

## REVIEW ARTICLE

# Outcome of Contemporary Nonsurgical Endodontic Retreatment: A Systematic Review of Randomized Controlled Trials and Cohort Studies

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## ABSTRACT

**Introduction:** The success rates of NS-ReTx have varied across decades of prior research. Nonetheless, recent endodontic advances have substantially enhanced case management. This systematic review aimed to identify rigorous studies on contemporary NS-ReTx, investigating both periapical healing—evaluated strictly for complete resolution or loosely for size reduction of periapical radiolucency—and success, denoting clinical normalcy combined with periapical healing. **Methods:** We systematically searched MEDLINE, Embase, Web of Science, the Cochrane Library, and gray literature from January 1988 to December 2022. Article selection and data extraction were independently conducted by 3 reviewers. Selected studies underwent risk of bias assessment, and evidence quality using the Grading of Recommendations, Assessment, Development, and Evaluation approach. Meta-analysis and meta-regression established pooled outcome rates, 95% confidence intervals (CIs), and significant clinical prognostic factors ( $P < .05$ ). **Results:** Twenty-nine articles were included. Pooled periapical healing rates using strict and loose criteria were 78.8% (95% CI: 75.2-82.4) and 87.5% (95% CI: 83.8-91.2), respectively. Pooled success rates using strict and loose criteria were 78.0% (95% CI: 74.9-81.2) and 86.4% (95% CI: 82.6-90.1), respectively. Meta-regression analyses revealed significant influences on NS-ReTx outcomes ( $P < .05$ ), including periapical status, lesion size, apical root filling extent, and follow-up duration. **Conclusions:** Contemporary NS-ReTx shows encouraging outcomes, achieving periapical healing and success rates ranging from approximately 78% (strict criteria) to 87% (loose criteria). The absence of or smaller preoperative lesions, adequate root filling length, and extended follow-ups significantly improve NS-ReTx outcomes. Integrating these factors into treatment planning is pivotal for optimizing the outcome of NS-ReTx. (*J Endod* 2024; ■:1–20.)

Despite the reported success rates of 78% to 91% for primary endodontic treatment<sup>1-8</sup>, failures can still occur. In addressing these failures, 3 main treatment options emerge: nonsurgical retreatment (NS-ReTx), surgical endodontics, or tooth extraction. To guide the decision-making process among these treatments, it is crucial to assess their benefits and risks based on studies with robust evidence, methodologies, and designs<sup>9,10</sup>.

Focusing specifically on NS-ReTx, earlier systematic reviews<sup>11-13</sup> have reported varying favorable outcome rates, ranging from 28% to 100%. However, these reviews spanned several decades, introducing variability and potentially reflecting outdated practices that do not align with the contemporary state of endodontics. In the current landscape, endodontics has evolved with recent advancements in tools and technologies. Innovations such as nickel-titanium rotary instruments, electromotors, apex locators, digital radiography, cone-beam computed tomography (CBCT), and microscopes represent the cutting edge of endodontic practice. This modern toolkit significantly enhances the management of challenging cases, signaling a departure from traditional methods and showcasing the integration of state-of-the-art equipment and techniques in the field of endodontics<sup>14</sup>.

## SIGNIFICANCE

This systematic review investigated contemporary non-surgical endodontic retreatment studies, uncovering positive outcomes characterized by high rates of periapical healing and success. Factors such as smaller or absent preoperative lesions, adequate root filling length, and extended follow-ups were found to significantly enhance outcomes. Incorporating these considerations into treatment planning can optimize endodontic retreatment.

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To bridge the knowledge gap between prior systematic reviews and current endodontic practices, this systematic review rigorously investigates studies with meticulous methodologies on contemporary NS-ReTx. It aims to address the focused research question: What outcomes and prognostic factors are associated with contemporary NS-ReTx? The significance of obtaining a comprehensive understanding of prognostic outcomes in NS-ReTx cannot be overstated, as it is pivotal for making informed treatment choices. The cornerstone of evidence-based decision-making lies in the critical reliance on high-quality studies. Hence, the overarching objective is to empower clinicians to make well-informed treatment decisions, thereby contributing to enhanced long-term outcomes in the management of failed root canal treatments.

## METHODS

The systematic review was registered in PROSPERO (CRD42020211825), and it strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist. The eligibility criteria for study inclusion were as follows.

- Population:** Previously endodontically treated permanent teeth in need of NS-ReTx.
- Intervention:** NS-ReTx.
- Comparison:** None.
- Outcome:** The following outcomes were either reported in the included studies or could be derived from the available raw data:
  - Periapical healing was assessed via radiographic evaluations, using either

strict criteria for complete resolution or loose criteria for size reduction of periapical radiolucency.

- Success required the simultaneous fulfillment of both clinical normalcy and periapical healing (strict or loose criteria).
- Study design:** Randomized controlled clinical trials and cohort studies conducted from 1988 onwards, with sample size  $\geq 30$ , and follow up  $\geq 2$  years were included. In cases of varying follow-up durations, the average follow-up period needed to be  $\geq 2$  years. When studies provided stratified data for different follow-up periods, data specifically related to follow-ups of  $\geq 2$  years were extracted for analysis.

Studies on primary dentition, irrelevant designs, animal/microbiological studies, *ex-vivo/in vitro* studies, case reports, and review articles were excluded.

### Search Methods for the Identification of Studies

Two reviewers (M.S., Y.C.) collaborated with a librarian to search Medline (PubMed), Embase, Web of Science, and the Cochrane Library using specified search terms or equivalent Medical Subject Heading (MeSH) terms (Supplementary Table 1). The search period ranged from January 1988 (after the introduction of nickel titanium rotary instruments) to December 2022, focusing on English studies available through local holdings. Ongoing and completed trials registered in the World Health Organization International Clinical Trials Registry Platform and [ClinicalTrials.gov](http://ClinicalTrials.gov), unpublished studies from sources like ProQuest and Google Scholar (limited to the first 100 hits), and the Open Grey database were included. Relevant information was manually searched in three key endodontic textbooks<sup>15-17</sup>. The references of included studies were cross-checked for completeness, and bibliographic software (Endnote X9, Thomson Reuters, New York) was utilized to manage the identified articles, removing duplicates.

### Screening and Data Extraction

Three independent reviewers (M.S., Y.C., and N.A.) initially screened titles and abstracts. Calibration was ensured through joint evaluation of the first 20 articles. Subsequently, the selected articles were independently assessed, and data extraction was performed (Supplementary Table 2). Disagreements were resolved through discussion and consulting a fourth reviewer (A.A.), who also verified the accuracy of data extraction. Reasons for exclusion at the full-text stage were recorded in Supplementary Table 3.

### Risk of Bias Assessment

Three reviewers (M.S., Y.C., and N.A.) rated the risk of bias. Randomized controlled trials (RCTs) were assessed using the Cochrane risk of bias tool (RoB 2)<sup>18</sup> across 5 domains as presented in Table 1. A classification of "low risk" was assigned if all domains were judged as having a low bias risk; "some concerns" if any domain had concerns; and "high risk" if any domain had a high bias risk. Cohort studies were examined using the Newcastle Ottawa Scale<sup>19</sup> across three domains as presented in Table 1. Scores of 7-9, 5-6, and  $<5$  were deemed "low", "some concerns", and "high risk", respectively. Disagreements were resolved by consulting a fourth reviewer (A.A.). Studies with a high risk of bias were excluded.

### Quality of Evidence

The quality of evidence was assessed using the five domains of Grading of Recommendations, Assessment, Development and Evaluation framework<sup>20</sup>, as presented in Table 2. Each domain was assessed for no concerns, minor concerns, or major concerns. Using this method, evidence quality was categorized as high, moderate, low, or very low. Disagreements were resolved by consulting a fourth reviewer (A.A.).

### Quantitative Analyses

Statistical analysis utilized Stata version 11 (StataCorp., College Station, TX, USA). Heterogeneity, measured by the  $I^2$  index, was assessed using the Cochran Q test, with  $I^2 > 50\%$  indicating high heterogeneity. Separate meta-analyses were conducted for periapical healing and success. Random-effects models were used when high heterogeneity was present; otherwise, fixed-effect models were employed. Specifically, for the periapical healing meta-analysis, data were sourced from studies reporting this outcome exclusively or as a separate component within success studies. Furthermore, this approach encompassed success studies that provided aggregated results without detailing its individual components. This approach acknowledges the potential underestimation of periapical healing in such situations, considering that even if periapical healing was achieved, the absence of clinical normalcy would categorize the outcome as a failure due to the need for simultaneous fulfillment of both criteria.

Publication bias was examined using funnel plots and Egger's test. In the presence of publication bias, outcome rates were adjusted using the trim-and-fill method<sup>21</sup>. To investigate potential sources of statistical

Availability of data and material: Data tables are included in the manuscript.

Competing interests: No financial affiliation or involvement with any commercial organization with a direct financial interest in the subject or materials discussed in this manuscript, nor have any such arrangements existed in the past three years.

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**TABLE 1 - Risk of Bias Summary: Review Authors' Judgements About Each Risk of Bias Item for Each Included Study**

	D1	D2	D3	D4	D5	D6	D7	D8	D9	Overall
Randomized controlled trials using RoB2										
Karaoglan 2022						N/A	N/A	N/A	N/A	
Cohort studies using Newcastle-Ottawa Scale										
Azim 2016	0	1	1	1	0	1	1	1	6	
Caliskan 2005	0	1	1	0	1	1	1	1	6	
Chybowski 2018	1	0	1	1	1	1	1	1	7	
De Cheigny 2008	0	1	1	1	1	1	1	0	6	
Eyuboglu 2017	1	0	1	1	0	1	1	0	5	
Fu 2011	0	1	1	1	0	1	1	0	5	
Goldberg 2020	0	1	1	1	0	1	1	1	6	
Gorni/Gagliani 2004	0	1	1	1	1	1	1	1	7	
He 2017	0	1	1	1	1	1	1	1	7	
Hoskinson 2002	1	1	1	1	1	1	1	0	7	
Imura 2007	1	1	1	1	0	1	1	0	6	
Krupp 2013	0	0	1	1	0	1	1	1	5	
Lee 2022	0	0	1	1	1	1	1	0	5	
Li 2022	0	1	1	1	0	1	1	1	6	
Mareschi 2020	0	0	1	1	1	1	1	0	5	
Mente 2014	0	0	1	1	1	1	1	1	6	
Neskovic 2016	0	1	1	1	1	1	1	1	7	
Ng 2011	0	1	1	1	0	1	1	0	5	
Olcay 2019	0	1	1	1	0	1	1	0	5	
Ozer 2020	0	1	1	1	1	0	1	0	5	
Pirani 2018	0	1	1	0	0	1	1	1	5	
Pirani 2019	0	1	1	1	1	1	1	0	6	
Ricucci 2011	0	1	1	1	0	1	1	0	5	
Serefoglu 2021	0	1	1	1	0	1	1	1	6	
Signor 2021	0	0	1	1	1	1	1	0	5	
Stenhagen 2020	0	1	1	1	0	1	1	0	5	
Touboul 2014	0	1	1	1	0	1	1	0	5	
Zhang 2021	0	0	1	1	1	1	1	0	5	

Notes:

RoB domains for randomized controlled trials

D1: Bias arising from the randomization process

D2: Bias due to deviations from intended intervention

D3: Bias due to missing outcome data

D4: Bias in measurement of the outcome

D5: Bias in selection of the reported result

Newcastle-Ottawa Scale domains for cohort studies:

D1: Representativeness of the exposed cohort

D2: Selection of non-exposed cohort

D3: Ascertainment of exposure

D4: Demonstration that outcome of interest was not present at start of study

D5: Comparability of cohort on the basis of the design and analysis controlled for confounders

D6: Assessment of outcome

D7: Was follow-up long enough for outcome to occur

D8: Adequacy of follow-up

D9: Quality score

Judgement of risk

Unclear

Low

TABLE 2 - Quality of Evidence as per the Grading of Recommendations, Assessment, Development, and Evaluation Approach

Pooled outcome	Radiographic assessment	No. of studies	Study design	Certainty assessment				Effect		
				Inconsistency	Indirectness	Imprecision	Other considerations	No. of individuals	Pooled rate (95% CI)	Certainty
Periapical healing	Strict	28	RCT; Cohort	S	NS	NS	None	5,066	78.8% (75.2-82.4)	Moderate
Success	Loose	17	RCT; Cohort	S	NS	NS	None	3,002	87.5% (83.8-91.2)	Moderate
	Strict	25	RCT; Cohort	S	NS	NS	None	4,053	78.0% (74.9-81.2)	Moderate
	Loose	16	RCT; Cohort	S	NS	NS	None	2,892	86.4% (82.6-90.1)	Moderate

NS, not serious; S, serious.

heterogeneity among study characteristics (if reported in >2 studies), meta-regression models were employed.  $P < .05$  was considered statistically significant.

## RESULTS

### Results of the Search Process

Electronic searches identified 3,437 articles, supplemented by 34 articles from manual searches in textbooks and references. After deduplication, 1,853 articles underwent title and abstract screening, followed by full-text review of 105 articles. Ultimately, 29 articles were included in the review (Fig. 1). These studies were published between 2002 and 2022 in the following locations: Europe (United Kingdom, Italy, Norway, Serbia, Germany, and France) ( $n = 12$ )<sup>7,8,22-31</sup>, Turkey ( $n = 6$ )<sup>32-37</sup>, North America (United

States and Canada) ( $n = 5$ )<sup>38-42</sup>, South America (Brazil and Argentina) ( $n = 3$ )<sup>43-45</sup>, and Asia (China) ( $n = 3$ )<sup>46-48</sup>. The excluded studies at the full-text stage are listed in Supplementary Table 3.

### Metrological Characteristics of the Included Studies

The search identified one RCT<sup>34</sup>, 8 prospective cohort studies<sup>7,8,27,32,37,40,42,48</sup>, 18 retrospective cohort studies<sup>22-25,28-30,33,35,36,38,39,41,43-47</sup>, and 2 ambispective cohort studies<sup>26,31</sup>. Six studies had a low risk of bias, and 23 studies had some concerns (Table 1). The overall quality of evidence was moderate (Table 2). The characteristics of the included studies are presented in Table 3 and summarized below:

Sample sizes varied from 30 to 1314. In 25 studies, teeth were the unit of analysis,

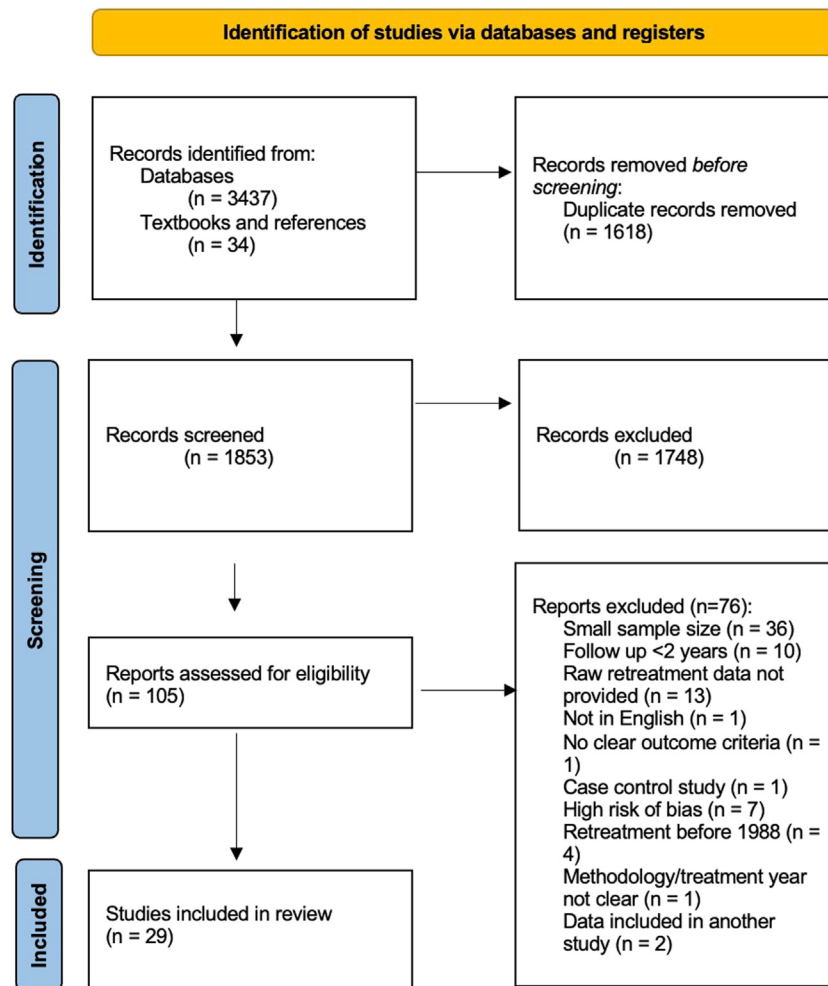


FIGURE 1 – The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for the study selection.

**TABLE 3 -** Characteristics of the Included Studies

Author year	Study design	Country	Operator	Sample size	Recall rate (%)	Assessment of outcome	Radiographic assessment criteria	Follow up (yrs)	Calibration	Reliability test	Statistical analysis
Azim et al. 2016	Retrospective	USA	DS	41 roots	N/A	C + R	S + L	2-4	—	—	Log. Reg.
Calışkan 2005	Prospective	Turkey	Sp	86 teeth	96	C + R	S + L	2-4	✓	✓	$\chi^2$
Chybowski et al. 2018	Retrospective	USA	Sp	72 teeth	N/A	C + R	S + L	2-4	✓	—	$\chi^2$
de Chevigny et al. 2008	Prospective	Canada	PG	229 teeth	41	C + R	S	$\geq 4$	✓	✓	$\chi^2$ , Fisher's exact, Log. Reg.
Eyuboglu et al. 2017	Retrospective	Turkey	Sp	110 teeth	47	C + R, R	S + L	2-4	✓	✓	Fisher's exact, Fisher-Freeman-Halton s, Log. Reg.
Fu et al. 2011	Retrospective	China	Sp	38 teeth	65	C + R	S	2-4	✓	—	$\chi^2$ , Fisher's exact, Log. Reg.
Goldberg et al. 2020	Retrospective	Argentina	Sp	77 teeth	N/A	R	S	$\geq 4$	✓	✓	Log. Reg.
Gorni & Gagliani 2004	Ambispective	Italy	Sp	452 teeth	94	C + R	S + L	2-4	✓	✓	Mann-Whitney U
He et al. 2017	Prospective	USA	PG	52 teeth	83	C + R, R	S + L	2-4	✓	—	Fisher's exact
Hoskinson et al 2002	Ambispective	UK	Sp	76 roots	42	C + R	S	$\geq 4$	—	✓	Log. Reg.
Imura et al. 2007	Retrospective	Brazil	Sp	624 teeth	N/A	C + R	S	$\geq 4$	—	—	$\chi^2$ , Fisher's exact, Log. Reg.
Karaoglan et al. 2022	RCT	Turkey	Sp	89 teeth	89	C + R	S + L	2-4	✓	✓	$\chi^2$ , Fisher's exact
Krupp et al. 2013	Retrospective	Germany	Sp	48 teeth	70	C + R	S	2-4	✓	✓	$\chi^2$ , Fisher's exact, student t
Lee et al. 2022	Retrospective	USA	N/A	165 teeth	45	C + R	S + L	$\geq 4$	✓	✓	$\chi^2$ , ANOVA
Li et al. 2022	Retrospective	China	Sp	44 teeth	N/A	C + R	S + L	2-4	—	—	Fisher's Exact
Mareschi et al. 2020	Retrospective	Italy	Sp	900 teeth	N/A	R	S	$\geq 4$	—	—	Log. Reg.
Mente et al. 2014	Ambispective	Germany	N/A	30 teeth	85	C + R	S	2-4	✓	✓	$\chi^2$ , Log. Reg.
Nesković et al. 2016	Prospective	Serbia	Sp	49 teeth	N/A	C + R, R	S + L	2-4	—	—	Mann-Whitney U
Ng et al. 2011	Prospective	UK	PG	1314 roots	67	C + R, R	S + L	$\geq 4$	✓	✓	Log. Reg.
Olçay et al. 2019	Retrospective	Turkey	Sp	101 teeth	43	C + R	S + L	2-4	✓	✓	$\chi^2$ , Fisher's exact, Fisher Freeman-Halton, Mann-Whitney U, Log. Reg.
Özer 2020	Retrospective	Turkey	Sp	83 teeth	63	C + R, R	S	$\geq 4$	—	✓	Holm-Sidak Multiple Comparative

(continued on next page)

TABLE 3 - Continued

Author year	Study design	Country	Operator	Sample size	Recall rate (%)	Assessment of outcome	Radiographic assessment criteria	Follow up (yrs)	Calibration	Reliability test	Statistical analysis
Pirani et al. 2018	Retrospective	Italy	PG	50 teeth	N/A	C + R	S	≥4	✓	—	Log. Reg.
Pirani et al. 2019	Retrospective	Italy	PG	55 teeth	39	C + R	S	≥4	✓	—	Log. Reg.
Ricucci et al. 2011	Prospective	Italy	GP	71 teeth; 114 roots	60	C + R	S + L	≥4	✓	—	Log. Reg.
Serifoglu et al. 2021	Prospective	Turkey	Sp	103 teeth	85	C + R, R	S + L	2-4	✓	✓	Log. rank
Signor et al. 2021	Retrospective	Brazil	PG	117 teeth	36	C + R	L	≥4	✓	✓	Fisher's exact, student's t-, Log. Reg.
Stenhagen et al. 2020	Retrospective	Norway	DS	36 teeth	14	R	S	≥4	✓	✓	χ <sup>2</sup> , Mann-Whitney U
Touboul et al. 2014	Ambispective	France	PG	108 teeth	38	C + R, R	S + L	2-4	✓	—	Fisher's exact
Zhang et al. 2021	Prospective	China	Sp	58 teeth	64	C + R, R	S + L	≥4	✓	✓	χ <sup>2</sup> , Fisher's exact, Log. Reg.

N/A, not available; RCT, randomized controlled trial; UK, United Kingdom; USA, United States of America; DS, dental student; GP, general dentist; PG, post-graduate resident; C + R, success (clinical and radiographic assessment); R, radiographic assessment only; S, Strict criteria for radiographic assessment; L, loose criteria for radiographic assessment; Log. Reg., logistic regression; χ<sup>2</sup>, Chi-square statistic. Notes: All studies had at least ≥2 radiographic assessors

whereas in 3 studies<sup>7,23,38</sup>, it was roots. One study<sup>8</sup> reported both teeth and roots as units of analysis.

NS-ReTx was performed by different operators: endodontists ( $n = 17$ )<sup>22-25,27,32-37,39,43,44,46-48</sup>, postgraduate endodontic residents ( $n = 7$ )<sup>7,28,29,31,40,42,45</sup>, dental students ( $n = 2$ )<sup>30,38</sup> and general dentists ( $n = 1$ )<sup>8</sup>. Two studies<sup>26,41</sup> did not report such information. None of the included studies compared the NS-ReTx outcome by qualification of operators.

The follow-up duration after treatment completion varied from 2 to 10 years. Nine studies had a follow-up of >4 years<sup>8,23,28-30,36,42,43,48</sup>, 16 studies had a follow-up of 2-4 years<sup>7,22,24,26,27,31,33-35,37-40,45-47</sup>, and one study had a follow-up of 3-5 years<sup>25</sup>. Three studies<sup>32,41,44</sup> reported success rates for both >4 years and 2-4 years of follow-up. The recall rates were reported in 21 studies<sup>7,8,22-24,26,29-37,40-42,45,46,48</sup> and ranged from 14% to 96%, with a median of 63%.

The determination of treatment outcome varied: 3 studies relied solely on radiographic examination ( $n = 3$ )<sup>25,30,43</sup>, and 26 studies considered both clinical normalcy and periapical healing for defining success. Among the 26 studies that reported success, 18 did not present findings on radiographic assessment separately<sup>8,22-24,26,28,29,32,34,35,38,39,41,42,44-47</sup>. In contrast, the remaining 8 studies<sup>7,27,31,33,36,37,40,48</sup> provided results for both clinical and radiographic assessments separately. For radiographic evaluations, 12 studies<sup>23-26,28-30,36,42-44,46</sup> exclusively applied strict criteria for complete resolution of periapical radiolucency, while a single study<sup>45</sup> solely utilized loose criteria for size reduction of periapical radiolucency. Additionally, 16 studies<sup>7,8,22,27,31-35,37-41,47,48</sup> reported findings based on both sets of criteria.

At least 2 observers performed the radiographic assessment in all studies. 22 studies<sup>7,8,22,24,26,28-35,37,39-43,45,46,48</sup> calibrated the observers and 17 studies<sup>7,22-24,26,30,32-37,41-43,45,48</sup> performed inter- or intra-reliability tests. Chi-square test, Fisher's exact test, Mann-Whitney U test, and t-test were used to assess prognostic factors. Eighteen studies also included multivariate analyses<sup>7,8,23,25,26,28,29,33,35,36,38,41-46,48</sup>.

**Preoperative Characteristics of the Included Studies**

The influence of the following preoperative clinical factors on the success of NS-ReTx was investigated: gender ( $n = 7$ )<sup>7,33,35,37,40,45,48</sup>, age ( $n = 7$ )<sup>33,35,37,40,44,45,48</sup>, health status ( $n = 1$ )<sup>45</sup>,



tooth type ( $n = 6$ )<sup>7,33,35,44,45,48</sup>, arch type ( $n = 5$ )<sup>7,33,35,40,45</sup>, periapical status ( $n = 12$ )<sup>7,8,22,27-29,33,35,40,42,44,45</sup>, lesion size ( $n = 9$ )<sup>7,8,32-35,37,40,48</sup>, preoperative mishaps [fractured instrument ( $n = 3$ )<sup>7,22,45</sup>, perforations ( $n = 5$ )<sup>7,22,35,42,45</sup>, canal obstruction ( $n = 2$ )<sup>7,22</sup>], preoperative root filling [apical extent ( $n = 4$ )<sup>33,34,37,45</sup>, quality ( $n = 7$ )<sup>7,22,33,35,37,42,45</sup>], time since initial treatment ( $n = 1$ )<sup>35</sup>, and different obturation material ( $n = 3$ )<sup>7,33,35</sup>.

The outcome of NS-ReTx was also measured without direct comparison for the following preoperative clinical factors: health status ( $n = 11$ )<sup>25,26,28,29,31,32,34,37,39,40,46</sup>, mandibular arch ( $n = 1$ )<sup>37</sup>, molars ( $n = 2$ )<sup>37,40</sup>, preoperative periapical lesion ( $n = 5$ )<sup>32,34,36,37,48</sup>, fractured instrument ( $n = 1$ )<sup>46</sup>, perforations ( $n = 2$ )<sup>24,26</sup>, and no canal obstructions ( $n = 2$ )<sup>34,37</sup>.

### Intraoperative/Postoperative Characteristics of the Included Studies

The influence of the following clinical factors on the outcome of NS-ReTx was investigated: canal preparation apical size and taper ( $n = 1$ )<sup>7</sup>, fractured instrument ( $n = 1$ )<sup>7</sup>, different concentration or type of irrigation ( $n = 2$ )<sup>7,23</sup>, gutta-percha versus resilon ( $n = 1$ )<sup>40</sup>, warm vertical versus lateral condensation ( $n = 1$ )<sup>7</sup>, root filling [apical extent ( $n = 7$ )<sup>7,8,33,35,37,45,48</sup>, quality ( $n = 4$ )<sup>35,42,45,48</sup>], single versus multiple visits ( $n = 4$ )<sup>7,34,42,45</sup>, and final restoration [types ( $n = 5$ )<sup>7,33,35,37,45</sup> and quality ( $n = 3$ )<sup>7,33,35</sup>].

The outcome of NS-ReTx was also measured without direct comparison for the following intraoperative/postoperative clinical factors: rubber dam isolation ( $n = 21$ )<sup>7,8,23-25,28-30,32,34-40,42,43,46-48</sup>, use of microscopes ( $n = 10$ )<sup>24,26,31,37,39,40,42,46-48</sup>, files [hand ( $n = 8$ )<sup>8,23,27,28,32,34,44,48</sup>, nickel-titanium rotary ( $n = 13$ )<sup>7,22,25,29,30,33,37-40,42,43,47</sup>, different tapers [ $\leq 0.06$  ( $n = 1$ )<sup>40</sup>,  $> 0.06$  ( $n = 3$ )<sup>35,36,48</sup>], apical size  $> 30$  ( $n = 7$ )<sup>7,33-35,40,44,47</sup>, different irrigation [sodium hypochlorite only ( $n = 7$ )<sup>8,22,24,32,38,44,47</sup>, adjunct chlorhexidine ( $n = 4$ )<sup>36,37,42,48</sup> or EDTA ( $n = 13$ )<sup>23,25,27-29,31,33-35,39,40,43,45</sup>], intracanal medicament [calcium hydroxide alone ( $n = 12$ )<sup>8,23,32,34-38,40,42,45,48</sup> or with adjunct chlorhexidine ( $n = 1$ )<sup>27</sup>], different types of obturation materials [gutta-percha and sealer ( $n = 22$ )<sup>7,8,22-25,27,30-39,42-44,47,48</sup>, chloroform to soften gutta-percha for obturation ( $n = 1$ )<sup>7</sup>], different types of sealer [resin-based ( $n = 11$ )<sup>24,28-30,32-37,48</sup>, zinc oxide-based ( $n = 4$ )<sup>7,22,23,31</sup>, calcium hydroxide-based ( $n = 1$ )<sup>27</sup>, bioceramic ( $n = 2$ )<sup>39,47</sup>], different types of obturation [lateral compaction

( $n = 9$ )<sup>8,27,30,32,34,36,38,43,44</sup>, warm vertical compaction ( $n = 7$ )<sup>22-25,31,40,48</sup>, single cone ( $n = 4$ )<sup>33,37,39,47</sup>, carrier-based ( $n = 2$ )<sup>28,29</sup>, mineral trioxide aggregate apical plug ( $n = 1$ )<sup>43</sup>, apical extent of root filling [adequate ( $n = 2$ )<sup>34,39</sup>, long ( $n = 1$ )<sup>43</sup>], number of visits [single ( $n = 4$ )<sup>33,39,43,45</sup>, multiple ( $n = 11$ )<sup>8,23,27,32,35-38,40,47,48</sup>], coronally restored with crown ( $n = 2$ )<sup>23,40</sup>, and quality of restoration ( $n = 4$ )<sup>37,39,40,43</sup>.

### Treatment Outcome

#### Periapical Healing

A total of 10 studies<sup>7,25,27,30,31,36,37,40,43,48</sup> and 7 studies<sup>7,27,31,33,37,40,48</sup> reported periapical healing using strict and loose radiographic criteria, respectively. Eighteen studies<sup>8,22-24,26,28,29,32-35,38,39,41,42,44,46,47</sup> and 10 studies<sup>8,22,32,34,35,38,39,41,45,47</sup> reported success based on clinical normalcy and periapical healing, employing strict and loose criteria, respectively. However, they did not present radiographic assessment separately. The reported range of periapical healing rates, based on strict criteria, was 64.1%<sup>37</sup> to 93.7%<sup>25</sup>, and using loose criteria, it ranged from 68.8%<sup>22</sup> to 96.4%<sup>33</sup>. In the pooled analysis, the periapical healing rate using strict criteria was 78.8% (95% CI: 75.2-82.4%), and using loose criteria, it was 87.5% (95% CI: 83.8-91.2%) (Fig. 2).

#### Success

A total of 25 studies<sup>7,8,22-24,26-29,31-42,44,46-48</sup> and 16 studies<sup>7,8,22,27,31,32,34,35,37-41,45,47,48</sup> reported clinical normalcy in combination with strict or loose periapical healing, respectively. The reported range of success rates, based on strict criteria, was 64.1%<sup>37</sup> to 90.9%<sup>33</sup>, and using loose criteria, it ranged from 68.8%<sup>22</sup> to 95.5%<sup>47</sup>. In the pooled analysis, the success rate using strict criteria was 78.0% (95% CI: 74.9-81.2%), and using loose criteria, it was 86.4% (95% CI: 82.6-90.1%) (Fig. 3).

### Clinical Prognostic Factors Affecting the Outcome of NS-ReTx

Table 4 presents pooled success rates for collected variables, and Table 5 outlines significant prognostic factors from meta-regression analysis. Four factors significantly influenced NS-ReTx outcomes.

#### Periapical Status

The pooled periapical healing rate was greater in cases without periapical lesions [12 studies; strict: 97.9% (95% CI: 94.6-99.8); loose: 95.7% (95% CI: 87.1-100.0)]<sup>7,8,22,27-29,33,35,40,42,44,45</sup> compared to those with preoperative lesions [17 studies; strict: 74.8% (95% CI: 69.2-80.4); loose: 84.0% (95% CI:

76.1-91.9)]<sup>7,8,22,27-29,32-37,40,42,44,45,48</sup> (Table 4).

Similarly, the pooled success rate was greater in cases without periapical lesions [12 studies; strict: 97.9% (95% CI: 94.6-99.8); loose: 95.7% (95% CI: 87.1-100.0)]<sup>7,8,22,27-29,33,35,40,42,44,45</sup> compared to those with preoperative lesions [17 studies; strict: 75.1% (95% CI: 69.2-80.5); loose: 84.6% (95% CI: 75.5-92.0)]<sup>7,8,22,27-29,32-37,40,42,44,45,48</sup> (Table 4).

This variable significantly influenced both outcomes using strict criteria ( $P < .05$ , Table 5).

#### Size of Periapical Lesion

Nine studies<sup>7,8,32-35,37,40,48</sup> investigated the outcomes of NS-ReTx for different periapical lesion sizes, categorized as  $\leq 5$  mm vs.  $> 5$  mm in PA and  $\leq 65$  mm<sup>3</sup> vs.  $> 65$  mm<sup>3</sup> in CBCT.

The pooled periapical healing rate was greater in cases with smaller periapical lesions [strict: 87.0% (95% CI: 77.3-94.5); loose: 92.9% (95% CI: 86.1-97.8)] compared to those with larger lesions [strict: 62.3% (95% CI: 56.8-67.6); loose: 86.7% (95% CI: 80.9-91.7)].

Similarly, the pooled success rate was greater in cases with smaller periapical lesions [strict: 87.0% (95% CI: 77.3-94.5); loose: 92.9% (95% CI: 86.1-97.8)] compared to those with larger lesions [strict: 62.3% (95% CI: 56.8-67.6); loose: 86.7% (95% CI: 80.9-91.7)].

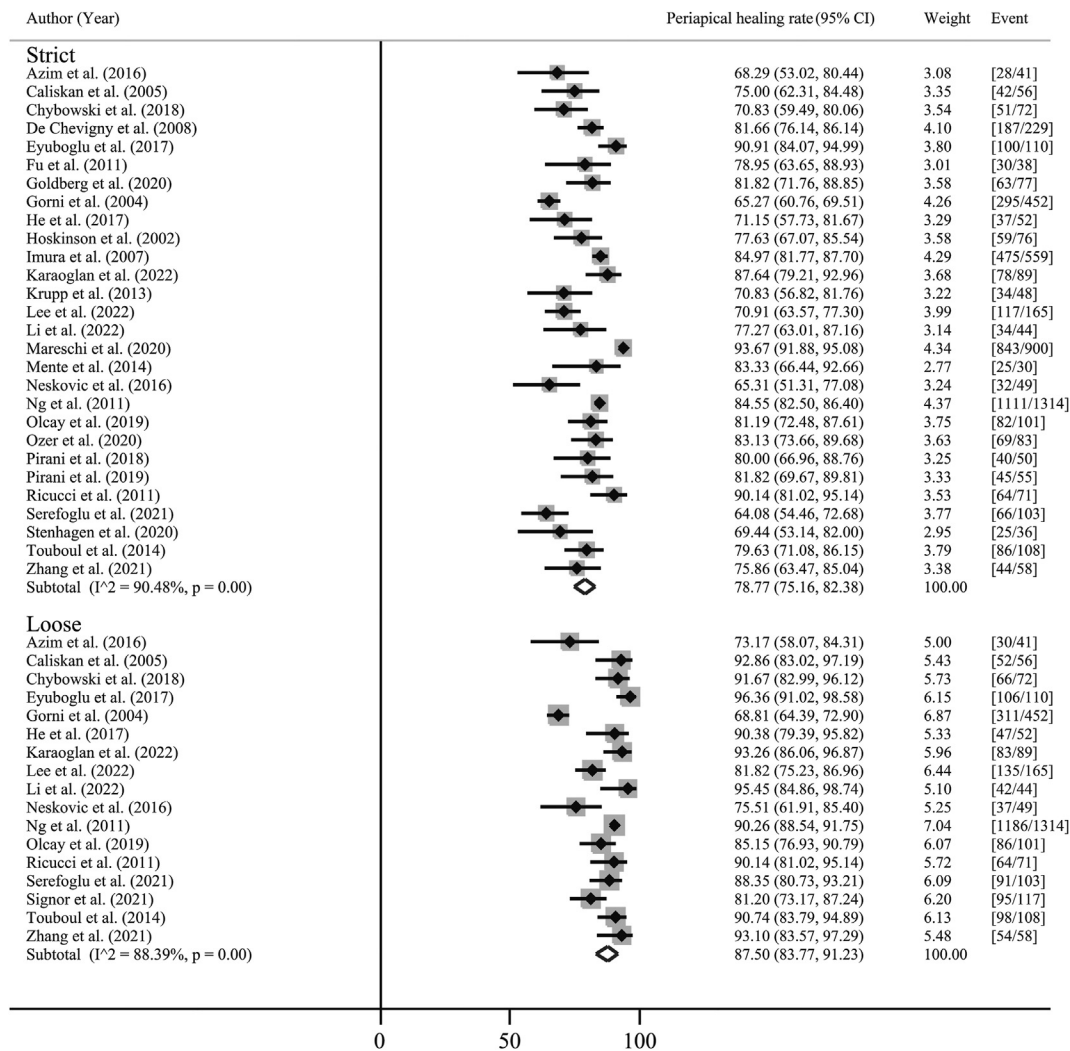
This variable significantly influenced both outcomes using strict criteria ( $P < .05$ , Table 5).

#### Apical Extent of Root Filling

The study categorized root filling length into three groups: short ( $> 2$  mm short of radiographic apex)<sup>7,8,33,35,37,45,48</sup>, adequate (0-2 mm of the radiographic apex)<sup>7,8,33-35,37,45,47,48</sup>, and long (extrusion)<sup>7,8,35,43,45,47,48</sup>.

The pooled periapical healing rates were comparable for adequate obturation [strict: 83.8% (95% CI: 77.4-89.3); loose: 89.2% (95% CI: 84.1-93.4)] and long obturation [strict: 78.0% (95% CI: 61.7-91.1); loose: 91.8% (95% CI: 76.5-100.0)], with reduced outcomes observed for short obturation [strict: 51.3% (95% CI: 27.2-75.2); loose: 72.2% (95% CI: 40.1-96.6)].

Similarly, the pooled success rates were comparable for adequate obturation [strict: 83.8% (95% CI: 77.4-89.3); loose: 89.2% (95% CI: 84.1-93.4)] and long obturation [strict: 77.2% (95% CI: 54.2-94.2); loose: 94.6% (95% CI: 70.4-100.0)], with reduced



**FIGURE 2** – Meta-analysis of studies reporting on the outcome of periapical healing.

outcomes observed for short obturation [strict: 51.3% (95% CI: 27.2-75.2); loose: 72.2% (95% CI: 40.1-96.6)].

A significant difference was noted between short and adequate obturation for both outcomes using strict criteria ( $P < .05$ , Table 5). Additionally, there was a statistically significant, although clinically small, difference between adequate and long obturation for periapical healing using loose criteria ( $P < .05$ , Table 5).

### Non-clinical Prognostic Factors Affecting the Outcome of NS-ReTx

The study also examined non-clinical factors influencing NS-ReTx outcomes and identified longer follow-up periods and more recent publication decades as contributors to improved results.

Specifically, cases with a follow-up period of  $\geq 4$  years showed greater periapical

healing rate [strict: 87.3% (95% CI: 82.3-91.6); loose: 89.7% (95% CI: 80.8-96.3)] compared to those followed up for 2-4 years [strict: 75.9% (95% CI: 72.3-81.0) loose: 83.1% (95% CI: 79.4-86.5)]. Similarly, cases with a follow-up period of  $\geq 4$  years showed greater success rates [strict: 84.6% (95% CI: 80.4-88.9); loose: 89.9% (95%CI: 82.6-97.3)] compared to those followed up for 2-4 years [strict: 75.4% (95% CI: 70.9-80.0); loose: 85.7% (95% CI: 81.6-89.8)]. This variable significantly influenced periapical healing using strict criteria ( $P < .05$ ) and success using loose criteria ( $P < .05$ ) (Table 5).

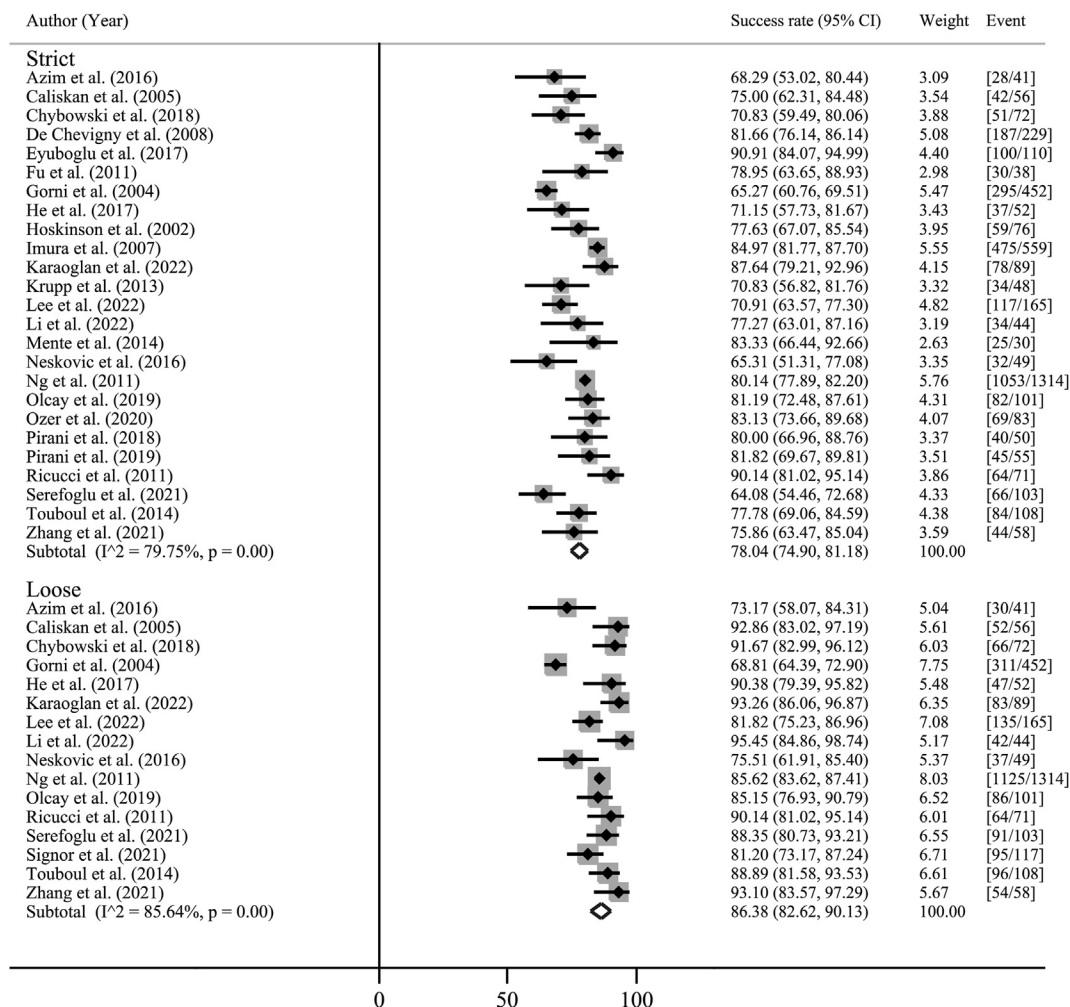
Additionally, studies published in the 2010s and 2020s demonstrated more favorable periapical healing rates [2010s; strict: 83.2% (95%CI: 81.5-84.8); loose: 90.3% (95%CI: 88.9-91.6)]; 2020s; strict: 87.8% (95% CI: 86.1-89.4); loose: 87.4% (95% CI: 84.5-90.0)] compared to those published in the 2000s [strict: 77.8% (95% CI:

75.5-80.0); loose: 59.8% (95% CI: 55.8-63.6)]. Similarly, studies published in the 2010s and 2020s showed greater success rates [2010s; strict: 79.4% (95% CI: 75.6-83.2); loose: 86.8% (95%CI: 83.7-89.8); 2020s; strict: 76.7% (95% CI: 69.2-84.1); loose: 89.0% (95% CI: 84.1-93.8)] compared to those published in the 2000s [strict: 77.0% (95% CI: 68.1-85.9); loose: 75.7% (95% CI: 72.1-79.3)]. The difference was statistically significant only for periapical healing using loose criteria ( $P < .05$ ) (Table 5).

### Publication Bias

Publication bias was assessed with Egger's test and the trim-and-fill method (Supplementary Table 4 and Fig. 4). A potential bias was noted for loose periapical healing only. Nevertheless, after applying the trim-and-fill adjustment, pooled rates remained similar.





**FIGURE 3** – Meta-analysis of studies reporting on the outcome of retreatment success.

## DISCUSSION

This systematic review analyzed 29 studies on contemporary NS-ReTx, providing a moderate overall evidence quality. The findings reveal favorable NS-ReTx outcomes, with periapical healing and success rates of about 78.8% and 78.0%, respectively, using strict criteria, and approximately 87.5% and 86.4%, respectively, using loose criteria. These results align with previous systematic reviews<sup>11,12,49</sup>. Ng et al.<sup>11</sup> in 2008 reported success rates of 76.4% (strict) and 82.7% (loose), while Torabinejad et al.<sup>49</sup> in 2009 reported a clinical and/or radiographic success rate of 78.0%. A systematic review in 2017<sup>12</sup> found retreatment outcomes between 84.1% and 88.6%, although it lacked specific assessment criteria and included both initial and NS-ReTx data without stratification. While our results align with previous reviews, we observed an increase in favorable

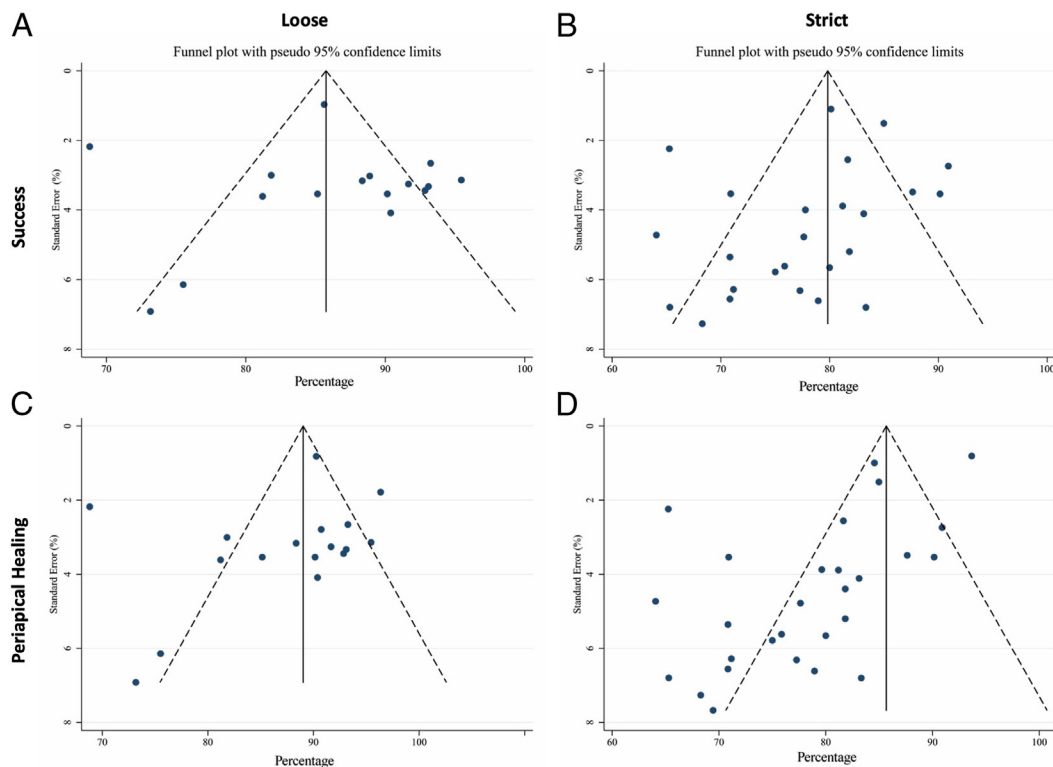
NS-ReTx outcomes spanning the 2000s, 2010s, and 2020s. This difference was statistically significant specifically for periapical healing using loose criteria. This improvement is likely due to technological advancements (e.g., imaging, instrumentation, obturation, and materials) and improved treatment protocols.

Our findings reveal that the presence of a preoperative periapical radiolucency can significantly diminish the rates of periapical healing and success, ranging from a decrease of 11% (loose criteria) to 23% (strict criteria). Ng et al.<sup>11</sup> also noted a significantly lower outcome (28%) for teeth with preoperative periapical lesions compared to those without. Previously treated teeth with persistent periapical lesions are more resistant to NS-ReTx<sup>50</sup>. Moreover, when a new coronal restoration is planned and existing root fillings are unsatisfactory, retreatment is commonly advised in cases without periapical lesions<sup>42</sup>. It

is worth noting that suboptimal root fillings in these cases may not necessarily indicate the presence of disease. Additionally, our results demonstrate that smaller preoperative lesions yield better treatment success and periapical healing, with differences of about 25% (strict criteria) and 6% (loose criteria). Conversely, larger lesions often indicate long-standing infections with challenging-to-remove biofilms, potentially making treatment more difficult<sup>51</sup>.

Our study emphasized the importance of the apical extent of root filling. Underfilled canals can harbor microbial biofilms in apical ramifications, hindering healing. Conversely, overextended fillings beyond the apex can trigger inflammation in periapical tissues via cytotoxic effects or immune responses<sup>7,52</sup>.

Healing of apical periodontitis is a slow process, involving immune responses and tissue remodeling<sup>53,54</sup>. Short-term observations may show signs of healing<sup>38</sup>, but a minimum follow-up of 3-4 years is



**FIGURE 4** – Funnel plot to assess publication bias in endodontic retreatment success (A) loose criteria; (B) strict criteria and periapical healing; (C) loose criteria; (D) strict criteria.

recommended for reliable assessment of treatment outcomes<sup>55-57</sup>. In fact, complete lesion resolution may take over a decade<sup>53,54</sup>. Our review highlights the importance of longer follow-up durations to assess periapical healing and subtle changes. We found that extending the follow-up duration from 2-4 years to over 4 years led to an increase in periapical healing by 6.6% (loose) to 11.4% (strict), and an improvement in success rates by 4.2% (loose) to 9.2% (strict). Long-term follow-up enables comprehensive evaluation of bone regeneration and lesion resolution, emphasizing the relevance of loose criteria as an outcome measure.

This systematic review has several potential limitations.

1. Including only English articles could have excluded relevant studies in other languages.
2. Including studies that focused on the history of previous NS-ReTx<sup>32</sup>, mishaps such as perforations<sup>24,26</sup>, fractured instruments<sup>46</sup>, and extruded root fillings<sup>43</sup>, and the use of "root" as a unit of measurement<sup>7,23,38</sup>, could have influenced the overall findings. To address this potential impact, we conducted sensitivity analyses by excluding these studies and

observed similar pooled results. As a result, we decided to retain them in our analysis.

3. This systematic review incorporated a study conducted by Zhang et al.<sup>48</sup>, focusing on the four-year outcome of NS-ReTx using CBCT. Notably, CBCT imaging demonstrated a twofold increase in the likelihood of lesion detection compared to intraoral periapical radiography (OR = 2.04, 95% CI, 1.52-2.73)<sup>58</sup>. However, when evaluating apical periodontitis against *ex vivo* human jaw histopathology, CBCT's diagnostic accuracy was found to be contingent on the tooth's treatment status, exhibiting diminished accuracy for root-filled roots<sup>59</sup>. The inclusion of Zhang et al.'s study<sup>48</sup> in our analysis might have influenced our overall findings. Their study revealed a periapical healing rate of 75.9% under strict assessment criteria and 93.1% under loose criteria. Nevertheless, our sensitivity analysis, excluding this study, yielded similar pooled results. Consequently, we retained this study in our analysis to maintain a comprehensive perspective. It is noteworthy that both the American Association of Endodontists and the American Academy of Oral and Maxillofacial Radiology currently discourage the utilization of CBCT for

diagnosis or screening without evident clinical signs or symptoms. They emphasize the sufficiency of conventional lower-dose radiographic modalities<sup>60</sup>. Consequently, less than 10% of endodontic outcome studies within the last decade incorporated CBCT imaging<sup>61</sup>. In light of the escalating popularity of CBCT in clinical practice, forthcoming retrospective studies from practice-based research networks can leverage pre-existing information to assess prognostic factors in endodontic outcomes<sup>61</sup>. As more cohort studies utilizing CBCT become available, future systematic reviews may contemplate defining subgroup analyses to present outcomes based on 2 different analysis methods with distinct diagnostic potentials separately.

4. The heterogeneity in study design, sample size, patient populations, treatment protocols, and methodology among the included studies (Supplementary Table 5) may limit the comparability and generalizability of the results.
5. Finally, this systematic review is limited in assessing specific prognostic factors due to constraints imposed by the available literature, specifically pertaining to parameters measured in prior

**TABLE 4 - Pooled Weighted Outcomes by Clinical Factors**

Subgroup		Preapical healing						Success					
		Strict			Loose			Strict			Loose		
		No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)
Publication decades	2000s	5	1058	77.8 (75.5-80.0)	2	363	59.8 (55.8-63.6)	5	1058	77.0 (68.1-85.9)	2	363	75.7 (72.1-79.3)
	2010s	14	1765	83.2 (81.5-84.8)	9	1720	90.3 (88.9-91.6)	14	1705	79.4 (75.6-83.2)	8	1551	86.8 (83.7-89.8)
	2020s	9	1339	87.8 (86.1-89.4)	6	500	87.4 (84.5-90.0)	6	408	76.7 (69.2-84.1)	6	500	89.0 (84.1-93.8)
Geographical location	America	7	958	80.7 (78.4-82.9)	5	373	83.9 (80.3-87.3)	6	895	76.1 (69.8-82.4)	6	373	85.2 (81.9-88.4)
	Europe	12	2659	84.8 (83.5-86.1)	5	1696	86.2 (84.6-87.7)	10	1731	77.4 (71.9-82.9)	5	1633	82.0 (73.6-90.3)
	Other	9	545	80.6 (77.5-83.6)	7	514	92.1 (89.6-94.3)	9	545	80.0 (74.2-85.7)	6	408	91.6 (88.6-94.5)
Operator	Dental student	2	53	68.8 (58.5-79.2)	1	30	73.2 (58.1-84.3)	1	28	68.3 (53.0-80.4)	1	30	73.2 (58.1-84.3)
	Postgraduate endodontic resident	6	1506	83.5 (81.8-85.2)	4	1426	88.9 (85.3-92.4)	6	1446	80.1 (78.2-81.9)	4	1363	86.1 (83.4-88.8)
	Specialist	17	2397	78.4 (72.9-84.0)	10	928	88.3 (81.7-94.9)	15	1491	77.1 (71.9-82.2)	9	822	87.3 (80.2-94.4)
Follow-up period	General dentist	1	64	90.1 (81.0-95.1)	1	64	90.1 (81.0-95.1)	1	64	90.1 (81.0-95.1)	1	64	90.1 (81.0-95.1)
	2-4 Years	17	2226	75.9 (72.3-81.0)	11	2439	83.1 (79.4-86.5)	17	2166	75.4 (70.9-80.0)	14	2270	85.7 (81.6-89.8)
Gender	>4 years	11	976	87.3 (82.3-91.6)	4	224	89.7 (80.8-96.3)	9	888	84.6 (80.4-88.9)	4	224	89.9 (82.6-97.3)
	Male	5	444	71.2 (59.2-83.3)	4	119	83.2 (77.1-89.3)	4	444	71.2 (59.2-83.3)	4	119	83.2 (77.1-89.3)
Age	Female	5	857	82.6 (76.7-88.4)	4	198	88.4 (84.3-92.5)	5	857	82.6 (76.7-88.4)	4	198	88.3 (83.2-93.5)
	<35 years (18-34)	1	36	65.5 (52.3-76.6)	1	51	92.7 (82.7-97.1)	1	36	65.5 (52.3-76.6)	1	51	92.7 (82.7-97.1)
	≥35 years (35-60)	1	30	62.5 (48.4-74.8)	1	40	83.3 (70.4-91.3)	1	30	62.5 (48.4-74.8)	1	40	83.3 (70.4-91.3)
	<45 years	2	85	85.2 (77.4-91.6)	1	44	80.0 (67.6-88.4)	2	85	85.2 (77.4-91.6)	1	44	80.0 (67.6-88.5)
	≥45 years	2	59	92.9 (83.0-99.2)	1	42	91.3 (79.7-96.6)	2	59	92.9 (83.0-99.2)	1	42	91.3 (79.7-96.6)
	<20 years	1	24	96.0 (80.5-99.3)	1	1	100.0 (20.7-100.0)	—	—	—	2	25	100.0 (93.7-100.0)
	20-29 years	—	—	—	—	—	—	1	52	75.4 (64.0-84.0)	—	—	—
	30-39 years	1	187	85.8 (80.5-89.8)	—	—	—	1	187	85.8 (80.5-89.8)	—	—	—
	40-49 years	1	153	85.5 (79.6-89.9)	—	—	—	1	153	85.5 (79.6-89.9)	—	—	—
	50-59 years	1	94	94.0 (87.5-97.2)	—	—	—	1	94	94.0 (87.5-97.2)	—	—	—
Health status	20-59 years	—	—	—	1	64	76.2 (66.1-84.0)	—	—	—	1	64	76.2 (66.1-84.0)
	<60 years Total	1	27	69.2 (53.6-81.4)	1	35	89.7(76.4-95.9)	1	27	69.2 (53.6-81.4)	1	35	89.7 (76.4-95.9)
Arch type	≥60 years Total	1	36	78.6 (64.9-89.8)	2	39	93.2 (82.5-99.5)	2	36	78.6 (64.9-89.8)	2	39	93.2 (82.5-99.5)
	Healthy	11	1343	79.1 (71.9-86.3)	7	476	90.9 (88.5-93.4)	10	498	77.0 (72.0-81.7)	7	474	90.2 (87.4-92.6)
Tooth type	Unhealthy	—	—	—	1	49	77.8 (66.1-86.3)	—	—	—	1	49	77.8 (66.1-86.3)
	Maxillary	3	653	85.2 (75.7-94.7)	3	128	89.0 (81.5-96.5)	3	653	85.3 (75.2-93.2)	3	128	88.4 (79.7-95.1)
Periapical status	Mandibular	4	603	76.1 (65.0-87.2)	4	190	85.4 (80.9-90.0)	3	537	80.3 (67.4-90.6)	3	99	80.8 (72.7-87.9)
	Anterior	4	367	88.1 (78.3-97.9)	2	49	83.7 (74.5-92.9)	4	367	88.3 (76.7-96.5)	2	49	82.1 (71.1-91.1)
	Premolar	4	349	82.6 (74.8-90.3)	2	77	92.5 (86.9-98.1)	4	349	82.7 (73.7-90.2)	2	77	91.8 (84.7-97.1)
Preapical lesion size	Molar	6	1120	76.5 (69.8-83.2)	4	193	84.1 (76.6-91.6)	5	1054	79.5 (72.9-85.4)	3	102	80.9 (67.7-91.4)
	PARL	15	1718	74.8 (69.2-80.4)	10	732	84.0 (76.1-91.9)	15	1718	75.1 (69.2-80.5)	10	732	84.6 (75.5-92.0)
	No PARL	10	970	97.9 (94.6-99.8)	6	188	95.7 (87.1-100.0)	10	970	97.9 (94.6-99.8)	6	188	95.7 (87.1-100.0)
	≤5 mm/ 65 mm <sup>3</sup>	8	925	87.0 (77.3-94.5)	6	230	92.9 (86.1-97.8)	8	925	87.0 (77.3-94.5)	6	230	92.9 (86.1-97.8)

(continued on next page)

TABLE 4 - Continued

Subgroup		Preapical healing						Success					
		Strict			Loose			Strict			Loose		
		No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)
	>5 mm/ 65 mm <sup>3</sup>	8	204	62.3 (56.8-67.6)	6	152	86.7 (80.9-91.7)	8	204	62.3 (56.8-67.6)	6	152	86.7 (80.9-91.7)
Preoperative fractured instrument	Present	3	153	91.3 (67.2-100.0)	2	63	97.5 (90.6-100.0)	3	153	91.3 (67.2-100.0)	2	63	97.5 (90.6-100.0)
	Absent	3	1291	69.2 (52.4-83.7)	3	433	78.4 (61.7-91.3)	3	1291	69.2 (52.4-83.7)	3	433	78.4 (61.7-91.3)
Preoperative canal content	GP	3	963	83.1 (74.7-90.2)	2	130	88.7 (82.9-93.4)	3	963	83.1 (74.7-90.2)	2	130	88.7 (82.9-93.4)
	Cement/Paste	2	40	82.3 (69.6-92.5)	1	8	80.0 (49.0-94.3)	2	40	82.3 (69.6-92.5)	1	8	80.0 (49.0-94.3)
	Thermafil	1	6	60.0 (31.3-83.2)	—	—	—	1	6	60.0 (31.3-83.2)	—	—	—
	Silver point	1	56	87.5 (77.2-93.5)	—	—	—	1	56	87.5 (77.2-93.5)	—	—	—
Preoperative perforation	Present	5	107	66.2 (54.1-77.5)	3	30	60.3 (44.0-75.7)	5	107	66.2 (54.1-77.5)	3	30	60.3 (44.0-75.7)
	Absent	7	2574	82.7 (73.4-90.3)	6	741	86.9 (76.6-94.6)	6	1731	80.2 (72.2-87.1)	5	635	84.3 (74.1-92.4)
Preoperative canal obstruction	Present	2	196	68.3 (62.8-73.6)	1	71	68.9 (59.5-77.1)	2	196	68.3 (62.8-73.6)	1	71	68.9 (59.5-77.1)
	Absent	4	1296	75.3 (63.4-85.6)	3	414	84.4 (66.1-96.5)	4	1296	75.3 (63.4-85.6)	3	414	84.4 (66.1-96.5)
Preoperative apical extent of root filling	Short	4	245	90.1 (70.6-99.9)	4	201	93.1 (80.9-99.7)	4	245	90.1 (70.6-99.9)	4	201	93.1 (80.9-99.7)
	Adequate	3	69	80.0 (61.5-94.0)	3	137	88.9 (76.2-97.5)	3	69	80.1 (61.5-94.0)	3	137	88.9 (76.2-97.5)
	Long	3	11	69.6 (42.4-91.9)	3	11	82.5 (42.1-100.0)	3	11	69.6 (42.4-91.9)	3	11	82.5 (42.1-100.0)
Preexisting root filling quality	Satisfactory	3	438	66.6 (52.2-79.6)	3	329	74.0 (52.2-91.0)	3	438	66.6 (52.2-79.6)	3	329	74.0 (52.2-91.0)
	Unsatisfactory	3	1097	91.9 (78.8-99.2)	3	146	93.3 (62.4-100.0)	3	1097	91.9 (78.8-99.2)	3	146	93.3 (62.4-100.0)
	Unfilled canal present	2	20	81.1 (62.4-95.0)	1	13	100.0 (77.2-100.0)	2	20	81.1 (62.4-95.0)	1	13	100.0 (77.2-100.0)
Preoperative root filling density	Good	2	26	61.4 (43.4-78.2)	1	35	83.3 (69.4-91.7)	2	26	61.4 (43.4-78.2)	1	35	83.3 (69.4-91.7)
	Poor	2	120	84.5 (78.0-90.1)	1	44	91.7 (80.5-96.7)	2	120	84.5 (78.0-90.1)	1	44	91.7 (80.5-96.7)
Time since initial treatment	≤3 years	—	—	—	1	50	79.4 (67.8-87.5)	—	—	—	1	50	79.4 (67.8-87.5)
	>3 years	—	—	—	1	36	94.7 (82.7-98.5)	—	—	—	1	36	94.7 (82.7-98.5)
Microscope	Yes	10	594	75.6 (71.2-79.7)	6	398	91.2 (88.3-93.8)	10	592	75.3 (71.0-79.4)	6	396	90.8 (87.8-93.4)
	No	17	3543	81.2 (76.0-85.9)	11	2185	85.5 (78.9-91.1)	15	2579	79.6 (75.1-83.7)	11	2124	85.0 (79.3-89.9)
File type	Hand file	8	834	80.9 (75.6-85.7)	5	290	90.0 (84.1-94.7)	8	834	80.9 (75.6-85.7)	5	290	90.0 (84.1-94.7)
	Rotary	13	2885	78.2 (71.0-84.8)	8	1879	88.0 (79.6-94.4)	10	1896	75.9 (69.8-81.5)	7	1712	85.4 (77.5-91.9)
Apical preparation size	≤#30	1	644	81.4 (78.6-84.0)	—	—	—	1	644	81.4 (78.6-84.0)	—	—	—
	>#30	8	1255	82.5 (78.3-86.4)	4	258	90.9 (86.0-94.8)	8	1255	82.5 (78.3-86.4)	4	258	90.9 (86.0-94.9)
Taper	≤0.06	2	595	79.4 (76.4-82.2)	1	47	90.4 (79.4-95.8)	2	595	79.4 (76.4-82.2)	1	47	90.4 (79.4-95.8)
	>0.06	4	690	80.8 (78.1-83.4)	—	—	—	4	690	80.8 (78.1-83.4)	2	140	88.4 (82.8-93.0)
Intraoperative fractured instrument	Present	1	6	50.0 (25.4-74.6)	—	—	—	1	6	50.0 (25.4-74.6)	—	—	—
	Absent	3	1191	78.2 (66.8-87.7)	2	174	90.8 (86.0-94.9)	3	1191	78.2 (66.8-87.7)	2	174	90.8 (86.2-94.6)
Irrigant	NaOCl	7	972	76.8 (67.0-85.3)	5	499	85.2 (71.4-95.2)	7	972	76.8 (67.0-85.3)	5	499	85.2 (71.4-95.2)
	NaOCl + Iodine	1	234	79.1 (74.1-83.3)	—	—	—	1	234	79.1 (74.1-83.3)	—	—	—

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TABLE 4 - Continued

Subgroup		Preapical healing						Success					
		Strict			Loose			Strict			Loose		
		No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)	No. study	Sample size	Pooled rate (95% CI)
Intracanal medicament	NaOCl + CHX	5	472	76.3 (69.5-82.6)	2	145	90.2 (85.0-94.5)	5	472	76.3 (69.5-82.6)	2	145	90.2 (85.0-94.5)
	NaOCl + EDTA	13	1839	81.9 (76.2-87.1)	8	618	89.0 (84.0-93.1)	11	931	80.4 (75.6-84.9)	7	510	87.2 (82.7-91.1)
	CaOH <sub>2</sub>	11	674	78.4 (73.5-83.0)	9	552	87.6 (83.8-91.0)	11	674	78.4 (73.5-83.0)	9	552	87.6 (83.8-91.0)
	CaOH <sub>2</sub> + CHX	1	32	65.3 (51.3-77.1)	1	37	75.5 (61.9-85.4)	1	32	65.3 (51.3-77.1)	1	37	75.5 (61.9-85.4)
	None	3	134	86.2 (68.7-97.5)	3	115	93.1 (86.0-98.2)	3	134	86.2 (68.7-97.5)	3	115	93.1 (86.0-98.2)
Root filling material	GP	21	2712	78.9 (73.2-84.1)	14	1140	88.4 (82.3-93.4)	19	1842	78.1 (73.5-82.4)	13	1032	87.4 (81.3-92.5)
	Thermafil	2	85	81.0 (72.8-88.1)	—	—	—	2	85	80.0 (72.8-88.1)	—	—	—
	Resilon	1	19	63.3 (45.5-78.1)	1	27	90.0 (74.4-96.5)	1	19	63.3 (45.5-78.1)	1	27	90.0 (74.4-96.5)
Obturation technique	Warm Vertical	8	1589	78.1 (66.1-88.1)	4	510	86.4 (71.2-96.7)	6	707	75.2 (67.6-82.1)	3	461	84.3 (66.1-96.5)
	Cold lateral	10	1727	80.7 (76.6-84.5)	5	266	86.5 (77.8-93.5)	8	1639	81.2 (76.7-85.3)	5	266	86.5 (77.8-93.5)
	Single cone	4	251	76.7 (61.7-89.0)	4	305	93.1 (88.8-96.6)	4	251	76.7 (61.7-89.0)	3	199	91.1 (86.8-94.7)
Sealer	ZOE	4	1588	76.1 (65.2-85.6)	4	1642	85.7 (72.0-95.5)	5	1528	74.6 (66.4-82.1)	4	1579	83.6 (72.8-92.2)
	Resin	11	625	79.1 (73.5-84.3)	6	472	91.8 (88.0-95.0)	9	531	79.4 (72.8-85.3)	5	366	90.2 (86.9-93.2)
	CaOH <sub>2</sub>	1	32	65.3 (51.3-77.1)	1	37	75.5 (61.9-85.4)	1	32	65.3 (51.3-77.1)	1	37	75.5 (61.9-85.4)
	Bioceramic	2	85	73.4 (64.8-81.1)	2	108	93.2 (87.7-97.3)	2	85	73.4 (64.8-81.1)	2	108	93.2 (87.7-97.3)
Apical extent of root filling	Short	6	144	51.3 (27.2-75.2)	5	109	72.2 (40.1-96.6)	6	144	51.3 (27.2-75.2)	5	109	72.2 (40.1-96.6)
	Adequate	7	1279	83.8 (77.4-89.3)	6	425	89.2 (84.1-93.4)	7	1279	83.8 (77.4-89.3)	6	425	89.2 (84.1-93.4)
	Long	4	166	78.0 (61.7-91.1)	3	29	91.8 (76.5-100.0)	3	103	77.2 (54.2-94.2)	3	29	94.6 (70.4-100.0)
Root filling quality	Satisfactory	5	377	75.2 (64.3-84.7)	6	545	88.8 (83.6-93.1)	5	377	75.2 (64.3-84.7)	5	439	86.3 (82.8-89.5)
	Unsatisfactory	1	1	100.0 (20.7-100.0)	2	33	81.7 (62.9-96.1)	1	1	100.0 (20.7-100.0)	2	33	81.7 (62.9-96.1)
Number of visits	Single	6	298	86.4 (76.2-94.4)	4	221	95.3 (91.8-98.1)	5	235	87.0 (73.7-96.6)	3	115	93.1 (86.0-98.2)
	Multiple	14	1791	78.0 (74.3-81.5)	11	631	87.5 (83.5-91.1)	13	1722	77.5 (73.5-81.3)	11	631	87.5 (83.5-91.1)
Coronal restoration type	Cast	5	930	80.0 (72.9-86.2)	3	119	87.3 (80.9-92.6)	4	930	80.0 (72.9-86.2)	3	119	87.3 (80.9-92.6)
	Composite/GI/Amalgam	4	444	79.0 (69.5-87.2)	2	113	98.0 (94.3-100.0)	4	444	79.0 (69.5-87.2)	2	113	98.0 (94.3-100.0)
	Temporary	1	11	57.9 (36.3-76.9)	1	11	91.7 (64.6-98.5)	1	11	57.9 (36.3-76.9)	1	11	91.7 (64.6-98.5)
Coronal restoration quality	None	—	—	—	1	3	75.0 (30.1-95.4)	—	—	—	1	3	75.0 (30.1-95.4)
	Adequate	6	1317	77.7 (70.1-84.5)	4	287	88.5 (84.7-91.8)	5	1254	76.8 (67.6-84.9)	4	287	88.5 (84.7-91.8)
	Inadequate	2	53	70.8 (57.8-82.6)	1	3	100.0 (43.9-100.0)	2	53	70.8 (57.8-82.6)	1	3	100.0 (43.9-100.0)

Note: NaOCl, sodium hypochlorite; CHX, chlorhexidine; EDTA, Ethylenediaminetetraacetic acid; CaOH<sub>2</sub>, calcium hydroxide; GI, glass ionomer; GP, gutta percha; ZOE, zinc oxide-eugenol



**TABLE 5** - Summary of Meta-Regression Analyses for the Effects of Clinical Factors on NS-ReTx Outcome

Subgroup		Periapical healing				Success			
		Strict		Loose		Strict		Loose	
		Coefficient (95% CI)	P- value	Coefficient (95% CI)	P- value	Coefficient (95% CI)	P- value	Coefficient (95% CI)	P- value
Publication decade	2010s vs. 2000s	0.02 (-0.03-0.07)	.461	0.15 (0.10-0.21)	.001*	0.04 (-0.01-0.10)	.122	0.04 (-0.01-0.09)	.117
	2020s vs. 2000s	0.01 (-0.03-0.04)	.612	0.06 (0.00-0.11)	.048*	0.03 (-0.01-0.06)	.138	-0.01 (-0.04-0.05)	.747
	2020s vs. 2010s	0.01 (-0.05-0.06)	.084	-0.00 (-0.01-0.00)	.845	0.01 (-0.05-0.06)	.832	-0.02 (-0.07-0.03)	.369
Geographical location	America vs. Europe	-0.01 (-0.07-0.05)	.683	-0.00 (-0.08-0.09)	.915	-0.01 (-0.07-0.04)	.572	0.09 (-0.32-0.14)	.359
	America vs. Others	0.00 (-0.03-0.03)	.993	-0.02 (-0.06-0.01)	.225	-0.00 (-0.03-0.03)	.964	-0.02 (-0.11-0.08)	.624
	Others vs. Europe	-0.00 (-0.06-0.06)	.936	0.04 (-0.03-0.12)	.214	0.19 (-0.04-0.07)	.047*	0.05 (-0.03-0.13)	.171
Operator	Specialist vs. Postgraduate endodontic resident	-0.01 (-0.06-0.05)	.721	-0.02 (-0.09-0.05)	.638	-0.01 (-0.06-0.03)	.542	0.01 (-0.08-0.06)	.744
	Specialist vs. Dental student	0.03 (-0.04-0.09)	.427	0.03 (-0.07-0.13)	.494	0.02 (-0.07-0.11)	.619	0.03 (-0.08-0.13)	.543
	Specialist vs. General dentist	-0.05 (-0.10-0.21)	.465	-0.02 (-0.15-0.19)	.788	-0.07 (-0.21-0.08)	.345	-0.03 (-0.20-0.14)	.720
Follow-up period	>4 years vs. 2-4 Years	0.09 (0.01-0.18)	.031*	0.04 (-0.11-0.19)	.586	0.04 (-0.00-0.08)	.068	0.27 (0.09-0.45)	.007*
Gender	Male vs. Female	-0.02 (-0.15-0.11)	.704	-0.03 (-0.09-0.03)	.292	-0.03 (-0.09-0.03)	.292	-0.02 (-0.15-0.11)	.704
	Health status	Unhealthy vs. Healthy	—	-0.03 (-0.37-0.31)	.847	—	—	-0.60 (-0.22-0.10)	.395
Arch type	Maxillary vs. Mandibular	0.20 (-0.08-0.12)	.600	0.02 (-0.12-0.15)	.785	0.00 (-0.07-0.08)	.844	0.03 (-0.20-0.14)	.616
Tooth type	Anterior vs. Premolar	0.00 (-0.04-0.04)	.870	-0.03 (-0.27-0.21)	.612	-0.02 (-0.11-0.08)	.700	-0.05 (-0.03-0.41)	.612
	Molar vs. Anterior	-0.02 (-0.07-0.04)	.496	0.03 (-0.37-0.43)	.866	-0.00 (-0.04-0.03)	.828	-0.00 (-0.13-0.12)	.965
	Premolar vs. molar	0.01 (-0.06-0.07)	.752	0.04 (-0.14-0.21)	.590	0.00 (-0.06-0.07)	.883	0.05 (-0.03-0.17)	.499
Periapical status	No PARL vs. PARL	0.18 (-0.08-0.25)	.001*	0.03 (-0.04-0.10)	.340	0.09 (0.04-0.14)	.001*	0.05 (-0.05-0.15)	.340
Periapical lesion size	>5 mm <sup>3</sup> vs. ≤5 mm <sup>3</sup> /65 mm <sup>3</sup>	-0.11 (-0.17-0.04)	.004*	-0.03 (-0.14-0.08)	.589	-0.11 (-0.17-0.04)	.004*	0.03 (-0.14-0.08)	.589
Preoperative fractured instrument	Absent vs. Present	-0.08 (-0.25-0.95)	.284	-0.08 (-0.19-0.35)	.401	-0.08 (-0.25-0.10)	.284	-0.08 (-0.35-0.19)	.401

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TABLE 5 - Continued

Subgroup		Periapical healing				Success			
		Strict		Loose		Strict		Loose	
		Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value
Preoperative canal content	Cement/Paste vs. GP	-0.00 (-0.23-0.30)	.992	-0.03 (-1.32-1.38)	.835	-0.00 (-0.23-0.30)	.992	-0.04 (-1.99-2.07)	.835
	GP vs. Thermafil	0.02 (-0.16-0.20)	.684	—	—	0.05 (-0.28-0.39)	.560	—	—
	GP vs. Silver point	-0.21 (-0.16-1.12)	.560	—	—	-0.01 (-0.10-0.08)	.684	—	—
Preoperative perforation	Present vs. Absent	-0.08 (-0.19-0.03)	.133	-0.13 (-0.32-0.06)	.155	-0.06 (-0.17-0.04)	.200	-0.12 (-0.31-0.08)	.197
Preoperative ca-l obstruction	Present vs. Absent	-0.03 (-0.17-0.98)	.518	-0.06 (-0.43-0.31)	.542	-0.03 (-0.17-0.10)	.518	-0.06 (-0.43-0.31)	.542
Preoperative apical extent of root filling	Adequate vs. Short	-0.02 (-0.12-0.07)	.535	0.02 (-0.05-0.08)	.563	-0.05 (-0.23-0.14)	.535	-0.03 (-0.17-0.10)	.563
	Long vs. Short	-0.19 (-0.85-0.48)	.499	-0.14 (-0.05-0.89)	.608	-0.05 (-0.21-0.12)	.499	-0.04 (-0.20-0.13)	.608
Preexisting root filling quality	Unsatisfactory vs. Satisfactory	0.21 (-0.03-0.44)	.070	0.19 (-0.59-0.21)	.261	0.10 (-0.01-0.22)	.070	0.10 (-0.11-0.30)	.261
	Poor vs. Good	0.11 (-0.32-0.54)	.382	—	—	0.11 (-0.32-0.54)	.382	—	—
Preoperative root filling density	Good vs. Unfilled ca-l	0.05 (-0.21-0.32)	.493	—	—	0.05 (-0.21-0.32)	.493	—	—
	≤3 years vs. >3 years	—	—	—	—	—	—	—	—
Microscope	No vs. Yes	0.30 (-0.02-0.08)	.233	-0.04 (-0.10-0.03)	.271	0.02 (-0.03-0.06)	.480	-0.04 (-0.10-0.02)	.202
File type	Rotary vs. Hand file	-0.01 (-0.07-0.05)	.733	-0.02 (-0.11-0.06)	.603	-0.03 (-0.08-0.02)	.222	-0.04 (-0.12-0.05)	.343
Apical preparation size	≤#30 vs. >#30	-0.00 (-0.06-0.05)	.875	—	—	-0.00 (-0.06-0.05)	.875	—	—
Taper	>0.06 vs. ≤0.06	0.01 (-0.06-0.08)	.780	—	—	0.00 (-0.05-0.07)	.897	-0.01 (-1.02-1.00)	.907
Intraoperative fractured instrument	Present vs. absent	-0.29 (-1.73-1.15)	.477	—	—	-0.14 (-0.86-0.57)	.477	—	—
Irrigant	NaOCl + Iodine vs. NaOCl	0.01 (-0.08-0.10)	.803	—	—	0.01 (-0.12-0.15)	.803	—	—
	NaOCl + CHX vs. NaOCl	-0.00 (-0.05-0.05)	.099	0.10 (-0.40-0.20)	.428	-0.00 (-1.40-0.04)	.991	0.03 (-0.10-0.05)	.428
	NaOCl + EDTA vs. NaOCl	0.04 (-0.02-0.09)	.161	0.05 (-0.02-0.12)	.113	0.01 (-0.01-0.03)	.367	0.01 (-0.01-0.04)	.206
Intracanal medicament	CaOH <sub>2</sub> + CHX vs. CaOH <sub>2</sub>	-0.04 (-0.20-0.12)	.612	-0.08 (-0.25-0.09)	.330	-0.07 (-0.23-0.10)	.396	-0.06 (-0.23-0.11)	.461
	None vs. CaOH <sub>2</sub>	0.02 (-0.03-0.07)	.377	0.00 (-0.00-0.00)	.998	0.01 (-0.04-0.06)	.610	0.01 (-0.04-0.07)	.617
Root filling material	Thermafil vs. GP	0.00 (-0.07-0.08)	.899	—	—	0.02 (-0.10-0.13)	.765	—	—
	Resilon vs. GP	-0.16 (-0.57-0.25)	.421	0.01 (-0.13-0.16)	.842	-0.04 (-0.14-0.06)	.459	0.03 (-0.12-0.07)	.590

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TABLE 5 - Continued

Subgroup		Periapical healing				Success			
		Strict		Loose		Strict		Loose	
		Coefficient (95% CI)	P- value	Coefficient (95% CI)	P- value	Coefficient (95% CI)	P- value	Coefficient (95% CI)	P- value
Obturation technique	Warm vertical vs. Cold lateral	-0.00 (-0.03-0.03)	.773	-0.01 (-0.07-0.04)	.591	-0.04 (-0.09-0.01)	.082	-0.04 (-0.15-0.07)	.442
	Warm vertical vs. Single cone	0.01 (-0.08-0.11)	.765	-0.06 (-0.17-0.05)	.235	-0.01 (-0.05-0.04)	.800	0.03 (-0.10-0.04)	.319
	Single cone vs. Cold lateral	-0.03 (-0.09-0.04)	.416	0.03 (-0.06-0.12)	.488	-0.03 (-0.09-0.04)	.404	0.02 (-0.09-0.13)	.669
Sealer	ZOE vs. Resin	-0.03 (-0.15-0.10)	.066	-0.03 (-0.08-0.03)	.304	-0.02 (-0.08-0.04)	.440	-0.05 (-0.13-0.04)	.251
	ZOE vs. CaOH <sub>2</sub>	0.03 (-0.09-0.15)	.557	0.02 (-0.13-0.17)	.692	0.02 (-0.09-0.13)	.597	0.01 (-0.12-0.15)	.759
	ZOE vs. Bioceramic	0.01 (-0.06-0.07)	.823	-0.01 (-0.07-0.04)	.499	0.00 (-0.45-0.05)	.922	-0.02 (-0.08-0.04)	.377
	Resin vs. Bioceramic	0.15 (-0.04-0.07)	.562	-0.00 (-0.07-0.06)	.865	0.01 (-0.04-0.07)	.566	-0.01 (-0.08-0.06)	.774
Apical extent of root filling	Short vs. Adequate	-0.07 (-0.12-0.01)	.018*	-0.01 (-0.06-0.03)	.553	-0.10 (-0.18-0.02)	.018*	-0.05 (-0.03-0.13)	.171
	Short vs. Long	-0.10 (-0.31-0.11)	.299	-0.06 (-0.27-0.16)	.562	-0.00 (-0.07-0.06)	.889	-0.04 (-0.06-0.14)	.438
	Adequate vs. Long	0.02 (-0.04-0.41)	.924	-0.06 (-0.12-0.00)	.049*	0.09 (-0.00-0.19)	.061	-0.02 (-0.19-0.22)	.839
Root filling quality	Unsatisfactory vs. Satisfactory	0.13 (-1.01-1.27)	.770	-0.07 (-0.26-0.12)	.390	0.13 (-1.01-1.27)	.770	-0.06 (-0.26-0.14)	.461
Number of visits	Single vs. Multiple	0.06 (-0.06-0.18)	.346	0.02 (-0.03-0.08)	.344	0.03 (-0.04-0.10)	.326	0.03 (-0.08-0.13)	.594
Coronal restoration type	Composite/GI/ Amalgam vs. Cast	-0.11 (-0.08-0.04)	.483	0.04 (-0.16-0.24)	.563	-0.02 (-0.08-0.04)	.483	0.04 (-0.16-0.24)	.563
	Temporary vs. Cast	-0.05 (-0.17-0.08)	.366	0.01 (-0.24-0.26)	.885	-0.06 (-0.22-0.10)	.366	0.01 (-0.30-0.33)	.885
Coronal restoration quality	None vs. Cast	—	—	-0.03 (-0.54-0.48)	.828	—	—	-0.02 (-0.36-0.32)	.828
	Inadequate vs. Adequate	-0.13 (-0.41-0.15)	.314	0.04 (-0.53-0.61)	.842	-0.06 (-0.21-0.10)	.406	0.06 (-0.80-0.91)	.842

Note \*: significant at  $P < .05$ , -OCL, sodium hypochlorite; CHX, chlorhexidine; EDTA, Ethylenediaminetetraacetic acid; CaOH<sub>2</sub>, calcium hydroxide; GI, glass ionomer; GP, gutta percha; ZOE, zinc oxide-eugenol.

investigations on outcome predictors of NS-ReTx. Consequently, several clinical factors that could impact the NSReTx outcome were not evaluated in this paper. Notably, preoperative factors such as pain level, swelling, sinus tract presence, mobility, and periodontal defect, crown-to-root ratio, tooth function (in occlusal contact, type of opposing occlusion, number of proximal contacts last tooth in segment, single tooth, abutment for fixed or removable partial denture), crack or fracture presence, history of luxation injuries, presence of posts in preoperative restoration (especially fiber posts with a heightened risk of perforation during retrieval attempts), and intraoperative techniques (e.g. irrigation with standard needle or any new technology, and combining with laser or sonic/ultrasonic), and occlusal reduction were not systematically assessed in the included studies. Consequently, the comprehensive evaluation of these factors as potential contributors to the outcome of NSReTx was not feasible within the scope of this review. We hope future studies utilize available checklists, such as the proposed framework for standardized data collection and reporting of endodontic outcome studies as presented in our recent paper<sup>62</sup>. This approach will facilitate a more thorough evaluation of the potential impact of various factors, ultimately supporting evidence-based treatment decisions.

Having said these limitations, this review has notable strengths. It employed a systematic search process, applying strict criteria to identify relevant, and

methodologically robust studies. Our advanced meta-regression analyses also identified clinical factors which can influence the outcome of NS-ReTx. These findings can guide proper case selection and encourage future research to focus on prospective studies with long-term follow-up. Long-term monitoring of retreated teeth is recommended due to the gradual nature of periapical healing. Although the field of endodontics has advanced notably, we have identified inconsistencies pertaining to data standardization and substantial variability in outcome measures. Future research should adhere to guidelines for data collection and reporting<sup>62</sup>. There is also a pressing need for a reproducible and standardized core outcome set to serve as a uniform framework for researchers, clinicians, and patients<sup>61</sup>.

## CONCLUSION

Our review of contemporary NS-ReTx studies shows encouraging outcomes, achieving periapical healing and success rates of approximately 78% (strict criteria) and 87% (loose criteria), respectively. The absence of or smaller preoperative lesions, adequate root filling length, and extended follow-ups significantly improve NS-ReTx outcomes. The incorporation of these factors into treatment planning is pivotal for optimizing the outcome of NS-ReTx.

## CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

**M. Sabeti:** Conceptualization, Methodology, Data curation, Writing – original draft,

Supervision, Resources, Project administration. **Y.J. Chung:** Methodology, Data curation, Data extraction, Writing – original draft. **N. Aghamohammadi:** Data curation, Data extraction, Writing – review & editing. **A. Khansari:** Data curation, Data extraction, Writing – original draft, Writing – review & editing. **R. Pakzad:** Methodology, Software, Formal analysis, Validation, Writing – review & editing. **A. Azarpazhooh:** Conceptualization, Methodology, Formal analysis, Validation, Writing – review & editing, Supervision, Resources, Project administration.

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## SUPPLEMENTARY MATERIAL

*Supplementary material associated with this article can be found in the online version at [www.jendodon.com](http://www.jendodon.com) (<https://doi.org/10.1016/j.joen.2024.01.013>).*

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