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ADMINISTRATIVE INFORMATION

Support - Not applicable.

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 4 November 2025 and was last updated on 4 November 2025.

INTRODUCTION

Review question / Objective This meta-analysis aimed to evaluate the efficacy of intracanal cryotherapy in alleviating postoperative pain following root canal treatment.

Condition being studied Nevertheless, postoperative pain is a frequently encountered complication, which can impair patient comfort, elevate psychological stress, and increase the overall cost of care. With the increasing emphasis on minimally invasive techniques in endodontics, non-pharmacological modalities for pain relief have attracted growing interest.

METHODS

Search strategy Following the PRISMA 2020 recommendations,¹⁵ an extensive literature search was performed across four key databases—PubMed, Web of Science, Cochrane Library, and Embase—encompassing all relevant studies

published up to March 10, 2025. The English search terms included: “cryotherapy,” “intracanal cryotherapy,” “cold irrigation,” “endodontic pain,” “postoperative endodontic pain,” and “endodontic cryotherapy.” To ensure thoroughness, we also manually reviewed the reference lists of included studies to identify additional relevant publications. Detailed search strategy was displayed in supplementary materials.

Participant or population Participants diagnosed with pulp or periapical pathologies receiving non-surgical root canal treatment.

Intervention Intervention group treated with cold irrigating solutions (e.g., cold saline or sodium hypochlorite).

Comparator Control group irrigated with solutions at ambient (room) temperature.

Study designs to be included Systematic Review and Meta-Analysis.

Eligibility criteria The following eligibility criteria were applied to identify studies for inclusion:

- (1) Articles published in peer-reviewed journals in either Chinese or English;
- (2) Participants diagnosed with pulp or periapical pathologies receiving non-surgical root canal treatment;
- (3) Intervention group treated with cold irrigating solutions (e.g., cold saline or sodium hypochlorite);
- (4) Control group irrigated with solutions at ambient (room) temperature;
- (5) Primary outcomes included postoperative pain severity (measured by VAS or NRS) or the incidence of pain;
- (6) Study designs included randomized controlled trials (RCTs), cohort studies, or case-control studies.

Information sources PubMed, Web of Science, Cochrane Library, and Embase.

Main outcome(s) Primary outcomes included postoperative pain severity (measured by VAS or NRS) or the incidence of pain. A total of 739 records were retrieved from database searches. Following the removal of 277 duplicates and the exclusion of 288 articles deemed irrelevant after title and abstract screening, 174 full-text papers were evaluated for eligibility. Ultimately, 16 studies met the inclusion criteria and were incorporated into the meta-analysis.

Quality assessment / Risk of bias analysis The methodological rigor of the included studies was appraised using the Cochrane Risk of Bias tool.¹⁶ This evaluation encompassed critical aspects such as the generation of random sequences, allocation concealment, blinding of participants and personnel, completeness of outcome data, selective reporting, and other potential bias sources.

Strategy of data synthesis Two reviewers independently assessed the titles and abstracts according to the established inclusion criteria. Articles considered potentially eligible underwent a full-text evaluation to confirm their relevance. Disagreements between reviewers were resolved through discussion with a third reviewer. Extracted data were recorded using a standardized form and included study characteristics, patient demographics, intervention details, follow-up duration, and outcome measures.

Subgroup analysis Risk of bias was assessed using the Cochrane Collaboration's tool. Overall, the included RCTs showed acceptable methodological quality, although some studies

lacked details on allocation concealment and blinding (Figure 7, Supplementary Figure 1). Funnel plots indicated a symmetrical distribution of studies, suggesting no significant publication bias (Supplementary Figure 2). Additionally, the results of GRADE was displayed in Supplementary Table 1.

Sensitivity analysis Sensitivity analyses were performed for 6-hour, 24-hour, and 72-hour pain outcomes. For both 6-hour and 24-hour results, excluding studies one at a time did not materially alter the overall effect sizes, indicating robust findings. For 72-hour pain, exclusion of one study¹⁹ reduced heterogeneity from 65% to 0%, and the effect estimate was no longer statistically significant (SMD = -0.38; 95% CI: -0.83 to 0.07) (Supplementary Figure 3).

Country(ies) involved China.

Keywords Intracanal cryotherapy, Endodontic pain, Root canal treatment, Cold irrigation, Systematic review.

Contributions of each author

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