

A prospective study of the factors affecting outcomes of nonsurgical root canal treatment: part 1: periapical health

Y.-L. Ng¹, V. Mann² & K. Gulabivala¹

¹Unit of Endodontology, UCL Eastman Dental Institute, University College London, London; and ²Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK

Abstract

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Aim To investigate the probability of and factors influencing periapical status of teeth following primary (1°RCTx) or secondary (2°RCTx) root canal treatment.

Methodology This prospective study involved annual clinical and radiographic follow-up of 1°RCTx (1170 roots, 702 teeth and 534 patients) or 2°RCTx (1314 roots, 750 teeth and 559 patients) carried out by Endodontic postgraduate students for 2–4 (50%) years. Pre-, intra- and postoperative data were collected prospectively on customized forms. The proportion of roots with complete periapical healing was estimated, and prognostic factors were investigated using multiple logistic regression models. Clustering effects within patients were adjusted in all models using robust standard error.

Results The proportion of roots with complete periapical healing after 1°RCTx (83%; 95% CI: 81%, 85%) or 2°RCTx (80%; 95% CI: 78%, 82%) were similar. Eleven prognostic factors were identified. The conditions that were found to improve periapical healing

significantly were: the preoperative absence of a periapical lesion ($P = 0.003$); in presence of a periapical lesion, the smaller its size ($P \leq 0.001$), the better the treatment prognosis; the absence of a preoperative sinus tract ($P = 0.001$); achievement of patency at the canal terminus ($P = 0.001$); extension of canal cleaning as close as possible to its apical terminus ($P = 0.001$); the use of ethylene-diamine-tetra-acetic acid (EDTA) solution as a penultimate wash followed by final rinse with NaOCl solution in 2°RCTx cases ($P = 0.002$); abstaining from using 2% chlorhexidine as an adjunct irrigant to NaOCl solution ($P = 0.01$); absence of tooth/root perforation ($P = 0.06$); absence of interappointment flare-up (pain or swelling) ($P = 0.002$); absence of root-filling extrusion ($P \leq 0.001$); and presence of a satisfactory coronal restoration ($P \leq 0.001$).

Conclusions Success based on periapical health associated with roots following 1°RCTx (83%) or 2°RCTx (80%) was similar, with 10 factors having a common effect on both, whilst the 11th factor 'EDTA as an additional irrigant' had different effects on the two treatments.

Keywords: outcome, periapical healing, root canal treatment, success.

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Introduction

Periapical disease is an inflammatory response around root canal termini in response to intraradic-

ular bacterial infection. It can be prevented (in the case of pulp inflammation) or resolved (in the case of pulp infection) by root canal treatment. The principles for root canal treatment laid at the beginning of the last century (Hall 1928) remain consistent with contemporary quality guidelines approved by Endodontic societies in Europe and North America (British Endodontic Society 1983, European Society of Endodontology 1994, 2006, Canadian Academy of

Correspondence: Dr Yuan-Ling Ng, Unit of Endodontology, UCL Eastman Dental Institute, University College London, 256 Grays Inn Road, London WC1X 8LD, UK (e-mail: p.ng@eastman.ucl.ac.uk).

Endodontics 2006). Most of the stipulations in the guidelines are supported by clinical/microbiological evidence, but gold standard long-term clinical outcome data are lacking.

The outcome of primary (1°RCTx) and secondary (2°RCTx) root canal treatments has been assessed using a variety of measures, the chosen measure selected on the basis of its perceived importance to researchers, dentists or patients. Researchers interested in identifying prognostic factors, have tended to opt for radiographic and clinical signs of resolution of periapical disease (Ng *et al.* 2007). From the patient's perspective, the measures of utility have included resolution of symptoms (Bender *et al.* 1966a,b), functionality of the tooth (Friedman & Mor 2004) and quality of life (Dugas *et al.* 2002). For the health planning professional or dental insurance companies, survival of the root canal fillings/treatment (Cheung 2002, Cheung & Chan 2003, Stoll *et al.* 2005, Lumley *et al.* 2008, Tickle *et al.* 2008) and tooth retention/survival (Lazarski *et al.* 2001, Salehrabi & Rotstein 2004) may be the most interesting outcome. Classically, root canal treatment procedures have been evaluated by signs and symptoms of periapical healing, but alternative treatments, such as implant-retained prostheses, focus on survival of the osseointegrated fixture. In response, the American Association of Endodontists adopted revised definitions of success that included tooth survival (Friedman & Mor 2004).

Systematic reviews (Ng *et al.* 2007, 2008a,b) using clinical and radiographic measures of periapical healing revealed the estimated weighted pooled success rates of 1°RCTx completed at least 1 year prior to review, ranged between 68% and 85% when strict criteria (complete absence of periapical radiolucency) were used (Ng *et al.* 2007). The equivalent estimated weighted pooled success rates of 2°RCTx ranged between 70% and 86% (Ng *et al.* 2008b). The reported success rates for both treatments had not improved over the last four (or five) decades. Four conditions were found to be significantly associated with better periapical healing following treatment and these included: (i) the presence of a periapical lesion, (ii) the apical extent and quality of root filling and (iii) an adequate coronal restoration (Ng *et al.* 2008a,b).

Since the turn of the millennium, a number of studies (Lazarski *et al.* 2001, Caplan *et al.* 2002, Salehrabi & Rotstein 2004, Stoll *et al.* 2005) have reported on the survival of teeth after root canal treatment. A systematic review of tooth survival

following root canal treatment (Ng *et al.* 2010) found the pooled percentages over 2–10 years following RCTx ranged between 86% and 93%. Four conditions were found to significantly improve tooth survival. In descending order of influence, the conditions increasing the observed proportion of teeth surviving were (i) a crown restoration after RCTx, (ii) the presence of both mesial and distal proximal contacts, (iii) absence of utilization of tooth as an abutment for removable or fixed prosthesis, (iv) and tooth type (nonmolar teeth versus molar teeth).

Systematic reviews (Ng *et al.* 2007, 2008a,b, 2010) on periapical status and survival of teeth following nonsurgical root canal treatment revealed the quality of evidence for treatment factors affecting both 1°RCTx and 2°RCTx to be suboptimal, with substantial variation in the study designs. The problem was worse amongst studies investigating tooth survival compared to those investigating periapical healing. Substantially fewer studies had investigated the outcome of 2°RCTx than 1°RCTx.

The aims of this study were to investigate the probability of success and factors influencing the outcomes (both periapical healing and tooth survival) of 1°RCTx and 2°RCTx. The aim of this paper is to present the probability of and factors influencing periapical healing of teeth following 1°RCTx or 2°RCTx, whilst the second paper will report the probability of and factors influencing tooth survival following 1°RCTx or 2°RCTx (Ng *et al.* 2011).

Materials and methods

Ethical approval, inclusion and exclusion criteria

This project was approved by the Joint Research & Ethics Committee of UCL Hospitals NHS Trust (reference number 96/E195). Informed consent was obtained from all patients.

The sample population included all patients undergoing 1°RCTx or 2°RCTx, commencing from the 1st October 1997 until the end of June 2005 in the Unit of Endodontology (part of Department of Conservative Dentistry prior to 2004), UCL Eastman Dental Hospital, London, UK. The patients were referred from general dental practice, secondary dental or maxillo-facial referral centres and other Clinical Units of the dental hospital. All patients were over 15 years of age when treatment commenced and had either 1°RCTx or 2°RCTx completed and had at least a semi-permanent restoration placed.

Teeth were excluded from this study if they had preoperative periodontal disease or prior surgical endodontic treatment, or if the apex/apices under investigation was/were not discernible on any of the periapical radiographs. The teeth were excluded from the analysis of 'periapical status following treatment' if: (i) they were not followed-up for at least 2 years, (ii) they were extracted for reasons not related to endodontic problems, (iii) information on the periapical status at the time of the extraction was not available and (iv) a completed pre- and intraoperative data collection form was not available for each tooth.

Primary and secondary root canal treatment in the unit of Endodontology

The main group of clinicians consisted of Endodontic postgraduate students providing root canal treatment under the supervision of specialists. Standard principles of 1°RCTx or 2°RCTx, consistent with the European Society of Endodontology guidelines (European Society of Endodontology 2006) were followed, but the treatment was not restricted to a single protocol.

All treatments were performed under local anaesthesia and rubber dam isolation, ensuring absence of saliva leakage. After accessing the tooth, the canals were prepared by preflaring the coronal (or straight) portion prior to negotiation of the apical portion and determination of working length. Sodium hypochlorite solution was always used as an irrigant during the preflaring procedure. The location of the apical terminus was always aided by an electronic apex locator (EAL) [Root ZX (J Morita Co, Tustin, CA, USA); AFA Apex Finder (Analytic Endodontics, Orange, CA, USA); or Elements diagnostic (SybronEndo, Orange, CA, USA)]. The EAL determination was confirmed by taking a radiograph with the diagnostic file placed at the EAL '0' reading length or the maximal extent achievable with the smallest file. The initial size of file (*recorded as the initial canal size*) was the largest that could reach EAL '0' reading length without force to ensure good electrical contact and stability when taking a radiograph. The apical extent of instrumentation was then determined by the operator as a distance equal to or slightly short of the EAL '0' reading length.

Operators were free to choose various types of instruments and techniques for canal negotiation and shaping. The instruments available for use included: (i) K-flex files (Dentsply Maillefer, Ballaigues, Switzerland), (ii) Flex-O-files (Dentsply Maillefer), (iii) Hedström files

(Dentsply Maillefer), (iv) GT hand instruments (Dentsply Maillefer), (v) ProTaper hand instruments (Dentsply Maillefer), (vi) rotary GT instrument system (Dentsply Maillefer), (vii) rotary ProFile instrument system (Dentsply Maillefer), (viii) rotary ProTaper instrument system (Dentsply Maillefer) and (ix) rotary K3 instrument system (SybronEndo). The stainless steel instruments may have been used in push-pull filing (Abou-Rass *et al.* 1980), stem-winding (Backman *et al.* 1992) or balanced-force (Roane *et al.* 1985) motions. Patency of the apical terminus, if achieved, was maintained during canal enlargement by placing a small file of size 8 or 10 passively to 0.5 mm beyond the apical terminus between each instrumentation step during canal enlargement.

The recommended minimum or optimal apical size of canal preparation was size 30. If the initial apical size of the canal was larger than 30, it was not recommended to enlarge it further but the wall of the canal was gently planed using stainless steel instruments to facilitate disruption of the biofilm. After apical enlargement, the canal would be flared to various tapers as perceived to be necessary. For large canals, it was not recommended to create a predetermined taper in order to preserve root dentine. In this case, a 0.02 taper was recorded and subsequently confirmed by Y-LN during radiographic assessment by measuring the diameters at the cervical level and apical terminus and dividing the difference in the diameters by the distance between the two points. If the apical size of canal was larger than the largest available stainless steel instrument (size 140), the canal size was estimated by Y-LN from the preoperative radiograph by measuring the diameter of the canal apically. Using stainless steel instruments for canal preparation, the tapers were restricted to either 0.05 or 0.10 taper by introducing sequentially larger instruments at either 1.0 mm or 0.5 mm step-back intervals, respectively. By definition, canals could only be shaped to 0.04, 0.06, 0.08, 0.10 tapers if nickel-titanium instruments with such tapers were used. If the multiple tapered ProTaper instruments were used, the taper at the tip of the instrument (0.07–0.09) was recorded.

Sodium hypochlorite (NaOCl) solution (5% Teepol bleach; Teepol® products, Orpington, UK) was the standard root canal irrigant. Operators were free to choose the concentration of the NaOCl (2.5% or 5.0%) and to use any additional irrigant as clinically perceived necessary and approved by the specialist supervisor. The irrigants included 10% povidone-iodine (Betadine®; Seton Health Care PLC, Oldham, UK),

0.2% chlorhexidine gluconate (CHX) (Corsodyl®; Adam Health Care Ltd, Leeds, UK), 17% ethylene-diamine-tetra-acetic acid (EDTA) (AnalaR® grade; Merck BDH, Poole, UK and prepared in our laboratory) or Smear-Clear™ (SybronEndo). Canal irrigation was carried out using 27 gauge side-cut open end needles (Monoject® Luer lock syringe; Sherwood Medical, St. Louis, MO, USA); with or without supplementation by ultrasonic agitation. Ultrasonic agitation was only used after mechanical canal enlargement was completed, fresh NaOCl irrigant was introduced into the canal and agitated using an ultrasonically energized size 15 file (Dentsply Maillefer) with low power setting (EMS; Electro Medical Systems SA, Nyon, Switzerland or P5; Satelec Acteon group, Merignac, France). Calcium hydroxide (BDH Merck) and barium sulphate (AnalaR® grade; Merck BDH) powder (in a ratio of 7 : 1) mixed with sterile water was the standard interappointment medicament. Ledermix (Blackwell Supplies, Gillingham, UK) was occasionally used for teeth with acute pulpitis when extirpation of pulp tissues at the first visit was incomplete.

All root canals were filled with gutta-percha and zinc oxide-eugenol root canal sealer (Roth Dental Company, Chicago, IL, USA) using a technique of the operator's choice. Customization of the tip of the master gutta-percha cone using chloroform (Chloroform BP; JM Loveridge Ltd, Southampton, UK) was recommended as a routine measure (Van Zyl *et al.* 2005). The various techniques used included: (i) cold lateral compaction, (ii) thermoplastic lateral compaction using warm finger spreaders, (iii) thermoplastic lateral compaction using ultrasonically energized files, (iv) modified Schilder's warm vertical compaction technique (Van Zyl *et al.* 2005) and (v) continuous wave technique (Buchanan 1996). In some of the most recently completed cases, mineral trioxide aggregate (MTA) (ProRoot™ MTA; Dentsply Maillefer, Weybridge, UK) was used as filling material for roots with incompletely formed apices.

Upon completion of root canal treatment, a permanent core was placed in the access cavity with or without a base material (IRM® or glass-ionomer cement; Dentsply, Weybridge, UK), according to the operator's choice. Amalgam was the core material normally used to restore posterior teeth, whilst composite material was used for anterior teeth. A final radiograph was then taken by the operator. If indicated, a cast restoration was provided by the referring dentist and exceptionally it was provided by the endodontist. If a cast post and core was required

on an anterior tooth, the gutta-percha root filling was cut back leaving at least 5 mm of root filling apically, over which a 2-mm layer of IRM® would be placed, if at all possible. The tooth was then restored with a temporary postretained crown. If a cast post and core was indicated on a molar tooth, the pulp chamber was dressed with IRM® protected with a copper band and the final core and restoration were provided by the referring dentist.

Follow-up clinical examination

The intention was to follow-up all the treated teeth annually up to 4 years (50% of the cases) postoperatively. Appointment letters were sent to the patient 1 month in advance of the annual follow-up appointment by the receptionists in the Department. Those patients failing to attend for recall were contacted with a personal courtesy call by the author (Y-LN) and a further explanation letter to encourage them to attend follow-up appointments. The reasons for lack of attendance were recorded and analysed. Follow-up examination consisted of updating the general and endodontic history as well as clinical and radiographic examination. All subjects were interviewed and examined by Y-LN annually following completion of treatment. During the interview, the patient's personal, medical and dental details as well as the preoperative pain history were confirmed. A detailed pain interview was conducted on patients presenting with pain to exclude nonendodontic origin. Extra-oral examination included palpation of masticatory, neck and shoulder muscles for comparative tenderness. Auscultation and palpation of the temporo-mandibular joint and assessment of the range of mandibular movement was incorporated to exclude pain originating from these structures. Clinical details about the treated tooth included: (i) tenderness to pressure and percussion of the tooth, (ii) tenderness to palpation of adjacent soft tissues, (iii) presence of an associated sinus tract or swelling in the adjacent soft tissues, (iv) periodontal probing profile around the tooth, and (v) the type and presence of an adequate coronal restoration and 'seal'. The quality of restoration was classified into three categories: (i) obvious visual or tactile exposure of root-filling material when the root filling could be seen or probed clinically, (ii) clinically (probing) or radiographically detected coronal marginal discrepancy but without obvious visual or tactile exposure of the root filling to the oral cavity or (iii) satisfactory coronal restoration judged by good retention and marginal fit.

If the tooth had been re-treated or extracted, the timing and reasons for re-treatment or extraction were recorded. The adjacent and opposing teeth were also examined to exclude them as causes of pain or infection.

Radiographic assessment

All the relevant radiographs (F-speed; Eastman Kodak Company, Rochester, NY, USA): preoperative, file at EAL 'zero' length, master apical file at working length, postobturation and follow-up periapical radiographs were taken reproducing the same angulation by intuitive orientation of a beam-aiming device (Rinn; Dentsply Ltd, Weybridge, UK). In case of persistent discomfort from the treated tooth at follow-up, periapical radiographs at different horizontal angles were taken in order to detect any persistent radiolucent lesion superimposed upon the root. Those cases with persistent discomfort but no obvious evidence of periapical pathology on two periapical radiographs were investigated further using cross-sectional tomography (ScanOra; Orion Co, Espoo, Finland). If the patient was pregnant at the time of the follow-up appointment, the radiographic examination was deferred until after delivery.

All the preoperative, immediate postobturation and follow-up radiographs were viewed under standard conditions by Y-LN using a fluorescent light box (Kenro Ltd, Swindon, UK) and a magnifying viewer (Brynmol, $\times 2.5$ magnification; Trycare Ltd, Bradford, UK). The radiographs mounted in sequence and date order were viewed in a darkened room to determine the periapical status. The preoperative periapical status of each root was classified into three categories: (i) intact periodontal ligament, (ii) widened periodontal ligament or (iii) periapical lesion. The diameter of the lesion preoperatively and at follow-up was measured using a metal endodontic ruler with precision upto 0.5 mm under $\times 2.5$ magnification. The diameter for widened periodontal ligament was recorded as 0.5 mm. The quality of previous treatment was judged satisfactory if a well-compacted root filling extended to within 2 mm of the radiographic root apex.

To account for the subjectivity of radiographic assessment of healing, 30% of the radiographs (randomly selected) were re-examined by Y-LN 1 year later to determine intraobserver reliability and a second observer (KG) examined 30% of the radiographs to determine interobserver agreement. Both observers were experienced endodontists and blinded to the treatment procedures used. They were also precalibrated

using reference radiographs representing the four categories of radiographic healing: (i) complete, in the presence of a normal periodontal ligament space, (ii) incomplete, if there was reduction in size of the lesion without return to normal periodontal ligament space width, (iii) uncertain, when it was radiographically impossible to make a definitive decision on status of postoperative healing (*these cases were excluded from further analyses*) or (iv) failure, if a pre-existing periapical lesion had increased in or remained the same size; or a previously normal periodontal ligament space had increased in width or developed into a radiolucent area. In the event of interobserver disagreement, the two observers discussed their findings and agreed on the outcome. In case of no agreement, Y-LN arbitrated on the final decision. The periapical status of each root (presence or absence of widening of periodontal ligament space/periapical lesion) on final recall radiographs of 50 randomly selected teeth (129 roots) were also reassessed without referring to the preoperative radiograph and knowledge of the duration of follow-up.

The intraoperative and postobturation radiographic assessments consisted of length, apical extent and homogeneity judgments under $\times 2.5$ magnification and optimal lighting by Y-LN. In cases where canal terminus patency could not be achieved and EAL '0' reading length was not available, the discrepancy between the file tip and radiographic apex was measured on the diagnostic length radiograph. The apical extent of root filling and presence of voids within the apical 5 mm of root filling were determined from the postobturation radiograph. The discrepancies between the file tip location at EAL zero reading and apical extent of the root filling were measured using the radiographic apex as the reference point; any sealer extrusion was recorded. The fate of the extruded material was monitored on the follow-up radiographs.

Determination of outcome

Treatment success was assessed using two outcome measures. The primary outcome was clinical and radiographic evidence of absence of apical periodontitis or healing by each root. The secondary outcome was tooth survival (the outcomes of which will be presented in the second part of this paper) (Ng et al. 2011).

For this part of the study, successful treatment based on strict criteria was defined as absence of pain, clinical evidence of inflammation or swelling and conventional radiographic measures of complete healing/presence of a normal periodontal ligament space. Successful

treatment based on loose criteria was defined as absence of pain, clinical evidence of inflammation or swelling and conventional radiographic measures of complete healing/presence of a normal periodontal ligament space or incomplete healing (if there was reduction in size of the lesion without return to normal periodontal ligament space width). If a tooth had been extracted because of endodontic problems (persistent pain, swelling, sinus or periapical radiolucent lesion), the treatment was considered failed. Tooth extraction without any exit data on postoperative periapical status excluded it from further 'periapical healing' analysis.

Data management

Comprehensive prospective pre- and intraoperative data for each patient had been meticulously recorded by Endodontic postgraduate students (under supervision by specialists) and staff on custom-designed data-collection-forms since October 1997. The customized forms were also available for recording follow-up information and radiographic assessments.

All the patient's medical conditions were self-reported onto a standard medical history form at the first consultation appointment and was verified and updated by interview prior to treatment and at the follow-up appointment by Y-LN. All conditions reported by the patient were recorded, but only those that were prevalent amongst the patient cohort or previously reported to have significant association with treatment outcome were analysed.

Relevant demographic data, medical history, preoperative pain history, diagnostic and treatment details of the tooth were extracted from the data collection forms and entered onto an electronic database (Microsoft Office Access software™). The Data protection act 1998 (http://www.dh.gov.uk/en/Managingyourorganisation/Informationpolicy/Recordsmanagement/DH_4000489) was complied with when handling patients' personal data. All data were anonymised on the electronic database.

Statistical analysis

Statistical analyses were performed with STATA version 9.2 (STATA Corporation, College Station, TX, USA, 2005) statistical software package. The age and gender of the patients and the preoperative pulpal and periapical status of the teeth which were excluded or lost at different stages were compared with those included for analysis.

Cohen's kappa coefficients were calculated to assess both intra- and interobserver agreement on radiographic examination. The 95% confidence interval was estimated using bias corrected bootstrap estimates (Reichenheim 2004). Good agreement was taken as >0.8, substantial as 0.61–0.8 and moderate as 0.4–0.6 (Petrie & Watson 1999).

Associations between potential prognostic factors and the proportion of teeth with successful treatment based on strict criteria (absence of apical periodontitis after treatment) were initially assessed using univariable logistic regression. To account for the clustering effect of multiple roots within the same tooth/patient or multiple teeth within patient, logistic regressions with cluster sandwich estimator for robust standard error was used in all of the logistic regression models. In case of a potential prognostic factor having more than two categories, the overall effect of the factor was assessed using the Wald test to assess heterogeneity.

Initial analyses were performed separately for 1°RCTx and 2°RCTx to find potential prognostic factors. Factors affecting success at the 5% significance level or showing a large effect ($OR \geq 1.5$ or $OR \leq 0.5$) at the 10% significance level were then entered simultaneously with 'preoperative periapical status' into logistic regression models one by one. The effect of those factors which remained prognostic were further adjusted for 'size of preoperative periapical lesion' in models already including the 'preoperative periapical status'.

The effect of type of treatment (1°RCTx, 2°RCTx) and its potential interaction with prognostic factors (identified from the analyses on separate datasets) was assessed in a combined data set incorporating both 1° and 2°RCTx.

Using the combined data set, the final model to investigate factors affecting the success of any type of root canal treatment was built as follows. Potential prognostic factors, previously identified in the separate datasets, were entered one by one into logistic regressions including 'preoperative periapical status' and 'size of preoperative periapical lesion'. A factor was considered to have prognostic value based on previously defined criteria.

The final multiple logistic regression model was built through three stages. First, all the *preoperative factors* having prognostic value from the previous models were entered together into the logistic regression model including the 'type of treatment', 'preoperative periapical status' and 'size of preoperative periapical lesion'. Those factors that lost their prognostic value, according to the above definition, were removed from the model.

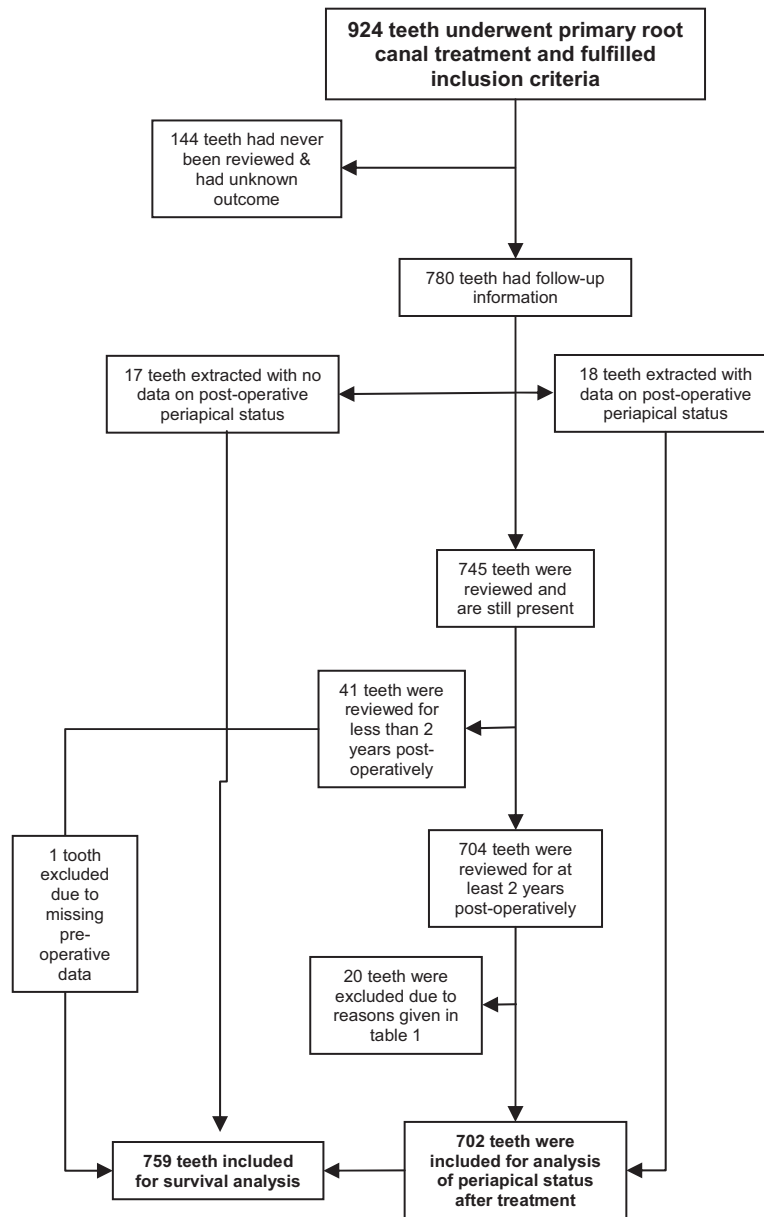


Figure 1 Flow chart showing study flow of teeth undergoing primary root canal treatment and fulfilling initial inclusion criteria.

Secondly, all the *intraoperative factors* with prognostic values were entered into the model resulting from stage 1. As in stage 1, those factors that lost their prognostic values in this model were removed. Finally, all the *postoperative factors* (restoration after root canal treatment) with prognostic values were added to the model resulting from stage 2 and retained according to the criteria given earlier. Those factors that lost their prognostic value at any of the above stages were tested again in stage 3. Interaction between intraoperative factors and type of treatment was also explored in this last stage.

The goodness-of-fit of the final model was assessed using the Hosmer and Lemeshow method as well as through Pearson and deviance residuals. If the model was appropriate, the ratios of the sum of these squared residuals to the residual degree of freedom should be close to 1 (Hosmer & Lemeshow 1980).

Results

A total of 924 teeth had undergone 1°RCTx and 1113 teeth had undergone 2°RCTx and fulfilled inclusion criteria; of these, 144 teeth and 230 teeth, respectively,

were never reviewed because of the failure of the patients to attend any of the review appointments (Figs 1 and 2). The reasons for patient's absence from review appointments or exclusion of teeth for analysis (of periapical healing outcome) are presented in Table 1.

A total of 702 1°RCTx teeth (534 patients, 1170 roots) and 750 2°RCTx teeth (559 patients, 1314 roots) were finally included in this prospective study. The characteristics of patients and teeth (age, gender distribution and periapical status) by exclusion and inclusion of teeth are presented in Table 2. The data

revealed that the proportion of teeth with a periapical lesion was significantly ($P < 0.05$) larger amongst the studied teeth than amongst the excluded teeth, regardless of type of treatment. The mean values for the diameter of periapical lesions associated with the studied teeth were minimally (0.3 mm) but significantly ($P < 0.001$) larger than those associated with the excluded teeth, regardless of type of treatment.

The intraobserver (Kappa 0.80 [95% CI: 0.77, 0.86]; 0.82 [95% CI: 0.79, 0.87]) and interobserver agreement (kappa 0.83 [95% CI 0.82, 0.89]; 0.81 [95% CI:

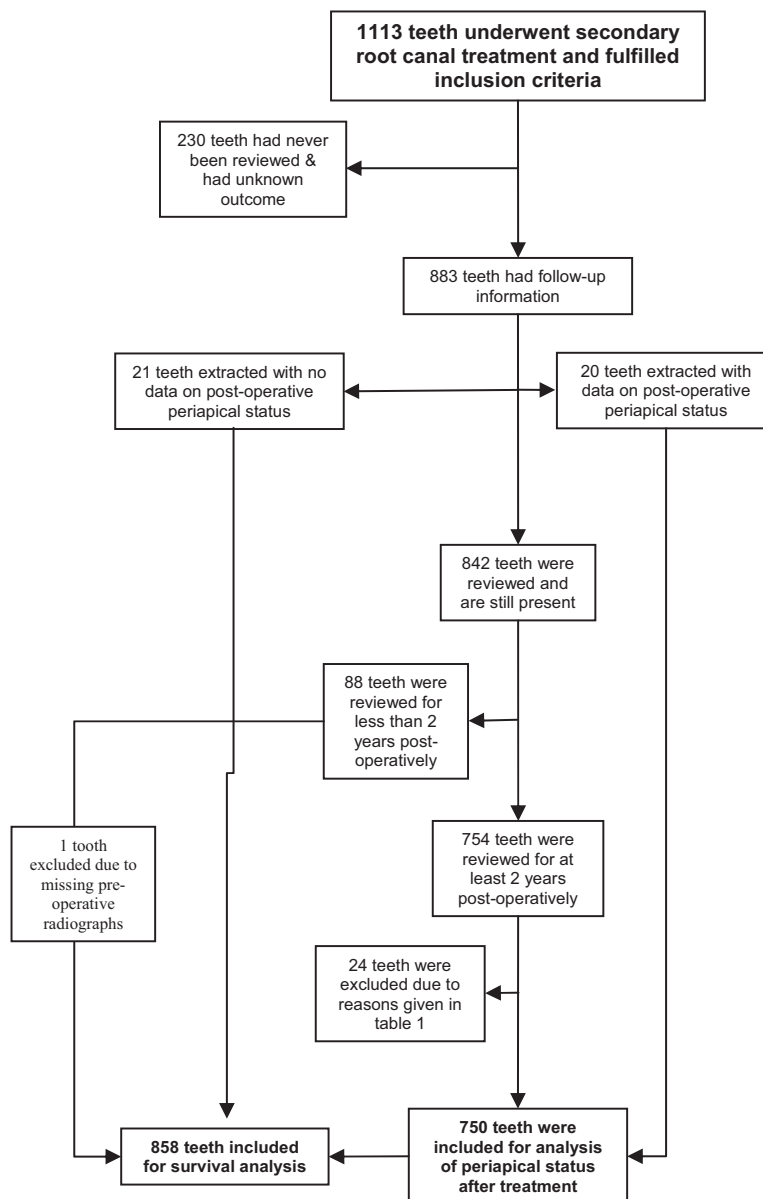


Figure 2 Flow chart showing study flow of teeth undergoing secondary root canal treatment and fulfilling initial inclusion criteria.

Table 1 Reasons for patients' nonattendance at recall and for exclusion of teeth with at least 2-year follow-up

	1°RCTx	2°RCTx
<i>Reasons for not attending for recall</i>		
No contact – reason unknown	117	189
Moved away	3	10
Deceased	3	3
Ill health/care home	1	1
Busy	20	27
<i>Reasons for exclusion for those who had been followed up for 2 or more years</i>		
Apex of roots not discernible on pre- or intraoperative radiographs	12	10
Pre- or intraoperative radiographs missing	4	6
Pre- or intraoperative data collection form missing	3	7
Tooth did not have final root filling at the Eastman	1	0
Retreatment by referring dentist for unknown reason	0	1

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment.

Table 2 Characteristics of patients and teeth at inception and those included in the final analyses of absence of clinical and radiographic signs of apical periodontitis after treatment

	Inception cohort		Study cohort	
	1°RCTx (n = 924)	2°RCTx (n = 1113)	1°RCTx (n = 702)	2°RCTx (n = 750)
Age (mean, years)	40.9	41.1	41.5	42.4
Female patients (%)	57.8	62.3	58.1	64.3
Male patients (%)	42.2	37.7	41.9	35.7
Vital pulp (%)	18.9	–	19.2	–
Nonvital pulp (%)	81.1	–	80.8	–
Intact PDL (%)	24.5	19.1	20.7	14.6
Widened PDL (%)	10.9	10.2	13.0	11.2
Periapical lesion (%)	63.3	69.0	66.3	74.2
Unable to assess periapical status (%)	1.3	1.7	–	–
Size of lesion (mean, mm)	2.6	2.3	2.9	2.6

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment; PDL, periodontal ligament.

0.78, 0.88]) for 696 roots and the 129 roots, respectively, were good.

Proportion of teeth successful by different examination methods

The distribution of different clinical and radiographic outcomes (2–4 years post-treatment) is presented in Table 3. Data on the number of years taken for a

periapical lesion to (radiographically) heal completely were available for 277 of 639 1°RCTx cases and for 384 of 775 2°RCTx cases. The majority of the 277 lesions associated with 1°RCTx healed completely within 1 year (71.9%, $n = 207$) and another large proportion healed completely between 1–2 years (19.4%, $n = 56$), postoperatively. Similarly, the majority of the 384 lesions associated with 2°RCTx healed completely within 1 year (71.4%, $n = 274$) and a similar large proportion between 1–2 years (24.2%, $n = 93$), postoperatively. Only a small percentage (4.9%, $n = 14$ for 1°RCTx; 4.5%, $n = 17$ for 2°RCTx) required 3 years or more to heal completely. The factors affecting the rate of healing of periapical lesions were not investigated because of insufficient data.

Identification of potential prognostic factors predicting probability of success using logistic regression

The proportion of roots with successful treatment defined by absence of periapical disease listed by each potential prognostic factor and the results of univariable logistic regression analyses investigating the effect of each on treatment outcome are presented in Tables 4–9. Those factors found to have prognostic value by this means were tested further by entering them simultaneously with 'preoperative periapical status' into logistic regression models one by one. Each of those factors retaining their prognostic value (results not shown) were entered simultaneously into a multiple logistic regression model with 'preoperative periapical status' and 'size of lesion' as covariates. Ten factors for 1°RCTx and 11 for 2°RCTx reached statistical significance at the 5% level or had a large effect at the 10% level, respectively (Table 10). Of the potential prognostic factors influencing the success of 2°RCTx, only one factor (fate of preoperative foreign material) was unique to 2°RCTx. Clinically, the 'fate of preoperative foreign material' was a surrogate measure for the ability to clean or fill the canal to the apical terminus. 'Fate of preoperative foreign material' was therefore not investigated further.

Considering that all remaining potential prognostic factors (except preoperative pulpal status) were common to both types of treatment, it was decided to combine the two data sets to increase the statistical power. The interactions between 'type of treatment' and other potential factors (shown in previous analyses to have different effects on 1°RCTx and 2°RCTx) were investigated further.

Table 3 Clinical signs and symptoms and radiographic outcome after root canal treatment

(a) Clinical assessment	Total number of roots	Absence of signs and symptoms [<i>n</i> (%)]	Presence of signs and symptoms [<i>n</i> (%)]	
1°RCTx	1170	1068 (91.3% [89.5%, 92.8%])	102 (8.7% [7.1%, 10.4%])	
2°RCTx	1314	1178 (89.6% [87.9%, 91.2%])	136 (10.4% [8.8%, 12.1%])	
(b) Radiographic assessment	Total number of roots	Complete healing [<i>n</i> (%)]	Incomplete healing [<i>n</i> (%)]	Failed [<i>n</i> (%)]
1°RCTx	1170	1017 (86.9% [84.9%, 88.8%])	85 (7.3% [5.8%, 8.9%])	68 (5.8% [4.5%, 7.3%])
2°RCTx	1314	1111 (84.6% [82.5%, 86.5%])	75 (5.7% [4.5%, 7.1%])	128 (9.7% [8.2%, 11.5%])
(c) Combined assessments	Total number of roots	Successful [<i>n</i> (%)]	Unsuccessful [<i>n</i> (%)]	
1°RCTx	1170			
Strict criteria		969 (82.8% [80.5%, 84.9%])	201 (17.2% [15.0%, 19.3%])	
Loose criteria		1043 (89.1% [87.4%, 90.9%])	127 (10.9% [9.1%, 12.6%])	
2°RCTx	1314			
Strict criteria		1053 (80.1% [77.9%, 82.3%])	261 (19.9% [17.7%, 22.0%])	
Loose criteria		1125 (85.6% [83.7%, 87.5%])	189 (14.4% [12.5%, 16.3%])	

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment.

Final multiple logistic regression model using the combined data set

Initially, each of the factors with prognostic value (Table 10) was entered simultaneously with 'preoperative periapical status' and 'size of periapical lesion' into a multiple logistic regression model. All except two factors (preoperative pulpal status and apical size of canal preparation) retained their prognostic value (results not shown).

In all the subsequent analyses, three variables (type of treatment, preoperative periapical status and size of periapical lesion) were included in all multiple regression models. Although 'type of treatment' only reached significance at the 10% level in the previous analysis, it was included in the model for investigation of its potential interaction with other prognostic factors. Pain and swelling are likely to occur concomitantly during interappointment flare-up. Thus, these two factors, interappointment pain and interappointment swelling were combined for analyses in the following multiple regression models. In model 1 (Table 11), all four potential preoperative prognostic factors were entered simultaneously with the aforesaid three variables. Two factors, 'preoperative swelling' and 'preoperative periodontal probing depth', failed to retain their prognostic value.

In model 2 (Table 12), all seven potential intraoperative prognostic factors were entered into model 1 after removing the preoperative factors that had lost their prognostic values. 'Apical extent of instrumentation' and 'Apical extent of root filling' were significantly

correlated ($P < 0.001$). In order to include both factors simultaneously into the same model, 'apical extent of root filling' was converted into a binary variable (long root filling or not) to measure the extrusion of root filling material into the periapical tissues. The results of the analysis revealed that the 'type of treatment' and 'preoperative perforation' failed to reach significance at the 10% and 5% levels, respectively. Of the intraoperative factors, 'intraoperative perforation' also failed to reach significance at the 5% level. In the subsequent analyses, 'preoperative perforation' and 'intraoperative perforation' were combined into one variable as 'pre- or intraoperative perforation' as they were significantly ($P < 0.001$) correlated with each other.

In model 3 (Table 13), the 'quality of restoration' was entered into model 2 (Table 12) after removing those factors that lost their prognostic values. As the effect of 'additional use of EDTA as irrigant' was found to have the same effects but to different extents on the 1°RCTx and 2°RCTx when the two data sets were analysed separately, an interaction term 'type of treatment \times EDTA' was incorporated in the model to explore this potential interaction. In this model (Table 13), all the factors incorporated, with the exception of three factors: 'type of treatment', 'pre- or intraoperative perforation', 'interaction between type of treatment and additional use of EDTA', reached statistical significance at the 5% level. The type of treatment failed to reach significance at the 10% level, but the other two factors did. This model was therefore adopted as the final model to describe the prognostic factors for 1°RCTx and 2°RCTx. The goodness-of-fit tests from

Table 4 Unadjusted effects of patient characteristics, tooth and root type using logistic regression analysis

Factors	1°RCTx			2°RCTx		
	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
Age (continuous data)	–	–	1.004 (0.99, 1.01)	–	–	0.999 (0.99, 1.01)
Sex						
Female	699	84.4	1	864	81.4	1
Male	471	80.5	0.76 (0.56, 1.03)	450	77.8	0.80 (0.61, 1.06)
Diabetic						
No	1143	82.9	1	1283	80.1	1
Yes	27	77.8	0.72 (0.29, 1.80)	31	80.6	1.03 (0.42, 2.55)
Allergic						
No	881	82.3	1	1000	80.1	1
Yes	289	84.4	1.17 (0.81, 1.68)	314	80.3	1.01 (0.73, 1.39)
Systemic steroid						
No	1153	82.7	1	1294	80.3	1
Yes	17	88.2	1.56 (0.34, 6.70)	20	70.0	0.57 (0.22, 1.50)
Long term antibiotics						
No	1154	82.9	1	1307	80.1	1
Yes	16	75.0	0.62 (0.20, 1.93)	7	85.7	1.49 (0.18, 12.43)
Thyroxin therapy						
No	1120	82.8	1	1270	79.8	1
Yes	50	84.0	1.09 (0.51, 2.36)	44	90.9	2.54 (0.90, 7.16)
Hormone replacement						
No	1109	82.8	1	1279	80.4	1
Yes	61	83.6	1.06 (0.53, 2.12)	35	71.4	0.61 (0.29, 1.29)
Coronary heart disease						
No	1082	83.4	1	1217	79.8	1
Yes	88	76.1	0.63 (0.38, 1.07)	97	84.5	1.38 (0.78, 2.44)
Tooth type			$P = 0.01^{**}$			$P = 0.1^{**}$
Upper incisors/canine	199	75.9	1	137	72.3	1
Upper premolars	81	72.8	0.85 (0.47, 1.53)	131	73.3	1.05 (0.61, 1.80)
Upper molars	413	87.2	2.16 (1.40, 3.33)	464	82.5	1.81 (1.16, 2.83)
Lower incisors/canine	74	73.0	0.86 (0.47, 1.57)	61	75.4	1.18 (0.59, 2.35)
Lower premolars	39	82.1	1.45 (0.60, 3.50)	48	83.3	1.92 (0.82, 4.47)
Lower molars	364	86.0	1.95 (1.28, 3.03)	473	82.2	1.78 (1.14, 2.77)
Root type			$P = 0.05^{**}$			$P < 0.0001^{**}$
Single rooted teeth	363	76.0	1	339	74.0	1
Buccal of 2 rooted premolar	26	69.2	0.71 (0.30, 1.69)	27	70.4	0.83 (0.35, 1.97)
Palatal of upper premolar/molar	161	85.7	1.89 (1.14, 3.13)	179	86.0	2.16 (1.33, 3.52)
Mesio-buccal of upper molar	131	85.5	1.86 (1.08, 3.20)	151	76.2	1.12 (0.92, 1.75)
Disto-buccal of upper molar	131	89.3	2.63 (1.44, 4.82)	148	87.2	2.39 (1.39, 4.08)
Mesial of lower molar	179	86.0	1.94 (1.19, 3.16)	233	77.7	1.22 (0.82, 1.81)
Distal of lower molar	177	85.9	1.92 (1.18, 3.12)	230	85.7	2.09 (1.34, 3.25)
Disto-lingual of lower molar	2	100.0	Not analysed***	7	100.0	Not analysed***
Developmental anomalies						
No	1160	83.0	1	1313	80.2	Not analysed***
Yes	10	60.0	0.31 (0.09, 1.10)	1	0	

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.** P value of test for heterogeneity for categorical factors.

***The effect of the respective factor was not analysed because of the small number of positive cases.

Deviance statistic and Pearson chi-squared statistic, divided by residual degree of freedom, were both close to one, 0.83 and 0.99, respectively. This indicated that there was no evidence of over-dispersion in the final

model. The fit of the final model was also assessed using Hosmer–Lemeshow goodness-of-fit test (Hosmer & Lemeshow 1980), which did not detect lack of fit (Hosmer–Lemeshow χ^2 5.33 [8df], $P = 0.72$).

Table 5 Unadjusted effects of preoperative tooth factors (common to both 1° and 2°RCTx) using logistic regression analysis

Factors	1°RCTx			2°RCTx		
	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
<i>History of luxation injuries</i>						
No	1012	83.9	1	1249	80.5	1
Yes	158	75.9	0.61 (0.41, 0.91)	65	72.3	0.63 (0.36, 1.11)
<i>History of tooth fracture or crack</i>						
No	949	83.0	1	1119	80.6	1
Fracture	121	86.0	1.25 (0.93, 2.14)	96	78.1	0.86 (0.52, 1.43)
Cracks	100	77.0	0.68 (0.42, 1.12)	99	76.8	0.79 (0.49, 1.30)
<i>Restoration type</i>						
Virgin tooth	179	77.1	1	–	–	–
Plastic restoration	454	83.7	1.53 (0.99, 2.34)	663	81.7	2.24 (0.89, 5.67)
Plastic + post	–	–	–	10	70.0	1.16 (0.23, 5.95)
Cast restoration	280	81.4	1.30 (0.82, 2.07)	454	81.1	2.14 (0.84, 5.46)
Cast restoration + post	10	80.0	1.19 (0.24, 5.82)	63	71.4	1.25 (0.43, 3.61)
Temporary dressing	225	87.6	2.09 (1.23, 3.54)	103	74.8	1.48 (0.54, 4.07)
Open cavity	22	81.8	1.34 (0.43, 4.17)	21	66.7	1
<i>Pain</i>						
No	682	84.0	1	722	80.2	1
Yes	488	81.1	0.82 (0.60, 1.11)	592	80.1	0.99 (0.76, 1.30)
<i>Tenderness to percussion</i>						
No	697	81.3	1	686	80.8	1
Yes	473	85.0	1.30 (0.94, 1.78)	628	79.5	0.92 (0.70, 1.21)
<i>Soft-tissue tenderness</i>						
No	840	84.5	1	866	82.6	1
Yes	330	78.5	0.67 (0.48, 0.92)	448	75.4	0.65 (0.49, 0.86)
<i>Soft-tissue swelling</i>						
No	1047	83.7	1	1187	81.3	1
Yes	123	75.6	0.61 (0.39, 0.94)	127	69.3	0.52 (0.35, 0.78)
<i>Sinus</i>						
No	1029	85.0	1	1178	82.4	1
Yes	141	66.7	0.35 (0.24, 0.52)	136	60.3	0.32 (0.22, 0.47)
<i>Periodontal probing depth</i>						
<5 mm	1128	83.7	1	1276	80.2	1
≥5 mm but not to apex	36	66.7	0.39 (0.19, 0.79)	38	78.9	0.93 (0.42, 2.05)
Extended to apex	6	16.7	0.04 (0.01, 0.34)	–	–	–
<i>Pulpal status</i>						
Nonvital	912	80.6	1	–	–	–
Vital	258	90.7	2.35 (1.50, 3.69)	–	–	–
<i>Periapical status</i>						
Intact PDL	387	92.5	1	376	89.1	1
Widened PDL	169	87.0	0.54 (0.30, 0.97)	175	89.7	1.07 (0.59, 1.92)
Periapical lesion	614	75.6	0.25 (0.16, 0.38)	763	73.5	0.34 (0.24, 0.49)
<i>Size of periapical lesion</i>						
Continuous (each mm)	783	–	0.83 (0.80, 0.88)	938	–	0.75 (0.71, 0.80)
<5	605	85.7	1	803	83.2	1
≥5	178	66.9	0.34 (0.24, 0.48)	135	53.3	0.23 (0.16, 0.33)
<i>Root resorption</i>						
No	1072	83.6	1	1238	80.9	1
Internal	20	90.0	1.77 (0.41, 7.68)	9	88.9	1.89 (0.24, 15.22)
External (apical)	57	70.2	0.46 (0.26, 0.83)	64	65.6	0.45 (0.26, 0.77)
External (lateral)	10	80.0	0.79 (0.17, 3.73)	3	66.7	0.47 (0.04, 5.24)
Internal and external apical	2	100.0	Not analysed***	0	0	–
Cervical	9	55.6	0.25 (0.07, 0.92)	0	0	–
<i>Root perforation</i>						
None	1156	82.7	1	1288	80.4	1

Table 5 (Continued)

Factors	1°RCTx			2°RCTx		
	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
Apical	–	–	–	2	100.0	Not analysed***
Subcrestal	2	100.0	Not analysed***	10	40.0	0.16 (0.05, 0.58)
Supra-osseous	12	91.7	2.30 (0.29, 17.53)	14	78.6	0.89 (0.25, 3.22)

PDL, periodontal ligament space; 1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

***P* value of test for heterogeneity for categorical factors.

***The effect of the respective factor was not analysed because of the small number of positive cases.

Table 6 Unadjusted effects of preoperative tooth factors, unique to secondary root canal treatment, using logistic regression analysis

Factors	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
<i>Satisfactory root filling</i>			
No	1048	81.3	1
Yes	266	75.6	0.71 (0.52, 0.98)
<i>Canal content</i>			
Un-instrumented	59	84.7	1
Empty but instrumented	14	71.4	0.45 (0.12, 1.75)
Foreign material	1241	80.0	0.72 (0.35, 1.49)
<i>Type of foreign material</i>			
Ca(OH) ₂	8	37.5	0.14 (0.03, 0.60)
Gutta-percha	1026	80.9	1
Cement	39	84.6	1.30 (0.54, 3.14)
Thermafil®	10	60.0	0.35 (0.10, 1.27)
Silver point	64	87.5	1.65 (0.78, 3.52)
Fractured instrument	94	69.1	0.53 (0.33, 0.84)
<i>Type of fractured instrument</i>			
None	1220	81.0	1
K-file	49	67.3	0.48 (0.26, 0.89)
H-file	28	71.4	0.59 (0.26, 1.35)
NiTi	3	100.0	Not analysed
Spiral filler	11	54.5	0.28 (0.09, 0.93)
Gates Glidden drill	3	100.0	Not analysed***
<i>Fate of foreign material</i>			
Remained the same	56	51.8	1
Bypassed	25	84.0	4.89 (1.49, 16.08)
Removed	1146	81.8	4.17 (2.42, 7.20)
Extruded apically	14	42.9	0.70 (0.21, 2.28)

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

***P* value of test for heterogeneity for categorical factors.

***The effect of the respective factor was not analysed because of the small number of positive cases.

Consequently, the final logistic regression model was considered appropriate.

Discussion

The goal of this observational prospective clinical study was to identify the prognostic factors for nonsurgical

root canal treatment. By definition, the disadvantage of an observational design is that the preoperative factors and some of the intraoperative factors under investigation in the present study cannot be controlled but they can be accounted for through the analytical method used. The design of this study was informed by the previous meta-analyses (Ng *et al.* 2007, 2008a,b).

The meta-analyses had indicated that using strict criteria for judging treatment success (Ng *et al.* 2007), a minimum follow-up period of 3 years rather than 2 years should be adopted. However, in this prospective study, the majority of periapical lesions healed completely within 2 years; only 3–5% required three or more years for complete 'conventional radiographic healing'. This rate of healing was slightly faster than a previous report in which 87% of all lesions reduced to 2 mm or less within 2 years (Byström *et al.* 1987). The difference could be attributed to the smaller sample size (67 lesions) and a larger proportion of extruded root fillings (38%) in their study. The 2-year follow-up period was accepted because of the anticipated higher drop-out over longer recall periods given the population mobility in London, cost of travel and resistance to accrue work absence. The outcomes justified the strategy, which was also adopted by another London group (Chong *et al.* 2003) investigating endodontic surgery outcome.

The problems of conducting clinical trials in mobile populations are well documented, and many strategies have been adopted for improving recall rates, including prior agreement, financial or other inducements, personal contracts, and travel or health subscription (Sprague *et al.* 2003, Wang *et al.* 2004). Telephone calls to remind and explain the purpose of the recall appointment were effective in encouraging attendance, but extremely time-consuming. The approach was therefore rationalized by limiting telephone calls to those failing to attend at the first request. This strategy proved successful with recall rates (76% for 1°RCTx;

Table 7 Unadjusted effects of operator's qualification and prediction of prognosis and treatment visits using logistic regression analysis

Factors	1°RCTx			2°RCTx		
	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
<i>Operator's experience</i>			<i>P</i> = 0.7**	<i>P</i> = 0.4**		
1st year students	747	83.1	1	796	78.8	1
2nd year students	314	81.2	0.88 (0.62, 1.23)	407	81.3	1.17 (0.87, 1.59)
Staff member	109	85.3	1.18 (0.67, 2.07)	111	85.6	1.60 (0.92, 2.79)
<i>Estimated endodontic prognosis by operator</i>						
Poor	24	66.7	Not analysed***	28	71.4	Not analysed***
Fair	173	85.5		363	83.7	
Good	421	86.5		310	83.2	
<i>Number of treatment visits</i>						
1	14	100.0	Not analysed***	3	66.7	Not analysed***
2	434	83.2		425	81.6	
3	427	82.7		453	81.5	
4	167	85.0		289	78.2	
5	92	82.6		85	67.1	
6	22	68.2		39	92.3	
7	11	72.7		8	75.0	
8	0	–		12	83.3	
9	3	0.0		–	–	

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

***P* value of test for heterogeneity for categorical factor.

***The effect of the respective factor was not analysed because of missing data or presence of hidden confounders.

67% for 2°RCTx) much higher than the 53% median recall rates of previous studies for 1°RCTx but slightly lower than the 74% for 2°RCTx (Ng *et al.* 2008a,b). A comparatively lower 2-year recall rate (47%) was achieved in a randomized controlled trial based in London (Chong *et al.* 2003). More teeth with larger periapical lesions were included in the analyses than those excluded. This was as expected, as patients without tangible problems after treatment were more likely to drop out. The implication is that the reported success rate in this study may be slightly underestimated, as periapical lesions and their size reduce healing significantly. The final sample sizes of 1170 roots (702 teeth) for 1°RCTx and 1314 roots (750 teeth) for 2°RCTx were larger than most of the previous studies (Ng *et al.* 2007) using periapical healing as an outcome measure.

Root was used as a unit of measure in this part of the study, although this practice has been considered inappropriate and has a tendency to over-estimate success rates (Friedman 2002). However, one previous (Hoskinson *et al.* 2002) and the present study have not supported this contention. Hoskinson *et al.* (2002) included 80% of molar teeth in their sample population and revealed that the proportion of *teeth* with successful

treatment (77%) was similar to the proportion of *roots* with successful treatment (75%). The present study included 50% of molar teeth and the proportions of successful treatments based on tooth (77%) or root (81%) as a unit of measure were also similar. It was therefore decided to use root as a unit of measure. An additional justification was that the use of tooth would render investigation of some of the root-level independent variables (presence and size of the periapical lesion, presence of sinus tract, patency of the apical terminus, apical extent of instrumentation and root filling) problematic.

Consistent with previous systematic reviews (Ng *et al.* 2008a,b), the patients' gender and age had no significant influence on periapical healing following 1° or 2°RCTx. Previous evidence on the effect of general health on root canal treatment outcome is weak with contradictory findings (Storms 1969, Fouad & Burleson 2003, Marending *et al.* 2005, Quesnell *et al.* 2005, Shetty *et al.* 2006, Suchina *et al.* 2006, Doyle *et al.* 2007). Investigation of the influence of general health in the present study was compromised by the small proportion of patients (<10%) suffering from systemic diseases. Of the many medical conditions reported by study patients, only the more prevalent were selected

Table 8 Unadjusted effects of intraoperative factors (chemo-mechanical preparation) using logistic regression analysis

Factors	1°RCTx			2°RCTx		
	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
<i>Protect the tooth with a band</i>						
No	839	80.9	1	988	79.3	1
Yes	331	87.6	1.67 (1.15, 2.41)	326	82.8	1.26 (0.91, 1.75)
<i>Use of magnification</i>						
No	917	82.1	1	747	79.8	1
Yes	253	85.4	1.27 (0.86, 1.87)	567	80.6	1.05 (0.80, 1.38)
<i>Second canal found</i>						
No	878	82.3	1	902	81.5	1
Yes	292	84.2	1.15 (0.80, 1.64)	412	77.2	0.77 (0.58, 1.02)
<i>Instrument type</i>			<i>P</i> = 0.4**			<i>P</i> = 0.1**
Stainless steel file	1004	82.0	1	1144	78.9	1
Hand NiTi	52	88.5	1.68 (0.71, 4.01)	47	89.4	2.24 (0.88, 5.73)
Rotary NiTi	114	87.7	1.57 (0.88, 2.81)	123	87.8	1.92 (1.10, 3.36)
<i>Patent at apical terminus</i>						
No	76	76.3	1	184	69.6	1
Yes	1094	83.3	1.54 (0.89, 2.68)	1130	81.9	1.97 (1.39, 2.80)
<i>Apical extent of instrumentation</i>						
Each mm short of EAL '0' position (continuous variable)	–	–	0.91 (0.82, 1.02)	–	–	0.82 (0.76, 0.91)
<i>Binary variable (mm)</i>						
≤2	1141	83.2	2.23 (1.00, 4.96)	1216	81.5	2.56 (1.65, 3.95)
>2	29	69.0	1	98	63.3	1
≤1	1099	83.1	1.32 (0.70, 2.44)	1154	81.5	1.89 (1.25, 2.86)
>1	71	78.9	1	160	70.0	1
<i>Initial apical size of canal</i>						
(continuous: 0–300)	–	–	0.987 (0.980, 0.995)	–	–	1.00 (0.99, 1.01)
≤30	1069	84.0	1	1144	80.8	1
>30	101	70.3	0.45 (0.29, 0.71)	170	75.9	0.75 (0.51, 1.10)
<i>Apical size of preparation</i>						
(continuous: 20–300)	–	–	0.98 (0.98, 0.99)	–	–	1.00 (0.99, 1.01)
≤30	812	85.7	1	791	81.4	1
>30	358	76.3	0.54 (0.39, 0.73)	523	78.2	0.82 (0.62, 1.08)
<i>Taper of preparation</i>			<i>P</i> = 0.006**			<i>P</i> = 0.2**
0.02	8	37.5	0.12 (0.03, 0.51)	31	71.0	0.70 (0.31, 1.55)
0.04	14	71.4	0.50 (0.15, 1.62)	0	–	–
0.05	524	83.4	1	537	77.8	1
0.06	125	86.4	1.26 (0.72, 2.22)	132	89.4	2.40 (1.33, 4.33)
0.08	18	94.4	3.38 (0.44, 25.77)	23	78.3	1.02 (0.37, 2.82)
0.10	481	81.9	0.90 (0.65, 1.25)	591	80.7	1.19 (0.89, 1.59)
<i>Perforation</i>						
No	1134	82.8	1	1302	80.4	1
Yes	36	83.3	1.04 (0.43, 2.53)	12	50.0	0.24 (0.02, 0.76)
<i>Blockage of canal</i>						
No	1100	83.2	1	1298	80.4	1
Yes	70	77.1	0.68 (0.38, 1.22)	16	56.3	0.31 (0.12, 0.85)
<i>Fracture of instrument</i>						
No	1155	82.9	1	1302	80.4	1
Yes	15	80.0	0.83 (0.23, 2.96)	12	50.0	0.24 (0.08, 0.76)
<i>Perforation repair material</i>						
EBA/IRM [®]	2	100.0	Not analysed	4	50.0	Not analysed
Glass-ionomer cement	23	82.6		19	63.2	
MTA [™]	7	85.7		7	57.1	
Gutta-percha	10	90.0		7	71.4	
Amalgam	1	100.0		1	0.0	

Table 8 (Continued)

Factors	1°RCTx			2°RCTx		
	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
<i>NaOCl concentration (%)</i>						
2.5	1082	82.8	1	1214	80.3	1
4–5	88	83.0	1.01 (0.57, 1.80)	100	78.0	0.87 (0.53, 1.42)
<i>Additional use of iodine</i>						
No	1088	83.2	1	1018	80.5	1
Yes	82	78.0	0.72 (0.42, 1.24)	296	79.1	0.92 (0.67, 0.13)
<i>Additional use of CHX</i>						
No	1129	83.4	1	1172	80.8	1
Yes	41	65.9	0.38 (0.20, 0.74)	142	74.6	0.70 (0.47, 1.05)
<i>Additional use of EDTA</i>						
No	887	82.3	1	942	77.5	1
Yes	283	84.5	1.17 (0.81, 1.68)	372	86.8	1.91 (1.37, 2.68)
<i>Interappointment pain</i>						
No	1018	83.7	1	1073	80.7	1
Yes	138	75.4	0.60 (0.39, 0.91)	238	77.7	0.84 (0.59, 1.18)
<i>Interappointment swelling</i>						
No	1122	83.3	1	1272	80.4	1
Yes	34	61.8	0.33 (0.16, 0.66)	39	71.8	0.62 (0.30, 1.26)
<i>Use of systemic antibiotics</i>						
No	1131	83.0	1	1302	80.1	1
Yes	25	68.0	0.43 (0.18, 1.02)	9	88.9	1.99 (0.25, 15.98)

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment; MTA, mineral trioxide aggregate; EAL, electronic apex locator; CHX, 0.2% chlorhexidine gluconate; EDTA, 17% ethylene-diamine-tetra-acetic acid.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

***P* value of test for heterogeneity for categorical factors.

for statistical analyses. The present patient cohort is unlikely to be a true representation of the medical problems in a UK population, e.g. the prevalence of diabetes in England was 4% (Forouhi *et al.* 2006), but only 2% of the studied patients reported this condition. The discrepancy may be explained by the fact that patients with severe medical problems are referred to Special Needs Clinics in Community Dental Centres and regional hospitals.

Preoperative conditions of the teeth (pulpal and periapical status, size of periapical lesion, history of trauma, presence of resorption, fracture, cracks, swelling and sinus) may all potentially have an impact on treatment outcome. Given the limitations in the sensitivity and specificity of available diagnostic methods (Dummer *et al.* 1980, Hyman & Cohen 1984), in the present study, the pulpal status was tentatively determined using thermal and electric pulp tests and visually confirmed after accessing the root canal during treatment. In agreement with the findings of a previous systematic review (Ng *et al.* 2008a), the periapical status was found to have a more dominant effect than the pulpal condition on periapical healing; the odds ratio for absence/presence of periapical lesion was 1.96

(95% CI 1.25, 3.13), similar to the estimate (OR = 1.95 [95% CI 1.35, 2.81]) in the previous meta-analysis. The issue of sensitivity of conventional radiographs for detecting periapical lesions and healing progress in endodontic outcome studies has been raised previously and re-emphasized recently in the context of new technology (Wu *et al.* 2009). Four per cent of the cases in the present study presented with no detectable periapical radiolucent lesion but were associated with pain, sinus or swelling at follow-up. Without the facility of cone beam volumetric tomography, those cases with persistent pain but absence of periapical lesion on conventional radiographs were further investigated using cross-sectional tomography (ScanOra[®]; Orion Co). The diagnostic value of this instrument was reduced by the relative imprecision of the focal trough to localize the relevant root apex. The quality of image is also reduced when taking images at an oblique angle to the site of interest (Peltola & Mattila 2004). The use of cone beam volumetric tomography in these cases may potentially have higher diagnostic yield (de Paula-Silva *et al.* 2009a,b).

The effect of size of periapical lesion was analysed as a continuous variable and was found to have a

Table 9 Unadjusted effects of intraoperative factors related to root filling, and postoperative restorative factors using logistic regression analysis

Factors	1°RCTx			2°RCTx		
	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a	No. of roots	Success rates (%)	Odds ratio (95% CI) ^a
<i>Root filling technique</i>			<i>P</i> = 0.8**			<i>P</i> = 0.06**
LC – cold spreader (sp)	272	84.2	1	295	81.0	1
LC – warm spreader	327	81.0	0.80 (0.52, 1.23)	404	80.7	0.98 (0.67, 1.43)
LC – U/S energized sp	347	83.6	0.96 (0.62, 1.47)	365	78.4	0.85 (0.58, 1.24)
Warm vertical compaction	160	83.8	0.97 (0.57, 1.65)	189	81.5	1.03 (0.65, 1.65)
Continuous wave	44	79.5	0.73 (0.33, 1.63)	42	88.1	1.73 (0.65, 4.62)
Obtura	14	71.4	0.47 (0.14, 1.57)	15	53.3	0.27 (0.09, 0.77)
MTA	2	100.0	Not analysed	4	75.0	0.70 (0.07, 6.88)
Tagger hybrid	4	100.0	Not analysed	0	–	–
<i>Apical extent of root filling^b</i>			<i>P</i> < 0.0001**			<i>P</i> < 0.0001**
Flush	954	85.8	1	1035	84.6	1
Short	70	74.3	0.48 (0.27, 0.84)	162	64.8	0.33 (0.23, 0.48)
Long	146	67.1	0.34 (0.23, 0.50)	117	61.5	0.29 (0.19, 0.44)
<i>Void within apical 5 mm of root filling</i>						
No	1155	82.8	1	1307	80.3	1
Yes	15	86.7	1.35 (0.30, 6.04)	7	42.9	0.18 (0.04, 0.83)
<i>Extrusion of sealer</i>						
No	865	84.2	1	942	81.1	1
Yes	305	79.0	0.71 (0.51, 0.99)	372	77.7	0.81 (0.60, 1.09)
<i>Core restorative material</i>			<i>P</i> = 0.03**			<i>P</i> = 0.4**
Amalgam	769	84.9	1	874	81.5	1
Composite	221	75.1	0.54 (0.37, 0.77)	145	77.9	0.80 (0.52, 1.23)
Glass-ionomer cement	83	88.0	1.30 (0.65, 2.58)	118	74.6	0.67 (0.43, 1.04)
IRM [®]	20	65.0	0.64 (0.33, 1.24)	27	70.4	0.73 (0.44, 1.22)
Post and amalgam	22	95.5	0.33 (0.13, 0.84)	57	87.7	0.54 (0.23, 1.26)
Cast post and core	55	78.2	3.73 (0.50, 28.0)	93	76.3	1.63 (0.72, 3.65)
<i>Core lining used</i>			<i>P</i> = 0.02**			<i>P</i> = 0.9**
None	630	84.3	1	732	80.6	1
GIC	81	69.1	0.42 (0.25, 0.70)	71	81.7	1.07 (0.57, 2.01)
IRM	459	83.2	0.92 (0.67, 1.28)	511	79.3	0.92 (0.69, 1.22)
<i>Type of restoration</i>			<i>P</i> = 0.07**			<i>P</i> = 0.03**
GIC/composite	265	75.8	1	165	73.3	1
Amalgam	207	83.6	1.62 (1.02, 2.57)	207	81.2	1.57 (0.96, 2.56)
Cast restoration	690	85.4	1.86 (1.31, 2.64)	923	81.6	1.61 (1.10, 2.36)
Temporary filling	8	75.0	0.96 (0.19, 4.85)	19	57.9	0.50 (0.19, 1.32)
<i>Quality of restoration</i>			<i>P</i> = 0.02**			<i>P</i> = 0.02**
Exposed root filling	15	40	1	8	37.5	1
Marginal defect	38	81.6	6.64 (1.78, 24.8)	69	69.6	3.81 (0.83, 17.43)
Satisfactory	1117	83.4	7.56 (2.66, 21.5)	1237	81.0	7.09 (1.68, 29.89)

LC, lateral compaction technique; sp, spreading; U/S, ultrasonic; 1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment; MTA, mineral trioxide aggregate.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

^bFlush = 0–2 mm from apex locator '0' reading position; Short = >2 mm short of '0' reading position; Long = extruded beyond the '0' reading position.

***P* value of test for heterogeneity for categorical factor.

significant influence (OR = 0.86; 95% CI: 0.81, 0.91) on the success of both 1° and 2°RCTx, even after adjusting the results by presence of periapical lesion and duration after treatment. This was in agreement with two previous studies (Chugal *et al.* 2001, Hoskinson *et al.* 2002), which also analysed this factor as a

continuous variable but contradicted other studies (Strindberg 1956, Byström *et al.* 1987, Sjögren *et al.* 1990, 1997) which found no significant difference in success rates between teeth with small (<5 mm) or large (≥5 mm) lesions. The discrepancy highlights the problems in dichotomization of a continuous variable

Table 10 Factors found to have prognostic value after adjusting for preoperative periapical status and size of lesion

1°RCTx	2°RCTx
Preoperative pulpal status	Preoperative sinus
Preoperative periodontal probing depth	Preoperative swelling
Preoperative sinus	Fate of preoperative foreign material
Apical extent of instrumentation	Preoperative perforation
Apical size of canal preparation (≤30, >30)	Patency at apical foramen
Additional use of CHX for irrigation	Apical extent of instrumentation
Interappointment pain	Intraoperative canal perforation
Interappointment swelling	Intraoperative canal blockage
Apical extent of root filling	Additional use of EDTA for irrigation
Quality of restoration	Apical extent of root filling
	Quality of restoration

All the factors were significant at the 5% level.

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment; EDTA, ethylene-diamine-tetra-acetic acid.

Table 11 Multiple logistic regression model incorporating preoperative periapical status, size of preoperative lesion and type of treatment together with other potential preoperative factors as predictors

Model 1			
Factors	OR	95% CI for OR ^a	P value
<i>Type of treatment</i>			
1°RCTx	1		
2°RCTx	0.78	0.60, 1.01	0.06
<i>Periapical status</i>			
Intact periodontal ligament	1		
Widened periodontal ligament	0.79	0.57, 1.07	0.1
Periapical lesion	0.50	0.37, 0.67	<0.001
<i>Size of periapical lesion</i>			
Continuous variable	0.88	0.84, 0.92	<0.001
<i>Preoperative sinus</i>			
No	1		
Yes	0.51	0.34, 0.76	0.001
<i>Preoperative periodontal probing depth >5 mm</i>			
No	1		
Yes	0.85	0.64, 1.14	0.3
<i>Preoperative swelling</i>			
No	1		
Yes	0.95	0.63, 1.45	0.8
<i>Preoperative perforation</i>			
No	1		
Yes	0.44	0.21, 0.95	0.04

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

Table 12 Multiple logistic regression model incorporating preoperative periapical status, size of preoperative lesion and type of treatment, the other two significant preoperative factors together with all the seven potential intraoperative factors as predictors

Model 2			
Factors	OR	95% CI for OR ^a	P value
<i>Periapical status</i>			
Intact periodontal ligament	1		
Widened periodontal ligament	0.74	0.54, 1.03	0.07
Periapical lesion	0.46	0.34, 0.63	<0.001
<i>Size of periapical lesion</i>			
Continuous variable	0.88	0.84, 0.92	<0.001
<i>Type of treatment</i>			
1°RCTx	1		
2°RCTx	0.83	0.64, 1.09	0.2
<i>Preoperative sinus</i>			
No	1		
Yes	0.51	0.35, 0.73	<0.001
<i>Preoperative perforation</i>			
No	1		
Yes	0.48	0.21, 1.08	0.08
<i>Patency at canal terminus</i>			
No	1		
Yes	1.79	1.18, 2.72	0.006
<i>Apical extent of instrumentation</i>			
Continuous variable	0.89	0.81, 0.98	0.02
<i>Long root filling</i>			
No	1		
Yes	0.47	0.35, 0.61	<0.001
<i>Intraoperative perforation</i>			
No	1		
Yes	0.67	0.44, 1.03	0.07
<i>Additional use of CHX as irrigant</i>			
No	1		
Yes	0.57	0.35, 0.93	0.03
<i>Additional use of EDTA as irrigant</i>			
No	1		
Yes	1.56	1.12, 2.17	0.009
<i>Interappointment pain or swelling</i>			
No	1		
Yes	0.55	0.38, 0.77	0.001

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment; EDTA, ethylene-diamine-tetra-acetic acid.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

(Royston *et al.* 2006). The lack of influence by duration after treatment (OR = 1.01; 95% CI: 1.00, 1.02) was unexpected but evidently irrefutable, as 91–95% of periapical lesions healed completely within 2 years following treatment. The negative influence of larger lesions has a ready biological explanation, because the diversity of bacteria is greater in teeth associated with larger periapical lesions (Sundqvist 1976) and the infection is more likely to persist following treatment

Table 13 Final multiple logistic regression model incorporating preoperative periapical status, size of preoperative lesion, type of treatment, the other two significant preoperative factors, six significant intraoperative factors together with the quality of restoration as predictors

Model 3			
Factors	OR	95% CI for OR ^a	P value
<i>Type of treatment</i>			
1°RCTx	1		
2°RCTx	0.78	0.55, 1.10	0.2
<i>Periapical status</i>			
Intact periodontal ligament	1		
Widened periodontal ligament	0.86	0.52, 1.42	0.5
Periapical lesion	0.51	0.32, 0.80	0.003
<i>Size of periapical lesion</i>			
Continuous variable	0.86	0.81, 0.91	<0.001
<i>Preoperative sinus</i>			
No	1		
Yes	0.53	0.36, 0.77	0.001
<i>Pre- or intraoperative perforation</i>			
No	1		
Yes	0.46	0.21, 1.02	0.06
<i>Patency at canal terminus</i>			
No	1		
Yes	2.22	1.38, 3.59	0.001
<i>Apical extent of instrumentation</i>			
Continuous variable	0.87	0.79, 0.97	0.01
<i>Long root filling</i>			
No	1		
Yes	0.38	0.27, 0.54	<0.001
<i>Additional use of CHX as irrigant</i>			
No	1		
Yes	0.47	0.26, 0.83	0.01
<i>Type of treatment^a EDTA</i>			
No	1		
Yes	1.81	0.90, 3.64	0.09
<i>Additional use of EDTA as irrigant</i>			
1°RCTx			
No	1		
Yes	1.26	0.76, 2.09	0.4
2°RCTx			
No	1		
Yes	2.28	1.37, 3.81	0.002
<i>Interappointment pain or swelling</i>			
No	1		
Yes	0.53	0.36, 0.79	0.002
<i>Quality of restoration</i>			
Exposed root filling	1		
Marginal defect	7.69	2.28, 25.95	0.001
Satisfactory	10.73	3.65, 31.54	<0.001

1°RCTx, primary root canal treatment; 2°RCTx, secondary root canal treatment; EDTA, ethylene-diamine-tetra-acetic acid.

^aConfidence interval for odds ratio estimated using robust standard error to allow for clustering within patients.

(Byström & Sundqvist 1981). This may be because larger lesions are associated with longer-standing infections that have penetrated deeper into dentinal

tubules and the peripheral aspects of the complex canal system (Shovelton 1964) where mechanical and chemical decontamination procedures fail to readily reach. Larger lesions may also reflect cystic transformation or extra-radicular infections, which render nonsurgical root canal treatment ineffective (Nair 2006). Finally, larger lesions may represent a more exaggerated host response that responds less readily to ecological shifts effected in the canal infection by the treatment protocols (Nair *et al.* 2005). These speculative hypotheses are likely to crystallize into distinct questions for further biological research into the nature of interaction between host, bacterial infection and treatment intervention.

Most of the other investigated preoperative factors (pain, tenderness to tooth percussion, tenderness to soft-tissue palpation, soft-tissue swelling, sinus tract, periodontal probing defect of endodontic origin and root resorption) were essentially different clinical manifestations of apical periodontitis. The manifestations could be regarded as surrogate measures of periapical disease representing different reactions between infection and host within a broad continuous spectrum. If so, the preoperative presenting condition may be an important predictor of treatment outcome; of those tested, only 'presence of sinus' was found to be a significant prognostic indicator, even after adjusting for presence and size of lesion and other prognostic factors. This finding contrasts with that of Chugal *et al.* (2001) who reported that 'presence of sinus' did not add any prognostic value to that provided by presence and size of lesion. The discrepancy may be attributed to the much smaller sample size (200 teeth and 441 roots) in their study. The negative impact of sinus tract on periapical healing is not readily explained by the diversity of the implicated intraradicular microbiota (*Porphyromonas endodontalis*, *Leptotrichia buccalis*, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*) (Sassone *et al.* 2008), which are putatively susceptible to contemporary root canal decontamination procedures. The sinus tract may, however, facilitate the influx of bacteria from the oral cavity to colonize the periapex and predispose to extra-radicular infection. Refractory cases presenting with persistent sinus tracts have been reported to be associated with extra-radicular actinomyces infection (Happonen 1986) or coccal- and fungal-form micro-organisms (Ferreira *et al.* 2004).

Preoperative factors unique to 2°RCTx (time interval between 1° and 2°RCTx, quality of pre-existing root filling, pre-existing canal content, root perforation and root canal obstruction) have been poorly investigated

in previous studies (Ng *et al.* 2008b). All of these factors except 'time interval between 1° and 2°RCTx' were investigated in the present study. The time interval could not be analysed because the precise time of completion of 1°RCTx by referring or other dentists was unknown. None of the investigated factors were found to have a direct influence on the success of 2°RCTx. The present study found that the success rates for roots with satisfactory pre-existing root fillings (absence of voids and extending to within 2 mm of the radiographic apex) were 6% lower than those with unsatisfactory pre-existing root fillings, but the difference was not significant after adjusting the results for the presence of periapical lesion. A similar but statistically significant trend was revealed in the Toronto study (Farzaneh *et al.* 2004, de Chevigny *et al.* 2008), where the success rate for teeth with satisfactory pre-existing root filling was significantly lower (19–22%). They advanced two explanations that may apply in the present study: (i) in teeth with adequate preoperative root filling, the persisting infection may have been less susceptible to routine 2°RCTx procedures; (ii) the persistent lesion may have been caused by extraradicular infection, a true cyst or foreign body reaction unresponsive to 1°RCTx. In contrast, canals with under-extended pre-existing root fillings in the present study were caused by natural or iatrogenic blockages that prevented negotiation to the apical terminus during 2°RCTx and therefore compromised outcome. It is interesting to note that there was no significant difference in the outcome for 1° and 2°RCTx in the present study, in contrast to the findings by Sjögren *et al.* (1990). The difference in findings may be attributable to the substantially large proportion of unsatisfactory existing root filling in the present 2°RCTx cases which responded similarly to the 1°RCTx cases to chemo-mechanical debridement.

The type and fate of preoperative foreign materials/separated instruments were all found to have a significant influence on 2°RCTx outcome in univariable regression analyses. Clinically, the type of foreign material/fractured instrument, fate of foreign material and ability to achieve patency at the canal terminus were in the same confounding pathway and significantly correlated with each other. Only 'patency at canal terminus' was analysed further because it had a more direct influence on treatment outcome from a clinical perspective. The results may infer that as long as patency could be achieved at the canal terminus, success of 2°RCTx would not be affected by type of foreign material whether it was removed or bypassed.

The aetiology of procedural errors is well described and may influence outcome through either canal obstruction (through poor irrigation or instrument separation) or perforation (through uncontrolled dentine removal), both of which were investigated in the present study. The presence of root perforation at the coronal or mid-root level was found to significantly reduce the odds of success by 70%, possibly attributable to bacterial contamination during or after treatment. This was consistent with the Toronto study (Farzaneh *et al.* 2004, de Chevigny *et al.* 2008). The suggestion that MTA™ as perforation repair material may improve the success in such cases (Main *et al.* 2004, de Chevigny *et al.* 2008) was not robustly confirmed as the present data did not favour any particular repair material.

Of the factors related to mechanical preparation of canals ('type of instrument', 'patency at canal terminus', 'apical size', 'taper and extent of canal instrumentation'), only 'patency at canal terminus' and 'apical extent of canal instrumentation', which are putatively measures of the apical extent of canal cleaning, were found to be significant prognostic factors for root canal treatment. These findings are in agreement with previous studies showing that teeth with apically inaccessible canals were associated with significantly lower success rates (Strindberg 1956, Engström 1964, Sjögren *et al.* 1990). The adjusted odds ratio for 'apical extent of canal preparation' revealed by the present prospective study (OR = 0.87) was almost identical to the odds ratio of 0.86 (*adjusted for periapical status and density of root filling*) reported by Chugal *et al.* (2003).

Investigation of the influence of instrument type for canal enlargement was confounded by the teaching philosophy adopted for inculcating endodontic technical skills at the Eastman. The higher success rates for hand or rotary NiTi instruments revealed in this study correlated with those postgraduates who had already acquired better technical skills to obtain and maintain apical patency as well as to avoid procedural errors, an observation also made by Pettiette *et al.* (2001). Their randomized controlled trial revealed treatments carried out by undergraduate students using NiTi K-type files for canal preparation were associated with less procedural errors and a significantly higher chance of success compared to those using stainless steel K-type files. The adopted philosophy at the Eastman is that learning root canal treatment skills is critically dependent on development of tactile skills. More than 20 years of collective experience shows that this is

best achieved through the use of stainless steel instruments. The training protocol requires the students to complete technical skills training on extracted teeth until proficiency is demonstrated in serial and in parallel with the development of clinical skills (clinical training is staggered behind laboratory skills training) through completion of 20–30 cases with such instruments to show consistency in controlled canal shaping. Once postgraduates show proficiency with stainless steel instruments, they graduate to using first, hand manipulation, and then rotary NiTi instruments, a range of which are used including rotary GT system, ProFile system, ProTaper system and the K3 system. More importantly, such senior students are also likely to have acquired a better understanding of the biological aspects of root canal treatment by this stage.

Investigation of the influence of apical size of preparation was again confounded by the departmental protocol that all canals should be prepared to a minimum size 30, except for cases with very acute or double canal curvatures. The apical size of preparation was also confounded by the initial apical size of the canal because the protocol dictated that no further canal enlargement was necessary in those canals which were initially apical size 30 or larger. Investigation of the influence of canal preparation taper was confounded by the initial size of canal and type and taper of instrument used. Meaningful comparison could therefore only be made between 0.05 and 0.10 tapers created by stainless steel instruments, where an insignificant difference in success rates was found regardless of 1°RCTx (OR = 0.9 [0.7, 1.3]) or 2°RCTx (OR = 1.2 [0.9, 1.6]). Collating these results, it is suggested that over-enlarging the canal is not necessary; a preparation size of 30 with a 0.05 taper for stainless steel instrumentation or 0.06 taper for NiTi instrumentation is more than adequate and may even be optimal. Precisely what, 'adequate' means in this context is more difficult to define. Although a number of laboratory studies (Allison *et al.* 1979, Lee *et al.* 2004, Huang *et al.* 2008) have investigated the interaction between canal dimensions and irrigation dynamics or obturation dynamics, the precise physical, chemical or biological mechanism that ultimately facilitates periapical healing remains unknown. There is a need to initiate a cycle of laboratory experiments and clinical trials to identify the optimum balance between canal preparation dimension and irrigation protocol in order to conserve root dentine for tooth survival whilst achieving effective biofilm control to facilitate periapical healing.

Currently available clinical outcome evidence to guide selection of canal irrigant and dressing material is weak (Ng *et al.* 2008a,b). Although the present study was not a randomized controlled trial, it did reveal previously unreported findings on irrigants. The use of a higher concentration of sodium hypochlorite (4–5%) made no significant improvement to treatment outcome. This finding is consistent with other studies (Cvek *et al.* 1976, Byström & Sundqvist 1983) that had compared 0.5% or 5.0% NaOCl solutions for irrigation; the NaOCl concentration was not found to influence the proportion of teeth 'rendered culture-negative' (Byström & Sundqvist 1983) or the proportion that healed periapically (Cvek *et al.* 1976).

The additional use of other irrigation agents was found to have a significant impact. As iodine and sodium hypochlorite are both halogen-releasing agents attacking similar key protein groups (McDonnell & Russell 1999), the finding that the additional use of 10% povidone-iodine for irrigation had no accumulative influence on treatment success was not unexpected. Surprisingly, the additional use of 0.2% chlorhexidine solution for irrigation reduced the success of treatment, significantly. This finding did not support previous reports (Siqueira *et al.* 2007, Wang *et al.* 2007) on its equivalent or superior *in vivo* antibacterial efficacy when compared with sodium hypochlorite. The negative impact of using alternate irrigation with sodium hypochlorite and chlorhexidine solution on root canal treatment outcome may be attributed to their interaction product. It is an insoluble precipitate containing para-chloro-aniline, which is cytotoxic and carcinogenic (Basrani *et al.* 2007, Bui *et al.* 2008). The interaction may mutually deplete the active moieties for bacterial inactivation, whilst the precipitate may cause persistent irritation to the periapical tissue, as well as block dentinal tubules and accessory anatomy. This study did not investigate the sole use of chlorhexidine as an irrigant and cannot conclude on its independent effect on treatment outcome. Given the nonrandomized nature of this study, one may argue that the results may be confounded by the fact that chlorhexidine was only used in cases with persistent weeping canals, soft-tissue swelling, pain or sinus tract following chemo-mechanical debridement using NaOCl as an irrigant and Ca(OH)₂ as an interappointment medicament. The potential correlations between the supplementary use of chlorhexidine and these clinical conditions had been explored, and no significant correlation was found. In addition, the prognostic value of this factor remained

significant at the 5% level even after accounting for these clinical conditions (presence of preoperative sinus, presence and size of periapical lesion, and presence of interappointment flare-up). The present findings should therefore be considered as sufficiently robust, although the effect of the supplementary use of chlorhexidine should be further investigated in a randomized controlled trial.

The findings on the additional use of 17% EDTA solution for irrigation are also previously unreported. Its use had a marginal effect on the success of primary treatment (OR = 1.3 [0.8, 2.1]) but had a profound effect on secondary treatment (OR = 2.3 [1.4, 3.8]). The synergistic effect of sodium hypochlorite and EDTA has been demonstrated previously in a clinical microbiological study (Byström & Sundqvist 1985). The long-term (≥ 2 years) outcome of their cases stratified by various canal disinfection protocols [available from Byström's PhD thesis (1986)] was not consistent with their microbiological findings. The percentage of teeth with periapical healing for alternate irrigation with sodium hypochlorite and EDTA solutions was low (67%) when compared with that for irrigation using saline (91%), 0.5% sodium hypochlorite (92%) or 5% sodium hypochlorite (86%) (Byström 1986). Their outcome data were unexpected as preobturation negative bacterial culture was achieved in all cases. However, given the comprehensive microbiological investigations involved, each group consisted of only 11–15 teeth; these clinical outcomes should therefore be interpreted with caution. The synergistic effect of the two agents is attributed to their combined effects on inorganic and organic components within the root canal system. The actions of EDTA include its chelating properties, which assist in negotiation of narrow or sclerosed canals by demineralization of root dentine and help remove compacted fibrous tissue from uninstrumented canal anatomy. It may also facilitate deeper penetration of sodium hypochlorite solution into dentine by removing the smear layer from the instrumented surface and opening up dentinal tubules, and lastly it may help detach or breakup adherent biofilms (Gulabivala *et al.* 2005). In 2°RCTx cases, the previously treated canals may contain contaminated debris, smear layer, un-negotiable calcifications or iatrogenic blockages, and lastly bacterially contaminated filling material. The additional use of EDTA irrigation may help by aiding removal of such contaminated materials and opening up accessory anatomy and blocked canal exits. In contrast, the smear layer and debris generated from instrumentation of previously untreated canals

during 1°RCTx should be more accessible to and relatively easily decontaminated by sodium hypochlorite solution alone. This may possibly explain why the success of 1°RCTx was not significantly improved by additional EDTA irrigation, whilst that of 2°RCTx was.

After chemo-mechanical debridement of the root canal system, pain or swelling occurred in 18% of cases and was found to significantly reduce the success of treatment in the present study. The rate of occurrence was within the lower end of the range (2–88%) reported previously (Glennon *et al.* 2004). The present finding was in contrast to previous reports (Kerekes & Tronstad 1979, Byström *et al.* 1987, Sjögren *et al.* 1990) where acute 'flare-ups' during treatment were found to have no influence on treatment outcome. Considering the relatively low occurrence of interappointment pain or swelling, the three previous studies may lack statistical power as their sample sizes (79–635 teeth) were much smaller than the present study. Explanations for the present findings may only be speculative but include the hypothesis that 'flare-ups' were caused by extrusion of contaminated material during canal preparation. Such material may then elicit a foreign body reaction or (transient) extra-radicular infection, resulting in treatment failure in a proportion of such cases. Alternatively, acute symptoms may be a result of incomplete chemo-mechanical debridement at the first appointment leading to a shift in canal microbial ecology favouring the growth of more virulent micro-organisms or triggering expression of virulence genes and leading to postpreparation pain and treatment failure. The exact biological mechanisms of failure in these cases warrant further investigation.

The use of the radiographic root apex as the reference point for setting the apical extent of root filling in previous studies (Ng *et al.* 2008a) is open to criticism because of its imprecise estimation of the canal terminus (Mizutani *et al.* 1992). The present study used instead, the location of canal terminus (EAL 'O' reading) by EALs and verified by other guides (radiographic, tactile, paper-point, sensitivity). Consistent with previous findings (Ng *et al.* 2008a,b), the present study found that roots with 'flush' (0–2 mm from apex locator 'O' reading position) root fillings was associated with the highest success rate, which was followed by short and then long root fillings. The apical extent of instrumentation and root fillings were found to correlate with each other, which is consistent with the clinical practice of filling the canal to the terminus of the canal preparation. A single measure 'apical extent of root filling' could therefore inform both about the

apical extent of canal cleaning, as well as extrusion of foreign materials into the surrounding tissues. Extrusion of cleaning, medication or filling materials beyond the apical terminus into the surrounding tissues may result in delayed healing or even treatment failure because of a foreign body reaction (Yusuf 1982, Nair *et al.* 1990, Koppang *et al.* 1992, Sjögren *et al.* 1995). Magnesium and silicon from the talc-contaminated extruded gutta-percha have been clinically associated with a foreign body reaction (Nair *et al.* 1990), a finding subsequently verified in an animal study in which large pieces of subcutaneously implanted gutta-percha were well encapsulated in collagenous capsules, whilst fine particles induced an intense, localized tissue response (Sjögren *et al.* 1995). This could infer that extrusion of large pieces of gutta-percha may have no impact on periapical healing, but the present study did not support this inference. The discrepancy may be accounted for by the potential bacterial contamination of the extruded gutta-percha in the clinical cases. In contrast, extrusion of sealer did not seem to affect the success of 1° and 2°RCTx in the present study, consistent with the findings by Sari & Durutürk (2007). The radiographic assessment for presence and resorption of sealer is complicated by the radiolucent property of the basic components and the inadequate sensitivity of the conventional radiographic method to detect small traces of it. It is possible that in some cases, the disappearance of extruded sealer may simply be because of resorption of the radio-opaque additive, barium sulphate. The effect of extruded sealer on the rate of healing warrants further investigation.

The radiographic measure of 'quality of root filling' was found to have a significant influence on the success of 1°RCTx in a systematic review (Ng *et al.* 2008a). This factor could not be analysed in the present study because sub-standard root fillings were inevitably replaced by the students (as part of their training), with few exceptions (1.3% for 1°RCTx, 0.5% for 2°RCTx).

The effect of number of treatment visits on outcome is the subject of an on-going debate and controversy (Ng *et al.* 2008a). The present study could not evaluate this factor because of the inherent presence of many unquantifiable and hidden confounders.

The placement of a good-quality coronal restoration after root filling is considered the final step for completion of root canal treatment. Its importance was reinforced by the findings of the present study consistent with previous data (Ng *et al.* 2008a,b). Interestingly, the overall adjusted effect of the quality

of restoration (OR = 10.73; 95% CI: 3.65, 31.54) revealed from the present study was much larger than that reported in a meta-analysis for 1°RCTx (OR = 1.82; 95% CI: 1.48, 2.25) (Ng *et al.* 2008a), and 2°RCTx (OR = 3.31; 95% CI: 1.07, 10.30) (Ng *et al.* 2008b). The extremely profound effect estimated from the present study may be attributed to the clearer criteria adopted for assessing the quality of coronal restorations. Given that one of the roles of coronal restorations is to prevent postoperative root canal re-infection, the adopted criteria in Hoskinson *et al.* (2002) (marginal discrepancy, restoration margin discolouration or caries, history of de-cementation) were unable to discriminate coronal leakage when the inner core was still intact. The present study corrected this deficiency by adopting a modified definition for unsatisfactory restorations in order to differentiate between obvious and potential coronal leakage more effectively. The two groups of unsatisfactory restorations were: (i) obvious signs of exposed root filling and (ii) potential leakage indicated by marginal defects and history of de-cementation.

Unlike previous studies (Heling & Tamse 1970, 1971, Heling & Kischinovsky 1979, Heling & Shapira 1978, Allen *et al.* 1989, Cheung & Chan 2003, Fouad & Burleson 2003, Farzaneh *et al.* 2004, Chu *et al.* 2005), the present study found that *type* of coronal restoration had no significant influence on treatment success after adjusting the results for other factors including the quality of restoration. The present finding was consistent with Chugal *et al.* (2007). They reported that the type of restoration (temporary versus permanent) had no significant influence on periapical healing after adjusting the results by preoperative periapical lesion. This finding may be attributed to the underlying reasons for delaying the placement of permanent restorations by dentist or patient. The reasons include the fact that: (i) these teeth may be associated with persistent signs or symptoms of persistent apical periodontitis following treatment or (ii) some referring dentists may defer placement of final restoration on teeth with preoperative periapical lesions until there is radiographic evidence of periapical healing. It has often been recommended that it would be wise to provide a sub-seal over the root filling in case of loss of a restoration; the sub-seal would be glass-ionomer (GIC) or zinc oxide eugenol cement (Saunders & Saunders 1994, Hommez *et al.* 2002, Carrotte 2004, Yamauchi *et al.* 2006). The placement of a GIC or zinc oxide eugenol (IRM®) cement lining coronal to the gutta-percha filling and underneath the permanent core in

order to provide additional antibacterial coronal seal was found to have no additional beneficial effect on treatment success in the present study. This study supported the view that provision of a *good-quality* coronal restoration, regardless of type, should be considered an integral part of root canal treatment along with obturation to prevent postoperative re-infection.

Conclusion

The probabilities of success measured by absence of apical periodontitis using root as an unit of measure were 82.8% ($n = 969$) for 1°RCTx and 80.1% ($n = 1043$) for 2°RCTx; the difference (2.7%) was not significant ($P = 0.2$). Using odds of success (*not equivalent to chance of success*) as a dependent variable, four preoperative factors, six intraoperative factors and one postoperative factor were found to be significant prognostic indicators for the success of 1°RCTx and 2°RCTx. Those roots with a preoperative periapical lesion were significantly associated with 49% lower odds of success (OR = 0.51, 95% CI 0.32, 0.80) than roots without a lesion. The odds of success of treatment were found to decrease by 14% for every 1 mm increase in the diameter of the preoperative lesion (OR = 0.86, 95% CI 0.81, 0.91). The presence of a preoperative sinus (OR = 0.52, 95% CI 0.36, 0.77) or root perforation (OR = 0.44, 95% CI 0.21, 1.02) significantly reduced the odds of success by 48% and 56%, respectively. During treatment, achieving technical patency at the canal terminus significantly increased the odds of success twofold (OR 2.22, 95% CI 1.37, 3.59), whereas the odds of success was reduced by 12% (OR = 0.88, 95% CI 0.79, 0.97) for every 1 mm of the canal short of the terminus remaining 'un-instrumented'. In contrast, a long root filling reduced the odds of success by 62% (OR = 0.38, 95% CI 0.27, 0.54). The use of 0.2% chlorhexidine in addition to sodium hypochlorite solution for canal irrigation did not improve but reduced the odds of success by 53% (OR = 0.47; 95% CI 0.27, 0.83). Interestingly, the additional use of EDTA solution for canal irrigation had no significant effect (OR = 1.26, 95% CI 0.76, 2.09) on the success of 1°RCTx but significantly increased the odds of success of 2°RCTx by twofold (OR = 2.28, 95% CI 1.37, 3.81). The occurrence of interappointment complications (swelling or pain) reduced the odds of success by 47% (OR = 0.53; 95% CI 0.36, 0.79). Finally, a good-quality coronal

restoration significantly increased the odds of success by 11-fold (OR = 10.73, 95% CI 3.65, 31.54).

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