



## A Systematic Review and Meta-Analysis of Nonvital Pulp Therapy for Primary Teeth

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**Abstract: Purpose:** The purpose of this systematic review and meta-analysis was to assess success rates for nonvital treatment in primary teeth for caries/trauma. **Methods:** Databases were searched between 1960 and 2020 for randomized controlled trials, cohorts, case series, and in vitro studies. The primary outcome was overall success (clinical and radiographic) for pulpectomy and lesion sterilization tissue repair (LSTR). Included articles were independently determined, agreed upon, data extraction assessed, risk of bias, meta-analyses, and assignment of quality of evidence (GRADE). **Results:** Comparing teeth with and without root resorption, pulpectomy success was better ( $P < 0.001$ ) in teeth without preoperative root resorption. Success with pulpectomies performed with zinc oxide eugenol [ZOE] and with Endoflas (ZOE plus iodoform plus calcium hydroxide) did not differ from that observed using Vitapex or Metapex (iodoform plus calcium hydroxide;  $P \geq 0.50$ ) after 18 months; however, Endoflas and ZOE success rates remained near 90 percent versus 71 percent or less for iodoform. Network analysis ratings showed Endoflas and ZOE performed better than iodoform alone. Also, LSTR performed better ( $P < 0.001$ ) than pulpectomies in teeth with preoperative root resorption, but pulpectomy results were superior ( $P = 0.09$ ) if roots were intact. Rotary instrumentation of root canals was significantly faster ( $P < 0.001$ ) than manual instrumentation. Success rates were not impacted by method of obturation or root length determination, type of tooth, number of visits, irrigants, smear layer removal, or timing/type of final restoration. **Conclusions:** Eighteen-month success rates support Endoflas and zinc oxide eugenol pulpectomies over iodoform pulpectomies. Lesion sterilization tissue repair had limited indication for teeth with resorbed roots. (*Pediatr Dent* 2020;42(4):256-72.E11-E199) Received April 14, 2020 | Last Revision May 31, 2020 | Accepted June 1, 2020

KEYWORDS: PULPECTOMY, LSTR, SYSTEMATIC REVIEW/META-ANALYSIS

Though largely preventable, dental caries is the most common chronic disease in children and continues to present significant consequences.<sup>1,2</sup> Untreated caries has been shown to increase the risk of new carious lesions in both the primary and permanent dentitions and cause premature loss of teeth<sup>3,4</sup> as well as the number of emergency room visits<sup>5</sup> and missed school days,<sup>6</sup> thus reducing oral health-related quality of life.<sup>7</sup>

When caries is left untreated, it may progress and the tooth's pulp may remain vital or possibly become nonvital. Diagnosis of pulp status is based on both clinical and radiographic parameters, such as clinical symptoms, presence or absence of parulis, mobility, and radiographic evaluation of furcation or periapical pathology. If a nonvital pulp diagnosis is made, preservation of the tooth may be the best treatment for the maintenance of overall oral health, space, and arch integrity.<sup>8</sup>

A pulpectomy is a root canal procedure for primary teeth with irreversibly inflamed or necrotic pulp resulting from caries or trauma. This nonvital treatment (NVT) procedure begins with proper case selection and continues with appropriate use of local anesthesia, isolation of the tooth, access opening, pulp extirpation, root length determination, mechanical preparation, and debridement of the root canal(s). Next, the procedure continues with disinfection using irrigants, drying, and obturation of the canal(s) employing a resorbable biocompatible material. Finally, the tooth is restored with a definitive restoration that seals the tooth from microleakage. Factors that may influence nonvital pulp therapy are the complex root morphology of the primary teeth, age of the patient, desires of the parent/patient, behavior, medical history, pathologic root resorption, physiologic root resorption, and proximity to the succedaneous teeth.<sup>9</sup>

Other than traditional pulpectomies for nonvital teeth, recent studies have reported success with a technique called lesion sterilization tissue repair (LSTR).<sup>10,11</sup> The procedure usually has no instrumentation of the root canals; instead, an antibiotic mixture is placed in the pulp chamber which is intended to disinfect the root canals before the tooth is restored.

Numerous studies, both in vivo and in vitro, have been published on pulpectomy, LSTR, and other components of nonvital treatment, including the effectiveness of root length determination methods, mechanical preparation methods, antimicrobial activity of irrigants, and treatment success of different materials.<sup>9-16</sup> However, the variations in study designs and reporting outcomes present a significant challenge in determining the quality of evidence. Previous systematic reviews examined the effectiveness and success of pulpectomy obturation materials but did not assess other aspects of the pulpectomy procedure or LSTR.<sup>17,18</sup> Nonvital pulp therapy procedures are integral to

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Supplemental material available in the online version.

### HOW TO CITE:

Coll JA, Vargas K, Marghalani AA, et al. A Systematic Review and Meta-Analysis of Nonvital Pulp Therapy for Primary Teeth. *Pediatr Dent* 2020; 42(4):256-72.E11-E199.

the practice of pediatric dentistry; therefore, it is imperative to systematically analyze all of the existing evidence regarding nonvital pulp therapy in primary teeth to support informed clinical decisions.

The purposes of this systematic review and meta-analysis were to: (1) determine, after a minimum of six months follow-up, the overall clinical and radiographic success of nonvital treatment options for primary teeth with deep caries or trauma affecting the pulp; and (2) evaluate *in vivo* and *in vitro* elements of NVT that may have affected outcomes, such as using different methods of filing, obturation, root length determination, and use of antimicrobial agents.

## Methods

This systematic review was conducted in compliance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).<sup>19</sup> To ensure transparency and reproducibility of this systematic review, a protocol titled "Systematic review and meta-analysis of nonvital pulp therapy for primary teeth" was registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42018099107).<sup>20</sup>

**Selection criteria.** Inclusion and exclusion criteria were based on the population, intervention, comparison, outcomes, and study design (PICOS) method. The population was defined as healthy pediatric patients who required NVT in a primary tooth (unit of analysis) with irreversibly infected or necrotic pulps from deep caries or trauma. The clinical interventions were any nonvital pulp therapy or vital pulp treatment; however, for *in vitro* studies, interventions were examined on any aspect of NVT. The comparison was to any other NVT if the study design permitted a comparison. The clinical and radiographic outcomes were categorized separately, if given, and combined for the overall success after a minimum of six months. Randomized clinical trials (RCTs), nonrandomized studies (NRSs), cohort, case-control, and cross-sectional studies, *in vitro* or *in vivo* articles reporting on aspects of NVT, and case series were considered for inclusion; however, case reports were excluded.

**Search strategy.** The following databases from 1960 to January 30, 2020, were searched: MEDLINE (PubMed) 1960; EMBASE—Cochrane Central Register of Controlled Trials (CENTRAL); EBSCO—Dentistry and Oral Sciences Source; WHOINT (trials database); dissertation abstracts; and open grey literature. The search strategies used Medical Subject Headings (MeSH) terms and keywords to find both published and unpublished studies (see [Supplemental Electronic Appendix](#)) Additionally, relevant journals were individually searched from 1990 onward. The supplemental electronic appendix also has the list of journals individually searched. The resulting search strategy retrieved all nonvital pulp therapy included studies cited by the recent Cochrane pulp therapy review<sup>17</sup> and another systematic review and meta-analysis on pulpectomy.<sup>18</sup>

Titles and abstracts were screened by four calibrated reviewers independently to identify studies for inclusion in the systematic review. When a paper was in a non-English language and needed further review, a translation was requested. Two reviewers provided translations for Spanish and Chinese studies.

If an abstract was unclear, the full paper was accessed to determine eligibility for inclusion. A list of articles for possible inclusion and data extraction was made. If a study published results for different time frames in separate publications, data from all of the publications were considered for inclusion. All

papers were reviewed in duplicate by two of the four authors to determine inclusion.

**Data extraction.** Four reviewers independently performed the data extraction and risk-of-bias assessment for the included articles using a standardized electronic template. One author created a master data sheet and determined all areas of disagreement. Disagreements were resolved through discussion by the assigned reviewers. For RCTs with more than two arms, only relevant arms were considered. RCTs with split-mouth designs were combined with parallel designs.

Sixty-eight fields were extracted from each study when possible; if there were questions regarding data, attempts were made to contact the study authors. The following data were extracted: general information (study citation, year research published, country, funding source); study characteristics (study design, operator, study site, number of procedure visits, *in vivo* or *in vitro*); tooth characteristics (number and type of teeth); patient characteristics (setting, age, gender, number of participants recruited in each group, and number of participants on follow-up); intervention characteristics (isolation method, method of root length determination, type of NVT, type of filing method, irrigation agent used, type of antimicrobials used, pulp chamber/canal filling used and method of placement, and final restoration type and timing); outcomes (clinical results by success/failure rates at each follow-up time, radiographic results by success/failure rates at each follow-up time, overall success, number of teeth postoperatively with pain, and pathologic root resorption; and quality assessment (for risk of bias [ROB] assessment). An RCT was analyzed using the Cochrane Collaboration tool.<sup>21</sup> For any NRS that included observational and retrospective types of studies or *in vitro* studies, the authors used a ROB tool from the Office of Health Assessment and Translation (OHAT).<sup>22</sup>

**Data synthesis.** For binary outcomes, the authors used the Mantel-Haenszel random-effects model to obtain pooled relative risks (RR) and 95 percent confidence intervals (95% CI). The number needed to treat (NNT) was determined by reciprocating the pooled risk difference, which was reported when it was statistically significant or had clinical importance. For continuous outcomes, the authors used the random-effects models and inverse-variance method to obtain pooled mean difference (MD) along with 95% CI. Using the random-effects models, the authors also estimated the overall success with 95% CI by combining success from study arms. The heterogeneity was determined by using the  $I^2$  statistic and the Cochrane test for heterogeneity, with  $P < 0.1$  considered to be statistically significant. The authors utilized the Metaprop procedure, using STATA 15.1 software (StataCorp LP, College Station, Texas, USA) applying continuity correction, not to exclude studies with 100 percent success, in addition to Freeman-Tukey double arcsine transformation to adjust for heterogeneity between the studies. The authors conducted sensitivity analyses with and without high risk of bias studies. The authors performed network meta-analyses to rank the intervention options. All meta-analyses were done using RevMan 5.2.1 software (Cochrane, London, UK) and STATA 15.1.

**Primary outcomes.** The primary outcomes were overall success rates at different time intervals for pulpectomy and LSTR and the effect of different treatment methods for pulpectomy and LSTR.

**Overall success definition.** Overall success was defined as only those teeth that showed both clinical and radiographic success simultaneously in time frames starting at six months.

Due to the variability of outcome measurements among studies, some data were recalculated with the following rules to provide a consistent way of reporting success. Overall success was standardized by applying the following rules:

1. If a tooth showed no resolution or stasis of a pre-operative radiolucency, it was categorized as a failure.
2. If a tooth exfoliated in less than six months it was counted as a failure.
3. If a tooth exfoliated greater than six months after NVT, it was always counted as a success in all future time frames.
4. If a tooth failed in a time frame, it was counted as a failure in all future time frames.
5. If a child dropped out during any time frame, that child's tooth/teeth were removed from that time frame's denominator and all future time frames in calculating success.

**Secondary outcomes.** The secondary outcomes included: speed of canal preparation for pulpectomy with manual or rotary filing; quality of pulpectomy fill; type of tooth (molar versus incisor); pulpectomy success after trauma versus caries; and adverse effects of NVT, such as pulpectomy filler resorption/retention, succedaneous teeth with problems from nonvital treatment, smear layer removal, and pain.

**Outcome moderators/factors.** The hypothetical outcome moderators/factors included the number of visits, method of root length determination, irrigation methods, type of final restoration, and method of tooth isolation. These were evaluated for their potential significant effect on success using subgroup analyses. In vitro studies were evaluated qualitatively to assess any clinical relevance for the success of NVT. The criteria for irreversible pulpitis or necrosis and teeth considered to be non-restorable were determined.

**Risk of bias assessment.** The Cochrane Collaboration's risk-of-bias assessment tool was used to rate the ROB of RCTs.<sup>21</sup> The ROB ratings were used to create an overall assessment of the ROB for these articles. The six key ROB domains used were: (1) the randomization process; (2) deviations from intended interventions; (3) missing outcome data; (4) outcome measurement; (5) selective outcome reporting; and (6) other biases. A low ROB was when all of the key domains of bias were judged to have low risk. A ROB rated as "some concerns" had at least one key domain judged as some concerns. A high ROB had at least one key domain judged to have a high risk of bias.

The quality of ROB for NRSs was evaluated using the OHAT ROB Rating Tool<sup>22</sup> for Human and Animal Studies. The overall assessment of ROB for NRSs, cohort, case-control, cross-sectional, in vitro, and in vivo studies was based on seven key domains. This included ROB for selection, confounding, performance, attrition/exclusion, detection, selective reporting, and other bias. The overall ROB was determined as "low" ROB when all domains were judged as definitely low ROB; "some concerns" was determined if one or more domain was judged as probably low ROB or one domain was judged as probably high ROB; a "high ROB" determination was made when at least one domain had a high ROB or multiple domains were judged to have probably high ROB in a way that substantially lowered confidence in the result.

**Grading.** The authors used Grading of Recommendations Assessment, Development, and Evaluation (GRADE)<sup>23</sup> guidelines to summarize the overall quality of evidence of each

outcome included in the systematic review and meta-analyses. The quality of evidence for each outcome across all the studies was rated according to seven criteria outlined in the GRADE approach, but the authors excluded publication bias because the number of publications was not 10 or more. The seven criteria were: (1) study design, which included ROB/study limitations; (2) inconsistency of results based on excess heterogeneity; (3) imprecision based on sample size; (4) indirectness of evidence; (5) importance; (6) magnitude of the effect; and (7) effect of plausible residual confounding. The first five can lead to downgrading the quality of evidence. The remaining two criteria—large magnitude of an effect, and effect of plausible residual confounding—may lead to upgrading the quality of evidence and were considered for observational studies per the GRADE proposal.

For each outcome, the quality of evidence was downgraded from "high quality" by one level for serious (or by two levels for very serious) limitation or upgraded based on the assessments of the following seven considerations:

1. Study design including ROB was determined, as stated earlier, and the GRADE guidance was given on overall ROB. In the meta-analysis, the authors included studies of low ROB with some concerns but downgraded one level if a high ROB study was included.
2. Inconsistency was judged based on the  $I^2$  value of the heterogeneity of the studies in the meta-analysis and assigned as: not serious ( $I^2$  equals zero to 30 percent); serious ( $I^2$  equals 35 to 65 percent); and very serious ( $I^2$  equals greater than 75 percent).
3. Imprecision was based on the total sample size in each arm of the meta-analysis and assigned as: not serious (greater than 125 total teeth in each arm); serious (65 to 110 total teeth in each arm); and very serious (less than 50 total teeth in each arm).
4. Indirectness of evidence was judged as: not serious if the evidence directly compared the interventions, population, or outcomes; serious if the findings did not apply to the population; and very serious if an indirect comparison was made.
5. Importance was judged on length of follow-up, with 24 months or greater considered critical; 18 months was rated as important; 12 months was rated as somewhat less important; and six to 12 months was rated much less important.
6. Large magnitude of an effect was judged based on RR as large or very large. Large was assigned a RR greater than two or less than 0.5, and very large was assigned a RR greater than five or less than 0.2, which could increase the bias one or two levels.
7. Effect of plausible residual confounding was upgraded one level for observational studies when their confounding factors were expected to increase or reduce the treatment effect, but none was observed.

The overall quality of evidence was assessed for each primary and secondary outcome and categorized into four levels: (1) high (very confident that the true effect lies close to that of the estimate of the effect); (2) moderate (moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different); (3) low (the effect estimate is limited, and the true effect may be substantially different from the

estimate of the effect); and (4) very low (very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect).

## Results

**Description of studies.** A total of 8,769 articles on nonvital pulp therapy in primary teeth were initially identified through database searching, and 1,415 articles were identified through other sources (hand-searching and further database searches). After removing 4,309 duplicates, 5,875 nonduplicate titles remained. After reviewing the titles, 5,344 studies were found irrelevant because they were out of the scope of the present study. A total of 531 article abstracts were screened and 267 were excluded due to not matching this study's PICOS, resulting in 264 for full text screening. After full-text review for eligibility, 133 articles were excluded due to various reasons (e.g., permanent teeth, study design, wrong intervention, literature review, vital treatment, opinion, and other reasons), leaving 131 articles eligible for data extraction. The data from 17 studies were excluded because they were unique clinical studies that had no other comparative article, resulting in 114. There were 79 articles used for qualitative assessment and 35 quantitative articles used in one or more meta-analyses (see Figure 1).

The earliest of the 131 eligible articles was from 1972, which was a qualitative article,<sup>24</sup> but most were published after 2015. The 35 articles used in the quantitative analyses represented 1,829 children who had 2,309 teeth treated, including primary molars and anterior teeth. Their ages ranged from three to 13 years, with the majority treated in the four- to seven-year-old range. Data from the 35 articles used in forest plots were conducted primarily in pediatric dentistry departments

of universities by dentists or residents supervised by pediatric dental faculty.

Of the articles used in one or more meta-analyses, 16 compared the success of different pulpectomy fillers. Eight compared different LSTR treatments, six compared root canal filing methods, and five compared root length determination methods. The ROB table for the 114 included articles for qualitative and quantitative analysis as well as the characteristics of studies is found in the **Supplemental Electronic Appendix**. Among the 35 articles included for quantitative analysis, 15 were rated as low bias, 13 with some concerns, and seven rated as high bias. Among 79 articles included for qualitative analysis, 34 were rated as low bias, 24 with some concerns, 20 rated as high bias, and one study was a systematic review; therefore the ROB was not assessed.

**Quantitative data: different nonvital medicaments used in meta-analyses.** Twelve RCT articles had up to 18-month results comparing zinc oxide and eugenol (ZOE) pulpectomy to iodoform (iodoform plus calcium hydroxide), or calcium hydroxide (CH).<sup>9,12,15,25-33</sup> ZOE used for primary tooth pulpectomy is zinc oxide powder mixed with eugenol to a creamy or thick consistency and is radiopaque. Vitapex (Neo Dental International Inc., Burnaby, British Columbia) is one brand of iodoform composed primarily of 40.4 percent iodoform, 30 percent CH, 22.4 percent silicone, and 6.9 percent inert products; it is in a premixed syringe and radiopaque.<sup>34</sup> Metapex (Meta Biomed LTD, South Korea) is also a brand of iodoform in a premixed syringe, is composed of essentially the same products, except in slightly different percentages, and is radiopaque.<sup>35</sup> These were the two brands of iodoform analyzed in this paper. CH pastes (Calcicur, by Voco America Inc., USA, Apexit Plus by Ivoclar Vivadent AG, Schaan Liechtenstein, and Sealpex by Kerr Corp. USA) can be purchased in premixed syringes or mixed as a powder and water. There were five zinc oxide, iodoform, plus CH (ZOE/iodoform/CH) RCT studies that had up to 12-month results.<sup>12,30,31,36,37</sup> The brand Endoflas (Sanlor Laboratories, Cali Columbia) was the ZOE/iodoform/CH included in this paper and is composed of 40.6 percent iodoform, 56.5 percent zinc oxide, 1.07 percent CH, 1.63 percent barium sulfate, and a liquid mix of eugenol and paramonochlorophenol.<sup>31</sup> LSTR treatment consists of using antibiotic tablets crushed into a powder and mixed with propylene glycol and/or a macrogol vehicle to make a paste that is placed over the pulp canal orifices.<sup>11</sup>

Many of the aforementioned studies had multiple arms comparing different types of root canal fillers at various time frames. In this study's meta-analyses, the authors used the appropriate arms to make this study's comparisons at six, 12, 18, and 24 months. Twenty-four months' follow-up time was the longest for direct RCT data comparisons. The present study's grading of importance ranked 18 months and longer as important, 12 months as less important, and six months as much less important.

**Primary outcomes: long-term pulpectomy success.** Pulpectomy success of 12 months or longer, irrespective of the root canal filler type or method of canal obturation, was evaluated using 20 RCT studies<sup>9,11,12,15,16,26,27,29,31,32,37-45,79</sup> and seven nonrandomized observational studies.<sup>46-52</sup> The meta-analysis using the 12-month RCT success rates for teeth without root resorption was 89 percent versus 47 percent for those with root resorption, and these rates

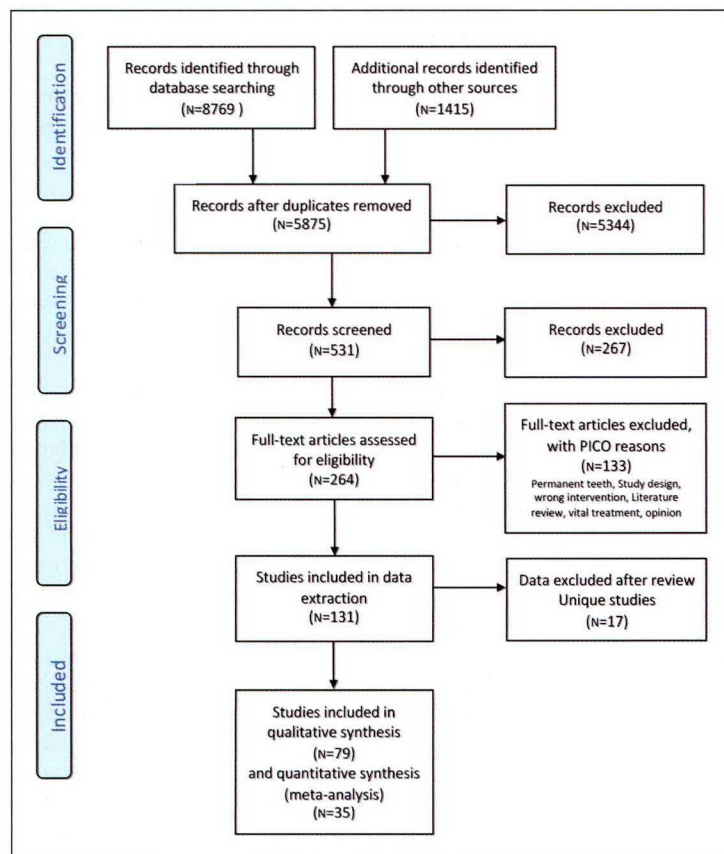


Figure 1. PRISMA flow diagram.

were significantly different ( $P < 0.001$ ; **Supplemental Electronic Appendix, sFigure 2a**) The quality of the evidence for this result was very low, according to GRADE at 12 months due to the “very serious” heterogeneity seen in the  $I^2$  statistic, and “very serious” indirectness.

There were only two RCT studies<sup>16,45</sup> with data for 24 months. These RCT studies’ 24-month findings were similar to 12-month data; however, since only one study had root resorption and one other study had no root resorption, the meta-analysis was not computed. A subgroup analysis for 24-month follow-up combining the RCT<sup>16,45</sup> and observational studies<sup>24,47,50</sup> success rates showed a significant difference between the teeth with or without preoperative root resorption ( $P < 0.001$ ) Teeth with resorption had significantly less success (59 percent) compared to teeth without resorption (88 percent; **Supplemental Electronic Appendix, sFigure 2b**). The quality of the evidence for this result was very low at 24 months, according to GRADE, due to the very serious heterogeneity and very serious indirectness.

For longer periods (24 to 60 months), pulpectomy success in teeth without preoperative root resorption had higher success, ranging from 84 to 90 percent versus teeth with preoperative root resorption (59 to 69 percent; **Supplemental Electronic Appendix, sTable 1a and b**). There were insufficient numbers of RCT studies that were available in each time frame to compare study results.

**ZOE versus iodoform pulpectomy success (six, 12, 18 months).** The two brands of iodoform were essentially the same composition, so their pulpectomy success results were combined. There were six articles<sup>9,15,26,29,32,33</sup> comparing the pulpectomy success of ZOE to one brand of iodoform at six months. Four articles compared ZOE to the other iodoform brand at six months.<sup>12,30,31,53</sup> The results showed the six-month ZOE success to be 83 percent versus 90 percent for iodoform, which was not significantly different (RR equals 0.96; 95% CI equals 0.87 to 1.06; **Supplemental Electronic Appendix, sFigure 3a**) The quality of the evidence for this result was low, according to GRADE, at six months due to the high ROB and serious heterogeneity in the  $I^2$  statistic. The sensitivity analysis removed the high ROB articles<sup>29-31</sup> and showed no difference (RR equals 1.00; 95% CI equals 0.96 to 1.04). The quality of the evidence for this result was moderate at six months, according to GRADE, due to serious heterogeneity in the  $I^2$  statistic. Based

on the six-month follow-up; this finding was judged as much less important.

Six articles<sup>9,15,26,29,32,41</sup> compared ZOE pulpectomy success to one brand of iodoform at 12 months. Two articles compared ZOE to the other iodoform brand at six months.<sup>12,31</sup> The ZOE success rate at 12 months was 91 percent versus 81 percent for iodoform. The meta-analysis showed no significant difference between these success rates (RR equals 1.04; 95% CI equals 0.89 to 1.22; **Supplemental Electronic Appendix, sFigure 3b**). The quality of the evidence for this result was very low at 12 months, according to GRADE, due to the very serious heterogeneity seen in the  $I^2$  statistic and high ROB. The sensitivity analysis removed the three high ROB articles<sup>29,31,41</sup> and showed no difference (RR equals 1.14; 95% CI equals 0.86 to 1.52). The quality of the evidence for this result was moderate at 12 months, according to GRADE, due to the serious heterogeneity seen in the  $I^2$  statistic. Based on the 12-month follow-up, this finding was judged to be somewhat less important.

Two articles<sup>15, 29</sup> compared ZOE pulpectomy success to one brand of iodoform at 18 months, and one article<sup>31</sup> compared ZOE to the other iodoform brand. The ZOE success rate was 92 percent compared to 71 percent for iodoform. The meta-analysis showed no significant difference between the ZOE and iodoform success rates (RR equals 1.14; 95% CI equals 0.74 to 1.77; Figure 2, **Supplemental Electronic Appendix, sFigure 3c**). Although there was no statistical difference, the ZOE success was 14 percent better than iodoform, with an NNT of 12. This NNT indicates that, after doing 12 pulpectomies, one failure may have been prevented using ZOE compared to iodoform. The quality of the evidence for this result was very low at 18 months, according to GRADE, due to the very serious heterogeneity in the  $I^2$  statistic, high ROB, and sample size issues. Based on the 18-month follow-up, this finding was judged as important.

**ZOE versus ZOE/iodoform/CH success (six, 12, 18 months).** Six articles at six months compared ZOE pulpectomy success to ZOE/iodoform/CH success.<sup>12,15,30,31,36,37</sup> The ZOE/iodoform/CH success rate was 97 percent versus 81 percent for ZOE. The rates were not significantly different (RR equals 1.23; 95% CI equals 0.89 to 1.68; **Supplemental Electronic Appendix, sFigure 4a**). The quality of the evidence for this result was very low, according to GRADE, due to the very serious heterogeneity in the  $I^2$  statistic and high ROB. The sensitivity analysis removed the high ROB articles<sup>30,31,36</sup> and also showed no difference between these fillers. The success rate for ZOE/iodoform/CH was 96 percent versus 88 percent for ZOE (RR equals 1.15; 95% CI equals 0.80 to 1.66). The quality of the evidence for this result was moderate, according to GRADE, due to the serious heterogeneity in the  $I^2$  statistic. Based on the six-month follow-up, this finding was judged to be much less important.

Four articles<sup>12,15,31,37</sup> compared ZOE pulpectomy success to ZOE/iodoform/CH at 12 months. The ZOE/iodoform/CH success rate was 94 percent compared to 84 percent for ZOE. The meta-analysis showed no significant difference between the ZOE/iodoform/CH and ZOE success rates (RR equals 1.17; 95% CI equals 0.81 to 1.69; **Supplemental Electronic**

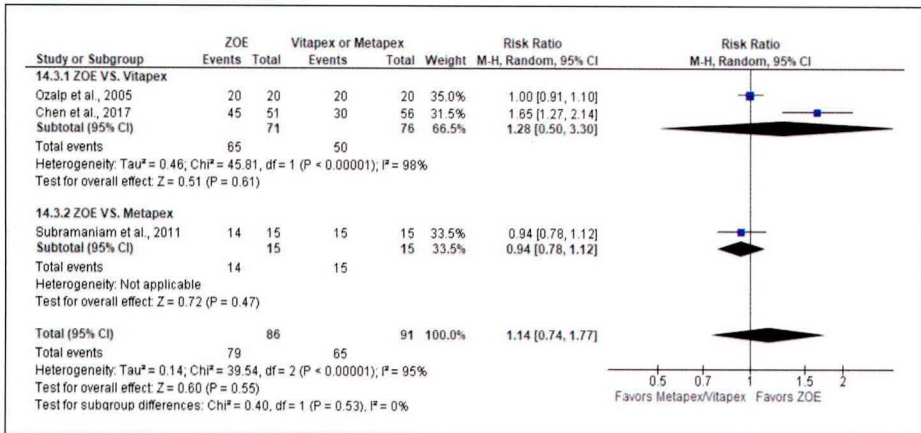


Figure 2. Zinc oxide eugenol (ZOE) versus iodoform (Metapex/Vitapex) pulpectomy at 18 months.\*

M-H, Mantel-Haenszel; CI, confidence interval.

\* Risk difference=0.09 (95% confidence interval=-0.22 to 0.40); number needed to treat=12.

**Appendix, sFigure 4b).** The quality of the evidence for this result was very low at 12 months, according to GRADE, due to the high ROB, serious imprecision seen in the sample sizes in each arm, and very serious heterogeneity observed in the  $I^2$  statistic. The sensitivity analysis removed the high ROB article<sup>31</sup> and showed no difference between these fillers. ZOE/iodoform/CH success was 94 percent, and ZOE success was 82 percent (RR equals 1.26; 95% CI equals 0.57 to 2.77). The quality of the evidence for this result was very low at 12 months, according to GRADE, due to the very serious heterogeneity seen in the  $I^2$  statistic and serious imprecision in the sample size. Based on the 12-month follow-up, this finding was judged as less important.

Two articles<sup>15,31</sup> compared ZOE pulpectomy success to ZOE/iodoform/CH at 18 months. The ZOE/iodoform/CH success rate was 93 percent compared to 89 percent for ZOE. The meta-analysis showed no significant difference between the ZOE/iodoform/CH and ZOE success rates, and the NNT equals 34 (RR equals 1.03; 95% CI equals 0.93 to 1.15; Figure 3, **Supplemental Electronic Appendix, sFigure 4c**). The quality of the evidence for this result was low at 18 months, according to GRADE, due to the high ROB and serious imprecision seen in the sample sizes in each arm. Based on the 18-month follow-up, this finding was judged as important.

**ZOE/iodoform/CH versus iodoform success (six, 12, 18 months).** Four articles compared ZOE/iodoform/CH pulpectomy success to iodoform success at six months.<sup>12,15,30,31</sup> The ZOE/iodoform/CH success rate was 94 percent compared to 92 percent for iodoforms. The meta-analysis showed no significant difference between the success rates (RR equals 1.05; 95% CI equals 0.99 to 1.12; **Supplemental Electronic Appendix, sFigure 5a**). The quality of the evidence for this result was moderate at six months, according to GRADE, due to the high ROB. Based on the six-month follow-up, this finding was judged as much less important.

Three articles compared ZOE/iodoform/CH pulpectomy success to iodoform success at 12 months.<sup>12,15,31</sup> The ZOE/iodoform/CH success rate was 95 percent compared to 70 percent for iodoforms. The meta-analysis showed no significant difference between the success rates (RR equals 1.19; 95% CI equals 0.76 to 1.84; **Supplemental Electronic Appendix, sFigure 5b**). The quality of the evidence for this result was very low at 12 months, according to GRADE, due to the high ROB, serious imprecision seen in the sample sizes in each arm, and very serious heterogeneity in the  $I^2$  statistic. Based on the 12-month follow-up, this finding was judged as less important.

Two articles compared ZOE/iodoform/CH pulpectomy success to iodoform success at 18 months.<sup>15,31</sup> The ZOE/iodoform/CH success rate was 93 percent compared to 63 percent for iodoforms. The meta-analysis showed no significant difference between the success

rates (RR equals 1.27; 95% CI equals 0.58 to 2.75; Figure 4, **Supplemental Electronic Appendix, Figure 5c**). The quality of the evidence for this result was very low at 18 months, according to GRADE, due to the high ROB, serious imprecision seen in the sample sizes in each arm, and very serious heterogeneity in the  $I^2$  statistic. The nonsignificant NNT equals seven, meaning after doing seven pulpectomies with iodoform one failure may have been prevented using ZOE/iodoform/CH. Based on the 18-month follow-up, this finding was judged as important.

**ZOE versus calcium hydroxide success (six, 12, 18 months).** When ZOE pulpectomy success was compared to CH success in studies that did not include iodoform with the CH, there were four articles with six-month follow-ups.<sup>25,27-29</sup> The ZOE success rate was 92 percent compared to 82 percent for CH. The meta-analysis showed no significant difference between the ZOE and CH success rates (RR equals 1.09; 95% CI equals 0.93 to 1.29; **Supplemental Electronic Appendix, sFigure 6a**). The sensitivity analysis removed the high ROB article<sup>29</sup> and showed no difference between these fillers. ZOE success was 90 percent, and CH success was 81 percent (RR equals 1.08; 95% CI equals 0.85 to 1.37). The quality of the evidence for this result was very low, according to GRADE, due to the very serious heterogeneity in the  $I^2$  statistic and high ROB. Based on the six-month follow-up, this finding was judged as much less important.

Two articles<sup>27,29</sup> compared ZOE pulpectomy success to CH at 12 months. The ZOE success rate was 99 percent compared to a CH success rate of 74 percent. The meta-analysis showed no significant difference between the ZOE and CH (Calcicur

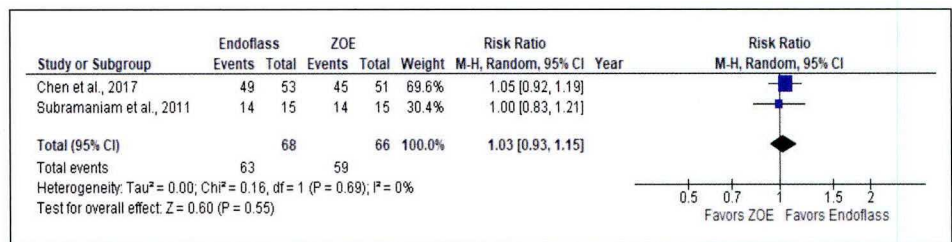


Figure 3. Zinc oxide eugenol (ZOE) versus iodoform (Metapex/Vitapex) pulpectomy at 18 months.\*  
M-H, Mantel- Haenszel; CI, confidence interval.

\* Risk difference=0.03 (95% confidence interval=-0.07 to 0.13); number needed to treat=34.

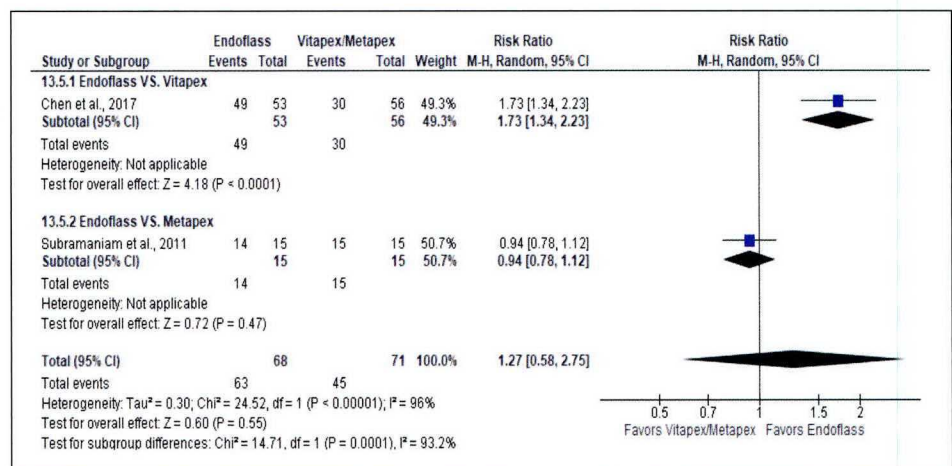


Figure 4. Endoflass (Zinc oxide eugenol/iodoform/calcium hydroxide) versus iodoforms ((Metapex/ Vitapex) at 18 months.\*

M-H, Mantel- Haenszel; CI, confidence interval.

\* Risk difference=0.16 (95% confidence interval=-0.33 to 0.65); number needed to treat=7.

and Apexit Plus) success rates (RR equals 1.26; 95% CI equals 0.95 to 1.67; **Supplemental Electronic Appendix, sFigure 6b**). The sensitivity analysis was conducted using the other CH brand of the Ozalap<sup>29</sup> study, (Apexit Plus and Sealapex) and the result was statistically different (RR equals 1.36; 95% CI equals 1.19 to 1.57). The NNT was four, meaning after 12 months one failure would be prevented using ZOE pulpectomy instead of CH. The quality of the evidence for this result was low at 12 months, according to GRADE, due to the high ROB and serious imprecision in the sample sizes. Based on the 12-month length of follow-up, this finding was judged as less important.

Only one article at 18 months compared ZOE to CH.<sup>29</sup> The article had different arms of CH comparing ZOE pulpectomy success to the different types of CH for 18 months. No meta-analysis was calculated since only one study was available.

**ZOE/iodoform/CH success versus calcium hydroxide success (six, 12, 18 months).** When the ZOE/iodoform/CH pulpectomy success was compared to CH success, there was only one article.<sup>29</sup> The article had different arms of CH comparing ZOE/iodoform/CH pulpectomy success to the different types of CH for six, 12, and 18 months. The authors could make no valid calculations using these pulpectomy success rates.

**Network analysis.** The objective of a network meta-analysis is to combine both the direct and indirect evidence across all studies. The network meta-analysis also ranks the effectiveness of the studied interventions.

The 12-month RCT direct comparisons of ZOE versus iodoform, ZOE versus ZOE/iodoform/CH, and ZOE/iodoform/CH versus iodoform cited previously in meta-analyses were used for network analysis. Since ZOE/iodoform/CH was not able to be compared to CH, and the sensitivity analysis of ZOE versus CH at 12 months showed that ZOE was significantly better (RR equals 1.36; 95% CI equals 1.19 to 1.57), CH was not included in the network analysis. The 12-month network analysis of pulpectomy filler success ranked ZOE/iodoform/CH as best; ZOE was second, and iodoform was the worst ranking (see **Supplemental Electronic Appendix, sFigure 7a**). The 12-month direct comparisons of ZOE/iodoform/CH versus ZOE showed a nonsignificant 17 percent

better success rate of ZOE/iodoform/CH compared to ZOE (RR equals 1.17; 95% CI equals 0.81 to 1.69). The ZOE versus iodoform success at 12 months showed a nonsignificant four percent better success rate for ZOE versus iodoform (RR equals 1.04; 95% CI equals 0.89 to 1.22). ZOE/iodoform/CH versus iodoform showed a nonsignificant 19 percent better success rate of ZOE/iodoform/CH versus iodoform (RR equals 1.19; 95% CI equals 0.76 to 1.84).

The 18-month network analysis of pulpectomy filler success ranked ZOE/iodoform/CH as best; ZOE was second, and iodoform had the worst ranking (**Supplemental Electronic Appendix, sFigure 7b**). The ZOE/iodoform/CH and ZOE 18-month success rates of 93 percent and 89 percent, respectively, showed no significant difference between them (RR equals 1.03; 95% CI equals 0.93 to 1.15; Figure 3, **Supplemental Electronic Appendix, sFigure 4c**). Even though there was no statistical difference between the ZOE success of 92 percent compared to 71 percent for iodoform, ZOE was 14 percent better than iodoform at 18 months with an NNT of 12 (RR equals 1.14; 95% CI equals 0.74 to 1.77; Figure 2, **Supplemental Electronic Appendix, sFigure 3c**). Similarly, the ZOE/iodoform/CH success rate at 18 months was 93 percent compared to 63 percent for iodoforms (RR equals 1.27; 95% CI equals 0.58 to 2.75; Figure 4, **Supplemental Electronic Appendix, sFigure 5c**). Although no statistical significance was found, ZOE/iodoform/CH was 30 percent better than iodoform at 18 months with an NNT of seven. From this data, ZOE/iodoform/CH or ZOE appeared to maintain an 18-month success rate near or above 90 percent over time while iodoform success decreased to 71 percent or less.

ZOE and ZOE/iodoform/CH appear to be better choices for pulpectomy success at 18 months, based on direct comparisons and the network analysis.

**LSTR versus pulpectomy.** Seven articles<sup>11,16,26,38,39,40,54</sup> compared LSTR to various types of pulpectomy success at 12 months. One study's<sup>54</sup> success data were based only on the rate of root resorption versus a contralateral tooth; therefore, it was not possible to determine the success of LSTR or pulpectomy and it was not used in the meta-analyses. The compound 3-Mix

is a combination of three antibiotics (metronidazole, minocycline, and ciprofloxacin)<sup>16</sup> placed in the pulp chamber after filing or not filing the canals in four LSTR studies,<sup>11,38,39,40</sup> while the other three studies<sup>16,26,54</sup> used other 3-Mix antibiotic combinations that excluded a tetracycline. Iodoform type pulpectomy was used in at least one arm of four studies,<sup>11,16,26,39</sup> while three studies used ZOE at least in one arm.<sup>26,38,40</sup>

For teeth with no external and internal root resorption,<sup>26,39,40</sup> the LSTR success rate was 65 percent compared to the pulpectomy success rate of 92 percent. The meta-analysis showed a nonsignificant difference between the LSTR and pulpectomy success rates favoring pulpectomy (RR equals 0.77; 95% CI equals 0.56 to 1.05). The NNT equals five, meaning after 12 months one failure may be prevented after every five teeth using pulpectomy instead of LSTR (Figure 5, **Supplemental Electronic**

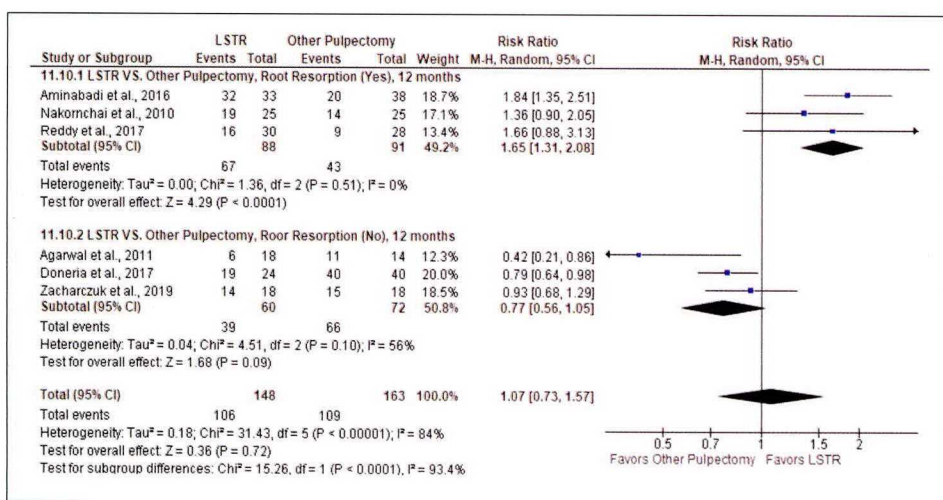


Figure 5. Lesion sterilization tissue repair (LSTR) versus pulpectomy at 12 months (with or without root root resorption).\*

M-H, Mantel- Haenszel; CI, confidence interval.

\* Root resorption (yes) at 12 months: risk difference=0.31 (95% confidence interval=0.13 to 0.48); number needed to treat=4. Root resorption (no) at 12 months: risk difference=-0.22 (95% confidence interval equals -0.41 to -0.03); number needed to treat=5.

**Appendix, sFigure 8a).** The quality of the evidence for this result was low at 12 months, according to GRADE, due to serious imprecision seen in the sample sizes and serious heterogeneity seen in the  $I^2$  statistic. Based on the 12-month follow-up, this finding was judged as less important.

For teeth with external and internal root resorption,<sup>11,16,38</sup> the LSTR success rate was 76 percent compared to the pulpectomy success rate of 47 percent. The meta-analysis showed a significant difference between the LSTR and pulpectomy success rates, with LSTR favored (RR equals 1.65; 95% CI equals 1.31 to 2.08). The NNT was four, meaning one failure would be prevented after every four teeth using LSTR instead of pulpectomy in teeth with root resorption. The 12-month data on LSTR versus pulpectomy showed that, if the roots were resorbed, LSTR had a better chance of success to save the tooth for up to 12 months (Figure 5, **Supplemental Electronic Appendix, Figure 8a**). The quality of the evidence for this result was moderate at 12 months, according to GRADE, due to the serious imprecision seen in the sample sizes. Based on the 12-month follow-up, this finding was judged as less important.

Qualitative data from Trairatvorakul<sup>59</sup> and Jaya<sup>57</sup> showed that the 24-month LSTR success was 37 percent; both are prospective studies. Grewal et al.'s study<sup>54</sup> is a 36-month RCT; they found that LSTR treatment harmed the eruption of the permanent tooth by causing interradicular bone loss, which in one case was associated with an odontogenic keratocyst. It seems LSTR should be used only to save primary molars for up to 12 months to maintain space and then be monitored closely for signs of failure at least every 12 months.

**LSTR success for 3Mix LSTR with tetracycline versus LSTR without a tetracycline.** This study's authors investigated the 12-month data of success from RCT studies comparing 3Mix with minocycline<sup>11,38-40,55-57,59,60</sup> to alternate antibiotic mixtures,<sup>16,26,56,61,62</sup> where a tetracycline was not included. There was statistically significant less success (56 percent) using 3-Mix with a tetracycline compared to 76 percent for 3-Mix without tetracycline ( $P=0.03$ ; **Supplemental Electronic Appendix, sFigure 9a**). The quality of the evidence for this result was very low at 12 months, according to GRADE, due to the very serious heterogeneity seen in the  $I^2$  statistic, and very serious indirectness due to the indirect comparison. There was also in vitro evidence on this finding. Rafatjou<sup>63</sup> found that the combination of clindamycin, metronidazole, and ciprofloxacin was as effective as the combination of minocycline, metronidazole, and ciprofloxacin, with no significant difference in reducing mean bacterial colony counts.

**LSTR success at 12 months with canals filed and/or broached versus not filed and/or broached.** There were 11 quantitative and qualitative studies of LSTR treatment with 12-month results where the canals were not filed or broached before placing the antibiotic paste.<sup>11,16,39,40,55-57,59-62</sup> There were four RCT articles on LSTR where the canals were filed and/or broached before the triple antibiotic paste was placed.<sup>26,38,55,61</sup> There was 72 percent success when the canals were filed and/or broached before the antibiotic paste was placed versus 62 percent success when the canals were not filed or broached before the antibiotic paste was placed. Cleaning the canals before LSTR treatment had a higher success rate, although it was not statistically different ( $P=0.29$ ) from not cleaning when doing LSTR treatment (see **Supplemental Electronic Appendix, sFigure 9b**). The quality of the evidence for this result was very low at 12 months, according to GRADE, due to the serious

heterogeneity seen in the  $I^2$  statistic and very serious indirectness due to the indirect comparison.

**Twenty-four-month and longer success follow-up: ZOE, iodoform, ZOE/iodoform/CH, calcium hydroxide, LSTR.** There were 24-month prospective and retrospective nonrandomized data on pulpectomy success for ZOE.<sup>24,64</sup> One study<sup>65</sup> used CH, and another used ZOE/iodoform/CH.<sup>66</sup> Only the Moskowitz<sup>66</sup> study had sufficient numbers of treated teeth showing ZOE/iodoform/CH success in 234 out of 242 teeth (96.7 percent).

LSTR 24-month success was achieved in 83 out of 154 teeth (53.9 percent) based on data from Jaya<sup>57</sup> (13 out of 30), Trairatvorakul<sup>59</sup> (22 out of 60), and Kargul<sup>67</sup> (48 out of 64). One study not included in this time frame<sup>68</sup> defined success as "mean function time"; the data for this study could not be evaluated for overall success like the remaining studies.

**Secondary outcomes: speed of canal preparation—manual versus rotary canal preparation time.** Six articles<sup>13,69-73</sup> compared manual files to rotary filing time of primary tooth root canals in vivo. There was one article<sup>13</sup> with two types of rotary file arms (ProTaper and K3 rotary), which are listed separately. The meta-analysis showed a significant difference favoring rotary filing that was approximately two minutes faster than manual (MD equals -126; 95% CI equals -167 to -85;  $P<0.0001$ ; **Supplemental Electronic Appendix, sFigure 10a**). The quality of the evidence for this result was high, according to GRADE. Although heterogeneity was seen in the  $I^2$  statistic, this was only due to faster rotary canal preparation versus manual preparation.

Only one study<sup>71</sup> compared pulpectomy success after manual versus rotary filing, with no significant difference observed after 24 months ( $P=0.78$ ). One other study<sup>27</sup> reported 12-month success, with no significant difference in rotary versus manual observed ( $P=0.80$ ). An antibacterial observational study by Subramaniam<sup>31</sup> demonstrated that manual versus rotary canal preparation showed no difference in bacterial reduction.

**Manual versus rotary adequacy of fill outcome: optimum (flush) filling to the apex.** The same six articles<sup>13,69-73</sup> compared manual to rotary files for optimal or flush filling to the root's apex of primary tooth root canals in vivo. The meta-analysis showed no statistical difference but favored rotary files achieving more flush apical fills (RR equals 1.32; 95% CI equals 0.98 to 1.79). Although there was no statistical difference, the use of rotary had 32 percent more flush fills than those using manual filing (NNT equals six). This NNT indicates that, after doing six pulpectomies with manual filing, one more flush apical fill may have occurred using rotary compared to manual (see **Supplemental Electronic Appendix, sFigure 10b**). The quality of the evidence for this result was moderate, according to GRADE, due to serious heterogeneity seen in the  $I^2$  statistic.

**Quality of pulpectomy fills using different methods of obturation.** Data from nine articles were used in a forest plot comparing the occurrence of pulpectomy flush fills done with lentulo spiral<sup>128,29,43,45,70,71,74-76</sup>; five used hand pluggers,<sup>13,31,41,76</sup> and nine used syringes.<sup>25,29,31,33,69,72,75,77,78</sup> Using a lentulo spiral resulted in 63 percent flush fills versus 48 percent with a hand plugger and 62 percent with a syringe (see **Supplemental Electronic Appendix, sFigure 11a**). There was no significant difference ( $P=0.13$ ) for the three methods of obturation achieving pulpectomy flush fills. This is a very low quality of evidence due to serious inconsistency in the  $I^2$  statistic and indirectness of evidence.



**Obturation method and pulpectomy success.** The 12-month success of pulpectomy done with lentulo spiral,<sup>9,12,15,27,29,32,37,43,49,50,58,65,79</sup> hand pluggers,<sup>24,31,39,40,51,80</sup> and syringe<sup>9,12,15,26,29,31,78</sup> were compared in a forest plot. As seen in the **Supplemental Electronic Appendix, sFigure 11b**, using a lentulo spiral resulted in 91 percent success versus 87 percent using hand pluggers and 87 percent with a syringe. There was no significant difference in the three methods of obturation achieving success ( $P=0.66$ ). The evidence consists of indirect comparisons from various types of study designs (RCTs and observational studies) and different follow-up times. This is a very low quality of evidence due to the very serious heterogeneity in the  $I^2$  statistic and indirect comparisons of evidence.

Five RCT studies directly compared pulpectomy success using lentulo spiral versus syringe fills after 12-months of follow-up.<sup>9,12,15,26,29</sup> The success rates were 91 percent for lentulo spiral versus 75 percent for syringes. The meta-analysis showed no significant difference in these two success rates (RR equals 1.16; 95% CI equals 0.91 to 1.49; **Supplemental Electronic Appendix, sFigure 11c**). This is a very low quality of evidence due to the high ROB in some studies and very serious inconsistency in the  $I^2$  statistic. Based on the 12-month follow-up, this finding was judged as less important.

The overfilling of the canals appears to be related to a lower success for pulpectomy. The data from various RCT and retrospective studies<sup>42,46,64,65,82</sup> show that overfilling the root canals in primary teeth tended to result in lowered success, especially for ZOE pulpectomies. All obturation techniques (hand plugger, lentulo spiral, Navi tip) produce voids when evaluated in vitro, and some techniques may cause more overfills (lentulo spiral) than others.<sup>83</sup> There were not enough clinical studies to evaluate these effects.

**Type of tooth (molar versus incisor) pulpectomy success.** Ten studies reported the success rate of the particular primary tooth treated with pulpectomy and the follow-up time. Three were RCTs<sup>43,45,84</sup> with a 12- to 36-month follow-up, and seven were retrospective observational studies with follow-ups ranging from six to over 91 months.<sup>24,46,47,82,85,86,87</sup> sTable 2 in the Supplemental Electronic Appendix lists the teeth treated, reason for treatment, and follow-up time for these studies. For teeth treated due to caries that were followed for at least 12 months, incisor success was observed in 144 out of 166 teeth (87 percent) and molar success was shown in 138 out of 155 teeth (89 percent). Success rates for first molars versus second molars were nearly the same (51 out of 56, 91 percent versus 69 out of 77, 90 percent, respectively).

The data in the Supplemental Electronic Appendix, sTable 2 indicates that tooth type does not appear to affect the success rates of primary incisor pulpectomies versus molar pulpectomies after 12 months. Incisor success was achieved in 144 out of 166 teeth (87 percent) if treatment was due to caries versus molar success observed in 138 out of 155 teeth (89 percent). No statistical comparison could be made, and the evidence consists of indirect comparisons from various types of study designs and follow-ups. No GRADE assessment of the quality of this evidence is possible.

**Pulpectomy success after incisor trauma versus caries.** Ten studies assessed the success of primary incisor pulpectomy after trauma and caries.<sup>24,43,45-47,82,84-87</sup> Three were RCTs,<sup>43,45,84</sup> and five were observational.<sup>47,46,82,85,86</sup> From sTable 2 in the Supplemental Electronic Appendix, the success rate of pulpotomy for traumatized anterior teeth after a minimum of 12

months was 77 percent (122 out of 159 teeth) versus 87 percent (144 out of 165) for incisors treated due to caries.

From this data, primary incisor pulpectomy success rates do not appear to be strikingly different if the tooth is treated due to trauma or caries after 12 months. However, two studies<sup>46,85</sup> found that traumatized incisors with a preoperative radiolucency and/or root resorption decreased pulpectomy success. No statistical comparison could be made, and the evidence consists of indirect comparisons from various types of study designs and follow-ups. No GRADE assessment of the quality of this evidence is possible. From one RCT study,<sup>47</sup> trauma did not decrease the success of an incisor pulpectomy unless the incisor was retraumatized. In that case, pulpectomy success decreased significantly to 41 percent ( $P=0.003$ ).

**Smear layer removal.** The smear layer is an accumulation of dentin and pulpal debris formed on the inside surface of the root canal during instrumentation for a pulpectomy.<sup>45</sup> Removing this smear layer may disinfect the canal walls and allow for a better adaptation of root canal filling materials. Not removing the smear layer may seal the dentinal tubules on the interior of the root canals and minimize bacterial penetration.

The effect of smear layer removal in primary teeth was evaluated in two RCTs.<sup>45,84</sup> They could not be evaluated statistically since one was a 24-month study<sup>45</sup> and the other a 36-month study.<sup>84</sup> Using a per-protocol recalculation of the data, the 24-month study showed a smear layer removal pulpectomy success rate of 94 percent (31 out of 33) and without its removal 82 percent (28 out of 34;  $P=0.26$ ). The 36-month study showed a smear layer removal pulpectomy success rate of 82 percent (14 out of 17) and without its removal 88 percent (15 out of 17;  $P=0.99$ ). Smear layer removal for pulpectomy in primary teeth does not seem to alter its success.

**Adverse effects of NVT: pulpectomy filler resorption.** There was qualitative data on filler resorption.<sup>9,32,86,88</sup> Apparently, ZOE resorbs slower than the primary tooth root in some cases. This may cause the permanent tooth's path of eruption to be deflected and result in anterior crossbite for incisors.<sup>86</sup> The iodoform fillers seemed to resorb at a faster rate than the root, resulting in the pulpectomy looking more like a pulpotomy after 12 to 18 months.<sup>9,15,32</sup> If filler is extruded beyond the apex, all iodoform fillers seem to resorb,<sup>9,32,33,38</sup> but ZOE resorbs slowly and can take years to resorb.<sup>15,32,88</sup> Teeth filled with ZOE for the pulpectomy had all or part of the filler retained in 138 out of 448 teeth (31 percent), based on data gathered from RCTs and NRSs.<sup>9,28,32,33,38,46,58,65,82,84,86,88,90</sup>

**Adverse effects of NVT: exfoliation NVT.** In the LSTR studies, Trairatvorakul<sup>32</sup> reported that six out of eight teeth exhibited abnormal exfoliation after a two-year follow-up. Grewal et al.'s study<sup>34</sup> was the longest LSTR follow-up of 36 months. It showed that LSTR-treated teeth did not resorb versus untreated contralateral teeth. Among studies on pulpectomy including RCTs and NRSs, nine studies<sup>12,45,46,50,58,84,86,89,90</sup> showed that 76 out of 317 (24 percent) pulpectomy-treated teeth had early exfoliation and 29 out of 319 teeth (nine percent) were overretained compared to contralateral teeth.

**Adverse effects of NVT: problems from nonvital treatment in succedaneous teeth.** Only one of the LSTR studies<sup>91</sup> reported an enamel defect in one out of 71 succedaneous teeth (one percent). Qualitative data on pulpectomy in NRSs<sup>46,50,84,86,90</sup> appears to show the pulpectomy procedure did not cause enamel defects in the succedaneous tooth. One study reported that it was related to the child's age<sup>50</sup> (especially among those

younger than four years) when the tooth became infected; other studies felt that excessive preoperative root resorption<sup>86</sup> or trauma<sup>46</sup> caused the defect. One study<sup>50</sup> involving 103 succedaneous teeth found only seven out of 103 teeth (6.8 percent) having a small enamel defect.

Grewal et al.<sup>54</sup> reported that LSTR teeth followed up through 36 months were overretained compared to the conventional pulpectomy treatment group, and some LSTR teeth were associated with interradicular bone loss surrounding the crown of a permanent successor.

**Adverse effects of NVT: pain.** Postoperative pain after the first 24 to 48 hours was only associated with a failed nonvital treatment. Immediate postoperative pain in the first 24 hours was assessed for pulpectomy in three studies.<sup>81,92,93</sup> Two were RCTs<sup>81,92</sup> comparing postoperative pain between rotary versus manual instrumentation. The other study<sup>93</sup> was an RCT comparing postoperative pain between single visits and multiple visits. Taking the three studies together, regardless of the different variables, the authors categorized the results into no pain, mild pain, and moderate to severe pain in three time intervals: six, 12, and 24 hours posttreatment (see [Supplemental Electronic Appendix, sTable 3](#)). The results at 24 hours showed the following: children having no postoperative pain (80 percent; 208 out of 261); children with mild pain (12 percent; 31 out of 261); and children with moderate to severe pain (eight percent; 22 out of 261). Severe pain from the pulpectomy procedure did not appear to be a major occurrence after 24 hours. No LSTR studies reported quantitative data on immediate postoperative pain.

**Outcome moderators/factors.** Different outcome moderators were analyzed to determine if they altered the success of the nonvital treatment. The number of visits to complete a pulpectomy, method of root length determination, type of irrigation, timing of final restoration, and method of tooth isolation were all evaluated to determine if they affected success.

**Number of visits.** Nineteen RCT studies<sup>11,12,26,27,31,32,37-40,55-58,59,60-62,79</sup> treated the teeth with a one-visit pulpectomy. Five other RCT studies<sup>15,38,41,42,45</sup> treated the teeth with a two-visit pulpectomy. The effect of whether a one- or two-visit pulpectomy altered success was tested with meta-analyses. For the one-visit group, the pooled success was 74 percent compared to 81 percent for the two-visit group. The two methods were not significantly different from the line of no effect for the pooled success confidence intervals ( $P=0.42$ ). The quality of the evidence for this finding was very low due to the very serious inconsistency in the  $I^2$  statistic and the indirect comparison (see [Supplemental Electronic Appendix, sFigure 12a](#)).

Qualitative data from Triches<sup>94</sup> showed significant reductions ( $P<0.05$ ) in the mean number of bacteria species after a single session of chemomechanical preparation in vivo. Another article<sup>95</sup> found that one percent chlorhexidine and a one percent metronidazole gel were ineffective for primary tooth pulpectomy in eliminating aerobic and facultative anaerobes from visit one to visit two.

**Root length determination method.** Only three RCT studies<sup>12,32,79</sup> used apex locator as the root canal length determination method; 13 other RCT studies<sup>9,11,15,16,27,29,31,39,40,41,42,44,45</sup> used radiographs for root length determination. The effect of whether the method of root length determination altered success was tested with meta-analyses. For the studies that used an apex locator, the pooled success was 79 percent compared to 86 percent for those that used radiographs. The two methods were not significantly different from the line of no effect for

the pooled success confidence intervals ( $P=0.28$ ). The quality of the evidence for this finding was very low due to the very serious inconsistency in the  $I^2$  statistic and indirect comparison (see [Supplemental Electronic Appendix, sFigure 13a](#)).

One study<sup>96</sup> of single-rooted primary anterior teeth used an apex locator, radiographs, and the tactile feel of the apex in the mouth to the actual length of the tooth after it was extracted; this article did not evaluate pulpectomy success. Of the 22 teeth without root resorption, the apex locator's and radiographs' mean length deviation from the actual mean length of 15.0 mm was insignificant while the tactile feel method was 1.0 mm shorter in the same teeth. In 29 teeth with apical root resorption, the mean lengths for tactile feel, radiographs, and apex locator were 0.1 mm shorter than the actual length. Three NRSs<sup>46,52,90</sup> used tactile feel for their primary tooth pulpectomies. Two of these studies<sup>52,90</sup> had success data that could be computed for 21 months on primary molars showing 513 out of 531 (96.6 percent) pulpectomy success. These same two studies had data for 46 months on primary incisor and molar pulpectomies, indicating success with 485 out of 517 teeth (93.8 percent). Apparently, using tactile feel for root length determination achieved high long-term pulpectomy success.

**Irrigation methods.** Table 4 in the Supplemental Electronic Appendix summarizes the effect the irrigation using water/saline, sodium hypochlorite, and chlorhexidine on pulpectomy success after 12 months. The data came from a mixture of RCTs and NRSs with different pulpectomy fillers and methods. The articles could not be appropriately grouped to conduct direct comparisons of the irrigation methods. Therefore, the authors are presenting the overall success of the three irrigation solutions. From the water/saline group,<sup>12,40,41,45,64,78,82,89</sup> the success of the pulpectomies was 341 out of 421 (81 percent). In the sodium hypochlorite group,<sup>15,24,26,27,31,32,39,42,44,46,51,52,65,71,79,84,85,87,90,98,99</sup> the success of the pulpectomies was 1,370 out of 1,538 (89 percent). For the chlorhexidine group,<sup>9,27,78</sup> the success of the pulpectomies was 162 out of 186 (87 percent).

Three studies<sup>15,32,79</sup> only used sodium hypochlorite (NaOCL) as the canal irrigation method. Three other studies<sup>12,31,42</sup> used NaOCL and either saline or distilled water during the canal preparation or as the final irrigation solution. The effect of whether these two direct comparisons of irrigation altered success was tested with meta-analyses. For the studies that used NaOCL only, the pooled success was 80 percent compared to 81 percent for the studies that used NaOCL plus saline and/or distilled water. The difference between the groups was not significant ( $P=0.99$ ), demonstrating that the confidence intervals overlapped the line of no effect comparing the irrigation solutions. The quality of the evidence for this result was very low, according to GRADE, due to the serious heterogeneity in the  $I^2$  and the indirectness of the comparisons (see [Supplemental Electronic Appendix, sFigure 14a](#)).

**Type and timing of the final restoration.** Fifteen studies documented teeth treated with a stainless steel crown.<sup>9,11,12,26,27,31,39,40,42,56,59,60,61,78,79</sup> Five other studies documented teeth treated with a filling (composite or amalgam).<sup>29,41,43,44,55</sup> The effect of whether the type of restoration altered success was tested with meta-analyses. For the steel crown group, the 12-month pooled success was 80 percent compared to 90 percent for the filling group. The difference between the groups was not significant ( $P=0.13$ ) from the line of no effect for the pooled success confidence intervals. The quality of the evidence for this result was very low, according to GRADE, due to the very serious heterogeneity in the  $I^2$  and indirect comparison (see [Supplemental](#)

**Electronic Appendix, sFigure 15a).** There were four NRSs with 24-month data on the type of restoration and success using a steel crown<sup>52,64,89,97</sup> and two articles describing the use of composite.<sup>84,85</sup> These articles were a mixture of RCT and observational studies. They showed that the steel crown success rate was 90 percent and the composite success rate was 77 percent after 24 months.

Twelve studies documented the placement of final restorations on the teeth on the same day as the pulpectomy,<sup>9,11,12,26,27,29,32,41,55,56,78,79</sup> and 10 studies related treating the teeth at a later date.<sup>15,31,37,39,40,42,45,60-62</sup> When treated on the same day, the pooled success after 12 months was 82 percent versus 83 percent for the restoration at a later date. The difference between the groups was not significant ( $P=0.87$ ) from the line of no effect for the pooled success confidence intervals. The quality of the evidence for this result was very low, according to GRADE, due to the very serious heterogeneity in the  $I^2$  and indirect comparison (see **Supplemental Electronic Appendix, sFigure 15b**).

**Tooth isolation (rubber dam).** All but five studies used a rubber dam. The five that did not use a rubber dam did not have usable data to evaluate.

**Criteria for teeth having irreversible pulpitis or pulp necrosis.** After reviewing RCT articles,<sup>9,12,15,25,29-32,36,38,41,42,79,98,100</sup> there was agreement that teeth with any of the following signs and symptoms had irreversible pulpitis and/or necrosis. Clinically: spontaneous pain, soft tissue swelling/pathology, abnormal mobility. Radiographically: furcation or periapical radiolucency, or pathologic root resorption.

Aminabadi<sup>16</sup> studied 108 infected and 57 noninfected primary molars needing pulpotomy and pulpectomy and found a dark red blood color can be easily detected with the eye and indicates a tooth with irreversible pulpitis. Another study<sup>101</sup> showed children presenting with pain and decay on radiographs closer than one mm to the pulp had irreversible pulpal inflammation in the coronal and radicular pulp.

According to the American Academy of Pediatric Dentistry's (AAPD) Best Practices for Pulp Therapy for Primary and Immature Permanent Teeth,<sup>8</sup> a tooth planned for pulpotomy where the hemorrhage cannot be "controlled with a damp cotton pellet applied for several minutes" exhibits signs of irreversible pulpitis. There is no reference for this statement. A recent study<sup>102</sup> concluded that "controlling bleeding at the exposure site or canal orifices does not provide an accurate assessment of inflammation at the canal orifice and may be misleading for diagnosing vital pulp treatment in primary teeth with a carious pulp exposure." Therefore, if there is a pulp exposure in a primary tooth without pain and none of the signs or symptoms of irreversible pulpitis, the inability to control pulpal hemorrhage after a few minutes may not always be a reliable indicator of irreversible pulpitis.

**Restorability criteria of teeth considered for nonvital pulp treatment.** Teeth that were candidates for pulpectomy or LSTR were not considered for pulpectomy or LSTR if they had an inadequate crown or root structure and were not restorable. After reviewing RCT articles<sup>12,15,25,38,41,42,79,100</sup> on pulpectomy and LSTR,<sup>11,16,26,60,62,67</sup> all articles agreed that non-restorable teeth were not candidates for nonvital treatment and were extracted.

**In vitro antimicrobial data: calcium hydroxide and iodoform filler qualitative data.** An agar diffusion article<sup>103</sup> showed that CH had large zones of inhibition only when the concentration was 40 to 60 percent. Vitapex, which has 30 percent calcium hydroxide, had significantly smaller zones of

inhibition than any other medicament. Navit<sup>104</sup> tested ZOE/iodoform/CH, ZOE, and other iodoforms for zones of inhibition against different microbial mixtures. ZOE/iodoform/CH and ZOE were not significantly different but were significantly better than iodoforms. Hegde<sup>105</sup> used agar diffusion for six filler materials against different bacterial strains and found that ZOE was more effective than CH-containing pastes. It appears that the root canal fillers with CH concentrations less than 40 to 60 percent have less antimicrobial action in vitro than ZOE and ZOE/iodoform/CH.

**Root canal irrigation antimicrobial effect.** One systematic review<sup>106</sup> evaluated intracanal irrigants in primary teeth, and seven studies met the review's inclusion criteria. They also found five studies comparing two percent chlorhexidine to saline but could not perform a meta-analysis due to differences in the methods or heterogeneity problems. The systematic review found two other studies that compared a mixture of tetracycline isomer, an acid, and a detergent, (MTDA) and oxidative water to NaOCl. There was no difference between the different irrigation solutions. Therefore, from this article<sup>106</sup> and the meta-analysis (see **Supplemental Electronic Appendix, sFigure 14a**) it appears that NaOCl or other antimicrobial agents are effective intracanal irrigation solutions.

**Characteristics of studies and ROB tables (see Supplemental Electronic Appendix, sTables 5, 6, and 7).** Table 5 lists the characteristics of studies for the 114 articles included for qualitative and quantitative analysis. Table 6 lists all the RCT articles with ROB assessments, and Table 7 lists all the NRS ROB assessments.

## Discussion

The primary motivation for this systematic review and meta-analysis was to assess the overall success of NVT in primary teeth and determine which factors may influence this success. The results showed varied success rates and levels of evidence. Although the the present study's authors looked at articles with at least six months of follow-up, this discussion will be focused on the longer follow-up times, since GRADE assessment at 18 months was rated as important. ZOE, iodoform, and ZOE/iodoform/CH were the only fillers with 18-month overall success results ranging from 93 percent (ZOE/iodoform/CH), 91 percent (ZOE), and 71 percent (iodoform). The CH (Calcicur and Apexit Plus) success of 74 percent was for 12 months and was significantly less success than ZOE. An interesting observation was seen when iodoforms were used as the filler material. As more time elapsed, the success rate went down. Their success at six months was 92 percent and at 12 months was 90 percent; but at 18 months, it was only 71 percent. A possible explanation for this is that both the CH and iodoform present in iodoform resorb over time,<sup>9,32</sup> resulting in loss of the antimicrobial properties (mainly high pH) and reinfection of the root canal system. On the other hand, since ZOE/iodoform/CH and ZOE remain in the canals and have been shown to have antimicrobial properties,<sup>32,104,105</sup> the success rates remain stable over time. Similarly, the in vitro antimicrobial studies<sup>103-105</sup> showed that ZOE had greater antimicrobial properties than calcium hydroxide pastes. The clinical results for ZOE/iodoform/CH in comparison to ZOE were also very similar. With data for 18 months, the 93 percent success of ZOE/iodoform/CH was not statistically different compared to the 89 percent success of ZOE (Figure 3). The 18-month network analysis showed ZOE/iodoform/CH to be the best choice, ZOE second, and iodoforms the worst choice based on success rates.

LSTR is a recent addition to the treatment options for non-vital pulp therapy. This study's results showed that, when teeth presented with preoperative internal/external root resorption, LSTR had a success rate of 76 percent after 12 months compared to a success rate of only 47 percent when a traditional pulpectomy was done. These results were statistically significant, although the quality of evidence was very low. On the other hand, when LSTR was used to treat teeth without preoperative internal or external root resorption, LSTR had a success rate of only 65 percent after 12 months compared to 92 percent success for traditional pulpectomy procedures. This difference was not statistically significant ( $P=0.09$ ) but had an NNT of five. The present study's qualitative results also showed that, beyond 12 months, success rates for teeth treated with LSTR having preoperative root resorption decreased dramatically to only 37 percent over 24 months.<sup>57,59</sup> Long-term LSTR treatment could result in permanent tooth damage, as described by Grewal et al.<sup>54</sup> They found over 36 months that significant bone loss not only could harm the eruption of the permanent tooth but could also influence the formation of cysts. These findings may suggest that bacterial colonization of root canals initiates internal resorption by activating macrophages and osteoclasts.<sup>107</sup> The high concentration of antibiotic in LSTR may give a temporary reduction in bacterial load, minimizing the progression of inflammatory root resorption. However, once the antimicrobial effect is reduced, recolonization occurs, osteoclast/macrophage activity resumes, and failures are seen at an accelerated rate. From this, the present study's authors can recommend using LSTR if maintenance in the developing arch is needed for function and/or space for 12 months followed by closely monitoring the LSTR-treated tooth with regular radiographs at least every 12 months.

The results of the present study's study's meta-analyses, comparing the use of lentulo spiral, hand pluggers, and syringes for pulpectomy obturation, showed no significant difference in the quality of fill, as determined by the percentage of flush apical fills. They also did not show any significant difference in the pulpectomy success rates for these three obturation methods (see **Supplemental Electronic Appendix, sFigure 11a and b**). Therefore, the dentist can choose the obturation method based on their clinical preference. The data comparing tooth type (incisor versus first or second molar) could not be evaluated statistically. It indicated that all teeth had comparable pulpectomy success when treated due to caries. Incisors treated due to trauma had a slightly lower pulpectomy success (77 percent) than if treated due to caries (87 percent), but this difference may have been due to repeated trauma reducing the pulpectomy's success (see **Supplemental Electronic Appendix, sTable 2**).

The outcome moderator comparisons were made to assess what factors other than filling material may impact the success of nonvital pulp treatments. The present study's authors found success of a pulpectomy was unaffected by the type of irrigation used, number of visits taken to complete the treatment, method of root length determination, and timing or type of final restoration (see **Supplemental Electronic Appendix, sFigure 12a, 13a, 14a, and 15a and b**).

Another area showing a significant difference was the speed with which a pulpectomy was completed. The use of a rotary instrument to prepare the root canals resulted in a completion time that was approximately two minutes faster than when manual instrumentation was used (see **Supplemental Electronic Appendix, sFigure 10a**). This was an expected

finding; if a practitioner believes saving time is critical, the use of a rotary file is supported.

The qualitative data on pulpectomy filler resorption<sup>9,32,88</sup> showed that ZOE tended to resorb slower than the primary tooth root. The iodoform pulpectomy fillers resorbed at a faster rate than the root so they could appear to look like a pulpectomy after 12 to 18 months.<sup>9,15,32</sup> The data on iodoform filler extruded beyond the apex indicates that it resorbs<sup>9,32,33,38</sup>; however, ZOE resorbs more slowly<sup>15,32,88</sup> and may be retained after exfoliation.<sup>9,28,32,33,38,46,58,65,82,84,86,88,90</sup> Qualitative data on ZOE/iodoform/CH indicates it resorbs at the same rate as the tooth's root.<sup>36,37</sup>

Results obtained from this systematic review showed that pulpectomy and LSTR procedures do not appear to cause enamel defects in the succedaneous tooth compared to untreated controls. Only one LSTR study<sup>91</sup> reported on the enamel defects of succedaneous teeth (one percent). Qualitative data on pulpectomy succedaneous enamel defects<sup>46,50,84,86,90</sup> appear to show the pulpectomy procedure did not cause enamel defects. Instead, this was related to the age of the patient, according to Stallaert.<sup>50</sup> A child younger than four years of age when the primary molar was treated is more vulnerable to the occurrence of enamel defects, possibly because the premolar is still forming. Coll<sup>86</sup> speculated that preoperative root resorption or trauma was the cause if an incisor was treated.<sup>46</sup>

**Results in context with previous studies.** The current review was more extensive than previously published systematic reviews for the treatment of nonvital primary teeth due to caries and trauma. The last Cochrane review published in 2018<sup>17</sup> had limitations compared to the present review. It did not include the LSTR studies, as the present paper did. Since LSTR treatment for nonvital primary teeth has been an alternative method since 2004, its omission as a treatment alternative and whether it is better than conventional pulpectomy is a shortcoming of their systematic review. The current review found 10 randomized controlled studies<sup>11,16,26,38-40,56,57,61,62</sup> comparing LSTR to pulpectomy success from six to 12 months. The present paper gives clear reasons for LSTR's success with teeth having resorbed and nonresorbed roots.

A second limitation to the 2018 systematic review<sup>17</sup> was the non-inclusion of some studies published before that paper's August 2017 review. The present review found a ZOE versus iodoform study published in 2003<sup>33</sup> that was not included. Also, the authors found two studies comparing ZOE/iodoform/CH to ZOE published in 2010<sup>30</sup> and 2016<sup>12</sup> that were missing. The missing data from the Cochrane report does not fairly judge these nonvital treatments. Lastly, the Cochrane report did not attempt to standardize the success and failure criteria, since authors from the original studies did not always classify success and failure similarly. When necessary, the present review recomputed the data from papers so that all the data represented common success and failure criteria.

A recent systematic review published in 2019<sup>18</sup> only evaluated the success ZOE compared to calcium hydroxide with iodoform in primary teeth. The present study's authors found nearly all of the same articles included in their meta-analyses. This study's results differ from their results, which can be attributed to several factors. First, the present study used risk ratios rather than odds ratios. Odds ratios, when used for common occurrences, like high success rates, will overestimate the real difference. Risk ratios are more appropriate. Second, the authors included multiple arms of studies in their forest plots, which is appropriate for a sensitivity analysis. However,

they used one arm of a study in a forest plot twice to compare its effect to two other arms. Therefore, if one inspects the Najjar article<sup>18</sup> on radiographic pulpectomy success at 18 months, it reveals that ZOE was significantly better than iodoform pastes. The present study's data shows ZOE was 14 percent better but not statistically better (RR equals 1.14; 95% CI equals 0.74 to 1.77). The reason for the difference seems to be that Najjar et al. counted the Chen 2017<sup>15</sup> data on iodoform success (30 out of 56) twice in the same forest plot, which significantly lowered its success. The authors agree with their conclusion that ZOE tends to give higher success at 18 months compared to iodoform.

**Strengths and weaknesses.** One of the strengths of the current paper was that, for the included RCT articles, the authors followed the Cochrane Handbook for Systemic Reviews of Interventions.<sup>21</sup> Additionally, the authors reviewed all titles, abstracts, full text, and data extractions in duplicate and assessed the quality of the evidence using GRADE, where possible.

Another strength was this study's inclusion of nonrandomized controlled trials and cohort studies, case-control studies, and case series. The authors assessed these studies' ROB using the OHAT<sup>22</sup> ROB tool. Their data can be used in the qualitative evidence section to help determine the long-term success of nonvital treatments and the effect of certain modifiers and *in vitro* results on pulpectomy.

A third strength was recalculating, if necessary, success/failure results using the present study's standardized success rules. This allowed all studies to be compared with one another, knowing all successes and failures were assessed the same. The Cochrane 2018<sup>17</sup> study used each author's assessment of success and failure rather than using one standardized method. In addition, the authors had workgroup members who could translate Chinese and Spanish articles so the authors could include more data from other sources.

A weakness was the present study's authors were unable to do a funnel plot to assess publication bias due to having less than 10 studies in any forest plot. However, many studies reported no significant difference in success for their nonvital results which the authors felt implied little publication bias.

Another perceived weakness was that the authors combined data from high, moderate, and low ROB because of the lack of sufficient trials in each ROB group for comparison but especially of low bias. However, for the meta-analyses, the ROB for the RCTs were usually of low or moderate bias, raising their credibility.

A third weakness was the exclusion of some pulpectomy fillers like calcium hydroxide and polyethylene glycol-based paste<sup>108</sup> from direct comparison analyses and the network analyses. This was due to the unique nature of these reports preventing the authors from comparing them to more traditional pulpectomy methods and fillers.

**Implications for practice.** These results suggest that filler material and amount of root resorption are the most important factors to consider when planning nonvital pulp therapy on a primary tooth. For 12 to 18 months, pulpectomies completed on teeth with no pathologic root resorption and filled with ZOE/iodoform/CH and ZOE were more likely to be successful than pulpectomies filled with any of the iodoform- or calcium hydroxide-based filler materials (see [Supplemental Electronic Appendix, Figures 3c, 4c, 5c, and 6b](#)). On the other hand, teeth with pathologic external or internal root resorption did not perform well when traditional pulpectomies were done. LSTR can be considered when preservation of the tooth for 12

months or less is important due to dental age or other factors at the time of treatment. For example, if the practitioner wishes to avoid the extraction of a primary second molar with root resorption before the six-year molar is present, LSTR may be offered as an alternative. LSTR may save the tooth for 12 months or possibly longer based on the moderate quality of evidence at 12 months, according to GRADE (Figure 5; [Supplemental Electronic Appendix, sFigure 8a](#)).

Another of this study's objectives was to determine if specific moderators/factors affected NVT success. The present study's authors could not find any moderators or secondary factors—including the type of irrigants, number of appointments taken to treat a tooth, method of root length determination, smear layer removal, and final restoration type or timing—that had any impact on the success of pulpectomies in the primary dentition. The results of this systematic review and meta-analysis will inform a revised AAPD Guideline for Pulp Therapy for Primary Teeth that will now be evidence-based.

**Implications for research.** For nonvital primary tooth pulp treatment, there are various criteria used to grade success. One consistent set of standards cited by every author would help future systematic reviewers make apple-to-apple comparisons. In the authors' opinion, a furcation radiolucency should decrease after six months or resolve and be determined a success for any nonvital pulp treatment. A static radiolucency means the infection is still present but just not causing clinical symptoms and should be a nonvital treatment failure.

Authors should ensure that their flow diagrams match their results and data in their tables. Also, reviewers should insist that their data matches so that future systematic reviewers can extract valid data for comparison. Flow diagrams should be made mandatory for publication by journals, and those diagrams should match the PRISMA flow diagram.

## Conclusions

Based on this study's results, the following conclusions can be made:

1. For nonvital teeth, pulpectomy is recommended for long-term success (greater than 24 months) in teeth when there is no root resorption present.
2. For long-term pulpectomy success (greater than 18 months), zinc oxide eugenol/iodoform/calcium hydroxide or ZOE fillers perform better than iodoform fillers.
3. Based on 12-month results, CH without iodoform pulpectomy fillers had lower success rates than ZOE.
4. Based on 12-month results, pulpectomy is preferred over lesion sterilization tissue repair in nonvital teeth with no root resorption.
5. LSTR is preferred over pulpectomy in nonvital teeth with root resorption when a tooth needs to be maintained in the arch for 12 months or less.
6. Rotary instrumentation decreases instrumentation time by approximately two minutes and tends to result in more flush fills.
7. The obturation method, number of treatment visits, method of root length determination, irrigation solutions, smear layer removal, or the timing/type of the final restoration do not impact the success rate of pulpectomies.
8. The type of tooth treated (molar versus incisor) does not influence the success rate of a pulpectomy.

9. The success rate of pulpectomies on anterior teeth is not impacted by trauma or caries.
10. Resorption of ZOE is slower than root resorption for iodoform and ZOE/iodoform/CH fillers.
11. Following a pulpectomy, severe to moderate post-operative pain is a rare occurrence.

### Acknowledgments

The authors wish to acknowledge Laurel Graham, MLS for her help in the initial literature search, Haider Alshami, BDS, Misr for performing the second literature search for this systematic review, and Nancy (Suzi) Seale Coll DDS, MSD who helped begin and participated in this research before her untimely death in 2018.

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