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REVIEW ARTICLE

Effectiveness of root canal treatment for vital pulps compared with necrotic pulps in the presence or absence of signs of periradicular pathosis: A systematic review and meta-analysis

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Abstract

Background: Preoperative pulpal status may influence the outcomes of root canal treatment (RCTx) according to various measures used.

Objectives: To compare the effectiveness of RCTx of teeth with a vital pulp versus a necrotic pulp, using a range of clinical and patient-related outcomes proposed for the development of S3-level clinical practice guidelines.

Methods: A search was conducted in the PubMed-MEDLINE, Scopus, EMBASE, Google scholar databases and available repositories, followed by hand searches, until 29 March 2022. Clinical studies published in the English language comparing the stipulated outcomes of RCTx of teeth with vital versus necrotic pulp were included. The Newcastle–Ottawa Scale was adapted to assess study quality. Effects of pulpal status were estimated and expressed as risk ratio (RR) using fixed- and random-effect meta-analyses. The quality of evidence was assessed through the Grading of Recommendations Assessment, Development and Evaluation tool.

Results: Twenty-eight studies published between 1961 and 2021 were included. Five studies have investigated the "tooth survival" outcome, four reported pulpal status was not a significant predictor, consistent with meta-analysis findings (RR: 1.00; 95% CI: 1.00, 1.00; $n = 3$). Seven studies reported pulpal status had no significant influence on postoperative pain, regardless of duration after treatment. Sixteen studies have analysed "periapical health," and 11 revealed pulpal status had no significant influence. Meta-analyses revealed the influence was not significant if preoperative periapical radiolucency was absent (RR: 0.95; 95% CI: 0.90, 1.00; $n = 9$) but significant if it was present (RR: 1.12; 95% CI: 1.05, 1.19; $n = 11$). Most studies were classified as "some concerns" ($n = 17$) to "low" ($n = 9$) risk of bias RoB.

Discussion: Evidence is limited and only available for three outcomes when comparing the effectiveness of RCTx in permanent teeth with vital pulp versus pulp necrosis. Nevertheless, the quality of available evidence was moderate to high. The "periapical health" data heterogeneity could be explained by preoperative radiolucency,

thus RCTx was found more effective for prevention than the resolution of apical periodontitis.

Conclusions: There was no significant difference in the "tooth survival," "postoperative pain" and "evidence of apical radiolucency" outcomes of RCTx in teeth with vital or necrotic pulps.

Registration: PROSPERO database (CRD42021260280).

KEYWORDS

apical periodontitis, meta-analysis, necrotic pulp, pain, root canal treatment, vital pulp

INTRODUCTION

The European Society of Endodontology (ESE) (Duncan et al., 2021) has recently initiated the development of S3-level clinical practice guidelines for the treatment of pulpitis and apical periodontitis since the latest guidelines were published in 2006 (European Society of Endodontology, 2006). Systematic reviews of available data based on appropriately constructed PICO questions with multiple outcome measures (OMs) identified by a panel of experts through a Delphi process is one of the crucial steps (Duncan et al., 2021). Thereby, a consensus was reached regarding further patient-reported and clinician-reported OMs and the associated follow-ups (Duncan et al., 2021), which are at the core of the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework (Guyatt et al., 2008; Sanz et al., 2020). The present systematic review with meta-analysis is part of the output from the ESE S3 working group 1 (WG1), which focuses on the treatment of pulpitis. The title of the present work, in particular, coded WG 1.4, is "Effectiveness of root canal treatment for vital pulps compared with necrotic pulps."

Incipient or established-but-limited pulpitis may be managed by vital pulp therapy when it is believed that a sufficient body of pulp tissue remains healthy and unaffected (Ricucci et al., 2014). The direct and uncontrolled spread of pulp inflammation leading to more advanced pulpitis causing the pulp to be unsavable with incipient involvement of the apical tissues may require extirpation to control pain and nonsurgical root canal treatment to maintain the health of apical tissues (Ricucci et al., 2014). Pulp necrosis in the absence of microbial contamination is often silent and its diagnosis is elusive. Where pulpal necrosis and infection have already eventually ensued with consequent apical inflammation, nonsurgical root canal treatment is required to manage the resident intraradicular infection. Other clinically relevant scenarios necessitating root canal treatment include the elective treatment of vital teeth, as part of a prosthodontic treatment plan, and noncontaminated pulp necrosis ensuing traumatic dental injuries.

Vital pulp therapy performed under guideline standards with an optimal coronal seal, achieved promising long-term success in teeth with carious, mechanical or traumatic exposures of healthy pulps (Cushley et al., 2021; Cvek, 1978). The most important factors affecting the outcome of vital pulp therapy measured as the health of the pulp are pre-existing health of the pulp; adequate removal of infected hard or soft tissues; careful operative technique to avoid damage to residual tissues and exclusion of microbial penetration around the final restoration (Bogen et al., 2008; Horsted et al., 1985; Mente et al., 2010). However, it can be difficult to gauge the health of the residual pulp clinically (Dummer et al., 1980; Ricucci et al., 2014; Seltzer et al., 1963a, 1963b). The degree of pulp bleeding upon exposure is a more reliable tool to judge the status of the pulp than the preoperative clinical signs and symptoms plus the results of commonly used special tests (Matsuo et al., 1996). Due to the challenges in making accurate pulpal diagnosis, the perceived unpredictable outcome of vital pulp therapy in teeth with pulpitis (Ward, 2002), and the compromised outcome of root canal treatment once the pulp has become necrotic with established infection (Kojima et al., 2004), pulp extirpation and subsequent root canal treatment are considered as the first management of choice for teeth with pulpitis by many clinicians to ensure immediate control of symptoms (Bjorndal & Reit, 2004; Oen et al., 2007). Apart from the prevention and treatment of apical periodontitis and the management of pain, the role of primary root canal treatment regarding broader outcomes of significance for clinicians and patients needs further understanding.

The present systematic review should therefore provide evidence to inform clinical decision-making and formulation of evidence-based guidelines. It fulfils the criteria, including the PICOTS framework, of the ESE S3-level clinical practice guidelines consensus (Duncan et al., 2021).

The focused question for the present systematic review is "In patients with vital pulp or pulp necrosis in permanent or immature teeth (P) what is the effectiveness of nonsurgical root canal treatment for managing teeth with a vital pulp (I) in comparison with nonsurgical root canal

treatment for managing teeth with pulp necrosis (nonvital) (C) in terms of clinical and patient-related outcomes (O)."

MATERIALS AND METHODS

The current review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement (Page et al., 2021) adapted to the *International Endodontic Journal* author guidelines. The protocol has been registered in the PROSPERO database (CRD42021260280) and is accessible at https://www.crd.york.ac.uk/prospero/.

PICOTS framework

Participants/population (P) were patients undergoing nonsurgical root canal treatment.

Intervention(s)/exposure(s) (I) group were teeth with a vital pulp.

Comparator(s)/control (C) group were teeth with pulp necrosis (nonvital) with or without signs of periradicular pathosis.

Outcomes (O) included a combination of patient and clinician-reported outcomes measures were assessed, as follows.

Main outcome(s)

The most critical outcome was "tooth survival." Other critical outcomes are "pain, tenderness, swelling, need for medication (analgesics, antibiotics)," "radiographic evidence of reduction of apical lesion size (loose criteria)" and "radiographic evidence of normal periodontal ligament space (strict criteria)" or "evidence of emerging apical radiolucency."

Additional outcome(s)

Important outcomes were as follows "tooth function (fracture, restoration longevity)," "need for further intervention," "adverse effects (including exacerbation, restoration integrity, allergy)," "oral health-related quality of life (OHRQoL)" and "presence of sinus tract."

Timing (T) was defined as a minimum of 1 year and a maximum of as long as possible for all outcome measures, except "pain, tenderness, swelling, need for medication (analgesics)," which is a minimum of 7 days and a maximum of 3 months and OHRQoL which is a minimum of 6 months and a maximum of as long as possible.

Study design (S) included human experimental studies (randomized control trials, comparative clinical trials—nonrandomized) and longitudinal observational studies (retrospective and prospective comparative cohort and case–control studies). The number of patients had to be at least 20 (10 in each arm) at the end of the study.

Searches

A systematic literature search was conducted using three electronic databases: Scopus (https://www.scopus.com/search/form.uri?zone=TopNavBar&origin=searchbasic&display=basic#basic), PubMed (https://pubmed.ncbi.nlm.nih.gov/) and Embase (https://www.embase.com/?phase=continueToApp#search), from inception to the 2 August 2021 with language restricted to English. The search terms are summarized in Table S1. To identify conference papers, and other grey literature, additional searches were performed using Google Scholar (first 100 returns on the 26 July 2021) and available repositories (Networked Digital Library of Theses and Dissertations, Open Access Theses and Dissertations, DART-Europe E-theses Portal—DEEP, Opening access to UK theses—EThOS—on the 22 July 2021). The hand search included reference lists of included papers and previously published reviews (Manfredi et al., 2016; Ng et al., 2008, 2010), plus the last 20 years of *International Endodontic Journal* (final search 23 July 2021) *and Journal of Endodontics* (final search 14 July 2021). Reference lists of included studies were analysed to assure the reliability of the data collected. Conducted searches were rerun on 29 March 2022, except for Google Scholar, with no further study fulfilling the PICOTS framework since the previous drafting of the manuscript.

The search strategy was performed by two independent reviewers (GR-F and Y-LN); disagreement and doubts would have been by discussing with a third reviewer (working group leads—IE-K and GK). Duplicates identified in the searches of the various databases were removed. Relevant and appropriate studies selected in the systematic review were performed based on a three-step process: identification, screening and eligibility.

Data extraction (selection and coding)

The data extraction was performed by two independent reviewers; two reviewers (GR-F and Y-LN) performed independently duplicate data extraction using a preestablished and piloted spreadsheet. Only published

data were included for analyses and no attempt was made to contact the authors to obtain missing data or clarify data discrepancies. In case of nonagreement between the reviewers, the data were not used until further clarification was available (resolved by discussing with IE-K and GK). In the case of multiple papers reporting on the same study, only the relevant data of interest was extracted.

The following details were included in the spreadsheet for each study and the final review: name and country of the first author, year published, name of the journal, type of study design, unit of outcome measure, the total number of units, age distribution, number of units with vital pulp and relative success, number of patients with necrotic pulp and relative success, intervention details (number of visits, irrigants and medicaments), duration of follow-up, outcome measures employed, type of radiographic assessment, method of outcome assessment and main findings. Studies using periapical index values ≤2 as their threshold to describe "healed" were considered as "loose criteria" for radiographic evidence of reduction of apical lesion size. The inter-reviewer reliability (percentage of agreement and kappa correlation coefficient) of the full-text analysis was calculated.

Risk of bias (quality) assessment

Critical appraisal of the included studies was performed using a customized version of the Newcastle–Ottawa Quality Assessment Scale for case–control studies (Wells et al., 2014), considering the risk of bias (RoB) related to the case (teeth with vital pulp) and control (teeth with necrotic pulp) selection, comparability and assessment of outcome(s) (Table 1). Studies with 8–7 or 6–4 stars assigned were considered to be of "low risk of bias" and "some concerns" quality respectively, whereas studies with 3 or fewer stars were regarded as "high risk of bias" studies.

Strategy for data synthesis

All data were analysed qualitatively as well as quantitatively and a narrative synthesis of the included studies was performed. Quantitative data for each outcome measure were pooled in a statistical meta-analysis using a fixed-effect or random-effect model to obtain a risk ratio (RR) and 95% CI. All analyses were performed using the STATA IC version 16.1 (STATA Corporation). The forest plots were calculated considering 95% of CI and *p*-values. A *p*-value ≤.05 was considered statistically significant.

TABLE 1 Criteria for assessment of risks of bias adapted from Newcastle–Ottawa quality assessment scale for case–control studies

A) Selection
1) Is the case (teeth with vital pulp) definition adequate?
a) Yes, with independent validation (pulp sensibility test or confirmation upon accessing or explicit mention of vital pulp treatment/extirpation or similar)
b) Yes, eg record linkage or based on self-reports
c) No description
2) Representativeness of the cases (teeth with vital pulp)
a) Consecutive or obviously representative series of cases
b) Potential for selection biases or not stated
3) Selection of controls (teeth with nonvital pulp)
a) Controls from the same setting
b) Controls from other setting(s)
c) No description
4) Definition of controls (teeth with nonvital pulp)
a) Validation of nonvital pulp (pulp sensibility test or confirmation upon accessing)
b) No description of the source
B) Comparability
1) Comparability of cases and controls on the basis of the design or analysis
a) Study controls for nonvital pulp with no radiographic evidence of periapical disease
b) Study controls for any additional factor (clinical protocols for case and control)
C) Outcome
1) Assessment of outcome
a) Independent blind assessment for clinician-reported outcome measures OR previously validated tool for patient-reported outcome measures
b) Record linkage
c) No description
2) Adequacy of follow up of cohorts
a) Complete follow up—all subjects accounted for
b) Subjects lost to follow up unlikely to introduce bias—small number lost— >70% follow up, or description provided of those lost)
c) Follow up rate <50% and no description of those lost
d) No statement

Note: A study can be awarded a maximum of one star for each numbered item within the selection and exposure categories.

Sensitivity analyses during meta-analysis

Sensitivity analysis was carried out using a random-effects model to calculate RR by assessment method and periapical status of necrotic pulp.

Contour-enhanced funnel plots were used to assess for small study effect via visual inspection for evidence of

asymmetry associated with: small studies showing more or less beneficial intervention effect estimates; studies displaying markedly different intervention effect estimates (outliers); studies that are highly influential in the meta-analysis or an isolated study causing an overall small *p* value.

Meta-regression and bubble plot were used to investigate the effect of the potential confounding factor (preoperative periapical radiolucency amongst teeth with necrotic pulp) on the pooled outcome. In case of significant influence, subgroup meta-analyses were carried out.

Quality of evidence assessment using GRADE

The overall quality of the evidence for each of the main outcomes ("tooth survival," "pain" and "evidence of apical radiolucency") was rated using the GRADE (Guyatt et al., 2008) approach by two review authors independently (GR-F and Y-LN). Disagreements were discussed until a decision was reached by consensus. The judgement was based on the design of the different component studies for each outcome, with the GRADE certainty of evidence being reduced depending on: (1) the RoB; (2) inconsistency of results based on the degree of heterogeneity I^2 value; (3) indirectness of evidence; (4) imprecision and (5) publication bias. Possible quality of evidence for each outcome was "very low," "low," "moderate" or "high."

RESULTS

Search output

The search strategy retrieved 3283 records in total, of which 28 fulfilled the inclusion criteria. The results of the search strategy are presented in Figure 1. The main reasons for excluding the 150 studies identified following the full-text assessment are summarized in Figure 1 and listed in Appendix S1.

Narrative synthesis of the 28 included studies

Five included studies (Kebke et al., 2021; Kwak et al., 2019; Landys Boren et al., 2015; Ng et al., 2011a; Pirani et al., 2018) compared teeth with vital versus necrotic pulp using the most critical outcome measure, tooth survival at 2–10 years postoperatively. Other critical outcomes: postoperatory pain at 7 days to 3 months was assessed in seven studies (Farzana et al., 2010; Makanjuola et al., 2018; Oginni & Udoye, 2004; Oliet, 1983; Prashanth et al., 2011; Sigurdsson et al., 2016; Wong, 2016); and post-treatment evidence

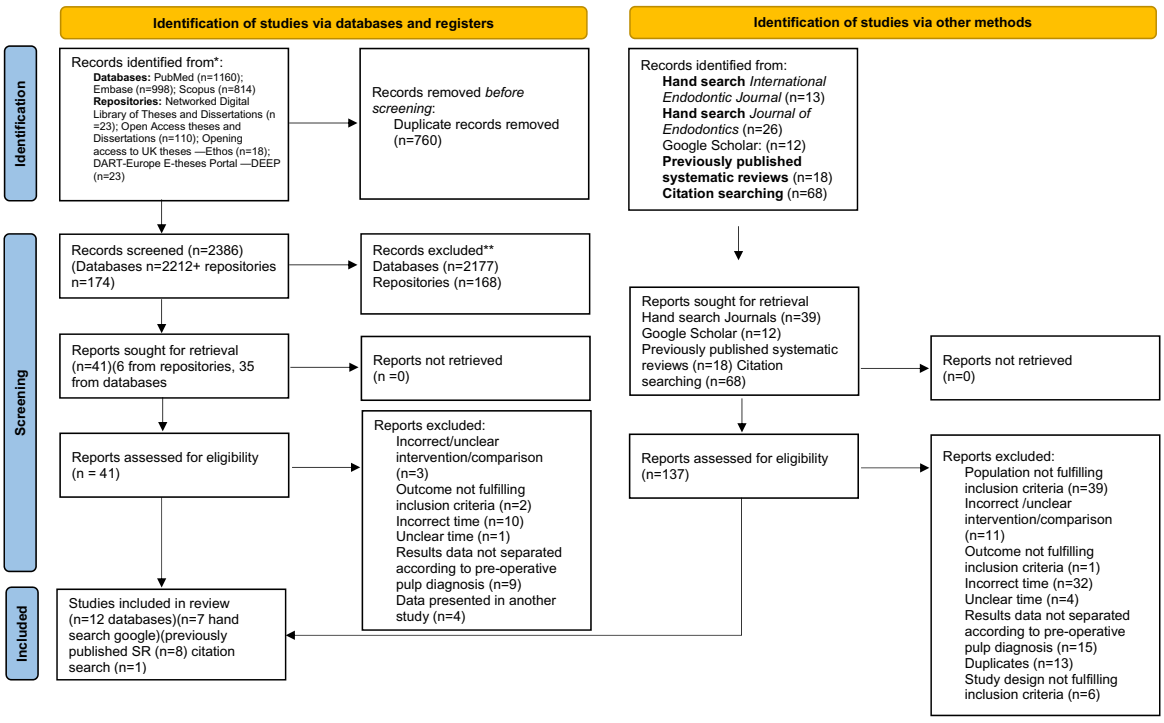

FIGURE 1 PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources.

of apical radiolucency at 1–30 years following treatment was investigated in 19 studies (Barbakow et al., 1980a, 1980b; Chugal et al., 2001; De Chevigny et al., 2008; De Quadros et al., 2005; Grahnen, 1961; Heling & Kischinovsky, 1979; Heling & Tamshe, 1970; Hoskinson et al., 2002; Jokinen et al., 1978; Nelson, 1982; Ng et al., 2011b; Oliet, 1983; Orstavik et al., 1987; Pirani et al., 2018; Ricucci et al., 2011; Salas et al., 2020; Sigurdsson et al., 2016; Sjogren et al., 1990; Smith et al., 1993). None of the included studies has reported on any of the further important outcomes including tooth function, need for further intervention, adverse effects or OHRQoL. Four studies have assessed evidence of apical radiolucency together with another outcome: postoperative pain (Oliet, 1983; Sigurdsson et al., 2016), or tooth survival (Ng et al., 2011a, 2011b; Pirani et al., 2018). The outcome presence of sinus tract has not been investigated as a separate measure, but its absence was included as a criterion for success for the "evidence of apical radiolucency" outcome. Further details of these studies are presented in Tables 2–4.

None of the studies reported a significant association between pulpal status and tooth survival outcome, regardless of the duration of follow-up (Table 2).

Of the seven studies investigating postoperative pain, two (Farzana et al., 2010; Wong, 2016) reported a low incidence of pain at day seven postoperatively and pulpal status did not have a significant ($p > .05$) influence. There was an absence of postoperative pain reported at 14-day, 30-day or 3-month post-treatment follow-up, regardless of pulpal status (Farzana et al., 2010; Makanjuola et al., 2018; Oginni & Udoye, 2004; Prashanth et al., 2011; Sigurdsson et al., 2016) (Table 3).

Of the 19 studies reporting "evidence of apical radiolucency" (periapical health) outcome, all with the exception of one study (Sjogren et al., 1990) reported

TABLE 2 Summary of included studies ($n = 5$) comparing tooth survival following root canal treatment of teeth with vital vs. necrotic pulp

First author	Country	Year	Journal	Study design	Age range (years)	Number of units				
						Total	Vital pulp	Vital pulp success	Necrotic pulp	Necrotic pulp success
Ng (a)	UK	2011	International Endodontic Journal	P		759 t	146	139	613	585
Landys Borén	Sweden	2015	Journal of Endodontics	R	14–91	242 p	111		131	
Pirani	Italy	2018	International Endodontic Journal	R	18–70	151 t	93	87	58	51
Kwak	Korea	2019	Journal of Endodontics	P		2 171 276 t	2 096 272	1 914 539	75 004	68 362
Kebke	Sweden	2021	International Endodontic Journal	H	10–80	210 t				

Note: Empty cells: missing data.

Abbreviations: $Ca(OH)_2$, calcium hydroxide; EDTA, ethylenediaminetetraacetic acid; H, Historical cohort; M, multiple visits; NaOCl, sodium hypochlorite; p, patients; P, Prospective cohort; Pa, periapical radiolucency; R, Retrospective cohort; S, single visit; t, teeth.

periapical health based on both clinical and radiographic examinations; 11 adopted strict radiographic criteria and 8 adopted loose radiographic criteria for determination of a successful outcome. Four studies (Grahnen, 1961; Heling & Tamshe, 1970; Jokinen et al., 1978; Smith et al., 1993) that did not account for the preoperative periapical radiolucency in the statistical analyses, reported root canal treatment on teeth with vital pulp was associated with significantly ($p < .05$) more favourable periapical health outcome than those teeth with necrotic pulp (Table 4). Six studies (Chugal et al., 2001, Hoskinson et al., 2002, De Chevigny et al., 2008, Ng et al., 2011b, Ricucci et al., 2011, Sigurdsson et al., 2016) revealed pulpal status was not a significant prognostic factor on periapical health outcome after adjusting for periapical status using multi-variable logistic regression models. There was excellent agreement in data entry (98.8%) for the 5544 data points including qualitative comments. Kappa correlation coefficient was 0.98 (95% CI: 0.985, 0.991) (almost perfect).

RoB assessment

The overall percentage of agreement in RoB assessment amongst all domains was high (90.8%) but the agreement of the initial assessment of RoB domain A1 was low (64.2%). All disagreements were resolved through discussion. Of the 28 studies included, nine were judged as having a *low RoB* (Barbakow et al., 1980b; De Chevigny et al., 2008; Makanjuola et al., 2018; Ng et al., 2011a, 2011b; Oginni & Udoye, 2004; Salas et al., 2020; Sigurdsson et al., 2016; Smith et al., 1993), two as *high RoB* (Kwak et al., 2019; Nelson, 1982) and the remaining 17 as *some concerns* (Chugal et al., 2001; De Quadros

		Intervention					
Necrotic pulp but no pa	**Necrotic pulp with pa**	**S/M commonly**	**Common irrigant(s)**	**Common medicament(s)**	**Duration of follow up (range, mean)**	**Method of outcome assessment**	**Main findings**
11	602	M	NaOCl 2.5%	$Ca(OH)_2$	2–4 years	Follow-up with clinical examination	Vital vs. necrotic pulp had no significant influence
27	104				10 years	Dental records, phone interview	Pulpal and periapical status did not have a significant influence
0	58	S	NaOCl 5%, EDTA 10%		5 ± 1 years	Follow-up	Vital had higher survival than necrotic with Pa, not confirmed as a predictor by multilevel analysis
75 004		M			5 years	Records	Pulpal status is not confirmed as a significant predictor
					10 years	Records	Pulpal diagnoses had no significant influence

TABLE 3 Summary of included studies ($n = 7$) comparing postoperative pain and/or swelling outcome following root canal treatment of teeth with vital vs. necrotic pulp

						Number of units				
First author	Country	Year	Journal	Study design	Age range (years)	Total	Vital pulp	Vital pulp success[a]	Necrotic pulp	Necrotic pulp success[a]
Oliet	USA	1983	Journal of Endodontics	P	10–60+	387 p	182		205	
Oginni	Nigeria	2004	BMC Oral Health	P		222 t				
Farzana	Bangladesh	2010	JAFMC	P		52 p	23	21 (23)	29	23 (29)
Prashanth	India	2011	Journal of Contemporary Dental Practice	P		32 t	16	16	16	16
Sigurdsson	USA	2016	Journal of Endodontics	P		75 t	61	61	14	14
Wong	Hong Kong	2016	HKU Thesis	P	18+	538 t	219		319	
Makanjuola	Nigeria	2018	Journal of the West African College of Surgeons	P	18–60	119 t	38	38	82	82

Note: Empty cells: missing data.

Abbreviations: $Ca(OH)_2$, calcium hydroxide; EDTA, ethylenediaminetetraacetic acid; M, Multiple visits; N/A, not applicable; NaOCl, sodium hypochlorite; p, patients; P, Prospective cohort; Pa, periapical radiolucency; S, single visit; t, teeth.

[a]Success: the absence of pain and/or swelling at follow-up.

et al., 2005; Farzana et al., 2010; Grahnen, 1961; Heling & Kischinovsky, 1979; Heling & Tamshe, 1970; Hoskinson et al., 2002; Jokinen et al., 1978; Kebke et al., 2021; Landys Boren et al., 2015; Oliet, 1983; Orstavik et al., 1987; Pirani et al., 2018; Prashanth et al., 2011; Ricucci et al., 2011; Sjogren et al., 1990; Wong, 2016), with the adequacy of follow up of cohort being the main domains of concern (Table 5).

		Intervention					
Necrotic pulp but no pa	**Necrotic pulp with pa**	**S/M commonly**	**Common irrigant(s)**	**Common medicament(s)**	**Duration of follow up (range, mean)**	**Method of outcome assessment**	**Main findings**
0	205	S/M	NaOCl 5%		7 days		Absence of postoperative pain persisted as long as 7 days
		S/M			30 days	Interview at follow-up: none, slight, moderate/ severe pain	Absence of postobturation pain persisted on day30
		M	NaOCl 1%	$Ca(OH)_2$	7 days, (30 days)	Interview using a previously published scale	7 days: similar postoperative pain comparing vital pulp and necrotic pulp; 30 day: no pain persisted
0	16	S/M	NaOCl 2.5%	Empty	1, 4, 6 weeks	Follow-up clinical examination	No incidence of pain at 1 week or longer follow-up.
		S	NaOCl 3%, EDTA 8%, GentleWave system		14 days	Visual Analogue Scale	7 days: 14 days: No incidence of pain
		S/M	NaOCl 5.25%, EDTA 17%	$Ca(OH)_2$	7 days	Follow-up Visual Analogue Scale used	Vital vs. necrotic pulp had no significant influence on 7-day postoperative pain
18	64	S	NaOCl 2.5%,	N/A	3 months	Review and use of pain scale Swelling:	No patients presented with pain or swelling at the 3-month review

Quantitative synthesis

Quantitative synthesis was possible for the comparison between vital versus necrotic pulp using "tooth survival" (data available from 3 studies) and "evidence of apical radiolucency" (periapical health) (data available from 16 studies) outcomes.

The fixed-effect meta-analyses of the pooled effect of pulpal status on tooth survival review negligible observed

TABLE 4 Summary of included studies ($n = 19$) comparing periapical health following root canal treatment of teeth with vital vs. necrotic pulp

						Number of units				
First author	**Country**	**Year**	**Journal**	**Study design**	**Age range (years)**	**Total**	**Vital pulp**	**Vital pulp success**	**Necrotic pulp**	**Necrotic pulp success**
Grahnén	Sweden	1961	Odontology Revy	R		775 r	570	485	205	168
Heling	Israel	1970	Oral Surgery	R	10–60	204 t	63	49	141	91
Jokinen	Finland	1978	Scandinavian Journal of Dental Research	R	16–75	2459 r	813	441	1646	863
Heling	Israel	1979	Journal of the British Endodontic Society	R	9–75	121 t	64	51	57	46
Barbakow	South Africa	1980	Journal of Endodontics	R	10–80	332 t	162	139	170	151
Nelson	UK	1982	International Endodontic Journal	R	<15–60<	295 t	97	86	198	153
Oliet	USA	1983	Journal of Endodontics	P	10–60+	338 t	146	127	195	173
Ørstavik	Norway	1987	Endodontics and Dental Traumatology	P	<20–80<	289 r	164	163	125	114
Sjögren	Sweden	1990	Journal of Endodontics	R	28–82	573 r	267	257	306	278
Smith	UK	1993	International Endodontic Journal	R	16–60+	821 t	216	192	605	500

		Intervention					
Necrotic pulp but no pa	Necrotic pulp with pa	S/M commonly	Common irrigant(s)	Common medicament(s)	Duration of follow up (range, mean)	Method of outcome assessment: radiographic criteria for success[a]	Main findings[b]
89	116	M	Vital: 10% I2; Necrotic: 50% H_2SO_4 and sodium bicarbonate, antiformin and chloroform	Grossman's solution and tricresol formalin	4–5 years	Strict	No significant difference between vital and necrotic pulp after adjusting for periapical status ($p > .05$)
			EDTA 15%	CMCP	1–5 years	Strict	Vital more favourable than necrotic pulp without accounting for periapical status ($p < .05$)
805	841	M	Vital: Organic acid Necrotic: H_2O_2 2%	Dexamethasone sodium phosphate, dequalone acetate	2–7 years	Strict	Vital more favourable than necrotic pulp; no Pa is more favourable than Pa ($p < .001$)
25	32		EDTA 15%, CMCP	CMCP	1–16 years	Loose	Vital similar to necrotic pulp; no Pa more favourable than Pa
52	118	M	NaOCl 5%, Endoprep	Cresenol most commonly	1–9 years	Strict	Vital similar to necrotic pulp; no difference amongst various vital pulpal status
54	144				2–30 years	Loose	No significant difference between vital and necrotic pulp ($p > .05$); No Pa is more favourable than Pa ($p < .001$)
0	192	S/M	NaOCl 5%		2 years	Strict	No significant difference between vital pulpitis and necrotic pulp with pa ($p > .05$)
46	79		Etedate, 5% chloramine T	Vital: chloramine T necrotic: 3.7% formaldehyde solution	4 years	Loose	Not analysed pulpal status
102	204	M	NaOCl 0.5%	$Ca(OH)_2$, I2 5%, CMCP	8–10 years	Strict	Vital and necrotic pulp with no pa had the same success rate (96%). Nonvital with no pa more favourable than with pa ($p < .05$)
124	481	M			5 years	Loose	Vital more favourable than necrotic pulp ($p < .05$) NoPa more favourable than Pa ($p < .05$)

TABLE 4 (Continued)

						Number of units				
First author	**Country**	**Year**	**Journal**	**Study design**	**Age range (years)**	**Total**	**Vital pulp**	**Vital pulp success**	**Necrotic pulp**	**Necrotic pulp success**
Chugal	USA	2001	Oral Surgery Oral Medicine Oral Pathology	R		322 t	143	126	179	123
Hoskinson	UK	2002	Oral Surgery Oral Medicine Oral Pathology	R		413 r	156	135	257	176
De Quadros	Brazil	2005	Journal of Dental Education	R	8–77					
de Chevigny	Canada	2008	Journal of Endodontics	P		510 t	178		332	
Ng (a)	UK	2011	International Endodontic Journal	P		1170 r	258	234	912	735
Ricucci	Italy	2011	Oral Surgery Oral Medicine Oral Pathology Oral radiology Endodontology	P		745 t	435	398	310	261
Sigurdsson	USA	2016	Journal of Endodontics	P		75 t	61	60	14	13
Pirani	Italy	2018	International Endodontic Journal	R	18–70	143 t	89	82	54	42
Salas	Peru	2020	Australian Endodontic Journal	P	29–72	47 t	26	22	21	16

Note: Empty cells: missing data.

Abbreviations: $Ca(OH)_2$, calcium hydroxide; CHX, chlorhexidine; CMPC, camphorated parachlorophenol; EDTA, ethylenediaminetetraacetic acid; H, Historical cohort; H_2O_2, hydrogen peroxide; H_2SO_4, sulphuric acid; M, multiple visits; NaOCl, sodium hypochlorite; p, patients; P, Prospective cohort; Pa, periapical radiolucency; R, Retrospective cohort; r, roots; S, single visit; t, teeth.

[a]Method of outcome assessment: All studies employed both clinical and plain film radiographic assessment using loose or strict criteria to determine the outcome, with the exception of Sjogren et al., 1990 which presented the data based on radiographic assessment only.

[b]Main findings: The absence of *p* value indicates observations were not supported by statistical analyses.

		Intervention					
Necrotic pulp but no pa	Necrotic pulp with pa	S/M commonly	Common irrigant(s)	Common medicament(s)	Duration of follow up (range, mean)	Method of outcome assessment: radiographic criteria for success[a]	Main findings[b]
					3.5–4.5 years	Strict	Vital pulpitis vs. necrotic pulp was not a significant predictor after adjusting for pa status ($p > .05$)
		S/M for teeth with Pa	NaOCl 1.5–3.0%, EDTA	Teeth with pa lesion $Ca(OH)_2$	4 years	Strict	Vital vs. necrotic pulp was not a significant predictor after adjusting for pa status ($p > .05$)
		M	NaOCl 1%, EDTA 17%, CHX 2%	$Ca(OH)_2$	1 years	Strict	Success rates (1 year): Healthy pulp: 96% Exposed pulp: 81% Pulpitis: 82% Necrotic: 63%
		M	NaOCl 2.5%, CHX 2%, EDTA 17%		4–6 years	Loose	Vital vs. necrotic pulp was not a significant predictor after adjusting for pa status ($p > .05$)
129	783	M	NaOCl 2.5%	$Ca(OH)_2$	2–4 years	Strict	Vital vs. necrotic pulp was not a significant predictor after adjusting for pa status ($p > .05$)
67	243	M	NaOCl 1%	$Ca(OH)_2$	5 years	Strict	Vital vs. necrotic pulp was not a significant predictor after adjusting for pa status ($p > .05$)
		S	NaOCl 3%, EDTA 8%, GentleWave system		1 years	Loose	Vital pulp with irreversible pulpitis and necrotic pulp was not significantly different ($p > .05$) PAI scores had a significant influence ($p < .05$)
0	54	S	NaOCl 5%, EDTA 10%		5 ± 1 years	Loose	Vital pulp higher Pa health rate than necrotic with apical periodontitis, not confirmed as a predictor by multilevel analysis
		S/M for necrotic pulp with Pa)	CHX 1.2–2%, (according to diagnosis), EDTA 17%	$Ca(OH)_2$ + CHX2%	1+ years	Loose	Vital pulp vs. necrotic pulp comparison was not significantly different ($p > .05$)

TABLE 5 Bias of individual studies ($n = 28$)

				Selection		
Name of the first author	**Year published**	**Outcome measures employed**	**Funding**	**A1) selection definition adequate**	**A2) selection Representativeness**	**A3) Selection control same setting**
Grahnén	1961	PARL	Nil	*	*	*
Heling	1970	PARL	Nil	Not described	*	*
Jokinen	1978	PARL	Nil	*	*	*
Heling	1979	PARL	Nil	*	*	*
Barbakow	1980	PARL	Nil	*	*	*
Nelson	1982	PARL	Nil	Not described	*	*
Oliet	1983	PARL/Pain	Nil	*	*	*
Ørstavik	1987	PARL	Nil	*	*	*
Sjögren	1990	PARL	Nil	*	*	*
Smith	1993	PARL	Nil	*	*	*
Chugal	2001	PARL	University of Connecticut Endodontic Alumni Association	Not described	*	*
Hoskinson	2002	PARL	Nil	*	*	*
Oginni	2004	Pain	Nil	*	*	*
De Quadros	2005	PARL	Brazilian agencies FAPESP, CNPq, and CAPES.	*	*	*
de Chevigny	2008	PARL	AAE Foundation, Canadian Academy of Endodontics Endowment.	*	*	*
Farzana	2010	Pain	Nil	*	*	*
Ng (a)	2011	PARL	NIHR Biomedical Research Centers funding scheme, UK	*	*	*

	Comparability	Outcome		
A4) Selection definition adequate	**B1) Comparability appropriate control**	**C1) Outcome assessment adequate**	**C2) Outcome follow-up adequate**	**Total***
Not described	* Different treatment protocols	*	44%	5
Not described	**	Not described	27%	4
*	* Different treatment protocols	*	46%	6
*	* Some vital teeth undergone chemical devitalisation	Not described	13%	5
*	**	*	59%	7
Not described	Periapical disease not controlled Treatment not described	*	No statement	3
Not described	* All necrotic teeth had apical radiolucency	Not described	No statement	4
*	* Different treatment protocols	*	36%	6
*	* Different apical extent of instrumentation for vital vs. necrotic teeth	*	46%	6
*	**	*	54%	7
Not described	* Treatment not described	*	19%	4
Not described	**	*	42%	6
*	* Preoperative pain and periapical disease not controlled	*	*	7
*	* Periapical disease not controlled	*	31%	6
*	**	*	32%	7
*	Preoperative pain or periapical disease not controlled	*	*	6
*	**	*	*	8

TABLE 5 (Continued)

Name of the first author	Year published	Outcome measures employed	Funding	Selection		
				A1) selection definition adequate	A2) selection Representativeness	A3) Selection control same setting
Ng (b)	2011	Survival	NIHR Biomedical Research Centers funding scheme, UK	*	*	*
Prashanth	2011	Pain	Nil	*	Not described	Not described
Ricucci	2011	PARL	Nil	*	*	*
Landys Boren	2015	Survival	Nil	Record linkage	*	*
Sigurdsson	2016	PARL/Pain	Sonendo Inc	*	*	*
Wong	2016	Pain	Nil	Not described	*	*
Makanjuola	2018	Pain; swelling	Nil	*	*	*
Pirani	2018	PARL/Survival	Nil	Not described	*	*
Kwak	2019	Survival	National Research Foundation, the Ministry of Education, Korea	Record linkage	*	*
Salas	2020	PARL	Nil	*	*	*
Kebke	2021	Survival	Norrbotten Public Dental Service, Sweden	*	*	*

Note: Total number of stars: 0–3 high risk of bias, 4–6 some concerns, 7–8 low risk of bias. *Awarded to low risk of bias for the respective domain; a maximum of 2* can be given to comparability.

heterogeneity ($I^2 = 0\%$) and produced a RR of 1.00 (df = 2; 95% CI: 1.00, 1.00; $p = .07$) (Figure 2). Summary estimates, the inclusion of value 1 in the 95% CI suggest that the meta-analytic effect is not statistically significant at the 5% level and did not favour root canal treatment of preoperative vital or necrotic pulp.

The random-effect meta-analyses of the pooled effect of pulpal status on periapical health outcome revealed significant heterogeneity ($I^2 = 69\%$) and produced a RR of 1.09 (df = 16; 95% CI: 1.05, 1.13; $p = .001$) (Figure 3). Summary estimates, noninclusion of value 1 in the 95% CI and *p*-values, plus the position of the diamond in the forest plot, suggest that the meta-analytic effect is statistically significant in favour of root canal treatment of vital pulp.

Publication bias across studies analysed with funnel plots and related statistical tests for the pooled survival outcome data were not justifiable due to the limited number of studies ($n = 3$).

Analysis with contour-enhanced funnel plot revealed no evidence of a small study effect on the pooled effect of pulpal status on a periapical health outcome (Appendix S2). Meta-regression and bubble plot revealed the negligible and insignificant effect of the proportion of

	Comparability	Outcome		
A4) Selection definition adequate	**B1) Comparability appropriate control**	**C1) Outcome assessment adequate**	**C2) Outcome follow-up adequate**	**Total***
*	**	*	*	8
*	* Preoperative pain or periapical disease not controlled.	*	*	5
*	* Treatment visit(s) different for vital vs. necrotic with periapical radiolucency	*	60%	6
Record linkage	* Treatment not described	*	No statement	4
*	**	*	*	8
Not described	* Preoperative pain prevalence or Periapical disease not controlled.	*	*	5
*	* Preoperative pain or periapical disease not controlled.	*	*	7
Not described	* Periapical disease not controlled	*	41%	4
Record linkage	Periapical disease not controlled Treatment not described	Not described	No statement	2
*	* Different treatment protocol	*	*	7
*	* Treatment not described	*	No statement	6

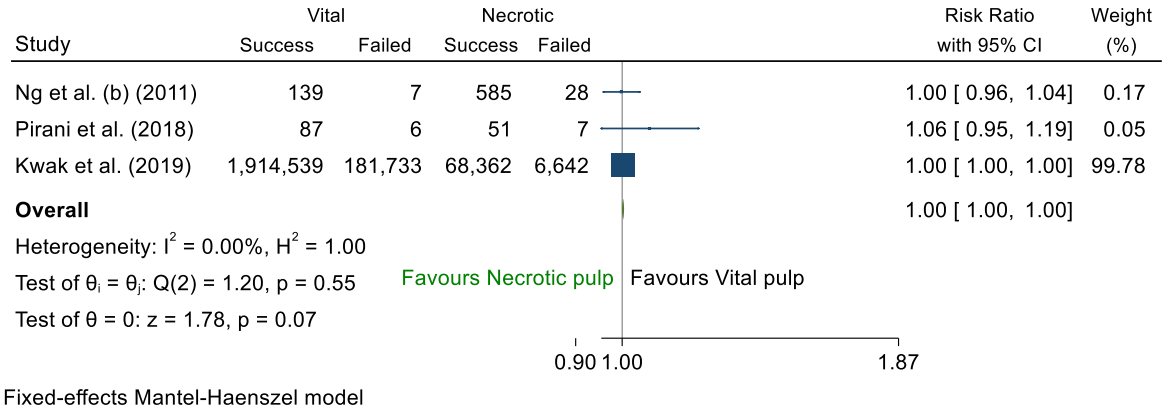

FIGURE 2 Forest plot showing pooled and individual studies' risk ratios (RR) for the survival of teeth undergoing root canal treatment with preoperative vital vs. necrotic pulp (pooled RR = 1.00; 95% CI: 1.00, 1.00).

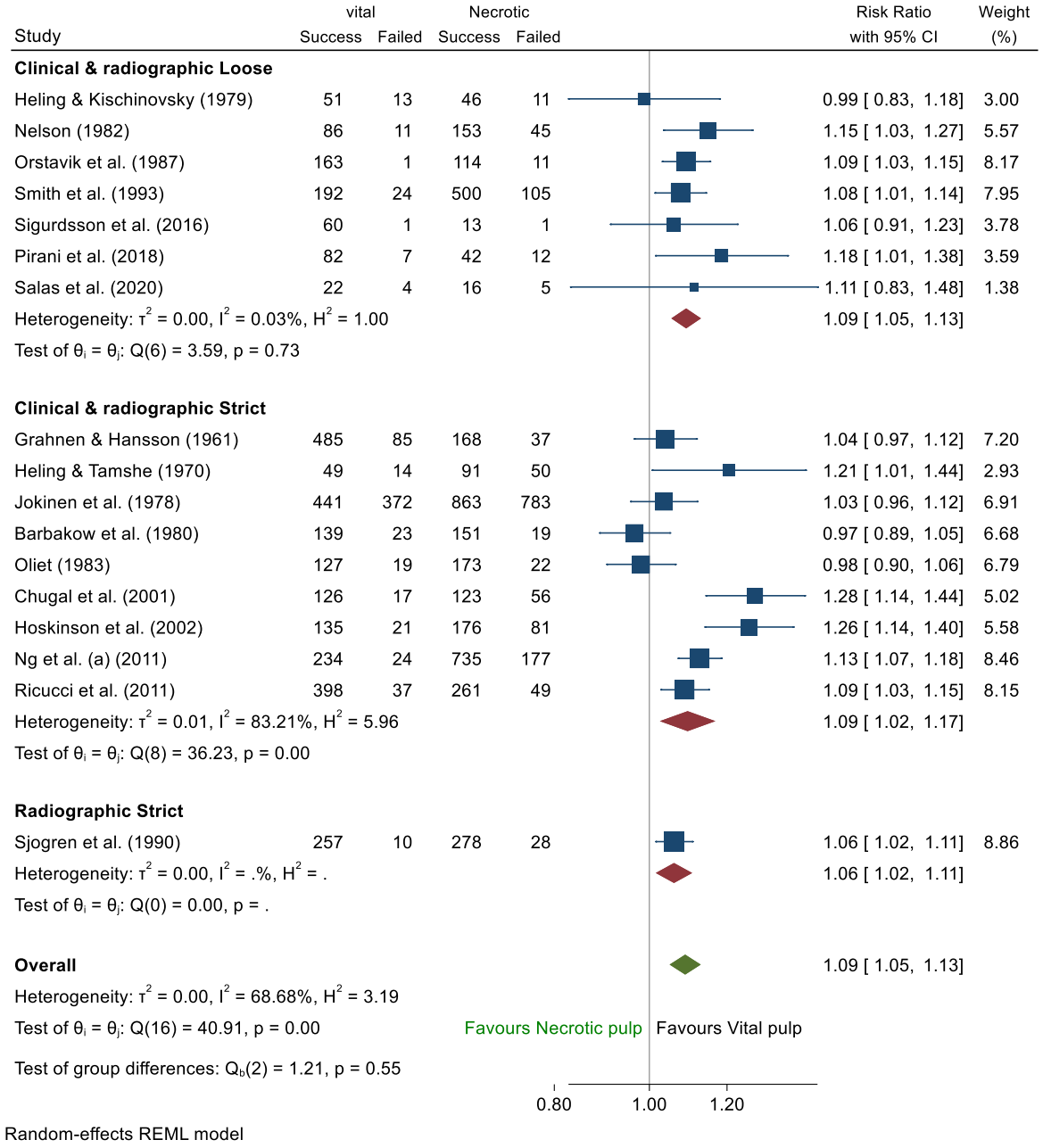

FIGURE 3 Forest plot showing overall pooled, subgroups' and individual studies' risk ratios (RR) for the absence of periapical radiolucency following root canal treatment with preoperative vital vs. necrotic pulp (pooled RR = 1.09; 95% CI: 1.05, 1.13).

teeth with no periapical radiolucency among those with necrotic pulp on the pooled effect of pulpal status on a periapical health outcome (coefficient = −0.02; 95% CI: −0.87, 0.22; $p = .2$) (Appendix S3).

Subgroup analyses by the periapical health assessment method revealed substantial heterogeneity of the data based on strict radiographic criteria ($I^2 = 83\%$) but minimal heterogeneity of the loose radiographic criteria data ($I^2 = 0.03\%$) (Figure 3). However, there was no significant difference in the pooled RR amongst the three groups ($p = .5$) (Figure 3).

Further sub-group analyses demonstrated different findings for periapical health outcome for roots/teeth with the absence (df = 8; RR = 0.95; 95% CI: 0.90, 1.00) (Figure 4) or presence (df = 10; RR = 1.12; 95% CI: 1.05, 1.19) (Figure 5) of preoperative periapical radiolucency. The inclusion of value 1 in the 95% CI of the pooled RR estimate indicates no significant difference in periapical health outcome following root canal treatment of teeth with preoperative vital versus necrotic pulp if periapical radiolucency is absent in the latter group.

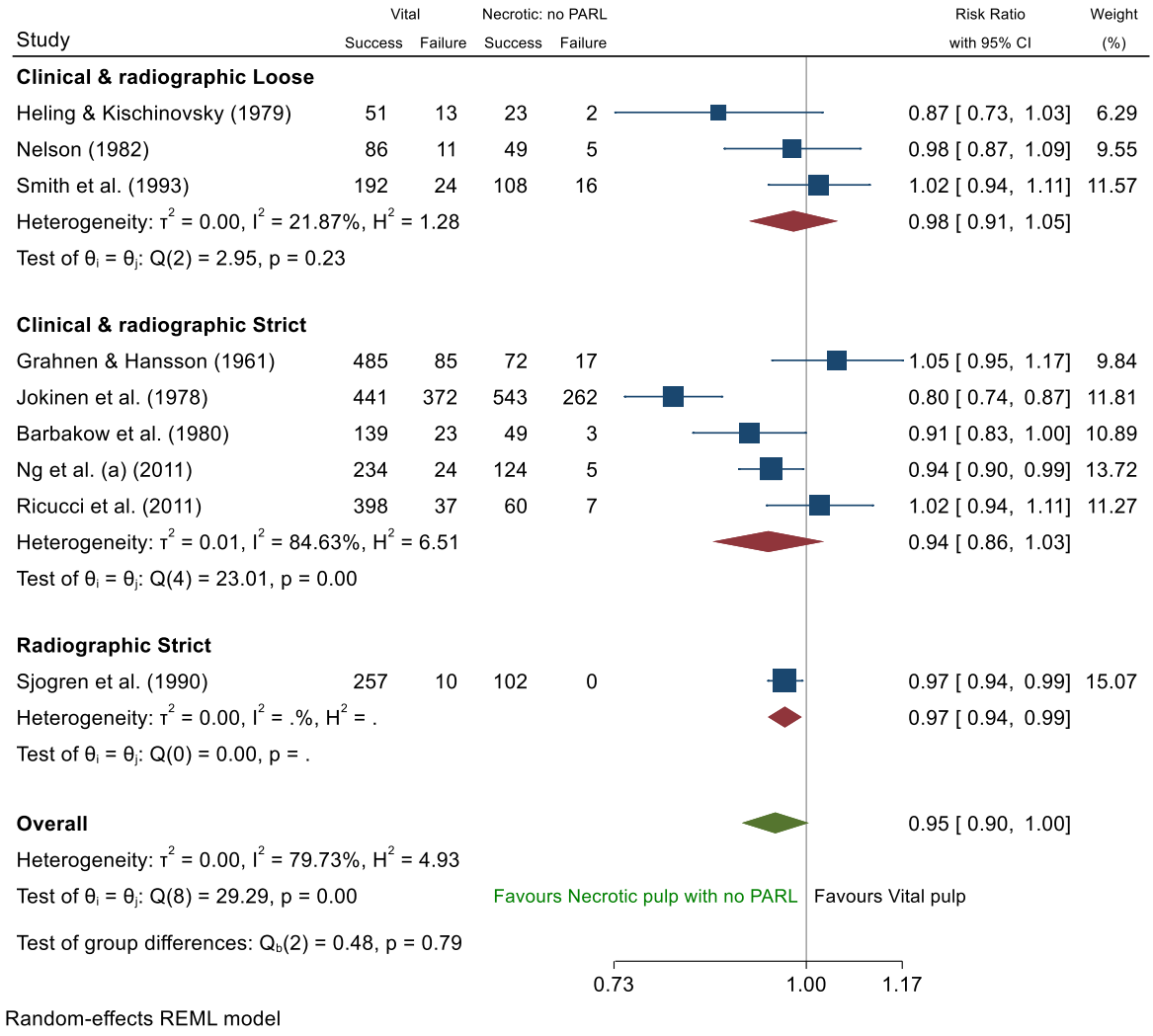

FIGURE 4 Forest plot showing overall pooled, subgroups' and individual studies' risk ratios (RR) for the absence of periapical radiolucency following root canal treatment of teeth with preoperative vital vs. necrotic pulp with no periapical radiolucency (PARL) (pooled RR = 0.95; 95% CI: 0.90, 1.00).

GRADE assessment of quality of the evidence

All component studies were classified as cohort studies. The quality of evidence for "tooth survival" outcome was considered to be moderate. The quality of evidence for "pain" and "periapical health" outcomes was considered to be moderate to high. The GRADE was dominated by the RoB and was not affected by heterogeneity I^2 value; indirectness of evidence; imprecision or publication bias (Table 6).

DISCUSSION

Strengths and limitations

The findings of the present systematic review highlighted the limitations of the evidence base on patient-reported and clinician-reported outcome measures used to compare the effectiveness of root canal treatment for vital versus necrotic pulps fulfilling the PICOTS framework formulated by the European Society of Endodontology for the present project.

The language restriction to English could be considered a limitation. However, the exclusion of publications in other languages was agreed upon by the ESE steering committee for the Quality Guidelines for Endodontic Treatment for consistency and to better manage the resources available. The search strategy of the present systematic review was sufficiently broad, including three commonly used databases, with a search strategy designed with the assistance of a research librarian with expertise in systematic reviews and was tailored to each database. Furthermore, included grey literature such as repositories and Google Scholar plus reference lists of the included studies. Finally, it was validated against the reference lists

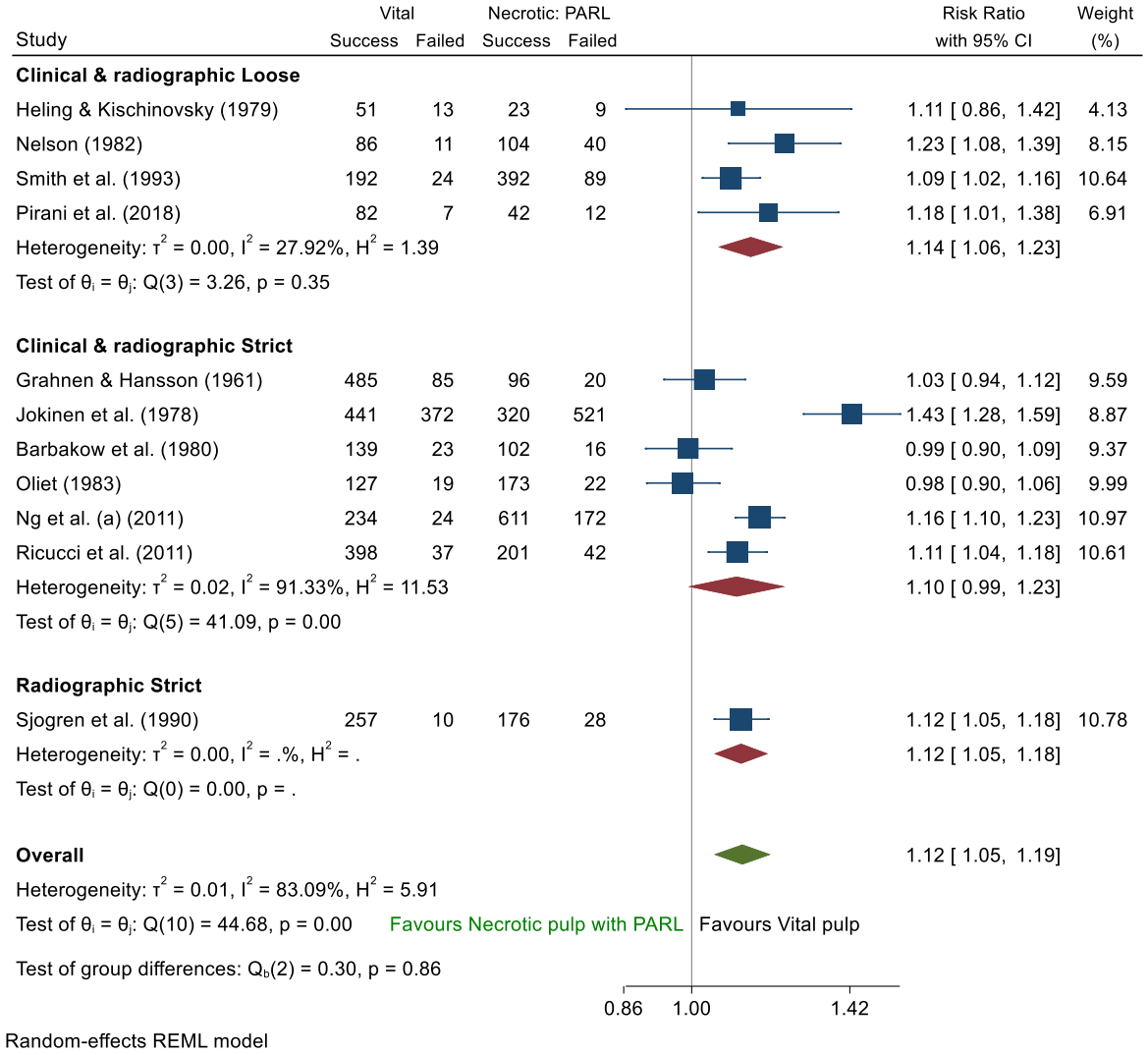

FIGURE 5 Forest plot showing overall pooled, subgroups' and individual studies' risk ratios (RR) for the absence of periapical radiolucency following root canal treatment of teeth with preoperative vital vs. necrotic pulp with periapical radiolucency (PARL) (pooled RR = 1.12; 95% CI: 1.05, 1.19).

of the included studies, previously published comparable systematic reviews and sentinel papers. A total of 3283 records were screened and the potential bias due to missing studies is low.

None of the studies has considered "tooth function" or "OHRQoL." Due to the strict study inclusion criteria, a couple of survival studies (Raedel et al., 2015; Stoll et al., 2005) that have investigated the "need for further intervention" outcome, were excluded from this review. Stoll et al. (2005) did not stratify the analyses or data by "tooth survival" and "need for further intervention" outcomes whilst Raedel et al. (2015) pooled data from retreatment cases. Hamasha and Hatiwsh (2013) have reported the impact of root canal treatment on OHRQoL was significantly greater if the teeth had preoperative vital pulp than necrotic pulp. However, this study measured OHRQoL 2 weeks after treatment and therefore excluded due to incompatibility with the "timing" criteria (T) of the PICOTS framework.

The timing item of the PICOTS framework may be considered a limitation of this review. The postoperative pain during the first week or persisting for 3 months or longer were not included in this review as agreed upon by the ESE steering committee. Postoperative pain is important for patients (Manfredi et al., 2016) and persistent dentoalveolar pain disorder (Nixdorf et al., 2012) following root canal treatment, presenting as persistent pain or discomfort following root canal treatment and signs of periapical healing for more than 3 months postoperatively, has been widely accepted as an important clinical problem. This outcome is particularly important for the present subject of investigation as it has been reported that teeth with responsive pulps diagnosed with irreversible pulpitis before treatment had fivefold higher odds of persistent

TABLE 6 GRADE assessment of the quality of the evidence for comparison of the effectiveness of root canal treatment for vital pulps compared with necrotic pulp for each outcome measure

Outcome	Time	RoB	I^2	Indirectness	Imprecision	Publication bias	Magnitude of effect	Quality of evidence
"Tooth survival"	2–4 years, 5 years, 10 years	Moderate	Low	Not downgraded	Not downgraded	Not analysed	No change	Moderate
"Pain"	7 days, 14 days, 30 days, 3 months	Moderate to high	Not analysed	Not downgraded	Not analysed	Not analysed	No change	Moderate to high
"Evidence of apical radiolucency"	1–10 years	Moderate to high	Low	Not downgraded	Not downgraded	Not downgraded	No change	Moderate to high

symptoms than those with nonvital pulp (OR = 5.2; 95% CI: 1.5, 18.1) (Philpott et al., 2019). Such observation was attributed to a deafferentation response initiated by pulpitis (Marbach, 1996). For evaluation of the impact on OHRQoL, the agreed timing was a minimum of 6 months whilst available data on immediate or short-term impact were excluded. However, Liu et al. (2014) reported most changes in OHRQoL after root canal treatment was found within 1 month and there was a small magnitude of further improvement between 1 and 6 months postoperatively. Given clinical signs and symptoms have a direct impact on OHRQoL it is also valuable to measure the short-term impact when the final restoration has been placed. Although further improvement albeit small may be observed in the longer term, it may risk a high drop-out rate, confounded by other oral health issues or dental intervention and bias related to inaccurate long-term memory.

The most important prognostic factor, preoperative periapical radiolucency for periapical health following root canal treatment (Ng et al., 2008) was accounted for when evaluating the "evidence of apical radiolucency" outcome. However, the influence of the status of vital pulp such as healthy pulp undergoing elective root canal treatment versus teeth with pulpitis undergoing emergency pulpectomy and root canal treatment could not be systematically analysed due to limited data. Nevertheless, some studies have only included teeth diagnosed with pulpitis in the vital pulp cohort (Chugal et al., 2001; Oliet, 1983) and inference could be drawn from them. For the postoperative "pain" outcome, preoperative pain intensity and duration as one of the significant predictors (Law et al., 2015) were only considered in the narrative syntheses due to the limited data for quantitative analyses. Whereas, the commonly found predictive factors for tooth survival, including the location of the tooth (Ng et al., 2010), and post-treatment restoration (Ng et al., 2010) were not considered due to limited studies included and the insignificant effect of pulpal status on tooth survival was found.

The RoB assessment adapted from the Newcastle-Ottawa Quality Assessment Scale for case–control studies demanded subjective interpretation of the information available in the papers resulting in a high rate (36%) of disagreement in determining RoB (Domain A1: Selection definition adequate) between the two reviewers at the initial assessment (data not presented), albeit agreements were reached after discussion. An inadequate follow-up rate was found to be the main source of bias in studies published in the last millennium and there was an inconsistent improvement in those studies published since 2000. Some studies did not present data on several risk domains and hence affecting the outcome of RoB assessment. Ideally, the authors could have been contacted for details, however, based on the reviewers' previous

experience, it was decided against this approach due to inconsistent compliance from study authors leading to potential bias. Although the submission of manuscripts using a validated template would ensure the availability of relevant data for future systematic review, it limits individuality and novelty in presentation, plus would have included several nonapplicable items. Nevertheless, the GRADE system revealed the evidence varied from moderate to high. It should be noted that the intervention and comparator for the PICOTS framework are preoperative factors, thus randomized trials to respond to the focused question of the present review are not possible. This is reflected in an upgrade on the quality rating of the evidence as reported in the results. Several studies received public funding that is unlikely to introduce bias to their results. Overall, the quality of evidence was moderate to high for the three assessed outcomes: "tooth survival," "pain" and "evidence of apical radiolucency."

Interpretation of findings

The outcomes of narrative syntheses were in congruence with the results of quantitative meta-analyses and revealed no significant influence of pulpal status on tooth survival and periapical health outcomes after controlling for the periapical status of teeth with necrotic pulp. Such findings were consistent with previous systematic reviews (Ng et al., 2008, 2010). For the "postoperative pain" outcome, all studies reported no incidence of pain after 14 days post-operatively, in contrast with the long-term studies on chronic persistent pain following root canal treatment (Law et al., 2015; Philpott et al., 2019). The absence of chronic pain in the included studies could be attributable to exclusion of teeth with acute symptoms (Oliet, 1983), and the exclusion of patients who defaulted after the first appointment (Farzana et al., 2010; Oginni & Udoye, 2004), low preoperative pain intensity amongst the study cohort with low proportion with preoperative pain (Makanjuola et al., 2018) or unknown distribution (Wong, 2016). Whereas two studies (Prashanth et al., 2011; Sigurdsson et al., 2016) did not provide details on preoperative pain status.

With regards to the effect of healthy versus diseased status of vital pulps, it was reported to have no significant influence on tooth survival (Kwak et al., 2019), or periapical health (Barbakow et al., 1980b). Sjogren et al. (1990) reported the same periapical health outcomes (96%) for teeth with preoperative healthy vital pulp versus those with pulpitis. Interestingly, Oliet (1983) reported no significant difference between vital pulpitis versus necrotic pulp with periapical radiolucency in the outcome periapical health. Whereas Chugal et al. (2001) found no significant difference between vital pulpitis and necrotic pulp after adjusting for periapical status for the latter group. The discrepancy may be attributable to the exclusion of teeth with acute symptoms where drainage via root canal was established, teeth with persistent exudation or teeth with treatment could not be completed within the available time in the former study.

It should be noted that the treatments in the majority of the included studies were carried out in hospital or institution settings by undergraduate or postgraduate students under the supervision and only some involved the primary care setting (Barbakow et al., 1980a, 1980b; Kebke et al., 2021; Kwak et al., 2019; Nelson, 1982; Oliet, 1983; Ricucci et al., 2011). Inference of the findings of the present systematic review can therefore not be necessarily drawn for the general dental practice setting. Furthermore, some earlier component studies used clinical techniques or materials not necessarily representative of contemporary endodontics.

Clinical implications

Since there is no significant difference in the treatment outcomes between teeth with preoperatively vital or necrotic pulp unless there is periapical radiolucency associated with the latter group, the current contemporary clinical practice for these two conditions may remain the same as long as the treatments are performed to the guideline standard. The goal of treatment is to prevent apical periodontitis by ensuring an aseptic treatment approach and preventing infection via coronal leakage. However, root canal treatment should not be delayed when irreversible pulpal disease or necrotic pulp is diagnosed, as it is more effective in preventing than resolving apical periodontitis. When apical periodontitis is evident as periapical radiolucency, the management challenge is the control of apical root canal infection. The treatment should therefore focus on ensuring chemo-mechanical debridement and obturation as close to the canal terminus as possible without periapical extrusion (Ng et al., 2011a, 2011b).

CONCLUSIONS

Within the limitations of this review, it could be concluded that there was no significant difference in the "tooth survival," "postoperative pain" and "evidence of apical radiolucency" outcomes of root canal treatment in teeth with vital or necrotic pulps. However, the delay in treatment of teeth with necrotic pulps until the periapical disease is evident as apical radiolucency that signifies infection of the apical portion of the root canal

system could compromise the "tooth survival" and "evidence of apical radiolucency" (periapical health) outcomes.

The evidence was missing for other critical ("need for medication") and important ("tooth function," "need for further intervention," "adverse effects" and "OHRQoL") outcomes to draw clinical implications.

AUTHOR CONTRIBUTIONS

The two authors contributed equally to conception, data analysis, writing and critical appraisal.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

DATA AVAILABILITY STATEMENT

Data derived from public domain resources.

ETHICS STATEMENT

This investigation did not involve human or animal subjects.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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