkcu et al., 2012; Lee et al., 2017; Lindgren et al., 2009; Kivovics et al., 2018; Nizam et al., 2018; Oh et al., 2019; de Oliveira et al., 2016; Pasquali et al., 2015; Payer et al., 2014; Stacchi et al., 2017; Torres et al., 2009; Wildburger et al., 2014; Zhang et al., 2012)	16	174
porcine xenograft (Porcine) (Lee et al., 2017)	1	8
biphasic calcium phosphate (BCP) (Cordaro et al., 2008; Flichy-Fernández et al., 2019; Jelusic et al., 2017; Lindgren et al., 2009; Meymandi et al., 2017; Nery et al., 2017; Oh et al., 2019)	7	121
beta-tricalcium-phosphate (ß-TCP) (Jelusic et al., 2017; Kılıç et al., 2017; Kurkcu et al., 2012; R. S. Pereira, Gorla, et al., 2017; Szabó et al., 2005; Wiltfang et al., 2003; Zerbo et al., 2004)	7	106
bioactive glass ceramic (Bioglass) (Pereira, Gorla, et al., 2017)	1	10
nanocrystalline hydroxyapatite (nano HA) (Stacchi et al., 2017)	1	26
nanocrystalline hydroxyapatite in silica gel (HA + silica gel) (Meimandi et al., 2017; Meymandi et al., 2017)	2	19
biodegradable copolymer (L-lactic, D-Lactic, and glycolic acid) (Felice et al., 2009)	1	10
bovine xenograft + autologous bone 1:1 (Bovine + AB 1:1) composite graft (Galindo-Moreno et al., 2008, 2011; Theodoro et al., 2018; Wagner et al., 2012)	4	54
bovine xenograft + autologous bone 1:1 composite graft followed by laser stimulation (Bovine + AB 1:1 + laser stimulation) (Theodoro et al., 2018)	1	6
bovine xenograft + autologous bone 4:1 (Bovine + AB 4:1) composite graft (Galindo-Moreno et al., 2011)	1	14
bovine xenograft + platelet-rich fibrin (Bovine + PRF) composite graft (Nizam et al., 2018; Zhang et al., 2012)	2	19
bovine xenograft + platelet-rich plasma (Bovine + PRP) composite graft (Torres et al., 2009)	1	5
bovine xenograft + plasma rich in growth factors (Bovine + PRGF) composite graft (Batas et al., 2019)	1	6
bovine xenograft + bone marrow aspirates (Bovine + BMA) composite graft (Payer et al., 2014)	1	6
bovine xenograft + bone marrow concentrate (Bovine + BMC) composite graft (de Oliveira et al., 2016; Pasquali et al., 2015; Wildburger et al., 2014)	3	21
bioactive glass ceramic + autologous bone 1:1 (Bioglass + AB 1:1) composite graft (Galindo-Moreno et al., 2008; Menezes et al., 2018; Pereira, Gorla, et al., 2017)	3	24
beta-tricalcium-phosphate + autologous bone 1:1 (ß-TCP + AB 1:1) composite graft (Pereira, Gorla, et al., 2017)	1	9
beta-tricalcium-phosphate + platelet-rich plasma (ß-TCP + PRP) composite graft (Kılıç et al., 2017; Wiltfang et al., 2003)	2	26

(Continues)

TABLE 3 (Continued)

Summary of network (5–8 months)		
Grafting material	**Number of trials**	**Number of MSA**
beta-tricalcium-phosphate + platelet-rich fibrin (ß-TCP + PRF) composite graft (Kılıç et al., 2017)	1	8
autologous bone + platelet-rich plasma (AB + PRP) composite graft (Khairy et al., 2013)	1	5
autologous bone + autologous platelet concentrate (AB + APC) composite graft (Bettega et al., 2009)	1	12
biphasic calcium phosphate + fibrin sealant (BCP + FS) composite graft (Wagner et al., 2012)	1	29
poly(lactic-co-glycolic acid)-based polymer (PLGA) coated biphasic calcium phosphate (BCP + PLGA) composite graft (Flichy-Fernández et al., 2019)	1	16
biphasic calcium phosphate + enamel matrix proteins (EMD) (BCP + EMD) composite graft (Nery et al., 2017)	1	10
nanocrystalline hydroxyapatite in silica gel + plasma rich in growth factors (HA + silica gel + PRGF) composite graft Meimandi et al., 2017)	1	10

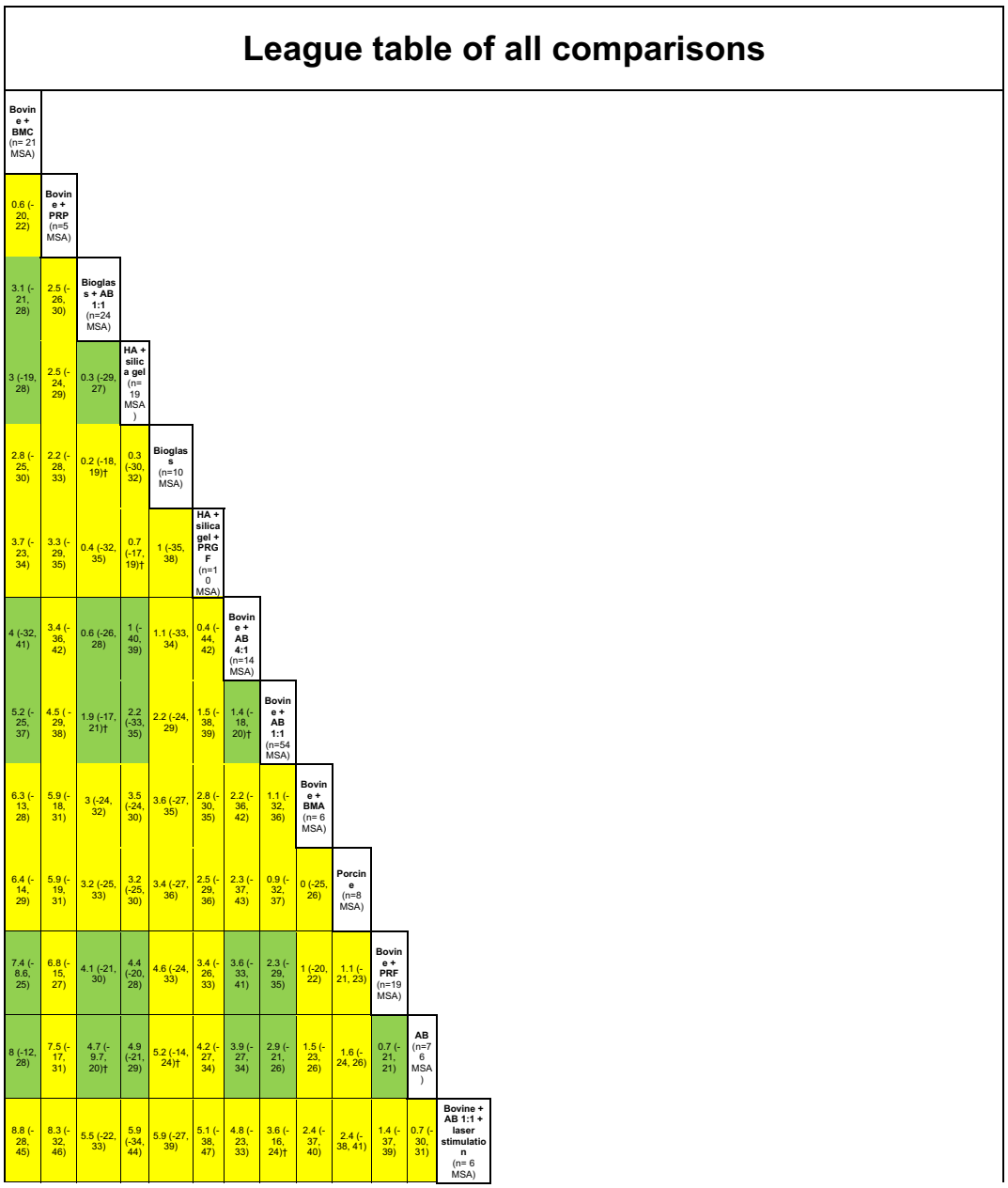
lowest amount of RG compared to other biomaterials. (b) The use of biomaterials (allografts, alloplasts, xenografts) resulted in non-significant differences in the amount of NB over various healing periods. (c) The healing periods have a significant effect on the NB formation, and a lower amount of NB is expected if the graft healing time was less than 4.5 months. (d) The combination of AB with alloplasts and xenografts shows no significant advantages over the same biomaterial with respect to NB formation. The same conclusions for the superiority of AB and the non-significant differences between biomaterials with respect to the amount of NB were obtained in another study that included five RCTs (Starch-Jensen et al., 2018). However, due to the different primary outcome measurement (survival rate of dental implant suprastructure), the included studies showed heterogeneity in the bone core biopsy harvesting methods (crestal and lateral method). In another narrative review, the results of 18 articles were synthesized (Stumbras et al., 2019), and slightly different conclusions were obtained: (a) AB has the best regenerative potential, (b) biomaterials combined with AB result in more matured NB and better graft osseointegration, and (c) platelet concentrates used together with biomaterials enhance bone formation and vascularization. Due to the heterogeneity of the included studies, quantitative analysis was not performed, and the differences in bone core biopsy harvesting methods (crestal and lateral method) and the applied healing periods among the studies were not considered. A recently published frequentist NMA (Al-Moraissi et al., 2020) concluded that AB showed the best performance only when a healing time of less than 6 months was applied, while the majority of biomaterials yielded similar histomorphometric results after a longer healing period. The addition of AB or autologous cell concentrates to any biomaterial may increase the NB capacity. The major differences between these two NMAs are: (a) that Al-Moraissi et al. applied eleven subgroups and pooled together biomaterials into commonly used categories (alloplast, xenograft, etc), which were separately analyzed in the present NMA, and (b) that they included the results of such RCTs, in which lateral bone core biopsy harvesting methods were applied and were excluded in the present NMA.

The main reason for the different conclusions between systematic reviews could be the differences in the applied inclusion criteria, which yielded a different database for the quantitative synthesis. The present NMA was conducted based exclusively on the histomorphometric results of RCTs in which delayed implant placement and crestal bone core biopsy harvesting protocol was applied. By applying these inclusion criteria, our goal was to reduce potential confounding factors. The other reason for the different conclusions could be the formation of subgroups according to healing periods and biomaterials applied, which always reduces sensitivity and could mask the slight differences between the histomorphometric results. In the present NMA, 28 subgroups were created for the applied biomaterials to represent their heterogeneity, and 3 predefined healing periods were applied. This resulted in small sample sizes in some subgroups, which was one of the limitations of the findings, but may have ensured higher sensitivity in the analysis for discovering the differences between NB formation capacities of biomaterials.

With consideration of the limitations of the present NMA, several biomaterials showed the same potential for NB formation after MSA. The combination of biomaterials with AB or autologous cell concentrates could be a feasible alternative for AB substitution to achieve high NB formation levels with a healing time frame of 5–8 months. From this point of view, the statement that AB alone as grafting material is the gold standard is questionable for this healing period, although there are other aspects of graft choice.

The AB graft has osteoinductive, osteoconductive, and osteogenic capabilities, which make it an ideal choice for guided bone regeneration, especially when shorter healing times are applied. However, AB grafts may show significant differences in osteogenic capacity and

TABLE 4 In the league table comparisons between biomaterials were highlighted with green if the sample size of both comparators reached the optimal information size (OIS) ($n > 11$). The coloring was changed to yellow if at least one of the comparators did not reach the OIS ($n < 11$). The values in each cell represent the relative treatment effect (and 95% credible intervals) of the treatment on the top versus the treatment on the left. Statistical significance was marked by an asterisk. If direct comparisons between grafting materials were available from trials, then the results were marked by a dagger sign. Abbreviations: maxillary sinus augmentation (MSA), autologous bone (AB), allograft (Allo), bovine xenograft (Bovine), porcine xenograft (Porcine), biphasic calcium phosphate (BCP), beta-tricalcium-phosphate (ß-TCP), bioactive glass ceramic (Bioglass), nanocrystalline hydroxyapatite (nanoHA), rigid biodegradable (L-lactic, D-lactic and glycolic acid) copolymer membrane (Biodegradable copolymer), bovine xenograft + autologous bone 1:1 (Bovine + AB 1:1), bovine xenograft + autologous bone 1:1 composite graft followed by laser stimulation (Bovine + AB 1:1 + laser stimulation), bovine xenograft + autologous bone 4:1 (Bovine + AB 4:1), bovine xenograft + platelet-rich fibrin (Bovine + PRF), bovine xenograft + platelet-rich plasma (Bovine + PRP), bovine xenograft + bone marrow aspirates (Bovine + BMA), bovine xenograft + bone marrow concentrate (Bovine + BMC), bioactive glass ceramic + autologous bone 1:1 (Bioglass + AB 1:1), beta-tricalcium-phosphate + autologous bone 1:1 (ß-TCP + AB 1:1), beta-tricalcium-phosphate + platelet-rich plasma (ß-TCP + PRP), beta-tricalcium-phosphate + platelet-rich fibrin (ß-TCP + PRF), autologous bone + platelet-rich plasma (AB + PRP), autologous bone + autologous platelet concentrate (AB + APC), biphasic calcium phosphate + fibrin sealant (BCP + FS), poly(lactic-co-glycolic acid)-based polymer (PLGA)-coated biphasic calcium phosphate (BCP + PLGA), biphasic calcium phosphate + enamel matrix proteins (EMD) (BCP + EMD), nanocrystalline hydroxyapatite in silica gel + plasma rich in growth factors (HA + silica gel + PRGF)



(Continues)

TABLE 4 (Continued)

9.6 (-4.2, 25)	8.9 (-11, 29)	6.4 (-15, 29)	6.6 (-12, 24)†	6.7 (-19, 33)	5.8 (-19, 30)	5.5 (-29, 41)	4.2 (-24, 34)	3.1 (-17, 24)	3.2 (-18, 25)	2.2 (-13, 18)	1.5 (-15, 19)	0.7 (-34, 36)	**BCP** (n=121 MSA)																	
10 (-10, 33)	9.6 (-15, 35)	6.9 (-15, 29)	7 (-18, 33)	7.5 (-18, 33)	6.5 (-24, 38)	6.4 (-28, 42)	4.9 (-24, 35)	3.5 (-22, 29)	3.7 (-22, 30)	2.7 (-19, 26)	2.2 (-14, 19)	1.5 (-32, 37)	0.5 (-17, 20)	**ß-TCP + PRP** (n= 26 MSA)															
10 (-13, 34)	9.2 (-17, 36)	6.7 (-21, 36)	6.9 (-19, 32)	7 (-24, 38)	6.2 (-24, 36)	5.6 (-33, 46)	4.7 (-29, 39)	3.3 (-23, 30)	3.5 (-23, 31)	2.6 (-21, 27)	2 (-22, 27)	0.9 (-37, 41)	0.4 (-18, 18)†	0.2 (-25, 26)	**BCP + EMD** (n=10 MSA)														
9.9 (-25, 46)	9.3 (-29, 47)	6.6 (-19, 33)	6.9 (-32, 44)	7.1 (-24, 39)	6.3 (-36, 46)	6.1 (-20, 32)	4.7 (-12, 22)†	3.5 (-34, 41)	3.5 (-35, 42)	2.5 (-34, 39)	1.8 (-27, 31)	1.4 (-25, 27)	0.3 (-34, 33)	0.5 (-33, 34)	0 (-37, 38)	**BCP + FS** (n=29 MSA)												
10 (-0.4, 22)†	9.5 (-8, 27)†	6.9 (-15, 30)	7.1 (-14, 27)	7.6 (-18, 33)	6.3 (-21, 33)	6.2 (-28, 42)	4.9 (-24, 34)	3.7 (-14, 21)†	3.7 (-15, 22)†	2.8 (-9.6, 15)†	2.1 (-14, 19)	1.3 (-32, 37)†	0.6 (-9.2, 10)†	0.2 (-19, 18)	0.4 (-20, 20)	0.1 (-33, 34)	**Bovine** (n=174 MSA)											
12 (-7.9, 35)	12 (-13, 38)	9.1 (-19, 39)	9.5 (-18, 37)	9.5 (-21, 41)	8.8 (-24, 41)	8.5 (-31, 49)	7.3 (-27, 42)	5.8 (-19, 32)	5.9 (-20, 33)	5 (-17, 28)	4.2 (-20, 31)	3.6 (-34, 45)	2.7 (-18, 24)	2.3 (-24, 28)	2.5 (-25, 31)	2.5 (-36, 41)	2.4 (-16, 21)†	**Bovine + PRGF** (n=6 MSA)										
12 (-11, 37)	12 (-16, 39)	9 (-19, 39)	9.3 (-17, 35)	9.6 (-21, 42)	8.6 (-23, 40)	8.1 (-31, 49)	6.8 (-26, 43)	5.9 (-22, 33)	6 (-22, 35)	4.8 (-19, 30)	4.3 (-20, 30)	3.5 (-36, 43)	3 (-16, 21)†	2 (-24, 28)	2.5 (-24, 28)	2.5 (-35, 42)	2.3 (-19, 23)	0.2 (-29, 28)	**BCP + PLGA** (n=16 MSA)									
13 (-13, 41)	13 (-17, 42)	10 (-12, 33)	11 (-20, 40)	11 (-15, 36)	9.6 (-25, 44)	9.6 (-25, 44)	8.2 (-20, 37)	6.9 (-24, 36)	7.1 (-24, 37)	6 (-22, 33)	5.5 (-12, 22)†	4.7 (-30, 39)	4 (-21, 28)	3.1 (-21, 27)	3.9 (-27, 33)	3.5 (-32, 37)	3.3 (-21, 27)	1.4 (-30, 30)	1 (-30, 31)	**AB + APC** (n=12 MSA)								
14 (-7.2, 36)	13 (-12, 38)	10 (-19, 39)	10 (-17, 38)	11 (-20, 42)	10 (-23, 43)	9.7 (-30, 49)	8.4 (-26, 43)	7.3 (-19, 32)	7 (-19, 33)	6.1 (-15, 28)	5.7 (-19, 31)	4.9 (-35, 45)	4.1 (-17, 25)	3.7 (-23, 30)	3.7 (-24, 31)	4 (-35, 42)	3.5 (-15, 22)†	1.4 (-25, 26)	1.2 (-28, 30)	0.1 (-30, 31)	**nanoHA** (n=26 MSA)						
15 (-7.6, 40)	15 (-13, 42)	12 (-12, 37)	12 (-16, 41)	12 (-15, 41)	12 (-23, 45)	11 (-25, 49)	10 (-21, 42)	8.8 (-19, 36)	8.8 (-20, 38)	8 (-17, 33)	7.2 (-12, 28)	6.6 (-30, 43)	5.6 (-16, 27)	5 (-12, 22)†	5.3 (-22, 33)	5.4 (-29, 42)	5.1 (-16, 26)	2.8 (-25, 31)	2.7 (-26, 32)	1.8 (-24, 29)	1.5 (-26, 31)	**ß-TCP + PRF** (n =8 MSA)					
16 (-0.3, 34)	16 (-6.4, 37)	13 (-4.6, 32)	13 (-9.8, 35)	13 (-8.5, 35)	12 (-17, 41)	12 (-20, 45)	11 (-14, 37)	9.8 (-12, 31)	9.8 (-13, 32)	8.9 (-9.3, 27)	8.2 (-2.4, 19)†	7.5 (-25, 41)	6.7 (-7.3, 20)†	6.1 (-6.7, 18)†	6.3 (-16, 28)	6.3 (-24, 37)	6.1 (-7, 19)†	3.8 (-19, 26)	3.8 (-20, 27)	2.8 (-18, 24)	2.6 (-20, 25)	1 (-16, 18)†	**ß-TCP** (n=106 MSA)				
19 (-12, 48)	19 (-7.3, 47)	16 (-7.2, 40)	16 (-14, 46)	17 (-9.7, 44)	16 (-20, 51)	16 (-21, 51)	14 (-16, 45)	13 (-18, 42)	13 (-18, 43)	12 (-16, 39)	12 (-6.5, 29)†	11 (-25, 46)	9.8 (-16, 34)	9.4 (-16, 33)	9.4 (-22, 39)	9.6 (-24, 44)	9.4 (-16, 33)	7.1 (-25, 37)	7.1 (-24, 38)	6 (-19, 31)	5.8 (-26, 37)	4.5 (-25, 31)	3.4 (-18, 24)	**AB + PRP** (n= 5 MSA)			
22 (2.5, 44)*	21 (-2.6, 46)	19 (-8.3, 48)	19 (-8.2, 46)	19 (-11, 50)	18 (-13, 50)	18 (-21, 58)	17 (-16, 52)	16 (-9, 40)	16 (-9.3, 41)	15 (-6.4, 36)	14 (-9.1, 39)	13 (-25, 53)	13 (-7.6, 32)	12 (-13, 37)	12 (-15, 39)	12 (-25, 50)	12 (-5.3, 29)†	9.8 (-16, 35)	9.8 (-18, 37)	8.7 (-20, 39)	8.3 (-17, 34)	6.8 (-21, 34)	5.9 (-15, 28)	2.4 (-27, 33)	**Biodegradable copolymer** (n=10 MSA)		
24 (-1.9, 53)	24 (-6.8, 53)	21 (-2.9, 46)	21 (-9.2, 51)	21 (-6.3, 50)	20 (-14, 56)	21 (-17, 58)	19 (-12, 50)	18 (-13, 48)	18 (-12, 48)	17 (-11, 45)	16 (-3.4, 36)†	16 (-20, 52)	15 (-10, 40)	14 (-10, 38)	14 (-15, 44)	14 (-22, 49)	14 (-10, 38)	12 (-19, 42)	12 (-19, 43)	11 (-15, 37)	11 (-20, 41)	9 (-18, 36)	7.9 (-12, 28)†	4.7 (-22, 31)	2.2 (-28, 32)	**ß-TCP + AB 1:1** (n= 9 MSA)	
24 (3.2, 46)*	23 (-0.9, 48)	21 (-7.2, 50)	21 (-6.9, 48)	21 (-8.8, 53)	20 (-12, 52)	20 (-19, 61)	18 (-14, 54)	17 (-7.7, 43)	18 (-7.8, 43)	16 (-5.7, 39)	16 (-8.1, 41)	15 (-23, 55)	14 (-6.4, 34)	14 (-13, 39)	14 (-14, 41)	14 (-24, 53)	14 (-4.2, 32)†	12 (-15, 37)	11 (-16, 39)	11 (-19, 41)	10 (-15, 36)	8.7 (-20, 37)	7.6 (-15, 30)	4.4 (-26, 36)	2 (-23, 27)	0.3 (-31, 31)	**Allo** (n=12 MSA)

resorption rate depending on the donor areas (Klijn et al., 2010). If the goal is to create the same tissue structure as the original one, AB grafting still seems to be the best option, although its resorption rate could be higher than xenografts or alloplasts (Danesh-Sani et al., 2016; Gerressen et al., 2015). The major disadvantages of using AB are the limited availability and the donor-site morbidity.

In contrast, consistent quality, extensive availability, and lack of donor-site morbidity are the advantageous characteristics of allografts, xenografts, and alloplastic biomaterials. These biomaterials offer some other advantages such as implant survival rates or graft volume stability, although the limitations of this study did not allow us to investigate other outcomes. With the slow, and in some cases not complete resorption rate, a higher volume stability can be achieved (Gorla et al., 2015; Schlegel et al., 2016). Systematic reviews of longitudinal trials have reported higher survival rates of dental implants placed in an area previously augmented with a biomaterial (Al-Nawas & Schiegnitz, 2014; Del Fabbro et al., 2008).

4.1 | Limitations of the systematic review

A common limitation encountered while performing systematic reviews is the data pool, which is based on the study-level instead of the patient-level data. The following confounding factors of the analyzed trials may influence the histomorphometric results of MSA: (a) the histomorphometric similarities between newly formed bone and residual graft particles of the AB group, (b) the method used for lateral window osteotomy (surgical burs, piezo-electric tips, bone-scraper), (c) the use of the lateral bony wall during the intervention (removed, reflected, or replaced), (d) the use of a barrier membrane to cover the osteotomy window or to protect the Schneiderian membrane, and (e) the volume of the preoperative residual ridge and the shape of the maxillary sinus (Avila et al., 2010; Avila-Ortiz et al., 2012).

Randomized controlled trials and systematic reviews of RCTs generally provide high quality of evidence. According to the GRADE approach, rating down of the quality of evidence should be considered based on five criteria. These elements were used for the judgment of confidence derived from the results.

4.1.1 | Limitations in study design (risk of bias)

Among the included studies, 5 had a low risk of bias, 20 had an unclear risk of bias, and 9 showed a high risk of bias, as described previously (Appendix S3).

4.1.2 | Inconsistency of results

Node-splitting analysis was performed for examination of consistency. There was no statistical difference between the results of direct, indirect, or network (mixed) comparisons (beta-tricalcium-phosphate versus biphasic calcium phosphate: $p = .48$ bovine versus biphasic calcium phosphate: $p = .47$, bovine versus beta-tricalcium-phosphate: $p = .49$), and the network of the included trials showed a consistent model (Appendix S5).

4.1.3 | Indirectness of evidence

According to the network geometry, the results of our NMA are based on indirect comparisons between most of the applied grafting materials. More details are shown in the league table (Table 4). The population, the intervention (surgical technique, bone core biopsy harvesting), and the outcome measurements were the same in all included trials. Nevertheless, the patient selection criteria were slightly different in each study. The anatomical conditions of the surgical sites (residual ridge height, sinus widths) might have influenced the histomorphometric results. The incomplete information available on these potentially confounding factors in several studies poses the risk of intransitivity.

4.1.4 | Imprecision

The optimal information size (OIS) was determined as 11 MSA procedures per group, based on the sample size calculation by Nizam et al. (2018), with an effect size of 1.1, power of 80%, alpha = 0.05, and $\Delta = 5.5\%$. Twelve biomaterial subgroups did not reach the OIS. More details are shown in the league table (Table 4).

4.1.5 | Publication bias

Funnel plots were performed with Egger's test with no evidence for publication bias ($p = .138$) (Appendix S6).

For various comparisons, the reason for downgrading the evidence was the imprecision (the number of MSAs did not reach the OIS), the indirectness (lack of information regarding potentially confounding factors in several studies), and the study limitations (risk of bias). If for some subgroup, the OIS limit was not reached, the results of these interventions should be interpreted with great caution. The quality of evidence of this NMA ranged from low to very low for all comparisons.

4.2 | Strengths of systematic review

The strengths of this study are the potential for quantitative analysis to rank the best available biomaterials for MSA according to their capacity for NB formation. The results are based on a high number of RCTs due to a comprehensive literature search. This systematic review applied the methods of Bayesian NMA, which can handle direct and indirect evidence from RCTs simultaneously. The application of various augmentation techniques (simultaneous implant placement, additional grafting of the ridge), the differences in the sites of bone

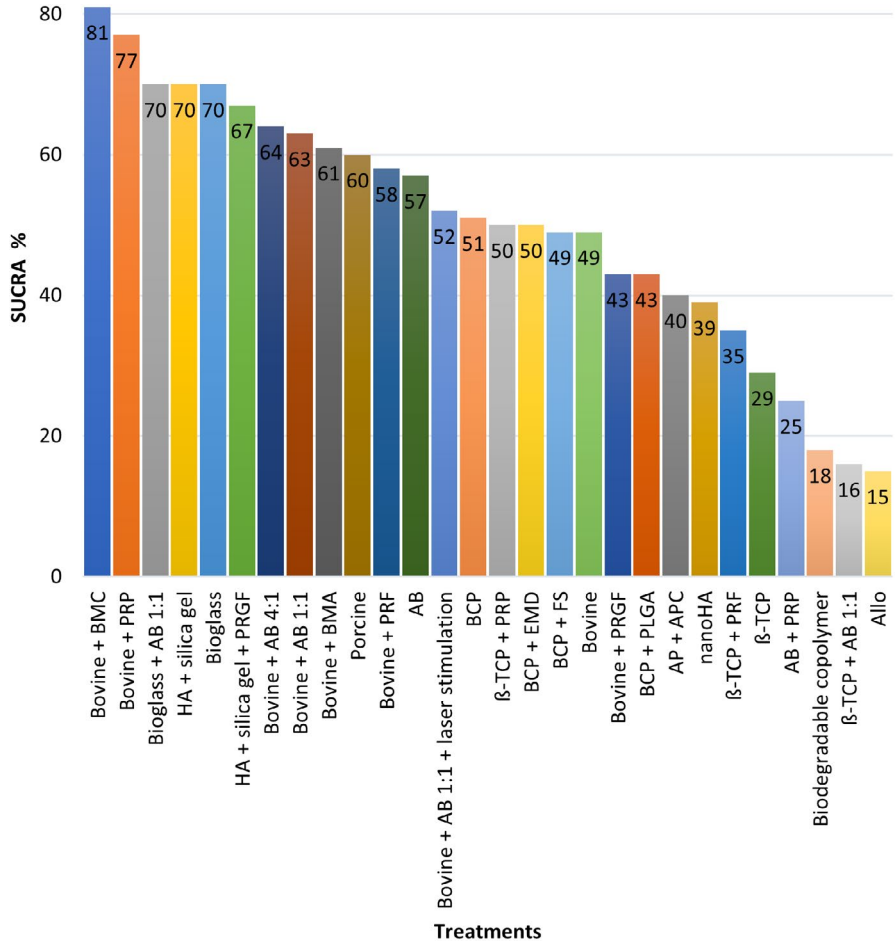


FIGURE 4 Surface under the cumulative ranking curves shows the ranking of interventions according to efficacy. The highest bar achieves the best rank. Abbreviations: autologous bone (AB), allograft (Allo), bovine xenograft (Bovine), porcine xenograft (Porcine), biphasic calcium phosphate (BCP), beta-tricalcium-phosphate (ß-TCP), bioactive glass ceramic (Bioglass), nanocrystalline hydroxyapatite (nanoHA), rigid biodegradable (L-lactic, D-lactic and glycolic acid)copolymer membrane (Biodegradable copolymer), bovine xenograft + autologous bone 1:1 (Bovine + AB 1:1), bovine xenograft + autologous bone 1:1 composite graft followed by laser stimulation (Bovine + AB 1:1 + laser stimulation), bovine xenograft + autologous bone 4:1 (Bovine + AB 4:1), bovine xenograft + platelet-rich fibrin (Bovine + PRF), bovine xenograft + platelet-rich plasma (Bovine + PRP), bovine xenograft + bone marrow aspirates (Bovine + BMA), bovine xenograft + bone marrow concentrate (Bovine + BMC), bioactive glass ceramic + autologous bone 1:1 (Bioglass + AB 1:1), beta-tricalcium-phosphate + autologous bone 1:1 (ß-TCP + AB 1:1), beta-tricalcium-phosphate + platelet-rich plasma (ß-TCP + PRP), beta-tricalcium-phosphate + platelet-rich fibrin (ß-TCP + PRF), autologous bone + platelet-rich plasma (AB + PRP), autologous bone + autologous platelet concentrate (AB + APC), biphasic calcium phosphate + fibrin sealant (BCP + FS), poly(lactic-co-glycolic acid)-based polymer (PLGA)-coated biphasic calcium phosphate (BCP + PLGA), biphasic calcium phosphate + enamel matrix proteins (EMD) (BCP + EMD), nanocrystalline hydroxyapatite in silica gel + plasma rich in growth factors (HA + silica gel + PRGF)

core biopsy sampling, and the variations in healing time among the MSA studies could be serious factors influencing the histomorphometric outcomes. To overcome these confounding factors, strict inclusion and exclusion criteria were applied. To solve the potential bias from the variations in time for graft healing among trials, predefined subgroup categories according to applied healing periods (early, normal, late) were used. Unlike the main biomaterial categories (xenograft, allograft, alloplast, etc.) used in other systematic reviews (Al-Moraissi et al., 2020; Danesh-Sani et al., 2017; Stumbras et al., 2019), pooling of biomaterials by their processing method and the formation of 28 separate groups may be a more sensitive approach to evaluate the histomorphometric performance.

5 | CONCLUSIONS

5.1 | Implications for practice

The results of the present NMA suggest that the use of biomaterials does not result in a statistically significant difference in the rate of NB formation compared to AB alone as grafting material. However, their use can significantly reduce the amount of AB graft required for MSA, resulting in a less invasive surgical intervention and shorter surgical time. The combination of biomaterials with AB or autologous cell concentrates, such as BMC, PRP, and platelet-rich fibrin, represents a feasible alternative for AB substitution to achieve high

NB formation levels with the conventionally used 5- to 8-month healing periods. If one of the attributes of superior bone quality is the higher proportion of newly formed bone, the superiority of AB transplantation to biomaterials for MSA in a healing time frame of 5–8 months cannot be justified. For shorter healing periods, faster remodeling ability of AB may be advantageous.

5.2 | Implications for research

Randomized clinical trials designed with OIS and a unified surgical protocol for bone core biopsy harvesting may be needed for verification of indirect evidence. As for the healing period of less than 5 months, the low number of available studies made it impossible to pool a network analysis, which could be a potential area of future research.

ACKNOWLEDGEMENTS

This study was supported by a Human Resources Development Operational Programme Grant (Grant Number: EFOP-3.6.2-16-2017-0006 – LIVE LONGER) and an Economic Development and Innovation Operative Program Grant (Grant number: GINOP-2.3.2-15-2016-00048 - STAY ALIVE). Both grants are co-financed by the European Union (European Regional Development Fund) within the framework of Programme Széchenyi 2020. The funders had no role in study design, data collection and analysis, preparation of the manuscript, or decision to publish.

CONFLICT OF INTERESTS

The authors have declared that no conflict of interests exist.

AUTHOR CONTRIBUTION

Bálint Trimmel: Investigation (equal); Methodology (supporting); Project administration (lead); Writing-original draft (equal). **Noémi Gede:** Data curation (equal); Formal analysis (lead); Validation (equal). **Péter Hegyi:** Investigation (lead); Methodology (equal); Supervision (lead); Writing-review & editing (equal). **Zsolt Szakács:** Formal analysis (equal); Methodology (lead); Supervision (supporting); Writing-review & editing (equal). **Gyöngyi Anna Mezey:** Data curation (equal); Formal analysis (supporting); Visualization (equal). **Eszter Varga:** Data curation (equal); Formal analysis (equal).

ORCID

Bálint Trimmel https://orcid.org/0000-0003-2308-2312
Péter Hegyi https://orcid.org/0000-0003-0399-7259
Zsolt Szakács https://orcid.org/0000-0002-7035-941X
Márton Kivovics https://orcid.org/0000-0003-0728-7027
Lilla Hanák https://orcid.org/0000-0003-4830-5658
György Szabó https://orcid.org/0000-0002-5828-6078

REFERENCES

Al-Moraissi, E. A., Alkhutari, A. S., Abotaleb, B., Altairi, N. H., & Del Fabbro, M. (2020). Do osteoconductive bone substitutes result in similar bone regeneration for maxillary sinus augmentation when compared to osteogenic and osteoinductive bone grafts? A systematic review and frequentist network meta-analysis. *International Journal of Oral & Maxillofacial Surgery*, *49*, 107–120. https://doi.org/10.1016/j.ijom.2019.05.004

Al-Nawas, B., & Schiegnitz, E. (2014). Augmentation procedures using bone substitute materials or autogenous bone - a systematic review and meta-analysis. *European Journal of Oral Implantology*, *7*, S219–S234.

Antonoglou, G. N., Stavropoulos, A., Samara, M. D., Ioannidis, A., Benic, G. I., Papageorgiou, S. N., & Sándor, G. K. (2018). Clinical performance of dental implants following sinus floor augmentation: A systematic review and meta-analysis of clinical trials with at least 3 years of follow-up. *The International Journal of Oral & Maxillofacial Implants*, *33*, e45–e65. https://doi.org/10.11607/jomi.6417

Avila, G., Wang, H. L., Galindo-Moreno, P., Misch, C. E., Bagramian, R. A., Rudek, I., Benavides, E., Moreno-Riestra, I., Braun, T., & Neiva, R. (2010). The influence of the bucco-palatal distance on sinus augmentation outcomes. *Journal of Periodontology*, *81*, 1041–1050. https://doi.org/10.1902/jop.2010.090686

Avila-Ortiz, G., Neiva, R., Galindo-Moreno, P., Rudek, I., Benavides, E., & Wang, H. L. (2012). Analysis of the influence of residual alveolar bone height on sinus augmentation outcomes. *Clinical Oral Implants Research*, *23*, 1082–1088. https://doi.org/10.1111/j.1600-0501.2011.02270.x

Batas, L., Tsalikis, L., & Stavropoulos, A. (2019). PRGF as adjunct to DBB in maxillary sinus floor augmentation: Histological results of a pilot split-mouth study. *International Journal of Implant Dentistry*, *5*, 14. https://doi.org/10.1186/s40729-019-0166-6

Bettega, G., Brun, J.-P., Boutonnat, J., Cracowski, J.-L., Quesada, J.-L., Hegelhofer, H., Drillat, P., & Richard, M. J. (2009). Autologous platelet concentrates for bone graft enhancement in sinus lift procedure. *Transfusion*, *49*, 779–785. https://doi.org/10.1111/j.1537-2995.2008.02036.x

Boyne, P. J., & James, R. A. (1980). Grafting of the maxillary sinus floor with autogenous marrow and bone. *Journal of Oral Surgery*, *38*, 613–616.

Chaimani, A., Caldwell, D. M., Li, T., Higgins, J. P. T., & Salanti, G. (2019). Chapter 11: Undertaking network meta-analyses. In: J. P. T. Higgins, J. Thomas, J. Chandler, M. Cumpston, T. Li, M. Page, & V. A. Welch (Eds.), *Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019)*. : Cochrane. Available from http://www.training.cochrane.org/handbook

Chanavaz, M., Donazzan, M., Ferri, J., Tatum, H., Francke, J. P., & Fenart, R. (1995). Sinusaugmentation statistical evaluation of 15 years of surgical experience (Manuel Chanavaz, 1979–1994)] [Article in French]. *Revue De Stomatologie Et De Chirurgie Maxillo-Faciale*, *96*, 267–273.

Corbella, S., Taschieri, S., Weinstein, R., & Del Fabbro, M. (2016). Histomorphometric outcomes after lateral sinus floor elevation procedure: A systematic review of the literature and meta-analysis. *Clinical Oral Implants Research*, *27*, 1106–1122. https://doi.org/10.1111/clr.12702

Cordaro, L., Bosshardt, D. D., Palattella, P., Rao, W., Serino, G., & Chiapasco, M. (2008). Maxillary sinus grafting with bio-oss® or straumann® bone ceramic: Histomorphometric results from a randomized controlled multicenter clinical trial. *Clinical Oral Implants Research*, *19*, 796–803. https://doi.org/10.1111/j.1600-0501.2008.01565.x

Danesh-Sani, S. A., Engebretson, S. P., & Janal, M. N. (2017). Histomorphometric results of different grafting materials and effect of healing time on bone maturation after sinus floor augmentation: A systematic review and meta-analysis. *Journal of Periodontal Research*, *52*, 301–312. https://doi.org/10.1111/jre.12402

Danesh-Sani, S. A., Loomer, P. M., & Wallace, S. S. (2016). A comprehensive clinical review of maxillary sinus floor elevation: Anatomy, techniques, biomaterials and complications. *British Journal of Oral and Maxillofacial Surgery*, *54*, 724–730. https://doi.org/10.1016/j.bjoms.2016.05.008

de Oliveira, T. A., Aloise, A. C., Orosz, J. E., Oliveira, R. D. M. E., de Carvalho, P., & Pelegrine, A. A. (2016). Double centrifugation versus single centrifugation of bone marrow aspirate concentrate in sinus floor elevation: A pilot study. *International Journal of Oral & Maxillofacial Implants*, *31*, 216–222. https://doi.org/10.11607/jomi.4170

Del Fabbro, M., Rosano, G., & Taschieri, S. (2008). Implant survival rates after maxillary sinus augmentation. *European Journal of Oral Sciences*, *116*, 497–506. https://doi.org/10.1111/j.1600-0722.2008.00571.x

Dias, S., & Caldwell, D. M. (2019). Network meta-analysis explained. *Archives of Disease in Childhood - Fetal and Neonatal Edition*, *104*, F8–F12. https://doi.org/10.1136/archdischild-2018-315224

Felice, P., Scarano, A., Pistilli, R., Checchi, L., Piattelli, M., Pellegrino, G., & Esposito, M. (2009). A comparison of two techniques to augment maxillary sinuses using the lateral window approach: Rigid synthetic resorbable barriers versus anorganic bovine bone. Five-month post-loading clinical and histological results of a pilot randomised controlled clinical trial. *European Journal of Oral Implantology*, *2*, 293–306.

Flichy-Fernández, A. J., Blaya-Tárraga, J. A., O'Valle, F., Padial-Molina, M., Peñarrocha-Diago, M., & Galindo-Moreno, P. (2019). Sinus floor elevation using particulate PLGA-coated biphasic calcium phosphate bone graft substitutes: A prospective histological and radiological study. *Clinical Implant Dentistry and Related Research*, *21*, 895–902. https://doi.org/10.1111/cid.12741

Galindo-Moreno, P., Ávila, G., Fernández-Barbero, J. E., Mesa, F., O'Valle-Ravassa, F., & Wang, H.-L. (2008). Clinical and histologic comparison of two different composite grafts for sinus augmentation: A pilot clinical trial. *Clinical Oral Implants Research*, *19*, 755–759. https://doi.org/10.1111/j.1600-0501.2008.01536.x

Galindo-Moreno, P., Moreno-Riestra, I., Avila, G., Padial-Molina, M., Paya, J. A., Wang, H.-L., & O'Valle, F. (2011). Effect of anorganic bovine bone to autogenous cortical bone ratio upon bone remodeling patterns following maxillary sinus augmentation. *Clinical Oral Implants Research*, *22*, 857–864. https://doi.org/10.1111/j.1600-0501.2010.02073.x

Gerressen, M., Riediger, D., Hilgers, R.-D., Hölzle, F., Noroozi, N., & Ghassemi, A. (2015). The volume behavior of autogenous iliac bone grafts after sinus floor elevation: A clinical pilot study. *The Journal of Oral Implantology*, *41*, 276–283. https://doi.org/10.1563/AAID-JOI-D-13-00246

Gorla, L. F. D. O., Spin-Neto, R., Boos, F. B. D. J., Pereira, R. D. S., Garcia-Junior, I. R., & Hochuli-Vieira, E. (2015). Use of autogenous bone and beta-tricalcium phosphate in maxillary sinus lifting: A prospective, randomized, volumetric computed tomography study. *International Journal of Oral and Maxillofacial Surgery*, *44*, 1486–1491. https://doi.org/10.1016/j.ijom.2015.07.003

Jelusic, D., Zirk, M. L., Fienitz, T., Plancak, D., Puhar, I., & Rothamel, D. (2017). Monophasic ß-TCP vs. biphasic HA/ß-TCP in two-stage sinus floor augmentation procedures - a prospective randomized clinical trial. *Clinical Oral Implants Research*, *28*, e175–e183. https://doi.org/10.1111/clr.12983

Khairy, N. M., Shendy, E. E., Askar, N. A., & El-Rouby, D. H. (2013). Effect of platelet rich plasma on bone regeneration in maxillary sinus augmentation (randomized clinical trial). *International Journal of Oral and Maxillofacial Surgery*, *42*, 249–255. https://doi.org/10.1016/j.ijom.2012.09.009

Kılıç, S. C., Güngörmüş, M., & Parlak, S. N. (2017). Histologic and histomorphometric assessment of sinus-floor augmentation with beta-tricalcium phosphate alone or in combination with pure-platelet-rich plasma or platelet-rich fibrin: A randomized clinical trial. *Clinical Implant Dentistry and Related Research*, *19*, 959–967. https://doi.org/10.1111/cid.12522

Klijn, R. J., Meijer, G. J., Bronkhorst, E. M., & Jansen, A. J. (2010). Sinus floor augmentation surgery using autologous bone grafts from various donor sites: A meta-analysis of the total bone volume. *Tissue Engineering Part B: Reviews*, *16*, 295–303. https://doi.org/10.1089/ten.TEB.2009.0558

Kurkcu, M., Benlidayi, M. E., Cam, B., & Sertdemir, Y. (2012). Anorganic bovine-derived hydroxyapatite vs β-tricalcium phosphate in sinus augmentation: A comparative histomorphometric study. *Journal of Oral Implantology*, *38*, 519–526. https://doi.org/10.1563/AAID-JOI-D-11-00061

Lee, J. S., Shin, H. K., Yun, J. H., & Cho, K. S. (2017). Randomized clinical trial of maxillary sinus grafting using deproteinized porcine and bovine bone mineral. *Clinical Implant Dentistry and Related Research*, *19*, 140–150. https://doi.org/10.1111/cid.12430

Lindgren, C., Sennerby, L., Mordenfield, A., & Hallman, M. (2009). Clinical histology of microimplants placed in two different biomaterials. *International Journal of Oral & Maxillofacial Implants*, *24*, 1093–1100.

Lutz, R. (2018). Material selection for sinus membrane elevation. *Implantologie*, *26*, 19–24.

Márton, K., Tamás, S., Orsolya, N., Béla, C., Ferenc, D., Péter, N., Csaba, D.-N., Lajos, C., Zsombor, L., Eitan, M., & György, S. (2018). Microarchitecture of the augmented bone following sinus elevation with an albumin impregnated demineralized freeze-dried bone allograft (bonealbumin) versus anorganic bovine bone mineral: a randomized prospective clinical, histomorphometric, and micro-computed tomography study. *Materials*, *11*, 202. https://doi.org/10.3390/ma11020202

Meimandi, M., Moghaddam, A. A., Gholami, A. G., Abbass, F. M., & Solati, M. (2017). Histomorphometric and histologic evaluation of nano-HA with and without PRGF in bilateral sinus lift augmentation: A randomized clinical trial. *Journal of Research in Medical and Dental Science*, *5*, 69–81.

Menezes, J. D., Pereira, R. D. S., Bonardi, J. P., Griza, L. G., Okamoto, R., & Hochuli-Vieira, E. (2018). Bioactive glass added to autogenous bone graft in maxillary sinus augmentation: A prospective histomorphometric, immunohistochemical, and bone graft resorption assessment. *Journal of Applied Oral Science*, *26*, e20170296. https://doi.org/10.1590/1678-7757-2017-0296

Meymandi, M., Solati, M., Ardakani, M. T., Abbas, F. M., & Moghaddam, A. A. (2017). Histologic and histomorphometric evaluation of maxillary sinus floor elevation using nanobone (R) and easy-graft (TM) crystal: A split-mouth clinical trial. *Journal of Research in Medical and Dental Science*, *5*, 35–43.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G.The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Medicine*, *6*(7), e1000097. https://doi.org/10.1371/journal.pmed1000097

Moy, P. K., Lundgren, S., & Holmes, R. E. (1993). Maxillary sinus augmentation: Histomorphometric analysis of graft materials for maxillary sinus floor augmentation. *Journal of Oral and Maxillofacial Surgery*, *51*, 857–862. https://doi.org/10.1016/S0278-2391(10)80103-X

Nery, J. C., Pereira, L. A. V. D., Guimaraes, G. F., Scardueli, C. R., França, F. M. G., Spin-Neto, R., & Stavropoulos, A. (2017). β-TCP/HA with or without enamel matrix proteins for maxillary sinus floor augmentation: A histomorphometric analysis of human biopsies. *International Journal of Implant Dentistry*, *3*, 18. https://doi.org/10.1186/s40729-017-0080-8

Nizam, N., Eren, G., Akcalı, A., & Donos, N. (2018). Maxillary sinus augmentation with leukocyte and platelet-rich fibrin and deproteinized bovine bone mineral: A split-mouth histological and histomorphometric study. *Clinical Oral Implants Research*, *29*, 67–75. https://doi.org/10.1111/clr.13044

Oh, J. S., Seo, Y. S., Lee, G. J., You, J. S., & Kim, S. G. (2019). A Comparative study with biphasic calcium phosphate to deproteinized bovine bone in maxillary sinus augmentation: A prospective randomized and controlled clinical trial. *The International Journal of Oral & Maxillofacial Implants*, *34*, 233–242. https://doi.org/10.11607/jomi.711

Pasquali, P. J., Teixeira, M. L., de Oliveira, T. A., de Macedo, L. G. S., Aloise, A. C., & Pelegrine, A. A. (2015). Maxillary sinus augmentation combining bio-oss with the bone marrow aspirate concentrate: A histomorphometric study in humans. *International Journal of Biomaterials*, *2015*, 1–7, https://doi.org/10.1155/2015/121286

Payer, M., Lohberger, B., Strunk, D., Reich, K. M., Acham, S., & Jakse, N. (2014). Effects of directly autotransplanted tibial bone marrow aspirates on bone regeneration and osseointegration of dental implants. *Clinical Oral Implants Research*, *25*, 468–474. https://doi.org/10.1111/clr.12172

Pereira, R. S., Gorla, L. F., Boos, F. B. J. D., Okamoto, R., Garcia Júnior, I. R., & Hochuli-Vieira, E. (2017). Use of autogenous bone and beta-tricalcium phosphate in maxillary sinus lifting: Histomorphometric study and immunohistochemical assessment of RUNX2 and VEGF. *International Journal of Oral and Maxillofacial Surgery*, *46*, 503–510. https://doi.org/10.1016/j.ijom.2017.01.002

Pereira, R. D. S., Menezes, J. D., Bonardi, J. P., Griza, G. L., Okamoto, R., & Hochuli-Vieira, E. (2017). Histomorphometric and immunohistochemical assessment of RUNX2 and VEGF of Biogran™ and autogenous bone graft in human maxillary sinus bone augmentation: A prospective and randomized study. *Clinical Implant Dentistry and Related Research*, *19*, 867–875. https://doi.org/10.1111/cid.12507

Pjetursson, B. E., Tan, W. C., Zwahlen, M., & Lang, N. P. (2008). A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation. *Journal of Clinical Periodontology*, *35*(8 Suppl), 216–240. https://doi.org/10.1111/j.1600-051X.2008.01272.x

Price, A., Van Dyke, T., & Karatzas, S. (1998). Histomorphometric analysis of bone cores from human sinus lift grafts. *Journal of Dental Research*, *77*, 839.

Raghoebar, G. M., Onclin, P., Boven, G. C., Vissink, A., & Meijer, H. J. A. (2019). Long-term effectiveness of maxillary sinus floor augmentation: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, *46*(Suppl 21), 307–318. https://doi.org/10.1111/jcpe.13055

Salanti, G., Ades, A. E., & Ioannidis, J. P. A. (2011). Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: An overview and tutorial. *Journal of Clinical Epidemiology*, *64*, 163–171. https://doi.org/10.1016/j.jclinepi.2010.03.016

Schlegel, K. A., Wiltfang, J., Lutz, R., Schmitt, C. M., & Moest, T. (2016). Hard tissue augmentation —material selection. *Implantologie*, *24*, 7–15.

Spiegelhalter, D. J., Abrams, K. R., & Myles, J. P. (2004). Bayesian approaches to clinical trials and health-care evaluation. *John Wiley & Sons*, *Ltd.*, https://doi.org/10.1002/0470092602

Stacchi, C., Lombardi, T., Oreglia, F., Maltoni, A. A., & Traini, T. (2017). Histologic and histomorphometric comparison between sintered nanohydroxyapatite and anorganic bovine xenograft in maxillary sinus grafting: A split-mouth randomized controlled clinical trial. *BioMed Research International*, *2017*, 1–10. https://doi.org/10.1155/2017/9489825

Starch-Jensen, T., Mordenfeld, A., Becktor, J. P., & Jensen, S. S. (2018). Maxillary sinus floor augmentation with synthetic bone substitutes compared with other grafting materials: A systematic review and meta-analysis. *Implant Dentistry*, *27*, 363–374. https://doi.org/10.1097/ID.0000000000000768

Stumbras, A., Krukis, M. M., Januzis, G., & Juodzbalys, G. (2019). Regenerative bone potential after sinus floor elevation using various bone graft materials: A systematic review. *Quintessence International*, *50*, 548–558. https://doi.org/10.3290/j.qi.a42482

Szabó, G., Huys, L., Coulthard, P., Maiorana, C., Garagiola, U., Barabás, J., Németh, Z., Hrabák, K., & Suba, Z. (2005). A prospective multicenter randomized clinical trial of autogenous bone versus beta-tricalcium phosphate graft alone for bilateral sinus elevation: Histologic and histomorphometric evaluation. *International Journal of Oral & Maxillofacial Implants*, *20*, 371–381. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-00513355/full

Tatum, O. H. Jr, Lebowitz, M. S., Tatum, C. A., & Borgner, R. A. (1993). Sinus augmentation. Rationale, development, long-term results. *The New York State Dental Journal*, *59*, 43–48.

Theodoro, L. H., Rocha, G. S., Ribeiro Junior, V. L., Sakakura, C. E., de Mello Neto, J. M., Garcia, V. G., Ervolino, E., & Marcantonio Junior, E. (2018). Bone formed after maxillary sinus floor augmentation by bone autografting with hydroxyapatite and low-level laser therapy: A randomized controlled trial with histomorphometrical and immunohistochemical analyses. *Implant Dentistry*, *27*, 547–554. https://doi.org/10.1097/id.0000000000000801

Ting, M., Rice, J. G., Braid, S. M., Lee, C. Y. S., & Suzuki, J. B. (2017). Maxillary sinus augmentation for dental implant rehabilitation of the edentulous ridge: A comprehensive overview of systematic reviews. *Implant Dentistry*, *26*, 438–464. https://doi.org/10.1097/ID.0000000000000606

Torres, J., Tamimi, F., Martinez, P.-P., Alkhraisat, M. H., Linares, R., Hernández, G., Torres-Macho, J., & López-Cabarcos, E. (2009). Effect of platelet-rich plasma on sinus lifting: A randomized-controlled clinical trial. *Journal of Clinical Periodontology*, *36*, 677–687. https://doi.org/10.1111/j.1600-051X.2009.01437.x

Wagner, W., Wiltfang, J., Pistner, H., Yildirim, M., Ploder, B., Chapman, M., Schiestl, N., & Hantak, E. (2012). Bone formation with a biphasic calcium phosphate combined with fibrin sealant in maxillary sinus floor elevation for delayed dental implant. *Clinical Oral Implants Research*, *23*, 1112–1117. https://doi.org/10.1111/j.1600-0501.2011.02275.x

Wildburger, A., Payer, M., Jakse, N., Strunk, D., Etchard-Liechtenstein, N., & Sauerbier, S. (2014). Impact of autogenous concentrated bone marrow aspirate on bone regeneration after sinus floor augmentation with a bovine bone substitute–a split-mouth pilot study. *Clinical Oral Implants Research*, *25*, 1175–1181. https://doi.org/10.1111/clr.12228

Wiltfang, J., Schlegel, K. A., Schultze-Mosgau, S., Nkenke, E., Zimmermann, R., & Kessler, P. (2003). Sinus floor augmentation with β-tricalciumphosphate (β-TCP): Does platelet-rich plasma promote its osseous integration and degradation? *Clinical Oral Implants Research*, *14*, 213–218. https://doi.org/10.1034/j.1600-0501.2003.140212.x

Zerbo, I. R., Zijderveld, S. A., de Boer, A., Bronckers, A. L. J. J., de Lange, G., ten Bruggenkate, C. M., & Burger, E. H. (2004). Histomorphometry of human sinus floor augmentation using a porous beta-tricalcium phosphate: A prospective study. *Clinical Oral Implants Research*, *15*, 724–732. https://doi.org/10.1111/j.1600-0501.2004.01055.x

Zhang, Y., Tangl, S., Huber, C. D., Lin, Y., Qiu, L., & Rausch-Fan, X. (2012). Effects of Choukroun's platelet-rich fibrin on bone regeneration in combination with deproteinized bovine bone mineral in maxillary sinus augmentation: A histological and histomorphometric study. *Journal of Cranio-Maxillofacial Surgery*, *40*, 321–328. https://doi.org/10.1016/j.jcms.2011.04.020

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Trimmel B, Gede N, Hegyi P, et al. Relative performance of various biomaterials used for maxillary sinus augmentation: A Bayesian network meta-analysis. *Clin Oral Impl Res*. 2021;32:135–153. https://doi.org/10.1111/clr.13690