INPLASY

Overview of systematic reviews comparing enamel matrix derivative (EMD) alone VS EMD plus bone graft in the treatment of infrabony periodontal defects

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Risk of bias assessment.

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 31 December 2025 and was last updated on 31 December 2025.

INTRODUCTION

Review question / Objective Primary objective "To assess and compare, based on systematic reviews published between 2009 and 2025, the clinical effectiveness of enamel matrix derivatives (EMD) used alone versus in combination with bone grafting in the treatment of periodontal intrabony defects."
Secondary objectives
To quantify, when data are available, the mean differences between the two therapeutic approaches in terms of:
Clinical attachment level gain (CAL, mm),
Probing depth reduction (PD, mm),
Bone fill (mm or %), assessed radiographically.
To assess the methodological quality of the included systematic reviews using the AMSTAR 2 tool and to determine the certainty of the body of evidence.

To analyze potential sources of heterogeneity.

To identify the methodological limitations of existing systematic reviews and to formulate recommendations for future clinical trials in periodontal regeneration.

Rationale "Periodontal regeneration aims to restore the structures destroyed by periodontitis, including the alveolar bone, periodontal ligament, and cementum. Since the late 1990s, enamel matrix derivatives (EMD) have been widely used as bioactive agents capable of promoting the formation of new cementum and Sharpey's fibers, thereby resulting in a measurable gain in clinical attachment.

In the context of deep intrabony defects, EMD may be combined with bone grafts (autogenous, allogeneic, xenogeneic, or alloplastic) with the objectives of:
(1) stabilizing the blood clot,
(2) maintaining the volume of the osseous defect, and

(3) providing an osteoconductive scaffold capable of supporting periodontal regeneration.

However, systematic reviews published between 2009 and 2025 have reported heterogeneous findings regarding the actual benefit of this combined therapeutic approach. While some reviews report a modest but statistically significant clinical gain (often >0.5 mm in clinical attachment level) in favor of adding a bone graft, others consider this advantage to be marginal or clinically irrelevant. This variability may be attributed to several factors, including:
(i) the configuration of the intrabony defect (number of residual bony walls),
(ii) the type of bone graft used,
(iii) differences in surgical protocols, and
(iv) the methodological quality of the systematic reviews themselves, which is sometimes inconsistent.

Despite the accumulation of primary studies and evidence syntheses over more than fifteen years, no umbrella review has, to date, assessed the overall robustness of this body of evidence or systematically compared the quality and consistency of conclusions drawn from the available systematic reviews.

Therefore, conducting an umbrella review is essential in order to:
• provide a hierarchical and critical overview of the existing level of evidence;
• guide clinicians in making an informed choice between the use of EMD alone or EMD combined with bone grafting;
• identify persistent sources of heterogeneity; and
• highlight current methodological gaps in order to propose recommendations for future clinical trials in periodontal regeneration."

Condition being studied "Although enamel matrix derivatives (EMD) have demonstrated proven efficacy in promoting periodontal regeneration, their optimal use in the management of intrabony periodontal defects remains a subject of debate. In particular, it is unclear whether combining EMD with bone grafting provides a clinically meaningful advantage over the use of EMD alone.

From a biological standpoint, bone grafts may enhance regenerative outcomes by stabilizing the blood clot, maintaining defect space, and providing an osteoconductive scaffold that supports tissue regeneration. These theoretical benefits have led to the frequent clinical use of EMD in combination with various grafting materials. However, clinical outcomes reported in the literature are inconsistent, with some studies suggesting additional gains in clinical attachment and bone fill, while others report marginal or negligible improvements.

This uncertainty is further reflected in the conclusions of published systematic reviews, which report heterogeneous results and differ in their methodological quality. As a consequence, clinicians are currently faced with conflicting evidence regarding the real added value of bone grafting when used adjunctively with EMD.

Addressing this question is therefore of major clinical relevance, as it may help determine whether the increased cost, surgical complexity, and potential morbidity associated with bone grafting are justified by superior regenerative outcomes. A comprehensive synthesis of the available evidence is needed to clarify whether EMD combined with bone grafting offers a true clinical advantage over EMD alone in the treatment of periodontal intrabony defects."
The final aim is to evaluate the clinical and radiographic outcomes associated with the use of enamel matrix derivatives (EMD), either alone or combined with various bone grafting materials, in the treatment of periodontal intrabony defects."

METHODS

Search strategy "A comprehensive and reproducible search strategy was developed to identify all systematic reviews and meta-analyses addressing the use of enamel matrix derivatives (EMD), either alone or in combination with bone grafting, in the treatment of periodontal intrabony lesions.
Databases searched: The electronic search was conducted in the following databases:
• PubMed/MEDLINE
• Cochrane Library
• Google Scholar
• ScienceDirect
• Mendeley Search
No geographical restrictions were applied.
The search period covered studies published from January 2009 to September 2025."
PubMed search strategy
Two complementary approaches were used: a broad search and a narrow search, in order to maximize sensitivity first and then specificity in the identification of relevant articles.
Broad search strategy: The broad search was designed to maximize sensitivity, ensuring that all potentially relevant systematic reviews were identified.

("enamel matrix derivative" OR emdogain OR amelogenin OR "enamel matrix protein*" OR EMD) AND ("bone graft*" OR "bone substitute*" OR xenograft* OR allograft* OR alloplast* OR grafting) AND (periodont* OR "intrabony defect*" OR "infrabony defect*" OR "intraosseous defect*") AND ("systematic review" OR "meta analysis" OR "review") AND
Narrow search strategy : The narrow search was designed to improve specificity, restricting the results to highly relevant publications.
("enamel matrix derivative"[tiab] OR emdogain[tiab] OR amelogenin[tiab] OR "enamel matrix protein*"[tiab]) AND ("bone graft*"[tiab] OR "bone substitut*"[tiab] OR xenograft*[tiab] OR allograft*[tiab] OR alloplast*[tiab]) AND ("intrabony defect*"[tiab] OR "intra-bony defect*"[tiab] OR "infrabony defect*"[tiab] OR "periodontal defect*"[tiab]) AND (systematic[sb] OR "systematic review"[tiab] OR "meta-analysis"[pt] OR "metaanalysis"[tiab]) NOT (implant*[tiab])
Cochrane Library search
(emdogain OR "enamel matrix derivative" OR "enamel matrix" OR amelogenin OR "enamel matrix proteins") AND (periodont* OR "periodontal regeneration" OR "intrabony defect" OR "infrabony defect" OR "bone defect" OR "bone regeneration")
Google Scholar search
("enamel matrix derivative" OR emdogain OR amelogenin OR "enamel matrix proteins") AND ("bone graft" OR "bone substitute" OR xenograft OR allograft OR alloplast) AND (periodontal OR "intrabony defect" OR "infrabony defect" OR "periodontal regeneration") AND ("systematic review" OR "meta analysis")
ScienceDirect search
Keywords used: “enamel matrix”, “derivative”, “intrabony defect”, “bone substitute”, “systematic review”, “meta-analysis”
Mendeley search
Keywords used: EMD, bone graft, intrabony defect
Manual search
Screening of the reference lists of included systematic reviews
Inclusion of relevant systematic reviews not identified through electronic searches.

Participant or population # Population : Adults (≥ 18 years) diagnosed with periodontitis presenting with at least one periodontal intrabony defect.

Intervention # Intervention: Enamel matrix derivatives (EMD) combined with bone grafting (autogenous, allogeneic, xenogeneic, or alloplastic grafts).

Comparator # Comparator: Enamel matrix derivatives (EMD) alone.

Study designs to be included Ssystematic reviews and meta-analysis.

Eligibility criteria
Inclusion criteria
Systematic reviews with or without meta analysis (2009–2025)
Reviews including primary studies (RCTs, cohort studies, etc.)
Explicit comparison between EMD alone and EMD combined with bone grafting
Language :English or French
Follow up ≥ 6 months
Exclusion criteria
Narrative reviews, scoping reviews, rapid reviews
In vitro studies, animal studies, peri implantitis studies
Comparisons not including EMD alone as a study arm
Studies published in languages other than English or French
Follow up < 6 months.

Information sources
Databases searched: The electronic search was conducted in the following databases:
• PubMed/MEDLINE
• Cochrane Library
• Google Scholar
• ScienceDirect
• Mendeley Search
and a manual search.

Main outcome(s) The primary outcomes will be clinical attachment level (CAL) gain and probing pocket depth (PPD) reduction as reported in the included systematic reviews.

Quality assessment / Risk of bias analysis The methodological quality of the studies included in the selected systematic reviews was assessed using the Cochrane Risk of Bias tool (RoB 2).

Strategy of data synthesis The methodological quality of the included systematic reviews will be assessed using the AMSTAR 2 tool, while the risk of bias will be evaluated using the ROBIS tool.

Subgroup analysis Groups treated with Enamel matrix derivatives (EMD) combined with bone grafting (autogenous, allogeneic, xenogeneic, or alloplastic grafts) and group treated with Enamel matrix derivatives (EMD) alone.

Sensitivity analysis Sensitivity analyses will be performed, if applicable, to assess the robustness of the findings by excluding systematic reviews

with critically low methodological quality (AMSTAR-2) or high risk of bias (ROBIS).

Language restriction yes , research restricted to english and frensh.

Country(ies) involved The study was conducted in Morocco, and the authors are from Morocco and Tunisia.

Keywords enamel matrix derivative; intrabony defect; bone substitute; systematic review; meta-analysis;bone graft; infrabony defect.

Contributions of each author

Author 1 - Bouchra El Houari - The first author contributed to the design of the study and co-led the literature search, article selection and evaluation, and the application of the AMSTAR 2 and ROBIS tools. he contributed to the manuscript. The author read, provided feedback and approved the final manuscript.
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Author 2 - MELAK TLILI - The first author contributed to the design of the study and co-led the literature search, article selection and evaluation, and the application of the AMSTAR 2 and ROBIS tools. he contributed to the manuscript.
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Author 3 - SIHAM CHEMLALI - The author provided statistical expertise.
Email: csihame15@yahoo.fr
Author 4 - ZINEB ESSADEQ - The author contributed to the literature search, article selection.
Email: zinebessadeq21@gmail.com
Author 5 - JAMILA KISSA - The author read, provided feedback and approved the final manuscript.
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