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Scaffold-Based Biomaterials for Periodontal Regeneration in Periodontitis: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 April 2026 and was last updated on 16 April 2026.

INTRODUCTION

Review question / Objective In adults with periodontitis presenting tooth-supported intrabony or furcation defects, do scaffold-based biomaterials used during regenerative periodontal surgery, with or without biologic enrichment, improve probing depth reduction, clinical attachment level gain, and radiographic/3D defect fill compared with conventional regenerative or surgical therapy?

Rationale Periodontitis causes progressive loss of cementum, periodontal ligament, and alveolar bone, and advanced disease frequently leaves residual pockets after non-surgical therapy. Conventional regenerative approaches such as guided tissue regeneration, grafting, and enamel matrix derivative can improve outcomes, but results are variable and highly dependent on defect morphology, technique, and patient factors. Scaffold-based biomaterials are intended to provide a three-dimensional matrix that supports cell adhesion, migration, proliferation, and differentiation while preserving space and guiding wound healing. Although the field now includes natural, synthetic, composite, and biologically enriched scaffolds, the clinical evidence remains heterogeneous. Existing reviews have largely focused on isolated regenerative modalities or have mixed periodontal and peri-implant indications. A focused systematic review and meta-analysis of scaffold-based biomaterials in tooth-supported periodontal intrabony and furcation defects is therefore justified.

Condition being studied Adults with periodontitis presenting intrabony (1–3 wall or combined) and/or furcation defects in the tooth-supported periodontium requiring regenerative periodontal surgery. The review evaluates periodontal tissue-engineering approaches based on scaffold-type biomaterials intended to support regeneration of alveolar bone, periodontal ligament, and cementum.

METHODS

Participant or population Adults diagnosed with chronic, aggressive, or stage II–IV periodontitis presenting tooth-supported intrabony or furcation defects treated with regenerative surgery. Studies must report defect-level or site-level outcomes when available. Studies involving mixed populations will be included only if the eligible periodontal-defect data can be extracted separately. Peri-implant sites and patients with systemic conditions likely to materially impair regeneration will be excluded.

Intervention Scaffold-based interventions (natural, synthetic, or composite scaffolds) used in periodontal regenerative surgery, with or without biologic enrichment (e.g., PRF/PRP, rhBMP-2, EMD, other growth factors or biologics).

Comparator Conventional regenerative or surgical controls, including open flap debridement, standard bone grafts or membranes, or scaling and root planing, without emerging scaffold technology.

Study designs to be included Randomized controlled clinical trials, including parallel-group and split-mouth designs, comparing eligible scaffold-based interventions with conventional regenerative or surgical controls.

Eligibility criteria Inclusion criteria: original full-text randomized controlled trials in English published between January 2020 and 1 March 2026; adults with tooth-supported intrabony or furcation periodontal defects; scaffold-based biomaterials used as part of regenerative periodontal therapy; and reporting at least one primary outcome (PD reduction, CAL gain, or radiographic/3D defect fill) at 6, 12, or 24 months where available. Studies will also be eligible when the intervention is not explicitly labeled a "scaffold" but functions as a scaffold-type biomaterial within the predefined PICO framework.

Exclusion criteria: non-original articles, conference abstracts without full data, in vitro, in silico, ex vivo, or animal studies, peri-implant studies, studies without relevant periodontal regenerative outcomes, studies without a scaffold-based biomaterial intervention, and studies where eligible data cannot be extracted separately.

Information sources MEDLINE (Ovid), Embase, CENTRAL, and Web of Science will be searched electronically. Record management, screening, and extraction support will be performed in Rayyan. When necessary, study authors will be contacted by email to clarify scaffold composition, biologic enrichment, or outcome reporting. Ongoing or unpublished trials identified during screening will be documented but not included in quantitative synthesis unless sufficient results are available.

Main outcome(s) Primary outcomes will be: (1) probing depth (PD) reduction in millimeters; (2) clinical attachment level (CAL) gain in millimeters; and (3) radiographic/3D defect fill in millimeters. Outcomes will be extracted at 6, 12, and 24 months when available. Continuous data will be synthesized using mean difference (MD) with 95% confidence intervals.

Additional outcome(s) Additional outcomes will include histologic evidence of periodontal regeneration, where reported, and subgroup effects according to scaffold type (natural, synthetic, composite), biologic enrichment (PRF/PRP versus no PRF/PRP), and follow-up duration. Other descriptive data will include defect morphology, surgical technique, and funding source.

Data management All records will be imported into Rayyan, where duplicates will be identified and removed. Two reviewers will independently screen titles/abstracts and then full texts against prespecified eligibility criteria. Data will be extracted in a standardized electronic form covering participant characteristics, defect type and morphology, intervention and control details, scaffold composition, biologic enrichment, follow-up duration, outcome data, and funding source. Disagreements will be resolved by discussion and consensus; if unresolved, a third reviewer will adjudicate. RevMan v5.4 will be used for meta-analysis.

Quality assessment / Risk of bias analysis Risk of bias in included randomized controlled trials will be assessed independently by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool. The five standard domains will be evaluated: bias arising from the randomization process; bias due to deviations from intended interventions; bias due to missing outcome data; bias in measurement of the outcome; and bias in selection of the reported result. Overall judgments will follow the RoB 2 algorithm. Certainty of evidence for each outcome/time point will be appraised using GRADE.

Strategy of data synthesis Quantitative synthesis will be conducted when at least two clinically comparable studies report the same outcome at similar follow-up intervals. Random-effects meta-

analysis will be used because clinical and methodological heterogeneity is expected. Continuous outcomes will be pooled as mean differences with 95% confidence intervals. Studies will be grouped by outcome and time point (6, 12, and 24 months). Site-level or defect-level data will be prioritized over tooth-level data. If outcome data are reported as medians with interquartile ranges and cannot be converted reliably, findings will be summarized narratively. Statistical heterogeneity will be assessed using the I^2 statistic and Cochran's Q test; I^2 values of 0–25%, 25–50%, and >50% will be considered low, moderate, and high heterogeneity, respectively.

Subgroup analysis Where sufficient studies are available, subgroup analyses will be performed according to scaffold type (natural, synthetic, composite) and biologic enrichment (PRF/PRP versus no PRF/PRP).

Sensitivity analysis Sensitivity analyses will exclude studies at high risk of bias or with methodological uncertainty in allocation concealment or outcome assessment. Additional analyses will use leave-one-out study removal and, where possible, restriction to studies with consistent outcome definitions and measurement methods to assess the robustness of pooled estimates and sources of heterogeneity.

Language restriction English-language studies only.

Country(ies) involved Romania.

Keywords Periodontal regeneration, Scaffold-based therapy, Tissue engineering, Probing depth reduction, Biomaterials.

Contributions of each author

Author 1 - Felicia Gabriela Beresescu - Author 1 conceived the review question, designed the protocol, screened studies, extracted data, performed analysis, and drafted the manuscript.
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