INPLASY

Efficacy of White Mineral Trioxide Aggregate in Regenerative Endodontics and Apexification for Immature Permanent Teeth: A Systematic Review and Meta-Analysis

INPLASY202630040
doi: 10.37766/inplasy2026.3.0040
Received: 11 March 2026
Published: 11 March 2026

Li, ZZ; Xu, Y; An, SL; Liu, H; Liu, L; Pan, YZ; Sun, TY; Kang, SY; Liu, R; Zhang, L.

Corresponding author:
Lin Zhang

zhanglinaries@tmmu.edu.cn

Author Affiliation:
Army Medical University.

ADMINISTRATIVE INFORMATION

Support - No fundings.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202630040

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 March 2026 and was last updated on 11 March 2026.

INTRODUCTION

Review question / Objective Review question: In children with non-vital immature permanent teeth (P), what is the comparative clinical and radiographic efficacy of different bioceramic-based treatments (I), including various materials (e.g., alternative bioceramics versus White Mineral Trioxide Aggregate) and scaffolds (e.g., platelet concentrates versus blood clot) (C), on outcomes such as clinical/radiographic success, root development, pulp sensibility, and discoloration (O)?
Objective: The objective of this systematic review and meta-analysis is to systematically synthesize and compare the clinical and radiographic outcomes of bioceramic-based treatments for non-vital immature permanent teeth in children. This review focuses on evaluating the comparative effectiveness of different bioceramic materials (such as WMTA and alternative formulations) and various scaffolds (including platelet concentrates and blood clots) used in apexification and regenerative endodontic procedures. Key outcomes assessed include clinical success rates, radiographic success (periapical healing), restoration of pulp sensibility, patterns of root maturation (lengthening vs. wall thickening), and the risk of tooth discoloration.

Condition being studied The condition being studied is pulp necrosis (non-vital pulp) in immature permanent teeth in children. When a permanent tooth with incomplete root development (immature tooth) suffers from pulp necrosis due to trauma, caries, or anatomical anomalies, the physiological process of root maturation (including root lengthening and dentinal wall thickening) is arrested. This leaves the tooth with thin, weak roots and an open apex, making it susceptible to fracture and compromising its long-term prognosis. Traditional management involves apexification to induce an apical barrier, while regenerative endodontic procedures aim to revitalize the pulp-dentin complex to allow continued root development. This review focuses on the treatment outcomes for this specific endodontic condition in the pediatric population.

METHODS

Search strategy A comprehensive literature search was conducted from database inception to September 1, 2025, without language restrictions. The primary search was performed in PubMed/ MEDLINE using the following detailed strategy:
((("Mineral Trioxide Aggregate" [Supplementary Concept] OR "white mineral trioxide aggregate" [All Fields] OR "white mineral trioxide aggregate" [Title/ Abstract] OR "WMTA" [All Fields] OR "WMTA" [Title/Abstract] OR "white MTA" [All Fields] OR "ProRoot MTA White" [All Fields]) AND (("pulp regeneration" [All Fields] OR "pulp regeneration" [Title/Abstract] OR "regenerative endodontics" [All Fields] OR "regenerative endodontics" [Title/ Abstract] OR "pulp revascularization" [All Fields] OR "revascularization" [Title/Abstract] OR "revascularization" [Title/Abstract] OR "Dental Pulp" [MeSH Terms] OR "apexification" [MeSH Terms] OR "apexification" [Title/Abstract]))
Additional searches were performed in Embase, Scopus, Web of Science, and Cochrane Library (Detailed in the Supplementary Methods).

Participant or population Children and adolescents with non-vital immature permanent teeth (open apex, pulp necrosis with or without apical periodontitis).

Intervention Use of WMTA as an apical plug in conventional apexification or as a coronal barrier in regenerative endodontic procedures (REP).

Comparator BC scaffold, PC (PRP, PRF, or PP), alternative bioceramics (e.g., Biodentine, Totalfill) when directly compared with WMTA, or no comparator in single-arm studies.

Study designs to be included Inclusion criteria were designed to identify studies evaluating WMTA in pulp regeneration for immature or necrotic permanent teeth. Priority was given to registered clinical trials (e.g., ClinicalTrials.gov), RCTs, and prospective cohort studies. To ensure a more comprehensive understanding of the topic, non-RCTs and case reports/ series were also considered.

Eligibility criteria Eligibility criteria were defined using the PICOS framework;
Population: children and adolescents with non-vital immature permanent teeth (open apex, pulp necrosis with or without apical periodontitis);
Intervention: use of WMTA as an apical plug in conventional apexification or as a coronal barrier in regenerative endodontic procedures (REP);
Comparator: BC scaffold, PC (PRP, PRF, or PP), alternative bioceramics (e.g., Biodentine, Totalfill) when directly compared with WMTA, or no comparator in single-arm studies;
Outcomes: primary endpoints including clinical success (absence of signs/ symptoms) and radiographic success (periapical healing or stability); secondary endpoints including continued root development (length and wall thickness), restoration of pulp sensibility, and tooth discoloration;
Study design: RCTs, non-RCTs, prospective/ retrospective cohort studies, case series (≥3 cases), and case reports providing usable outcome data, whereas in vitro studies, animal studies, reviews/ meta-analyses, and studies using only grey MTA or other bioceramics without a WMTA arm were excluded.

Information sources A comprehensive literature search was conducted to identify relevant studies. The following electronic databases were searched from their inception to September 1, 2025:
1) PubMed/MEDLINE; 2) Embase; 3) Scopus; 4) Web of Science; 5) Cochrane Library (including Cochrane Database of Systematic Reviews and Central Register of Controlled Trials)
Search strategy: The primary search strategy was developed for PubMed/MEDLINE using a combination of MeSH terms, keywords, and title/ abstract searches (e.g., "white mineral trioxide aggregate," "WMTA," "regenerative endodontics," "apexification"). The full search strings for each database are provided in the Supplementary Methods.
Additional searches:
Reference lists: The reference lists of all included studies and relevant review articles were manually screened to identify additional potentially eligible studies (snowballing).
Grey literature: Sources of grey literature (e.g., Google Scholar, conference proceedings, dissertations) were not explicitly searched as per the original protocol, though major databases include some conference abstracts.
Language restrictions: No language restrictions were applied during the search process.
Study registries: Clinical trial registries (e.g., ClinicalTrials.gov) were not systematically searched as part of this review.

Main outcome(s) Primary endpoints including clinical success (absence of signs/ symptoms) and radiographic success (periapical healing or stability); secondary endpoints including continued root development (length and wall thickness), restoration of pulp sensibility, and tooth discoloration.

Quality assessment / Risk of bias analysis RoB was assessed using appropriate tools. RCTs were evaluated with the Cochrane RoB2 tool, focusing on aspects such as randomization, intervention deviations, missing data, outcome measurement, and result selection. Non-RCTs were assessed using the ROBINS-I tool, which addressed confounding, selection bias, and additional domains. Case reports/ series followed case report guideline guidelines to ensure methodological rigor. The RoB was visualized through traffic light and summary bar plots for RCTs.

Strategy of data synthesis Statistical analyses were conducted using R with the meta package8. The included studies exhibited significant clinical and methodological differences regarding study design, scaffold types, population characteristics, and follow-up durations. Therefore, based on conceptual heterogeneity, the random-effects model was pre-specified as the primary analytical approach for all meta-analyses. This model was employed to pool proportions and odds ratios (ORs) with their corresponding 95% confidence interval (CI) for both single-arm and comparative analyses. For proportions approaching boundary values (e.g., success rates nearing 100.00%), the Freeman–Tukey double arcsine transformation and generalized linear mixed models were applied to stabilize variances and prevent CI from exceeding the (0, 1) rang8. Pooled effect estimates and their 95% CI derived from transformed data were subsequently back-transformed to report results on the original proportion scale. Subgroup analyses were performed stratified by scaffold type (PRP + WMTA, PRF + WMTA, PP + WMTA, and apexification + WMTA), with between-subgroup differences assessed using the Q statistic. Heterogeneity was comprehensively evaluated using the τ^2 statistic, the I^2 metric with its 95% CI, and Cochran's Q test (with $P < 0.10$ indicating statistically significant heterogeneity).

Subgroup analysis Subgroup analyses were conducted to explore potential sources of heterogeneity and compare treatment effects across different clinical scenarios based on the following variables:
1. Type of scaffold used in regenerative endodontic procedures: Platelet concentrates (PC) including PRP versus blood clot (BC).
2. Type of bioceramic material: White Mineral Trioxide Aggregate (WMTA) versus alternative bioceramic materials.
3. Treatment procedure type: Apexification versus regenerative endodontic procedures (REP).
These subgroup analyses aimed to assess whether the clinical and radiographic outcomes (e.g., root development patterns, discoloration risk, success rates) differ depending on the scaffold material, the specific bioceramic used, or the nature of the endodontic intervention.

Sensitivity analysis Sources of heterogeneity were explored through sensitivity analyses, which involved: (1) excluding non-randomized studies and case series/reports; and (2) restricting analyses to studies judged to have low risk of bias. Publication bias was assessed via visual inspection of funnel plot symmetry for all meta-analyses. Given that the number of studies included in each meta-analysis was ≤ 6, formal statistical tests for publication bias (e.g., Egger's regression test or Begg's rank correlation test) were not performed, as these tests are underpowered and potentially misleading with sparse data. Statistical significance was set at $P < 0.05$. The certainty of evidence for each outcome was evaluated using the GRADE approach (Grading of Recommendations Assessment, Development and Evaluation)9. Two reviewers independently assessed these domains, that is, risk of bias, inconsistency, indirectness, imprecision, and publication bias. When a specific domain was rated as having serious or very serious limitations, the corresponding evidence was downgraded accordingly. Each outcome was assigned an overall certainty rating of high, moderate, low, or very low. Any discrepancies in domain-level judgments between reviewers were resolved through discussion and, if necessary, consultation with a third reviewer. Further details regarding the GRADE methodology and implementation guidance are available at the official GRADE Working Group website (https://www.gradeworkinggroup.org).

Language restriction No.

Country(ies) involved China.

Keywords Mineral Trioxide Aggregate, Regenerative Endodontics, Apexification, Platelet-Rich Plasma, Root Development, Tooth Discoloration.

Contributions of each author
Author 1 - Zizhan Li - participated in data acquisition and interpretation, and drafted the manuscript.
Author 2 - Yue Xu - contributed to quality assessment, data analyses, and manuscript preparation.
Author 3 - Songlin An - contributed to data interpretation, and revised the manuscript.

Author 4 - Hui Liu - contributed to data interpretation, and revised the manuscript.
Author 5 - Li Liu.
Author 6 - Yingzi Pan - participated in data acquisition and interpretation, and drafted the manuscript.
Author 7 - Taiyi Sun - participated in data acquisition and interpretation, and drafted the manuscript.
Author 8 - Shiyun Kang - contributed to data interpretation, and revised the manuscript.
Author 9 - Rui Liu - participated in performing the analysis with constructive discussions and revised the manuscript.
Author 10 - Lin Zhang - participated in data acquisition and interpretation, and critically revised the manuscript.