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REVIEW

Outcome of secondary root canal treatment: a systematic review of the literature

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Abstract

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Aims (i) To investigate the effects of study characteristics on the reported success rates of secondary root canal treatment (2°RCT or root canal retreatment); and (ii) to investigate the effects of clinical factors on the success of 2°RCT.

Methodology Longitudinal human clinical studies investigating outcome of 2°RCT which were published upto the end of 2006 were identified electronically (MEDLINE and Cochrane database 1966–2006 Dec, week 4). Four journals (*Dental Traumatology, International Endodontic Journal, Journal of Endodontics, Oral Surgery Oral Medicine Oral Pathology Endodontics Radiology*), bibliographies of all relevant papers and review articles were hand-searched. Two reviewers (Y-LN, KG) independently assessed and selected the studies based on specified inclusion criteria and extracted the data onto a pre-designed proforma, independently. The criteria were: (i) Clinical studies on 2°RCT; (ii) Stratified analyses available for 2°RCT where 1°RCT data included; (iii) Sample size given and larger than 10; (iv) At least 6-month post-operative review; (v) Success based on clinical and/or radiographic criteria (*strict = absence of apical radiolucency; loose = reduction in size of radiolucency*); and (vi) Overall success rate given or could be calculated from the raw data. Three strands of evidence or analyses were used to triangulate a consensus view. The reported findings from individual studies, including those excluded for quantitative analysis, were utilized for the intuitive synthesis which constituted the first strand of evidence. Secondly, the pooled weighted success rates by each study characteristic and potential prognostic factor were estimated using the random effect model. Thirdly, the effects of study characteristics and prognostic factors (expressed as odds ratios) on success rates were estimated using fixed and random effects meta-analysis with DerSimonean and Laird's methods. Meta-regression models were used to explore potential sources of statistical heterogeneity. Study characteristics considered in the meta-regression analyses were: decade of publication, study-specific criteria for success (radiographic, combined radiographic & clinical), unit of outcome measure (tooth, root), duration after treatment when assessing success ('at least 4 years' or '<4 years'), geographic location of the study (North American, Scandinavian, other countries), and qualification of the operator (undergraduate students, postgraduate students, general dental practitioners, specialist or mixed group).

Results Of the 40 papers identified, 17 studies published between 1961 and 2005 were included; none were published in 2006. The majority of studies were retrospective ($n = 12$) and only five prospective. The pooled weighted success rate of 2°RCT judged by complete healing was 76.7% (95% CI 73.6%, 89.6%) and by incomplete healing, 77.2% (95% CI 61.1%, 88.1%). The success rates by 'decade of publication' and 'geographic location of study' were not significantly different at the 5% level. Eighteen clinical factors had been investigated in various combinations in previous studies. The most frequently and thoroughly investigated were 'periapical status' ($n = 13$), 'size of

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lesion' (n = 7), and 'apical extent of RF' (n = 5) which were found to be significant prognostic factors. The effect of different aspects of primary treatment history and re-treatment procedures has been poorly tested.

Conclusions The pooled estimated success rate of secondary root canal treatment was 77%. The presence of pre-operative periapical lesion, apical extent of root filling and quality of coronal restoration proved significant prognostic factors with concurrence between all three strands of evidence whilst the effects of 1°RCT history and 2°RCT protocol have been poorly investigated.

Keywords: meta-analysis, outcome, root canal re-treatment, success, systematic review.

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Introduction

A number of studies specifically evaluating clinical outcome of root canal re-treatment [secondary root canal treatment (2°RCT)] have been published in the literature since the comprehensive reports by Bergenholtz *et al.* (1979a,b). There is a general belief that the success rates for 2°RCT are lower than those for primary treatment (Selden 1974, Pekruhn 1986, Sjögren *et al.* 1990, Friedman *et al.* 1995) but this is not universally supported (Molven & Halse 1988, Chugal *et al.* 2001). At the time of writing, there was only one systematic review (Paik *et al.* 2004) examining the level of evidence for the outcome of 2°RCT. The effect of study characteristics and the effect of individual clinical factors on 2°RCT outcome have not been investigated systematically. Such information would be useful for guiding clinical decision-making on re-treatment options as well as to inform the design of future randomized controlled trials on 2°RCT. The lack of randomized controlled trials for 2°RCT (Paik *et al.* 2004) should predict a substantial statistical heterogeneity due to variation in study designs, therefore this systematic review adopted the approach previously used for primary root canal treatment (1°RCT) (Ng *et al.* 2007), that is to use a process of 'triangulation' of three different analytical approaches.

The aims of this systematic review were: (i) to investigate the effects of study characteristics on the reported success rates of secondary root canal treatment (2°RCT or root canal re-treatment); and (ii) to investigate the effects of clinical factors on the success of 2°RCT.

Materials and methods

Literature search

Longitudinal clinical studies investigating the outcome of secondary root canal treatment that were published upto December 2006 were identified electronically (MEDLINE database 1966–2006 Dec, week 4) using 5 keywords (1. root canal re-treatment, 2. endodontic re-treatment, 3. endodontics, 4. treatment outcome, 5. success) and 6 strategies (1 AND 4, 1 AND 5, 2 AND 4, 2 AND 5, 3 AND 4, 3 AND 5). A Cochrane Library search was also conducted. PubMed was independently searched using the 'related articles' feature. Four journals (*Dental Traumatology, International Endodontic Journal, Journal of Endodontics, Oral Surgery Oral Medicine Oral Pathology Endodontics Radiology*), bibliographies of all relevant papers and review articles were hand-searched. Unpublished studies were identified by searching abstracts and conference proceedings. Personal contacts were also used to identify ongoing or unpublished studies. Full articles were obtained for all the titles and abstracts (when available).

Study selection, quality assessment and data extraction

Two reviewers (Y-LN, KG) independently assessed and selected the studies based on the following inclusion criteria:

1. Clinical study on secondary root canal treatment;
2. Stratified analyses available if primary root canal treatment cases had been included;
3. Sample size given and larger than 10;
4. At least a 6-month post-operative review;
5. Success based on clinical and/or radiographic (strict = absence of apical radiolucency; loose = reduction in size of radiolucency) criteria;
6. Overall success rate given or could be calculated from the raw data.

Disagreements on study inclusion were resolved by discussion. The reasons for study rejection at this or subsequent stages were recorded.

Data were extracted by two reviewers independently using custom-designed data collection forms. The data collection form had been piloted on several papers and modified for optimal utility before final use. The data extracted could be classified into six groups; success rates, study characteristics, patient demographic data, pre-, intra- and post-operative factors. Any disagreement was discussed and data were excluded if agreement could not be reached.

Data analyses

Pooled success rates and the influence of study characteristics

Stata version 9.2 statistical software (StataCorp LP, College Station, TX, USA) was used to perform all statistical analyses. The weighted pooled success rates were estimated using random effects meta-analysis with DerSimonian and Laird's methods (DerSimonian & Laird 1986). The effect of study characteristics on the pooled success rates were investigated by entering each factor as a covariate in the regression model. The study characteristics investigated were: decade of publication; study-specific criteria (radiographic, combined radiographic & clinical) for success, unit of outcome measure (tooth, root); duration after treatment when success was assessed ('at least 4 years' or '<4 years'); geographic location of the study (North American, Scandinavian, other countries); and qualification of the operator (undergraduate students, postgraduate students, specialist or mixed group).

Effects of clinical factors

The effects of various aspects of 2°RCT on success rate were analysed through three approaches:

1. Intuitive synthesis of reported findings from individual studies. Those studies excluded for the purpose of the statistical analyses, were included for this synthesis.

2. Weighted pooled success rate by each factor under investigation was estimated using random effects meta-analysis with DerSimonian and Laird's methods. In cases where data were only available from one study, the study reported success rate and 95% confidence interval was used.

3. Weighted effects (expressed as odds ratio) of these factors on success rates were estimated using fixed and random effects meta-analyses with DerSimonean and Laird's methods. Statistical heterogeneity amongst the studies was assessed by Cochran's (Q) test. Meta-regression models were used to explore any sources of statistical heterogeneity amongst the study characteristics. This analysis was only performed when success rates, stratified by clinical factor under investigation, were available from more than two studies.

Results

In total, 40 articles that had reported the outcome of 2°RCT, were identified and 21 were excluded for various reasons (recorded in Table 1). Some papers presented different parts of the same study; therefore

Table 1 Reasons for exclusion of the 21 studies

Article	Excluded because following condition not met
1. Puterbaugh (1926)	Overall success rate could not be calculated
2. Rhein *et al.* (1926)	At least 6-month post-operative review
3. Appleton (1932)	At least 6-month post-operative review, same data set as Rhein *et al.* (1926)
4. Buchbinder (1936)	Overall success rate could not be calculated
5. Strindberg (1956)	No stratified data for re-treatment cases
6. Frostell (1963)	No stratified data for re-treatment cases
7. Ingle *et al.* (1965)	No stratified data for re-treatment cases
8. Storms (1969)	Only 4 cases
9. Heling & Kischinovsky (1979)	Only 6 teeth
10. Kerekes & Tronstad (1979)	Overall success rate could not be calculated
11. Cheung (1993)	Not a clinical study
12. Gutknecht *et al.* (1996)	No stratified data for re-treatment cases
13. Hepworth & Friedman (1997)	Not a clinical study
14. Kvist & Reit (1999)	Overall success rate could not be calculated
15. Kvist & Reit (2000)	Not measuring clinical/ radiographic success
16. Fava (2001)	Not a clinical study
17. Hoen & Pink (2002)	Not measuring clinical/ radiographic success
18. Main *et al.* (2004)	Overall success rate could not be calculated (only considered healing of lesions at the perforation site)
19. Marending *et al.* (2005)	No stratified data for re-treatment cases
20. Spili *et al.* (2005)	No stratified data for re-treatment cases
21. De Quadros *et al.* (2005)	No stratified data for re-treatment cases

their data were combined for analyses: (1) Bergenholtz *et al.* (1979a,b), (2) Molven & Halse (1988) & Fristad *et al.* (2004).

Methodological characteristics of included studies

The 17 selected studies were published between 1961 and 2005 (Table 2); none were published in 2006. Most were retrospective studies and only five were prospective cohort studies, of which one (Danin *et al.* 1996) was a randomized controlled trial comparing the outcome of surgical and nonsurgical re-treatment of teeth with failed 1°RCT. The recall rates (percentage of patients attending for follow-up after treatment) were reported by 16 studies and ranged from 20% to 100% with a median of 73.5%. Either root ($n = 7$) or tooth ($n = 10$) was used as the unit of outcome measure. The sample size ranged from 18 to 452 teeth and 76 to 612 roots.

The treatment outcome was determined by radiographic examination alone (three studies) or in combination with clinical findings (14 studies) (Table 2). Most studies ($n = 14$) used strict radiographic criteria (complete resolution of periapical lesion at recall) for determination of success and eight studies followed up all the cases for at least 4 years (Table 2).

For the radiographic assessment of the outcome of treatment, 13 studies (Table 2) employed at least two observers to carry out the assessment. Observer(s) were calibrated prior to evaluation of radiographs in nine studies and intra- or inter-observer reliability tests were carried out in nine studies (Table 2).

The statistical methods used for analysing the association between potential influencing factors and treatment outcome were the chi-square test (10 studies), logistic regression models (three studies), Mann–Whitney *U*-test (one study), and logistic regression models using generalized estimating equations (one study) (Table 2). Two studies did not analyse the data statistically or did not present such information.

Success rates by study characteristics

Assessment of outcome and criteria for success

The reported success rates in individual studies ranged from 28% to 90% with a median of 79%. When stratifying the data by 'strict' or 'loose' criteria, the ranges were 62% to 90% based on strict criteria and 28% to 93% based on loose criteria. The pooled weighted success rate from data based on 'strict' criteria (data available from 14 studies) [76.7% (95% CI: 73.6%, 89.6%)] (Fig. 1) was similar to that from data based on 'loose' criteria (data available from eight studies) [77.2%, (95% CI: 61.1%, 88.1%)] (Fig. 2). Some studies provided outcome data by both criteria. For the data based on strict criteria, the pooled success rates by the method of assessment (radiographic & clinical examination versus radiographic examination alone) were similar. However, using loose criteria for determination of success, there was a substantial difference in the pooled success rate based on radiographic & clinical examination (83%) compared with that based on radiographic examination alone (28%) (Table 3). Notably, there was only one study contributing to the latter dataset (Table 3).

Duration of follow-up after treatment completion

Most studies did not standardize duration of review after treatment which ranged from 6 months to 20 years. Attempts to pool data on success rates by different follow-up durations were confounded by either no data or relatively small number of studies in most groups, rendering comparisons less meaningful (Table 3).

Year of publication

The data for outcomes stratified by decades are presented in Table 3. The pooled success rates for treatments carried out in the ''2000's'' appeared to be the lowest ($P < 0.05$) regardless of whether 'Strict' or 'Loose' outcome criteria were used.

Geographic location of study

About 40% of the studies were carried out in Scandinavian countries (seven studies, Sweden/Norway) and the rest were carried out in North American (USA/Canada) (five studies) or other countries (five studies) including: UK [1], Belgium [1], Italy [1], Saudi Arabia [1], and Turkey [1]. In one study (Friedman *et al.* 1995), the treatments were carried out in USA, Germany or Israel (Table 2). Based on the loose criteria, the pooled weighted estimate of success rate of treatment carried out in Scandinavian countries (56%) was much lower than in North American (85%) and other (81%) countries. In contrast, the pooled estimate of success rate from outcome data based on strict criteria from the Scandinavian countries (82%) was higher than that from the North American countries (75%) (Table 3). Meta-regression analyses revealed the geographic location of study did not have a significant influence on the success rates of 2°RCT on teeth with ($P = 0.1$) or without ($P = 0.2$) pre-operative periapical lesion.

Table 2 Study characteristics

Study ID	Authors	Geographic location	Operator	Study design	Recall rate (%)	Sample size (units)	Unit of measure	Assessment of success	Radiographic criteria of success	≥4 year after treatment	≥2 radiographic observers	Calibration	Reliability test	Statistical analysis
1	Grahnén & Hanssen (1961)	Sweden	UG	R	64	502	Ro	C&R	S	✔	✔	–	–	–
2	Engström *et al.* (1964)	Sweden	UG	R	72	153	T	C&R	L	✔	✔	–	–	χ^2
3	Selden (1974)	USA	Sp	R	20	52	T	C&R	L	–	–	–	–	χ^2
4	Bergenholtz *et al.* (1979a,b)	Sweden	UG	R	66	556	Ro	C&R	S	–	✔	–	✔	–
5	Pekruhn (1986)	Saudi Arabia	Sp	R	81	36	T	C&R	S	–	–	–	–	χ^2
6	Molven & Halse (1988) & Fristad *et al.* (2004)	Norway	UG	R	50	226	Ro	Ra	S	✔	✔	✔	✔	χ^2
7	Allen *et al.* (1989)	USA	–	R	53	315	T	C&R	S	–	–	✔	–	χ^2
8	Sjögren *et al.* (1990)	Sweden	UG	R	46	267	Ro	C&R	S	✔	✔	✔	✔	LR
9	Van Nieuwenhuysen *et al.* (1994)	Belgium	–	R	–	612	Ro	C&R	S	–	✔	✔	✔	χ^2
10	Friedman *et al.* (1995)	Canada[a]	Sp	C	78	128	T	C&R	S	–	–	–	–	χ^2
11	Danin *et al.* (1996)	Sweden	Sp	RCT	100	18	T	Ra	L	–	✔	✔	✔	χ^2
12	Sundqvist *et al.* (1998)	Sweden	UG	C	93	50	T	C&R	S	✔	✔	–	–	χ^2
13	Chugal *et al.* (2001)	USA	PG	R	75	85	Ro	Ra	S	✔	✔	–	–	LR
14	Hoskinson *et al.* (2002)	UK	Sp	R	78	76	Ro	C&R	S	✔	✔	✔	✔	GEE
15	Farzaneh *et al.* (2004)	Canada	Sp	C	22	103	T	C&R	S	–	✔	✔	✔	LR
16	Gorni & Gagliani (2004)	Italy	PG	C	94	452	T	C&R	S	✔	✔	✔	✔	M-W
17	Çalişkan (2005)	Turkey	Sp	R	96	86	T	C&R	S	–	✔	✔	✔	χ^2

'–', missing information; UG, undergraduate students; PG, postgraduate students; Sp, specialist endodontists; R, retrospective study; C, prospective cohort study; RCT, randomized controlled trial; T, teeth; Ro, root; C&R, combined clinical and radiographic examination; Ra, radiographic examination only; S, strict criteria; L, loose criteria; LR, single level logistic regression; GEE, generalized estimating equations; χ^2, chi-square test; M-W, Mann–Whitney *U*-test.

[a]The treatments were carried out in Germany, Israel or USA by three different operators.

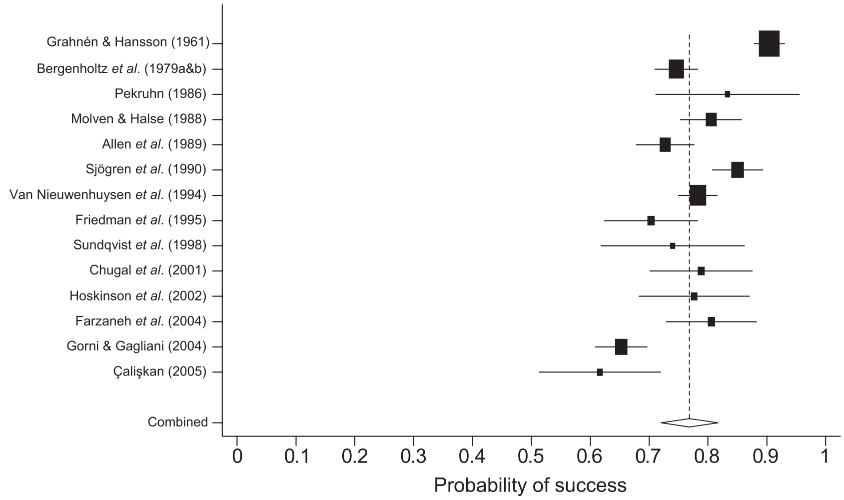

Figure 1 Probability of success based on strict radiographic criteria.

Qualification of operators (Undergraduate, postgraduate, specialist)

None of the reviewed studies had compared the outcome of 2°RCT by qualification of operators. The majority of the reviewed studies classified operator qualification as: undergraduate students (six studies), postgraduate students (two studies) or specialists (seven studies) (Table 2). The operators in the other two studies (Allen *et al.* 1989, Van Nieuwenhuysen *et al.* 1994) were a mixed group of dentists (undergraduate & postgraduate students, specialists) and a single dentist, respectively. From the pooled data, treatment carried out by specialists gave the lowest estimate of success, regardless of strict or loose criteria (Table 3). Meta-regression analysis, however, revealed that 'qualification of operator' had no significant influence on the outcome of 2°RCT on teeth with ($P = 0.6$) or without ($P = 0.2$) pre-operative lesion. The current data did not allow further stratified analyses by case complexity, thus the results should be interpreted with caution.

Success rates by clinical factors

Different studies have evaluated the influence of a range of different prognostic factors on outcome but the combinations of factors reported vary (Table 4).

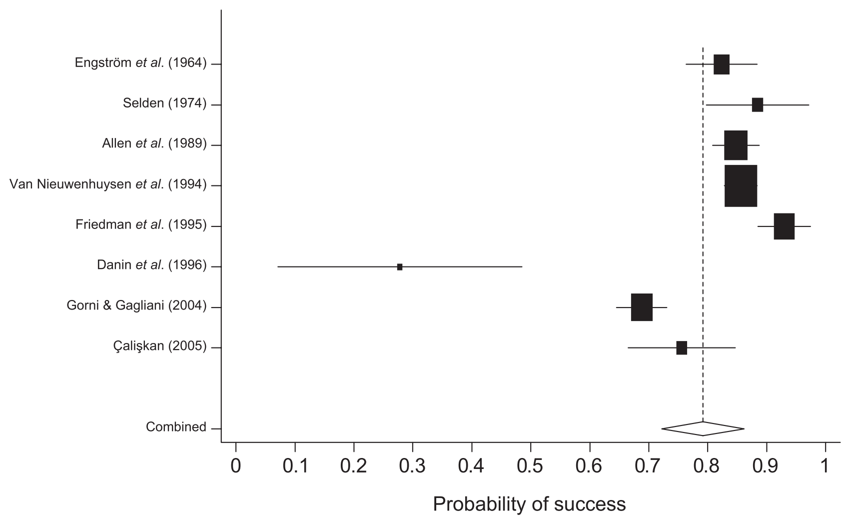

Figure 2 Probability of success based on loose radiographic criteria.

Table 3 Estimated success rates by study characteristics

Factor/categories	No. of studies identified[a]	Strict radiographic criteria: No. of studies	No. of units	Weighted pooled success rate (%)[b]	Loose radiographic criteria: No. of studies	No. of units	Weighted pooled success rate (%)[b]
Outcome measure used				76.7			77.2
Radiographic	3	2	311	80.1 (75.6, 84.5)	1	18	27.8 (7.1, 48.5)
Clinical + radiographic	14	12	3183	76.4 (70.9, 81.8)	7	1798	82.7 (76.5, 88.9)
Duration after treatment (months)							
6	1	0	–	–	1	155	94.2 (89.3, 97.3)
12	2	1	36	83.3 (67.1, 93.6)	1	18	27.8 (9.7, 53.5)
24	2	2	1008	70.0 (60.9, 79.2)	0	–	–
36	0	0	–	–	0	–	–
48	7	6	1082	85.5 (80.8, 90.1)	1	153	82.4 (75.4, 88.0)
>48	1	1	226	80.5 (74.8, 85.5)	0	–	–
Year of publication							
1960s	2	1	502	90.4 (87.9, 93.0)	1	153	82.4 (76.3, 88.4)
1970s	2	1	556	74.6 (71.0, 78.3)	1	52	88.5 (79.8, 97.1)
1980s	3	3	577	77.8 (71.3, 84.3)	1	315	84.8 (80.8, 88.7)
1990s	5	4	1057	77.9 (72.0, 83.9)	3	758	76.1 (62.0, 90.1)
2000s	5	5	802	72.7 (64.9, 80.5)	2	538	70.0 (66.2, 73.9)
Geographic location of study[c]							
N. American countries	5	4	503	74.7 (71.4, 78.1)	2	367	85.4 (81.8, 89.0)
Scandinavian countries	7	5	1601	81.5 (74.3, 88.7)	2	171	56.0 (2.5, 109.5)
Other countries	5	5	1390	72.9 (65.0, 80.9)	4	1278	80.9 (70.4, 91.5)
Qualification of operators							
Undergraduate students	6	5	1601	81.5 (74.3, 88.7)	1	153	81.0 (76.3, 88.4)
Postgraduate students	2	2	188	79.8 (74.1, 85.6)	0	–	–
Specialist	7	5	778	70.8 (64.0, 77.6)	5	736	73.2 (58.7, 87.7)

[a]Some of the studies identified for the respective factor provided success rates based on both strict and loose radiographic criteria.
[b]When data were available from only one study for a given factor, the success rate reported by that individual study is presented in this table.
[c]N. American countries = USA, Canada; Scandinavian countries = Norway, Sweden; Other countries = UK, Belgium, Italy, Saudi Arabia, Turkey.

Attempts to evaluate the effect of individual factors call for the pooling of various equivalent subsets of these studies. The results of the three approaches of analyses: (i) Intuitive synthesis of reported findings from individual studies; (ii) weighted pooled success rate by stratification of groups under each factor; and (iii) weighted effects (weighted pooled odds ratio) of these factors on success rates are presented in that order for each factor below. Considering only three studies had provided stratified data by clinical factors based on loose outcome criteria, *the quantitative analyses were only carried out on data based on strict criteria*.

Pre-operative factors

Gender. Only two ([1]Sjögren *et al.* 1990, Van Nieuwenhuysen *et al.* 1994) of the previous studies had investigated the influence of this factor but did not find any significant association between gender and success rate.

The above two studies did not provide the raw data for effect of gender; such data could however, be obtained from another study (Hoskinson *et al.* 2002) that had not analysed the data statistically (Table 5). The success rates for female patients were 44% higher than those for male patients. This result should be interpreted with caution because of the small sample size and substantially smaller number of male than female patients who had received 2°RCT in their study. Furthermore, all the treated teeth in the male patients were associated with a pre-operative periapical lesion whilst a smaller 70% of the teeth in the female patients were associated with a pre-operative lesion.

Age. Two studies ([2]Sjögren *et al.* 1990, Van Nieuwenhuysen *et al.* 1994) had analysed the influence of age on treatment outcome. The former

[1] Studies excluded from quantitative analyses for reasons given in Table 1.

Table 4 Clinical prognostic factors included in studies

Study ID	Author (Year)	Gender	Age	Health	Tooth type	Periapical status	Size of periapical lesion	Time interval before re-treatment	Pre-operative canal content	Pre-operative perforation	Pre-operative obstruction	Quality of pre-existing RF	Rubber dam isolation	Apical size of canal preparation	Taper of canal preparation	Separation of instrument	Irrigant	Medicament	Culture test	RF material technique	Sealer	Apical extent of RF	Quality of RF	No. of treatment visits	Restoration after 2RCT
1	Grahnén & Hanssen (1961)					✔											✔	✔		✔		✔		✔	
2	Engström *et al.* (1964)					✔	✔				☑						✔	✔	✔	✔		☑		✔	
3	Selden (1974)				☑	✔	✔																		
4	Bergenholtz *et al.* (1979a,b)				✔	✔	✔	✔					✔							✔		✔			
5	Pekruhn (1986)				☑								✔				✔	✔		✔	✔			✔	
6	Molven & Halse (1988)					✔														✔				✔	
7	Allen *et al.* (1989)				☑			☑	☑											✔					☑
8	Sjögren *et al.* (1990)	☑	☑		✔	✔	✔				☑		✔				✔		✔	✔		✔	✔	✔	☑
9	Van Nieuwenhuysen *et al.* (1994)	☑	☑				☑						☑				✔			✔	✔	☑	☑	☑	
10	Friedman *et al.* (1995)					✔											✔	✔		✔	✔	☑			☑
11	Danin *et al.* (1996)					✔	✔					✔	✔				✔	✔		✔				✔	
12	Sundqvist *et al.* (1998)					✔	☑	✔					✔				✔	✔	✔	✔		☑		✔	
13	Chugal *et al.* (2001)					☑	☑																		
14	Hoskinson *et al.* (2002)	✔	✔			✔	✔						✔	✔	✔		✔			✔	✔	✔	✔	✔	✔
15	Farzaneh *et al.* (2004)					✔		✔		✔		✔	✔				✔	✔		✔	✔	✔	☑	✔	✔
16	Gorni & Gagliani (2004)					✔			✔	✔	✔						✔	✔		✔					
17	Çalişkan (2005)			✔		✔	✔	✔	✔				✔				✔	✔		✔	✔			✔	
	Total no. of studies with raw data	1	1	1	2	13	7	4	2	2	1	2	8	1	1	0	12	9	3	15	6	5	2	10	2

RF, root filling; ✔, raw data available for estimation of pooled success rates or effects of the respective factor; —, the effect of the respective factor had been analysed statistically by individual study but raw data was not available for estimation of the effect in this review.

Table 5 Pooled weighted success rates by pre-operative clinical factors based on strict criteria

Factor	No. of studies	No. of cases	Weighted pooled success rate (%)[a]	Study ID[c]
Gender				
Female	1	56	89.2 (78.1, 96.0)	14
Male	1	20	45.0 (23.1, 68.5)	14
Age				
25–50 years	1	32	81.3 (63.6, 92.8)	14
>50 years	1	43	76.7 (61.4, 88.2)	14
Patient's health				
Healthy	1	86	61.6 (50.5, 71.9)	17
Unhealthy	No data	–	–	–
Tooth type				
Maxillary incisors/canines	2	108	62.6 (14.1, 111.2)	4, 8
Mandibular incisors/canines	2	49	59.1 (33.4, 84.8)	4, 8
Maxillary premolars	2	136	65.0 (31.3, 98.6)	4, 8
Mandibular premolars	2	89	71.8 (27.8, 115.9)	4, 8
Maxillary molars	2	49	68.0 (55.2, 80.9)	4, 8
Mandibular molars	2	70	85.0 (62.9, 107.1)	4, 8
Presence of periapical lesion				
Without Pa lesion	7(9)[b]	1117	93.5 (92.1, 95.0)	1, (2), 4, 6, 8, 10[d], 14–16
		1227	93.4 (91.6, 95.1)[d]	when #10 is included
With Pa lesion	10(13)[b]	1145	65.7 (58.6, 72.7)	1, (2), (3), 4, 6, 8, 10, (11), 12, 14–17
Size of periapical lesion				
Pa <5 mm	4(7)[b]	1386	67.3 (51.7, 83.0)	(2), 4, 8, (11), 14, 17
Pa >5 mm	4(7)[b]	875	41.7 (32.6, 50.8)	(2), (3), 4, 8, (11), 14, 17
Time interval between previous treatment and re-treatment				
≤1 year	1	17	70.6 (44.0, 89.7)	15
>1 year	4	452	66.2 (28.8, 83.7)	4, 12, 15, 17
Pre-operative canal content				
Gutta-percha	1	75	64.0 (52.1, 74.8)	17
Separated instrument	1	61	95.1 (86.3, 99.0)	16
Pre-operative perforation				
No	2	561	72.9 (40.3, 105.6)	15, 16
Yes	2	80	41.2 (30.5, 52.0)	15, 16
Pre-operative canal obstruction				
Calcification or presence of apical stop	1	103	66.0 (56.0, 75.1)	16
No obstruction	1	349	65.0 (59.8, 70.0)	16
Quality of pre-operative root fillings				
Satisfactory	1(2)[b]	19	68.4 (43.4, 87.4)	(11), 15
Unsatisfactory	1(2)[b]	80	87.5 (78.2, 93.8)	(11), 15

[a]Weighted pooled success rates were estimated using random effect model (where there was only one study, its reported success rate was presented).
[b]Number in bracket was the total number of studies using loose or strict radiographic criteria for determination of success.
[c]Study in bracket was not included in the estimation of pooled success rate because its outcome data for the given factor was based on loose radiographic criteria.
[d]Un-weighted pooled success rate was presented because 100% success rate for the associated category was reported by the respective study.

found no statistically significant difference in success rates stratified by age but the latter reported that the success rates reduced with increase in age.

Outcome data was only provided by one study (Hoskinson *et al.* 2002) (Table 5) and showed that treatments carried out in patients within the age band 25–50 years had a 4% higher chance of success than those carried out in older patients (>50 years). The results should again be interpreted with caution because of the small sample size.

General medical health. [2]Marending *et al.* (2005) had reported that conditions associated with impaired

[2]1°RCT cases were included in the stratified data by potential influencing factors.

nonspecific immune responses reduced the success of root canal treatment. However, they did not stratify this analysis by 1°RCT or 2°RCT. Çalişkan (2005) reported that only healthy patients were included in their study. No further quantitative analyses were carried out due to absence of raw data for comparison.

Tooth type. Three studies ([2]Selden 1974, [2]Pekruhn 1986, Allen *et al.* 1989) had compared the outcome of treatment between tooth types. Only Allen *et al.* (1989) found statistically significant differences in success rates between tooth types. They reported that maxillary teeth were associated with a significantly higher success rate compared with mandibular teeth. This difference however was not significant when only molar teeth were included in the analysis.

The above three studies did not present raw outcome data by tooth type (maxillary incisor & canine, maxillary premolar, maxillary molar, mandibular incisor & canine, mandibular premolar, mandibular molar); such raw data *were* however provided by Bergenholtz *et al.* (1979a,b) and Sjögren *et al.* (1990). The weighted pooled success rates for mandibular molar teeth were the highest followed by those for mandibular premolar teeth and then maxillary premolar and molars and then incisors/canines (Table 5).

Periapical status. Five studies (Molven & Halse 1988, Friedman *et al.* 1995, [1]Chugal *et al.* 2001, Hoskinson *et al.* 2002, Gorni & Gagliani 2004) had compared the success rates of teeth/roots with or without periapical lesions, all found the former were associated with significantly lower success rates than the latter. Stratified outcome data were provided by thirteen studies (Table 4). The weighted pooled success rates for those without periapical lesion were 28% higher than for those with periapical lesion pre-operatively (Table 5).

Of the 13 studies providing data for estimation of pooled success rates by periapical status, 8 (Grahnén & Hanssen 1961, Engström *et al.* 1964, Bergenholtz *et al.* 1979a,b, Molven & Halse 1988, Sjögren *et al.* 1990, Hoskinson *et al.* 2002, Gorni & Gagliani 2004, Farzaneh *et al.* 2004) provided stratified outcome data by both teeth with and without periapical lesion for meta-analysis. It was evident that teeth without periapical lesion had 6.32 (95% CI: 4.04, 9.90) times higher odds of success than teeth with periapical lesions (Table 7a). The heterogeneity 16.3 (7 df) was substantial (Table 7a) and could be partly explained by the 'decade of publication' and 'duration after treatment' when investigated using meta-regression models (*results not shown*).

Size of periapical lesion. Seven studies had statistically compared the success rates of teeth with pre-operative, large or small periapical lesions; four (Bergenholtz *et al.* 1979a,b, Van Nieuwenhuysen *et al.* 1994, Sundqvist *et al.* 1998, [1]Chugal *et al.* 2001) found that teeth with smaller lesions were associated with significantly higher success rates than those with larger lesions. In contrast, Sjögren *et al.* (1990), Danin *et al.* (1996) and Çalişkan (2005) found no statistical difference.

Seven reviewed studies (Table 4) provided outcome data by the size of lesion. By pooling the data for lesion size into <5 mm or ≥5 mm in diameter, the weighted pooled success rate for small lesions was 25% higher than that for large lesions (Table 5). The estimated pooled odds of success for small lesions was significantly higher when compared to the pooled odds of success for large lesions (OR = 2.64; 95% CI: 1.67, 4.17) (Table 7b). Selden (1974) was excluded from the meta-analysis because all the cases with small lesion were successful. Although, the heterogeneity 7.0 (5 df, $P = 0.224$) in the estimate was not significant, it could partly be explained by the 'duration after treatment'. In addition, the effect of the size of lesion only reached the 10% significance level when the covariate 'duration after treatment' was entered simultaneously into the meta-analysis regression model.

Time interval between 1°RCT and 2°RCT. Only two studies ([2]Allen *et al.* 1989, Farzaneh *et al.* 2004) had investigated the effect of this factor on outcome and both found no significant association. Three other studies had only included teeth receiving 1°RCT at least 2 years (Bergenholtz *et al.* 1979a,b, Çalişkan 2005) or 4–5 years (Sundqvist *et al.* 1998) previously. By pooling the data for time interval between 1°RCT and 2°RCT into ≤1 year or >1 year, the difference in weighted pooled success rates was 5% in favour of those cases with previous root canal treatments (1°RCT) of ≤1 year duration. No further meta-analysis was carried out due to insufficient data.

Pre-operative canal content. The success rates of 2°RCT related to the presence of different pre-operative foreign materials in the root canal system had only been investigated by [2]Allen *et al.* (1989) but they included data from surgical re-treatment cases (54% of the samples) in the analysis. They found that teeth with 'cement' root filling pre-operatively were associated with significantly lower success rates than those teeth with 'gutta-percha' or 'silver point' root fillings pre-operatively. Stratified outcome data by teeth with pre-operative gutta-percha root fillings or presence of separated instrument were given by Çalişkan (2005) and Gorni & Gagliani (2004), respectively (Table 5). No further meta-analysis was carried out due to insufficient data.

Procedural errors in previous canal preparation (1°RCT). The procedural errors investigated had included: canal perforation, obstruction and 'root canal morphology alteration by previous treatment' which was defined by Gorni & Gagliani (2004) as presence of transportation, perforation, stripping or internal resorption, the last condition was, however not related to the previous treatment (1°RCT).

Only one study (Farzaneh *et al.* 2004) had investigated the effect of pre-existing perforation on outcome; the success rates were significantly reduced by the presence of this procedural error. However, [1]Main *et al.* (2004) reported the periradicular radiolucency associated with the perforations were completely resolved in all cases with pre-existing perforation. Success rates stratified by this factor were provided by two studies (Farzaneh *et al.* 2004, Gorni & Gagliani 2004); the weighted pooled success rate for teeth without pre-operative perforation was 32% higher than that for teeth with pre-operative perforation (Table 5).

Four studies had investigated the effects of pre-operative canal obstruction ([1]Strindberg 1956, [2]Engström *et al.* 1964, Sjögren *et al.* 1990, Gorni & Gagliani 2004). The former two studies found that teeth with canals inaccessible towards the apex were associated with significantly lower success rates, whereas the latter two studies did not find any significant association. Sjögren *et al.* (1990) declared that they could not make any distinction between canals obliterated by denticles, tertiary dentine and/or obturations caused by improper previous (1°RCT) instrumentation and had not presented stratified outcome data for this factor. The stratified success rates *were* however, provided by Gorni & Gagliani (2004) (Table 5) but no further meta-analysis was carried out due to insufficient data.

Quality of pre-operative root fillings. Two studies (Danin *et al.* 1996, Farzaneh *et al.* 2004) have compared the success rates of 2°RCT on teeth with satisfactory versus unsatisfactory pre-existing root fillings (1°RCT). The former did not find any significant influence by the apical extent of pre-existing root filling but the latter found the success rates for those teeth with adequate pre-operative root fillings (extended to 0–2 mm from the radiographic root end with no voids) were significantly lower than those for teeth with inadequate pre-operative root fillings, in the case for teeth with pre-operative periapical lesions. The outcome data by this factor from Farzaneh *et al.* (2004) is presented in Table 5.

Intra-operative factors

Use of rubber dam isolation during treatment. Eight studies (Table 4) reported the routine use of rubber dam during treatment whilst nine studies did not mention the use of rubber dam isolation in their treatment protocol. One study (Van Nieuwenhuysen *et al.* 1994) had compared the outcome of 2°RCT using rubber dam versus cotton roll isolation. They found the use of the former was associated with significantly higher success rates but the requisite raw data were not available. The weighted pooled success rates of treatment using rubber dam isolation in those studies ($n = 7$) was 77.1%, based on strict criteria (Table 6). There was insufficient data for further analysis.

Apical extent of instrumentation. Only one study (Bergenholtz *et al.* 1979a) had investigated the effect of this factor (Table 4). It had been dichotomized into instrumentation beyond the apex or not: instrumentation beyond the apex was deemed a cleaned apex. The former cases (56%) were associated with significantly lower success rate than the latter cases (88%), regardless of the pre-operative periapical status of teeth (Table 6). They pointed out that the majority of failures occurring amongst 'clean roots' were complicated by overfilling during 2°RCT. No further meta-analysis was carried out due to insufficient data.

Apical size of canal preparation. Three previous studies ([1]Strindberg 1956, [1]Kerekes & Tronstad 1979, Hoskinson *et al.* 2002) (Table 4) had analysed the effect of apical size of canal preparation on treatment outcome; they found no significant association. Their analyses were however, not stratified by 1°RCT and 2°RCT and only a small proportion of re-treatment cases (30%, 9%, 16%, respectively) were included in their studies. The raw data for 2°RCT from the study by

Table 6 Pooled weighted success rates by intra-& post-operative clinical factors

Factor	No. of studies	No. of cases	Weighted pooled success rate (%)[a]	Study ID[c]
Use of rubber dam isolation				
Yes	7(8)[b]	1174	77.1 (71.6, 82.7)	4, 5, 8, (11), 12, 14, 15, 17
No	No data	–	–	–
Instrumentation beyond apex				
Yes	1	228	55.7 (49.3, 62.1)	4
No	1	328	87.8 (84.3, 91.3)	4
Apical size of canal preparation (ISO size)				
≤30	1	58	84.5 (75.2, 93.8)	14
>30	1	18	55.6 (32.6, 78.5)	14
Taper of canal preparation				
0.05	1	44	79.5 (67.6, 91.5)	14
0.10	1	32	75.0 (60.0, 90.0)	14
Type of irrigant				
NaOCl	8(10)[b]	1198	74.7 (67.6, 81.8)	(2), 5, 8, 10, (11), 12, 14–17
H_2SO_4	1	502	90.4 (87.9, 93.0)	1
NaOCl & EDTA	1	612	78.3 (75.0, 81.5)	9
Type of medicament				
$Ca(OH)_2$	5(6)[b]	792	69.1 (63.8, 74.4)	10, (11), 12, 14, 16, 17
Iodine	0(1)[b]	–	–	(2)
Creosote	1	502	90.4 (87.9, 93.0)	1
None	1	36	83.3 (71.2, 95.5)	5
Culture results prior to obturation				
Negative culture	2(3)[b]	392	84.4 (80.4, 88.4)	(2), 8, 12
Positive culture	1(2)[b]	16	27.0 (4.3, 77.7)	(2), 12
Negative culture – no pa	0(1)[b]	–	–	(2)
Positive culture – no pa	0(1)[b]	–	–	(2)
Negative culture – pa	1(2)[b]	44	79.5 (67.6, 91.5)	(2), 12
Positive culture – pa	1(2)[b]	6	33.3 (4.3, 77.7)	(2), 12
Root filling material/technique				
Gutta-percha with sealer	8	1808	73.5 (68.5, 78.4)	5, 7, 9, 10, 14–17
Kloropercha	5(7)[b]	1601	81.5 (74.3, 88.7)	1, (2), 4, 6, 8, (11), 12
Type of sealer				
Zinc oxide eugenol based	4	1176	75.4 (66.8, 83.9)	5, 9, 14, 15
Glass ionomer based (Ketac Endo®)	1	128	70.3 (62.4, 78.2)	10
Polyvinyl resin based (Diaket®)	1	86	61.6 (51.4, 71.9)	17
Apical extent of root filling				
Short-filled	3	229	87.4 (74.2, 100.7)	1, 8, 14
Flush-filled	4	310	80.5 (68.6, 92.4)	1, 8, 14, 15
Long-filled	4	406	63.1 (42.9, 83.4)	1, 4, 8, 14
Short-fill – no pa	2	159	100.0	1, 14
Flush-fill – no pa	2	120	97.2 (94.3, 100.1)	1, 14
Long-fill – no pa	2(3)[d]	179	84.0 (78.8, 89.1)	1, 4, [d]14
		194	84.0 (78.8, 89.3)[d]	When #14 included
Short-fill – pa	3	70	78.5 (69.0, 88.0)	1, 8, 14
Flush-fill – pa	3	112	72.2 (64.0, 80.4)	1, 8, 14
Long-fill – pa	4	212	54.2 (30.8, 77.6)	1, 4, 8, 14
Quality of root filling				
Satisfactory	2	157	71.8 (64.8, 8.8)	8, 14
Unsatisfactory	1(2)[d]	13	30.8 (5.68, 55.9)	8, 14[d]
		15	26.6 (4.3, 49.0)[d]	When #14 was included
Number of treatment visits				
Single visit	1(2)[d]	52	83.3 (71.2, 95.5)	5, 15[d]
			86.1 (27.7, 144.4)[d]	When #15 was included
Multiple visits	7(9)[b]	1461	79.5 (73.2, 85.8)	1, (2), 6, 8, (11), 12, 14, 15, 17
Quality of restoration				
Satisfactory	2	155	84.1 (78.4, 89.9)	14, 15

Table 6 (Continued)

Factor	No. of studies	No. of cases	Weighted pooled success rate (%)[a]	Study ID[c]
Unsatisfactory	2	20	60.0 (38.6, 81.5)	14, 15

[a] Weighted pooled success rates were estimated using random effect model (where there was only one study, its reported success rate was presented).
[b] Number in bracket was the total number of studies using loose or strict radiographic criteria for determination of success.
[c] Study in bracket was not included in the estimation of pooled success rate because its outcome data for the given factor was based on loose radiographic criteria.
[d] Study excluded for estimation of the weighted pooled success rate because the success rate for the associated category was 100% or 0%.

Hoskinson *et al.* (2002) (Table 4) showed that the success rate for small (size 20–30) apical preparations (85%) was higher than that for large (size 35–90) apical preparations (56%) (Table 6). The effect of size of preparation could not be analysed further due to insufficient data.

Taper of canal preparation. Only one study (Hoskinson *et al.* 2002) (Table 4) analysed the influence of canal preparation taper on 2°RCT; they did not find any significant difference in success rate between 0.05 and 0.10 canal tapers. However, the result of their analysis might have been confounded by the concomitant change in the concentration of the sodium hypochlorite irrigant and the root filling technique. The success rates stratified by taper of canal preparation are presented in Table 6. The effect of taper of canal preparation could not be analysed further due to insufficient data.

Separation of instrument during 2°RCT. [1]Strindberg (1956) found that instrument separation during 2°RCT reduced the success rate significantly. None of the studies selected had stratified outcome data for this factor.

Irrigant. Different types of irrigants have been used singly or in various combinations in the studies

Table 7 Summary of meta-analyses for the effects of clinical factors on success rates of 2°RCT

Comparisons	No. of studies	Odds ratio	95% CI	Heterogeneity	
				χ^2-value	*P*-value
(a) Effects of presence of pre-operative periapical lesion					
Present	8	1	–	–	–
Absent		6.32	4.04, 9.90	16.3	0.022
(b) Effects of size of pre-operative lesion					
Large radiolucency	6	1	–	–	–
Small radiolucency		2.64	1.67, 4.17	7.0	0.224
(c) Effects of pre-obturation culture results					
+ve culture result	2	1	–	–	–
–ve culture result		4.30	0.34, 54.9	6.9	0.009
(d) Effects of pre-obturation culture results (teeth with pre-operative periapical lesion)					
+ve culture result	2	1	–	–	–
–ve culture result		4.81	0.72, 32.23	3.4	0.066
(e) Effects of apical extent of root filling					
Long	3	1	–	–	–
Flush		2.36	1.36, 4.10	1.4	0.500
Short		4.11	2.10, 8.07	2.5	0.286
(f) Effects of apical extent of root filling (teeth with pre-operative lesion)					
Long	3	1	–	–	–
Flush		1.65	0.86, 3.16	0.39	0.824
Short		1.72	0.81, 3.64	1.17	0.558
(g) Effects of quality of coronal restoration					
Unsatisfactory	2	1	–	–	–
Satisfactory		3.31	1.07, 10.3	0.21	0.647

reviewed, including solutions of: sodium hypochlorite ($n = 10$ studies), sulphuric acid (50%) or sodium bicarbonate (Grahnén & Hanssen 1961); a combination of sodium hypochlorite, ethylene-diamine-tetra-acetic acid (EDTA) solution and urea peroxide has also been utilized (Van Nieuwenhuysen *et al.* 1994). Some studies (five studies) did not present this information. None of the studies had systematically investigated the effect of irrigant on success rates. The weighted pooled success rates by different types of irrigant are presented in Table 6. The effect of this factor could not be analysed further due to insufficient data.

Medicament. Some studies standardized the type of medicaments used, and included: calcium hydroxide ($n = 6$), creosote ($n = 1$) and iodine ($n = 1$). In contrast, Sjögren *et al.* (1990) reported the use of calcium hydroxide in most cases but potassium iodide and camphorated phenol were sometimes used. Whilst, Van Nieuwenhuysen *et al.* (1994) reported the use of paraformaldehyde in the early part of their study, replaced later by calcium hydroxide. No inter-appointment medicament was used by Pekruhn (1986) because all the cases were completed in one visit. Six studies did not provide this information.

The pooled success rates stratified by different types of medicament are presented in Table 6. There were no data on success rates of treatment using iodine, based on strict criteria. Interestingly, the pooled success rate of 2°RCT using $Ca(OH)_2$ (68.2%) was much lower than that using creosote (90.4%) as the inter-appointment medicament. Although the data for creosote originated from a single study (Grahnén & Hanssen 1961), the total number of cases treated using $Ca(OH)_2$ in the pooled data ($n = 792$) was comparable to the number treated with creosote ($n = 502$). It is worthy of note that the majority (76%) of the roots in the creosote data were not associated with a pre-operative periapical lesion. No further meta-analysis was carried out due to insufficient data.

Root canal bacterial culture test results (positive or negative) prior to obturation Comparison of pre-obturation root canal culture test results for any periapical status. Two studies (Engström *et al.* 1964, Sundqvist *et al.* 1998) had investigated the influence of pre-obturation bacterial culture results on outcome of 2°RCT and found that canals with negative culture results prior to obturation were associated with significantly higher success rates than those with positive culture results. In one study (Sjögren *et al.* 1990), the teeth were root filled only when a negative bacterial culture result was obtained.

The pooled weighted success rates for teeth with negative culture results were higher than those with positive culture results by 57% (Table 6). The meta-analyses showed the odds of success of teeth with pre-obturation negative culture were higher than those of teeth with a positive culture (OR = 4.3; 95% CI: 0.3, 55.0) but the difference was not statistically significant (Table 7). Although the heterogeneity [6.9 (1 df)] was significant ($P = 0.009$), further meta-regression analysis was not carried out because of insufficient data.

Comparison of pre-obturation root canal culture test results for teeth without periapical lesion. For those teeth without a pre-operative periapical lesion (data provided by Engström *et al.* 1964), the success rate for teeth with negative culture results was 9% higher than for those teeth with positive cultures. However, their data was based on loose criteria and was therefore not presented in Table 6. The effect was not estimated because of insufficient data.

Comparison of pre-obturation root canal culture test results for teeth with periapical lesions. Sundqvist *et al.* (1998) found that culture results had a significant influence on outcome of re-treatment on teeth associated with periapical lesions. For those teeth with pre-operative periapical lesions, the success rates reported by Sundqvist *et al.* (1998) for teeth with negative bacterial cultures prior to root filling were 46% higher than those for teeth with positive cultures (Table 6). The effect estimated using meta-analysis was not statistically significant (OR = 4.8; 95% CI: 0.72, 32.2) with substantial heterogeneity 3.4 (df = 1, $P = 0.066$) but no further meta-regression was carried out due to insufficient data (Table 7d).

Root filling material and technique. The types of root filling materials reported were gutta-percha with various types of sealer ($n = 8$) or gutta-percha softened in chloroform ($n = 7$), but three studies did not provide such information. Of the eight studies using gutta-percha and sealer, only three studies (Pekruhn 1986, Gorni & Gagliani 2004, Çalişkan 2005) standardized the obturation technique. The former two used warm vertical compaction technique whilst Çalişkan (2005) used cold lateral compaction technique. Four studies (Van Nieuwenhuysen *et al.* 1994, Friedman *et al.* 1995, Hoskinson *et al.* 2002, Farzaneh *et al.* 2004) did not standardize the root filling technique and one (Allen *et al.* 1989) did not provide such information. Van Nieuwenhuysen *et al.* (1994) found the use of lateral compaction technique was associated with significantly higher success rate than the use of a single cone technique, in contrast to [1]Strindberg (1956) and [2]Friedman *et al.* (1995) who did not find any significant influence of root filling technique on success rates. The pooled success rate for teeth root filled with gutta-percha and sealer was 7% lower than for those filled with gutta-percha softened in chloroform (Table 6). The effects of root filling techniques and materials were not estimated due to insufficient data.

Three types of sealer have been used, including: Zinc oxide eugenol based sealers (4 studies), glass ionomer based sealers (KetacEndo®; ESPE Gmbh, Seefeld, Germany) (1 study) or resin based sealer (Diaket®; ESPE Gmbh, Seefeld, Germany) (one study). Eleven studies did not provide such information (Table 4). None of the previous studies had investigated the effect of sealer on the outcome of 2°RCT. The pooled success rates for teeth filled with the resin based sealer (62%) was lower than those obturated with zinc oxide eugenol based (75%) or glass ionomer based (70%) sealers (Table 6). The effect of type of sealers was not investigated further due to insufficient data.

Apical extent of root filling. Nine studies ([2]Grahnén & Hanssen 1961, [2]Engström *et al.* 1964, Bergenholtz *et al.* 1979a,b, Sjögren *et al.* 1990, Van Nieuwenhuysen *et al.* 1994, [2]Friedman *et al.* 1995, Sundqvist *et al.* 1998, [2]Hoskinson *et al.* 2002, Farzaneh *et al.* 2004) had investigated the influence of apical extent of root filling on treatment outcome statistically. They classified the various extents into three categories for statistical analyses: >2 mm short of radiographic apex (short), within 0–2 mm of the radiographic apex (flush) and extruded beyond the radiographic apex (long). Five studies ([2]Grahnén & Hanssen 1961, [2]Engström *et al.* 1964, Bergenholtz *et al.* 1979a,b, Van Nieuwenhuysen *et al.* 1994, [2]Friedman *et al.* 1995) found that this factor had significant influence on the success rates; long root fillings were associated with the lowest success rates ([2]Grahnén & Hanssen 1961, [2]Engström *et al.* 1964, Bergenholtz *et al.* 1979a,b) whilst flush root fillings were associated with the highest success rates ([2]Friedman *et al.* 1995, Farzaneh *et al.* 2004). The pooled success rates by apical extent of root fillings in descending order were: short (87%), flush (81%) and long (63%) root fillings but worse in the presence of a periapical lesion (Table 6). The rank order remained the same regardless of the periapical status.

Some studies provided the success rates stratified by periapical status and apical extent of root filling. Sjögren *et al.* (1990) found the apical extent of root filling did not influence the outcome of 2°RCT on teeth with periapical lesions. The pooled success rates for long root fillings were the lowest regardless of the periapical status (Table 6).

Only three studies presented success rates by all three extents (short, flush, long) of root filling for meta-analyses. Teeth with short (OR = 4.11; 95% CI: 2.10, 8.07) or flush (OR = 2.36; 95% CI: 1.36, 4.10) root fillings had significantly higher success rates than those with long root fillings (Table 7e). The results of meta-analyses on the data from teeth with pre-operative periapical lesions revealed similar trends with lower odds ratios and statistically insignificant findings (Table 7f). The heterogeneity was not significant, therefore further meta-regression analysis was not performed.

Quality of root filling. Out of the four studies (Table 4) which had analysed this aspect statistically, three (Sjögren *et al.* 1990, Van Nieuwenhuysen *et al.* 1994, Farzaneh *et al.* 2004) found that teeth with satisfactory root fillings were associated with significantly higher success rates than those with unsatisfactory root fillings. Satisfactory root fillings had been defined as 'adequate seal', 'good apical seal', 'absence of voids', whilst Van Nieuwenhuysen *et al.* (1994) also considered the apical extent of root fillings.

Only two studies provided stratified data by quality of root filling. The pooled success rate for teeth with satisfactory root fillings was 41% higher than for those teeth with unsatisfactory root fillings (Table 6). There were, however no successful cases with unsatisfactory root filling in one study (Hoskinson *et al.* 2002), therefore no further meta-analysis was carried out due to insufficient data.

Number of treatment visits. Five studies completed treatment in either one or multiple visits, eight studies carried out treatments over multiple visits only, only one study completed all treatment in one visit, whereas others (three studies) did not provide this information. Two studies (Van Nieuwenhuysen *et al.* 1994, Farzaneh *et al.* 2004) compared the outcome of treatment carried out over single or multiple visits, the former found the outcome of 2°RCT was significantly improved by multiple visit treatment and better still if the canal preparation and disinfection were completed in the first visit. In contrast, the latter study did not find any significant difference. The pooled success rate for single-visit treatment was 4.8% higher than the success rate for multiple-visit treatment but only one study had contributed to the data based on strict criteria for single-visit treatment (Table 6). The effect of number of treatment visits was not estimated due to insufficient data.

Type and quality of coronal restoration after 2°RCT. Five studies had analysed the influence of type or quality of coronal restoration on treatment outcome. Different comparisons had been made: restored versus unrestored teeth ([2]Friedman *et al.* 1995), permanent versus temporary restorations (Allen *et al.* 1989, [2]Friedman *et al.* 1995, Farzaneh *et al.* 2004), crown versus plastic restorations (Sjögren *et al.* 1990, [2]Friedman *et al.* 1995), presence versus absence of post ([2]Friedman *et al.* 1995), nonabutment versus abutment (Sjögren *et al.* 1990) and satisfactory versus unsatisfactory restorations ([2]Hoskinson *et al.* 2002). Hoskinson *et al.* (2002) defined satisfactory restorations as those with no evidence of marginal discrepancy, discolouration or recurrent caries at the restoration margin with no history of decementation. Teeth that had been restored or permanently restored were associated with significantly higher success rates than their contrary counterpart (Allen *et al.* 1989, [2]Friedman *et al.* 1995, Farzaneh *et al.* 2004). The type of restoration (Sjögren *et al.* 1990, [2]Friedman *et al.* 1995) was found to have no significant influence on the outcome of 2°RCT. Stratified data were provided by two studies (Hoskinson *et al.* 2002, Farzaneh *et al.* 2004) (Table 4) and the pooled success rate for teeth with satisfactory restorations was 24% higher than for those with unsatisfactory restorations (Table 6). The effect of quality of coronal restoration (OR = 3.31; 95% CI: 1.07, 10.3) was estimated based on the data from these two studies and found to be significant at the 5% level (Table 7g). The heterogeneity was not significant therefore further meta-regression analysis was not carried out.

Discussion

The number of clinical outcome studies on 2°RCT (n = 40 upto end of 2006) identified for this review was much smaller than those on 1°RCT (n = 119 upto end of 2003) (Ng *et al.* 2007). It was also noted that half of the articles on 2°RCT were published in the 1990s and 2000s whilst the number of those on 1°RCT were more evenly distributed amongst the different decades since 1960. This difference may reflect the general increase in awareness of dental health, tooth preservation and expansion in availability of aids and techniques to facilitate nonsurgical root canal re-treatment (Carr 1992). From 1992 to 2002, the number of surgical re-treatments carried out within the National Health Service in UK was reduced by one-third and this figure has continued to decline in recent years (Dental Practice Board 2005).

Most of the selected studies were prospective cohort or retrospective studies, therefore the levels of evidence provided were rated as Grade B (levels 2 or 3) based on the criteria given by the Oxford Centre for Evidence-Based Medicine (Phillips *et al.* 1998). This level of evidence was similar to the quality of 1°RCT outcome studies (Ng *et al.* 2007). The literature search identified two randomized controlled trials (Danin *et al.* 1996, Kvist & Reit 1999) comparing the outcome of surgical versus nonsurgical re-treatment and their data were analysed in a recently published Cochrane review (Del Fabbro *et al.* 2007). The study by Kvist & Reit (1999) was excluded from the present quantitative analysis because the overall success rates could not be calculated from the data presented in their paper. Nevertheless, both studies reported that surgical re-treatment was associated with higher success rates than 2°RCT, at 1-year after treatment, although in both studies the differences were not significant. Danin *et al.* (1996) probably could not reach significance because of the small sample size (18–19 patients per group) and Kvist & Reit (1999) failed to show any difference in the outcome at four-years post-operatively. The latter group hypothesized that surgical re-treatment resulted in more rapid initial bone fill but were associated with a higher risk of 'late failures'. No randomized controlled trial has thus far investigated any aspect of 2°RCT procedures.

The substantial variations and short-comings in the design amongst studies on outcome of 2°RCT were similar to those on 1°RCT (Ng *et al.* 2007). However, the median recall rate reported by studies on 2°RCT (74%) was substantially higher than that reported in studies on 1°RCT (53%). The implications of recall rate on the results from outcome studies were fully discussed previously (Ng *et al.* 2007); the same arguments apply here. The employment of at least two radiographic observers was another 'good practice' more frequently employed in 2°RCT outcome studies compared to 1°RCT (76% vs. 14%). Specialists were more frequently employed as operators in 2°RCT studies (41%) than in 1°RCT studies (37%). The pooled success rate for 2°RCT performed by specialists was however lower than when performed by undergraduate or postgraduate students. In contrast, 1°RCT carried out by postgraduate students and specialists had the higher pooled success rates than that performed by undergraduate students (Ng *et al.* 2007). This discrepancy may possibly be attributable to specialists managing more complex biological or technical problems, perhaps involving perforations, blockages, separated instruments or persistent infections. As the studies did not report on these factors, this supposition could not be tested in the meta-analysis.

The weighted pooled success rates from the 17 studies reviewed were 76.7% and 77.2% based on strict or loose criteria for success, respectively. The negligible difference in the weighted pooled success rates determined by loose and strict criteria for 2°RCT in this review was unexpected and was in contrast to the findings for 1°RCT (Ng *et al.* 2007). The difference could be attributable to the substantially smaller number of studies contributing to the outcome data based on loose ($n = 8$) compared to strict ($n = 14$) criteria and a possible outlier (Danin *et al.* 1996) in the pool (Fig. 2). The sample size in the latter was small ($n = 18$) with the lowest reported success rate (28%) based on 'loose' criteria compared with other studies (69–93%). After excluding Danin *et al.* (1996), the pooled success rate for loose criteria was found to increase to 83% (95% CI: 77%, 89%), 7% higher than the weighted pooled success rate based on strict criteria. This difference was slightly lower than that for 1°RCT (Ng *et al.* 2007). The slightly higher weighted pooled success rate based on strict criteria for 2°RCT (77%, 14 studies) compared to 1°RCT (74%, 40 studies) (Ng *et al.* 2007) was also unexpected. This finding contradicts the commonly held belief (Selden 1974, Pekruhn 1986, Sjögren *et al.* 1990, Friedman *et al.* 1995) that 1°RCT is associated with better outcome than 2°RCT due to the difference in the nature (Gulabivala 2004) and location of root canal infection (Nair *et al.* 2005).

Eight of the studies had presented stratified outcome data for 1°RCT and 2°RCT, of which seven had presented data based on strict criteria. However, the relative proportion of roots/teeth which had 2°RCT versus 1°RCT included in these studies were low and ranged from 4% to 51%. This may have rendered the statistical comparison under-power which is apparent in the meta-analysis comparing 1° and 2°RCT (Fig. 3); it shows that 1°RCT was associated with higher odds of success (OR = 1.26; 95% CI: 0.77, 2.07) but the difference was not significant ($P = 0.365$) (Fig. 3). A further meta-analysis was carried out on the data from teeth with pre-operative lesions in four studies (Grahnén & Hanssen 1961, Selden 1974, Sjögren *et al.* 1990, Hoskinson *et al.* 2002), which revealed the odds ratio increased to 1.63 (95% CI: 0.75, 3.55) but the

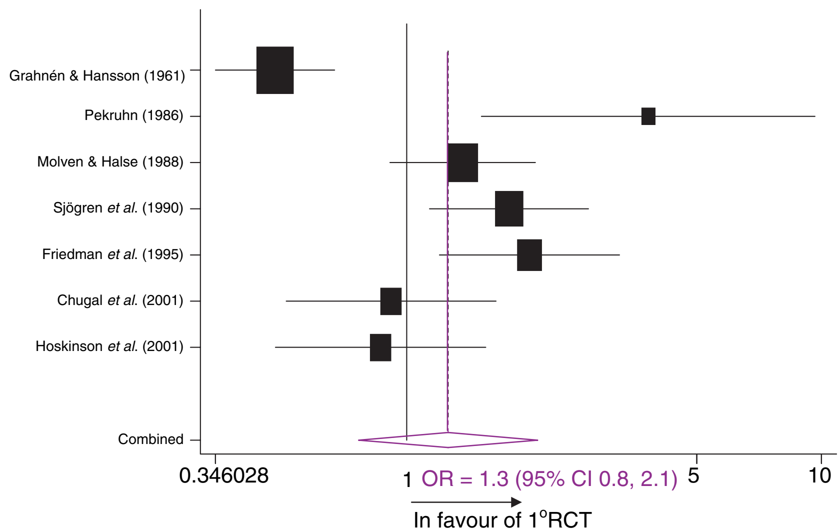

Figure 3 Comparison of the odds of success of 1°RCT and 2°RCT.

result was not statistically significant at the 5% level. It could be concluded that the differences in success rate between 1°RCT and 2°RCT are clinically genuine but there was insufficient statistical power (only four studies, $n = 999$ units for 1°RCT and $n = 309$ units for 2°RCT) to prove a significant difference. Further well designed prospective cohort studies are therefore required to confirm this relationship.

Given the small number of studies that could be included in this review, the meta-analyses on the effects of several prognostic factors could be considered to be compromised by the lack of statistical power to demonstrate a significant influence. Alternatively, the lack of power may have potentially over-estimated the magnitude of effect. The adoption of the previously used process of 'triangulation' of different analytical approaches (Ng *et al.* 2007, 2008) to draw meaningful conclusions would therefore seem sensible. Of the prognostic factors investigated, pre-operative presence and size of periapical lesion followed by apical extent of root fillings were the most frequently and thoroughly investigated. The observations were similar to those based on data for 1°RCT (Ng *et al.* 2008). Other pre-operative factors specifically relevant to 2°RCT (time interval between 1°RCT and 2°RCT, quality of pre-existing root filling, pre-existing canal content, root perforation, root canal obstruction) were poorly investigated. The deficiency in the data on intra-operative factors was more severe for 2°RCT than for 1°RCT (Ng *et al.* 2008) outcome studies.

On the influence of the periapical status on 2°RCT outcome, all three analytical approaches concurred and demonstrated a significantly higher (28%, OR = 6.3) success rate for teeth without periapical lesions compared with those with periapical lesions. The difference was larger than between such groups undergoing 1°RCT (10% difference in success rates, OR = 2.0) (Ng *et al.* 2008). The odds ratios for 2°RCT may have been over-estimated in the present review due to the small number of studies and the small sample size in the studies on 2°RCT. If the result is true, the greater impact of periapical status on 2°RCT may support the hypothesis that the infection in root-treated teeth with persistent periapical lesions could be more resistant to treatment (Gulabivala 2004). Alternatively, the problem may be one of inaccessible location of the infection within the root canal system, due to natural (Wada *et al.* 1998, Nair 2004, Nair *et al.* 2005) or iatrogenic (Seltzer *et al.* 1967) impediments. Although the success rates of 2°RCT on teeth with smaller lesions was significantly higher (25%, OR = 2.7) than for those with larger lesions, the difference failed to reach a statistically significant level (5%) when the covariate 'duration after treatment' was simultaneously entered into the meta-analysis regression model. The statistical heterogeneity could also be partly explained by the 'duration after treatment', consistent with the results of the systematic review on 1°RCT (Ng *et al.* 2008). It may therefore be concluded that larger lesions take longer to heal completely after 2°RCT, highlighting the importance of considering the confounder 'duration after treatment' when investigating the effect of prognostic factors.

Although the influence of bacterial culture results on the outcome of 2°RCT has only been investigated by two studies, the present review found a large but insignificant difference (52%, OR = 4.3) in success rates between those teeth with negative culture and those with positive culture. The difference was reduced slightly (46%) when only teeth with pre-operative lesion were included in the analysis. It may be hypothesized that the lack of significance was attributable to the small sample size since the bacterial culture results had a genuine negative impact on success of 2°RCT. The magnitude of impact of this factor on 2°RCT appeared to be much higher than on 1°RCT (Ng *et al.* 2008); this may again be due to over-estimation of the results because of the small sample size. Speculating that the result is true, the observation may be explained by difference in the nature of the residual bacteria present (Gulabivala 2004).

The intuitive (nine studies) and quantitative (three studies) analyses on the effects of the apical extent of root filling on 2°RCT gave somewhat different perspectives. These differences could be attributed to the substantial discrepancy in the number of studies contributing to the two analyses. The effect of this factor on 2°RCT outcome was profound and similar to its effect on 1°RCT (Ng *et al.* 2008). Teeth with long root fillings were associated with significantly lower pooled weighted success rates when compared with teeth with flush or short root fillings. Furthermore, for teeth with pre-operative periapical lesions, short root fillings were associated with higher success rates than flush root fillings, although the difference was small (7%) and statistically insignificant (OR = 0.84, 95% CI: 0.41, 1.72); this outcome was in contrast to the findings for 1°RCT (Ng *et al.* 2008). This finding was particularly unexpected because short root fillings could also be taken as a surrogate measure for inadequate cleaning of the apical canal terminus. This circumstance could be precipitated by either natural (calcification) or iatrogenic (pulpo-dentinal debris, foreign materials) obstructions. Previous reports on the effect of canal obstructions on the outcome of 1°RCT and 2°RCT have been contradictory and confusing ([1]Strindberg 1956, [2]Engström *et al.* 1964, Sjögren *et al.* 1990). The former two studies did not stratify their analyses by the two types of treatment and reported a significant influence from canal obstruction. In contrast, Sjögren *et al.* (1990) reported that the level of instrumentation as well as the apical extent of root fillings had no significant influence on the outcome of 2°RCT on teeth with apical periodontitis. To further accentuate the contrast, the same study (Sjögren *et al.* 1990) found a significant influence of canal obstruction on the outcome of teeth with apical periodontitis undergoing 1°RCT. The authors stressed that all cases with short root fillings and pre-operative periapical lesions were classified amongst those that could not be instrumented to their full length. Close inspection of their data revealed that 2°RCT teeth with pre-operative periapical lesions and long root fillings (50% of 26 roots) were associated with 15–17% lower success rate compared with those teeth with flush (0–2 mm short of radiographic apex) (67% of 51 roots) or short (≤2 mm short of radiographic apex) (65% of 17 roots) root fillings. The lack of statistical significance in the reported difference may again be due to insufficient sample size. The lack of difference in success rate between teeth with flush and short root fillings was also unexpected. The success rates for the 2°RCT (65%) and 1°RCT (68%) on teeth with pre-operative periapical lesions with short root fillings were similar. It could therefore be inferred that 'short' root fillings had the same effect on the outcome of both types of treatment. In contrast, the 2°RCT cases with flush root fillings (67%) were associated with a much lower (27%) success rate than their 1°RCT (94%) counterparts. It could be speculated that the canal termini in many of the 2°RCT cases may have been transported due to over-instrumentation and, therefore located further away from the radiographic apex compared to the previously untreated canals. Perhaps, given this complication, a direct comparison between flush root fillings in 1°RCT and 2°RCT cases may require different criteria, possibly facilitated by the use of electronic apex locators.

The effect of the quality of coronal restoration on 2°RCT (OR = 3.31; 95% CI: 1.07, 10.30) was similar to that on 1°RCT (OR = 1.82; 95% CI: 1.48, 2.25) (Ng *et al.* 2008) and supported by all three strands of evidence. The magnitude of the effect of coronal restoration on 2°RCT may have been over-estimated because of the small number of studies available but it may be inferred that coronal restorations fulfil a similar role in the two cases as the final stage of 2°RCT preventing re-infection of the root canal system.

In comparison with the gold standard, the evidence base for 2°RCT is weaker than that for 1°RCT. The pooled success rate of 2°RCT was approximately 77%, consistent with the findings for 1°RCT. Pre-operative periapical lesion, extrusion of root filling material, and unsatisfactory coronal restoration were all found to compromise the outcome of 2°RCT.

It may be concluded that according to the current best evidence, the primary goals of 2°RCT are to focus canal preparation on obtaining and maintaining access to the apical infection, achieving sufficient canal shaping to its terminus to facilitate adequate decontamination and then to provide a well condensed root filling extending to the canal system terminus without extrusion of any material. This should be followed as early as possible by the placement of a good quality coronal restoration to create a permanent (antibacterial) coronal seal.

In conclusion, the significant prognostic factors for 2°RCT identified from this review are similar to those for 1°RCT, strongly indicating that the principles and strategy for 2°RCT are identical to those for 1°RCT. The sole differences lie in the potentially compromised access to the said apical infection, either due to iatrogenic errors in canal preparation or inability to fully negotiate canal blockages due to natural or artificial materials. The outcome of 2°RCT should therefore be similar to 1°RCT as long as access to the apical infection can be re-established. There is therefore a need for clinicians to acquire the skill to diagnose and correct procedural errors as well as to prevent introduction of further iatrogenic errors during re-treatment. The acquisition of such skills must of necessity include the tactile skills necessary to manipulate stainless steel instruments back into previously patent (but now obstructed and deviated) canal termini. Nickel–titanium instruments, lacking the necessary physical properties to be appropriately pre-curved at the tip for re-direction, more-often-than-not prove unsuitable for the task. This may have important implications for training. These definitive observations are offered within the constraints of the limitations of the data available. There is still a palpable need for well designed prospective studies to evaluate the outcome of 1°RCT and 2°RCT at more detailed and sophisticated levels. In particular, there is a need to investigate the influence of numerous untested pre-operative prognostic factors specifically related to 2°RCT. Furthermore, it is imperative to carry out randomized controlled trials with sufficiently detailed data recording to establish optimal re-treatment protocols.

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