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A prospective study of the factors affecting outcomes of non-surgical root canal treatment: part 2: tooth survival

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Abstract

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

Methodology This prospective study involved annual follow-up of 2 (100%) to 4 years (50%) of 1°RCTx (759 teeth, 572 patients) and 2°RCTx (858 teeth, 642 patients) carried out by Endodontic postgraduate students. Pre-, intra- and post-operative data were collected prospectively from consented patients. Information about extraction of the root filled tooth was sought from the patient, the referring dentist or derived from the patient's records and included the timing and reasons for extraction. Tooth survival was estimated and prognostic factors were investigated using Cox regression. Clustering effects within patients were adjusted in all models using robust standard error.

Results The 4-year cumulative tooth survival following 1°RCTx [95.4% (93.6%, 96.8%)] or 2°RCTx [95.3% (93.6%, 96.5%)] was similar. Thirteen prognostic factors were identified. Significant patient factors included history of diabetes and systemic steroid therapy. Significant pre-operative factors included narrow but deep periodontal probing depth; pain; discharging sinus; and iatrogenic perforation (for 2°RCTx cases only). Significant intra-operative factors included iatrogenic perforation; patency at apical terminus; and extrusion of root fillings. Significant post-operative restorative factors included presence of cast restoration versus temporary restoration; presence of cast post and core; proximal contacts with both mesial and distal adjacent teeth; and terminal location of the tooth. The presence of pre-operative pain had a profound effect on tooth loss within the first 22 months after treatment [hazard ratio (HR) = 3.1; $P = 0.001$] with a lesser effect beyond 22 months (HR = 2.4; $P = 0.01$). Patency at the apical terminus reduced tooth loss (HR = 0.3; $P < 0.01$) within the first 22 months after treatment but had no significant effect on tooth survival beyond 22 months. Extrusion of gutta-percha root filling did not have any effect on tooth survival (HR = 1.1; $P = 0.2$) within the first 22 months but significantly increased the hazard of tooth loss beyond 22 months (HR = 3.0; $P = 0.003$).

Conclusions The 4-year tooth survival following primary or secondary root canal treatment was 95%, with thirteen prognostic factors common to both.

Keywords: outcome, root canal treatment, success, tooth survival.

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Introduction

Most previous studies investigating the factors affecting outcomes of primary (1°RCTx) or secondary (2°RCTx) root canal treatments have used clinical and/or radiographic signs of periapical healing as the outcome measure. Tooth survival has been used as an outcome measure in case-controlled study (Caplan *et al.* 2002) or large epidemiological surveys (Salehrabi & Rotstein 2004, Chen *et al.* 2008) published after 2000. A recent systematic review had assessed the pooled probabilities of tooth survival following RCTx and the associated prognostic factors based on the literature published up to 2007 (Ng *et al.* 2010); they found the pooled probabilities of tooth survival 2–10 years after root canal treatment to range from 86% to 93%. The substantial differences in study characteristics hindered effective direct comparison of findings. The evidence on the prognostic factors for tooth survival was very weak but the meta-analyses on available data showed that four conditions significantly improved tooth survival. Listed in descending order of influence, they were (i) tooth restoration with a crown after treatment; (ii) teeth having mesial and distal proximal contacts; (iii) teeth not functioning as abutments for removable or fixed prosthesis; and (iv) teeth other than molars. In essence, the available evidence supports the current intuitive premise that healthful tooth survival is likely to be influenced by the distribution, amount, strength and integrity of remaining tooth tissue, the occlusal and functional loading on the tooth and the manner in which that load is distributed within the remaining tooth structure (Gulabivala 2004). The review also highlighted the need for long-term prospective studies with comprehensive data collection on patient and tooth characteristics as well as their endodontic and restorative management. Ideally, the same sample should be used to investigate the prognostic factors for both periapical healing and tooth survival following root canal treatment. The aims of part two of this prospective study were to investigate the probability of, and factors influencing, tooth survival following 1°RCTx or 2°RCTx.

Materials and methods

The details of the ethical approval, sample inclusion and exclusion criteria, treatment protocol, follow-up examination, radiographic assessment and data management were presented in part one of this paper (Ng *et al.* 2011).

This is a prospective study involving annual follow-up for up to 4 years of 1°RCT (759 teeth) and 2°RCT (858 teeth) carried out by Endodontic postgraduate students. 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 maxillofacial referral centres and other clinical units of the dental hospital. All patients were over 15 years old 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 pre-operative periodontal disease (*teeth with narrow periodontal defect of endodontic origin were not excluded*) or prior surgical endodontic treatment or if the apex/apices under investigation was/were not discernible on any of the periapical radiographs. Pre-, intra- and post-operative data were collected prospectively on pre-designed proforma. The tooth was judged to have ‘survived’ if it was still present and potentially functional at the time of follow-up, regardless of the clinical or radiographic findings. It was considered to have failed to survive if the tooth had been extracted following treatment. The extraction outcome was reported either by the patient at the follow-up appointment, or without their attendance by phone or letter through the patient or referring dentist. The timing and reason(s) for tooth extraction were recorded.

Root-level independent variables were transposed to tooth-level variables based on the following criteria: tooth was considered to be non-vital or associated with a periapical lesion if any root was found to be non-vital, or associated with a periapical lesion. The size of the lesion was taken from the root with the largest lesion. Patency at canal terminus was recorded as positive if it was achieved in all roots. Blockage of canal was recorded as positive if any root canals were blocked during treatment. These two factors would account for those teeth with patency achieved in some but not all canals. Apical extent, size and taper of canal preparation were omitted in the survival analysis because of the lack of logical strategy for transposing these root-level variables to tooth-level. Extrusion of root filling or sealer from any root was considered as presence of extrusion for the entire tooth.

Tooth survival was estimated using STATA version 9.2 (STATA Corporation, College Station, TX, USA, 2005) statistical software package. When analysing the *survival of teeth* after treatment, the event of interest was extraction of the tooth. The zero time-point for these analyses was the date of completion of root canal treatment. Time to extraction of the tooth was recorded as the time interval (measured in months) between the date of the end of treatment and the date the tooth was extracted. Those teeth that were lost to follow-up (i.e. patients failing to return at the annual recall but were examined at least once after treatment was completed) were censored at the patient's last visit to the clinic (if the tooth was not extracted at this visit). Those teeth that were followed up for 4 years were censored at the 4-year recall date.

Cox proportional hazards regression models were used to investigate factors affecting the survival of the teeth after root canal treatment. Clustering within patients was accounted for by estimating robust standard error (Rogers 1993). The two data sets were combined for Cox regression analyses to increase the statistical power because of the small number of teeth lost after treatment. The type of treatment (1°RCTx, 2°RCTx) was included as a covariate in all models.

Initially, each of the potential prognostic factors was entered into a model simultaneously with 'type of treatment' one by one. Those factors that proved to be significant at the 5% level or demonstrated a large effect [Hazard ratio (HR) ≥ 1.5 or hazard ratio ≤ 0.5] but were only significant at the 10% level were considered to have prognostic value and were selected for further multiple analyses.

The final multiple Cox regression model was also built through two stages: *first*, all potential significant factors related to *patient's medical condition* were entered simultaneously into a model together with 'type of treatment' but those that lost their prognostic value were removed from the model and *secondly*, all potential significant *pre-, intra- and post-operative tooth factors* were added to the model resulting from the first stage of analysis. Again, those factors that lost their prognostic value in this model were removed.

During the building of the multiple model, if a factor was considered on clinical judgment to be acting as a surrogate measure for another factor, and one (or both) lost their significance in the more complex model, the former factor was excluded from further analyses. If there was no reason for exclusion of either of the factors, they were analysed separately in different models.

The proportionality assumption underlying the Cox regression was assessed using the Schoenfeld and scaled Schoenfeld residuals. This was carried out by graphical inspection and also by formally testing whether the slope of a smoothed regression line of the scaled Schoenfeld residuals versus analysis time was different from zero. For those factors for which the effects seemed to change with time, an interaction term with time period was introduced into the model after partitioning the time to have (approximately) equal numbers of failures in both time periods. If these interaction terms were significant (at $P < 0.10$), they were included in the final model. If not, the simpler model without interaction was used.

Results

In total, 759 of 924 teeth undergoing 1°RCTx and 858 of 1113 teeth undergoing 2°RCTx fulfilled the inclusion criteria and were available for the survival analysis (Ng *et al.* 2011). By the end of the study period, 95.4% (95% CI 93.6%, 96.8%) (724 of 759) of the teeth undergoing 1°RCTx and 95.2% (95% CI 93.6%, 96.5%) (817 of 858) of those undergoing 2°RCTx were still functionally present at their follow-up review (Fig. 1). Tooth loss by extraction occurred between 1–47 months for 1°RCTx and 3–48 months for 2°RCTx. Most of the lost teeth were extracted within 2 years after treatment. The hazard of tooth loss after 2°RCTx was slightly higher than that after 1°RCTx within the first year after treatment but there was no obvious difference after 1 year (Fig. 1). Preliminary univariable Cox regression analysis revealed the overall difference in hazard of tooth loss after primary or secondary root canal treatment was not significant at the 5% level (HR = 1.07; 95% CI 0.68, 1.70). The reasons for tooth extraction could be classified into six main groups (Table 1).

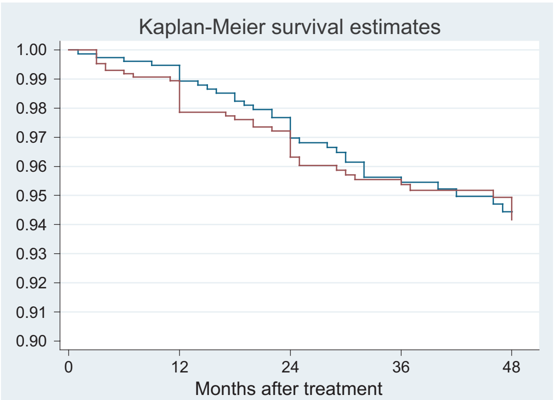

Figure 1 Kaplan–Meier survival estimates by primary (blue line) and secondary (red line) root canal treatment.

Table 1 Reasons for tooth extraction after 1°RCTx or 2°RCTx

Reasons	1°RCTx (*n* = 35)	2°RCTx (*n* = 41)
Endodontic problem		
Pain	3	6 (1 root fracture)[a]
Pain (chronic pain problem)	0	1
Pain and swelling	2 (1 periodontal problem)[a]	3
Pain after crown placement by GDP	1	0
Sinus	2	3
Sinus and pain	1	0
Sinus and swelling	1	0
Sinus and tooth facture	0	2 (1 tooth fracture, 1 tooth & root fracture)[a]
Swelling	0	1
Subtotal	10 (28.6%)	16 (39.0%)
Tooth/root fracture		
Root fracture	1	1
Tooth and root fracture (vertical)	0	1
Tooth fracture	9 (2 bruxers, 1 clencher)	10 (1 was bridge abutment, 1 replaced with implant)
Subtotal	10 (28.6%)	12 (29.3%)
Restoration failure		
Bridge failure	0	2
Bridge fracture	2 (1 was abutment, 1 replaced with implant)	0
Crown failure (tooth unrestorable)	5	6 (1 replaced with implant)
Plastic restoration failure	0	1
Post-perforation and fracture	1	0
Subtotal	8 (22.9%)	9 (22.0%)
Restorative or orthodontic treatment plan		
Aesthetic denture	0	1
Implant treatment	4	3
Orthodontic treatment plan	1	0
Subtotal	5 (14.3%)	4 (9.7%)
Periodontal problem		
	1	0
Subtotal	1 (2.8%)	0 (0.0%)
Other		
Concern about Hg poisoning	1	0
Subtotal	1 (2.8%)	0 (0%)
Total	35 (100%)	41 (100%)

[a]The conditions in bracket are not the main reason for tooth extraction and these cases have not been included under the 'Tooth/root fracture' and 'Periodontal problem' categories.

Identification of prognostic factors predicting tooth survival

Tables 2–6 present the results of univariable Cox survival regression analyses on the effect of each potential prognostic factor adjusted for the type of treatment using the combined data set. The clustering effect within patients was accounted for in all models. Sixteen potential prognostic factors were identified in the single prognostic factor model with type of

Table 2 Effects of each patient characteristic, tooth type and developmental anomaly on tooth loss by extraction adjusted for type of treatment using Cox regression analysis

Patient characteristics	1°RCT No. of teeth	1°RCT Loss (%)	2°RCT No. of teeth	2°RCT Loss (%)	HR adjusted for type of treatment (95% CI)[a]
Age (continuous data)	–	–	–	–	1.02 (0.10, 1.03)
Sex					
Female	441	5.2	552	4.2	1
Male	318	3.8	306	5.9	1.06 (0.64, 1.74)
Diabetic					
No	737	3.9	835	4.8	1
Yes	22	27.3	23	4.4	3.65 (1.43, 9.29)
Allergic					
No	588	4.1	654	4.7	1
Yes	171	6.4	204	4.9	1.21 (0.70, 2.09)
Systemic steroid					
No	748	4.7	846	4.5	1
Yes	11	0.0	12	25.0	2.80 (0.96, 9.09)
Long-term antibiotics					
No	752	4.7	852	4.8	Not analysed
Yes	7	0.0	6	0.0	
Thyroxin therapy					
No	733	4.5	831	4.5	1
Yes	26	7.7	27	14.8	2.53 (1.01, 6.39)
Hormone replacement					
No	727	4.8	837	4.8	1
Yes	32	0.0	21	4.8	0.38 (0.05, 2.78)
Coronary heart disease					
No	701	4.3	801	4.6	1
Yes	58	8.6	57	7.0	1.08 (0.68, 1.71)
Tooth type					$P = 0.1$[b]
Maxillary incisors/canine	219	4.6	149	2.7	1
Maxillary premolars	71	9.9	121	6.6	2.02 (0.90, 4.54)
Maxillary molars	156	3.9	186	3.2	0.93 (0.40, 2.18)
Mandibular incisors/canine	74	1.3	68	2.9	0.56 (0.16, 1.96)
Mandibular premolars	40	0.0	54	5.6	0.82 (0.23, 2.95)
Mandibular molars	199	5.5	280	6.4	1.64 (0.82, 3.25)
Developmental anomalies					
No	748	4.7	857	4.8	
Yes	11	0.0	1	0.0	Not analysed

[a]Confidence interval for hazard ratio (HR) estimated using robust standard error to allow for clustering within patients.
[b]*P* value of test for heterogeneity for categorical factor.

treatment as a covariate (Table 7). If one factor was deemed to act as a surrogate measure for another, the one with weaker effect on the hazard of tooth loss was excluded from further analyses.

Two of the pre-operative factors (presence of fractured instruments and fate of foreign material) were unique to 2°RCTx. 'Presence of fractured instruments' was significantly ($P < 0.001$) correlated with 'fate of foreign material'. In addition, 'fate of foreign material' was significantly ($P < 0.001$) correlated with 'patency at apical terminus'. As both of these two factors (presence of fractured instruments and fate of foreign

Table 3 Effects of pre-operative factors adjusted for type of treatment using Cox regression analysis

Factors	1°RCT No. of teeth	1°RCT Loss (%)	2°RCT No. of teeth	2°RCT Loss (%)	HR adjusted for type of treatment (95% CI)[a]
History of luxation injuries					
No	589	4.9	792	5.1	1
Yes	170	3.5	66	1.5	0.60 (0.25, 1.41)
History of fracture or crack					P = 0.7[b]
No	597	3.9	724	5.3	1
Fracture	98	9.2	71	1.4	1.36 (0.64, 2.89)
Cracks	64	4.7	63	3.2	0.92 (0.37, 2.31)
Restoration type					P = 0.9[b]
Un-restored tooth	179	3.4	–	–	0.72 (0.26, 1.98)
Plastic restoration	272	4.4	428	4.9	1
Plastic + post	–	–	6	0.0	–
Cast restoration	163	4.9	245	4.5	0.95 (0.54, 1.67)
Cast restoration + post	9	11.1	52	5.8	1.47 (0.51, 4.24)
Temporary dressing	120	5.8	112	4.5	1.26 (0.65, 2.41)
Open cavity	16	6.3	15	6.7	1.02 (0.62, 1.67)
Pain					
No	445	2.9	493	3.5	1
Yes	314	7.0	365	6.6	2.21 (1.34, 3.62)
Tenderness to percussion					
No	459	3.9	464	4.1	1
Yes	300	5.7	394	5.6	1.47 (0.92, 2.34)
Soft tissue tenderness					
No	543	3.9	568	4.8	1
Yes	216	6.5	290	4.8	1.32 (0.81, 2.13)
Soft tissue swelling					
No	678	4.4	770	4.7	1
Yes	81	6.2	88	5.7	1.32 (0.67, 2.60)
Sinus					
No	661	4.1	761	3.9	1
Yes	98	8.2	97	11.3	2.60 (1.54, 4.40)
Periodontal probing depth ≥ 5mm					
No	735	4.5	836	4.6	1
Yes	24	8.3	22	13.6	2.39 (0.95, 6.03)
Pulpal status					
Non-vital	613	4.6	–	–	1
Vital	146	4.8	858	4.8	1.07 (0.47, 2.43)
Periapical status					P = 1.0[b]
Intact PDL	157	3.8	125	6.4	1
Widened PDL	99	5.1	96	4.2	0.95 (0.40, 2.24)
Periapical lesion	503	4.8	637	4.6	0.95 (0.51, 1.76)
Size of periapical lesion					
Continuous variable	–	–	–	–	1.05 (0.98, 1.13)
Root resorption					P = 0.03[b]
No	663	4.7	787	5.1	1
Internal	19	0	8	0.0	Not analysed
External (apical)	56	3.6	60	1.7	0.52 (0.16, 1.66)
External (lateral)	10	0	3	0.0	Not analysed
Internal & external apical	2	0	–	–	Not analysed
Cervical	9	22.2	–	–	Not analysed
Perforation					P = 0.4[b]
No	745	4.4	832	4.7	1
Apical/mid-root level	–	–	4	0.0	Not analysed
Coronal (Subosseous)	3	33.3	10	10.0	3.23 (0.77, 13.49)
Coronal (Supraosseous)	11	9.1	12	8.3	1.87 (0.45, 7.77)
Coronal	14	4.6	22	9.1	2.37 (0.85, 6.59)

PDL, periodontal ligament space.

[a]Confidence interval for hazard ratio (HR) estimated using robust standard error to allow for clustering within patients.

[b]P value of test for heterogeneity for categorical factor.

Table 4 Unadjusted effects of pre-operative factors unique to 2°RCTx using Cox regression analysis

Factors	2°RCT No. of teeth	2°RCT Loss (%)	Unadjusted HR (95% CI)[a]
Satisfactory root filling			
No	145	6.9	1
Yes	713	4.4	1.50 (0.73, 3.09)
Canal content			
Un-instrumented	0	0.0	
Empty but instrumented	3	33.3	Not analysed
Foreign material	855	4.7	
Type of foreign material			$P = 0.03$[b]
$Ca(OH)_2$	7	1.1	0.61 (0.08, 4.69)
Gutta-percha	660	4.2	1
Cement	31	7.4	1.74 (0.42, 7.21)
Thermafil	6	0.0	Not analysed
Silver point	46	2.5	0.57 (0.08, 4.14)
Fractured instrument	105	11.4	2.94 (1.47, 5.93)
Presence of fractured instrument			
No	753	3.9	1
Yes	105	11.4	3.13 (1.62, 6.05)
Fate of foreign material			$P < 0.0001$[b]
Remained the same	56	16.1	1
Bypassed	25	4.0	0.26 (0.03, 2.12)
Removed	761	3.9	0.25 (0.12, 0.51)
Extruded apically	13	0.0	Not analysed

[a]Confidence interval for hazard ratio (HR) estimated using robust standard error to allow for clustering within patients.
[b]*P* value of test for heterogeneity for categorical factor.

material) were predictive for achieving patency at canal terminus, they were not analysed further in multiple regression models.

The two factors (pre-operative perforation and intra-operative perforation) were combined into a single binary factor 'presence of pre- or intra-operative perforation at mid- or coronal level' for further analyses because (i) there were only a small number of cases with such procedural errors and (ii) perforation at a more coronal level may increase the risk of bacterial leakage or tooth fracture.

Of the post-operative restorative factors, 'number of proximal contacts' and 'terminal tooth' were significantly ($P < 0.001$) correlated as a terminal tooth could only have one proximal contact. There was, however, no reason for excluding one or the other; therefore, their effects were analysed in two different models.

Final multiple Cox regression model building

Initially, the three medical conditions (diabetes, steroid therapy and thyroxine therapy) were entered simultaneously into a multiple Cox regression model together with type of treatment (*Results not shown*). Both steroid therapy and thyroxine therapy did not reach the 5% significance level and were found to be significantly ($P < 0.05$) correlated; therefore, they were not entered simultaneously into the same model in the further analyses.

In the next phase (*Results not shown*), type of treatment and the two medical conditions (diabetic, systemic steroid therapy) were entered simultaneously together with all the potential significant pre-operative, intra-operative and post-operative factors into a multiple Cox regression model. 'Systemic steroid therapy' proved to have prognostic value (HR = 2.95; 95% CI 0.98, 8.83). When 'thyroxine therapy' was entered into the model after excluding 'systemic steroid therapy', 'thyroxine therapy' was found to have no prognostic value (HR = 1.80; 95% CI 0.57, 5.72); thus, 'thyroxine therapy' was not analysed further.

'Patency at apical terminus' (HR = 0.66; 95% CI 0.26, 1.68) and 'blockage of canal during treatment' (HR = 1.48; 95% CI 0.69, 3.16) failed to retain their prognostic value when they were entered into the same model. Patency at canal terminus describes the apical level to which the canal could be cleaned by the instruments and chemical disinfectant. Those canals that became blocked at a later stage during canal enlargement might have been cleaned well enough during the earlier stages. Therefore, it was decided to keep 'patency at apical terminus' in the model but to exclude 'blockage of canal' from further analyses.

Two of the post-operative restorative factors, 'terminal tooth' (HR = 1.16; 95% CI 0.51, 2.65) and 'two proximal contacts' (HR = 0.62; 95% CI 0.36, 1.09), were also found to have no prognostic value when they were entered into the same model. They were found to be significantly ($P < 0.05$) correlated with each other; therefore, these two factors were analysed in separate models subsequently as there was no reason for excluding either of them.

In the final phase, the remaining 12 potential prognostic factors with exclusion of 'terminal tooth' were entered simultaneously with type of treatment into the penultimate model 1 (*Results not shown*). It was noted that the HR of 'pre-operative periodontal probing depth' had a wide confidence interval. When 'two proximal contacts' was replaced with 'terminal tooth' in the penultimate model 2 (*Results not shown*), the magnitude and direction of effect of all other prognostic factors in this model were almost the same as in the penultimate model 1. It was also noted that the HRs of

Table 5 Effects of intra-operative factors adjusted for type of treatment (1°RCTx vs. 2°RCTx) using Cox regression analysis

Factors	1°RCT No. of teeth	1°RCT Loss (%)	2°RCT No. of teeth	2°RCT Loss (%)	HR adjusted for type of treatment (95% CI)[a]
Protect the tooth with a band					
No	604	4.2	681	5.0	1
Yes	155	5.8	177	4.0	1.06 (0.59, 1.90)
Use of magnification					
No	620	4.8	530	4.3	1
Yes	139	3.6	328	5.5	1.14 (0.70, 1.87)
Patency at canal terminus					
No	39	10.3	70	7.1	1
Yes	720	4.3	788	4.6	0.49 (0.24, 1.01)
Blockage of canal					
No	687	4.5	685	4.1	1
Yes	72	5.6	173	7.5	1.77 (1.03, 3.03)
Perforation					
No	728	4.3	848	4.5	1
Yes	31	12.9	10	20.0	2.04 (1.33, 3.13)
Fracture of instrument					
No	745	4.7	842	4.8	1
Yes	14	0.0	16	6.3	1.45 (0.16, 13.53)
NaOCl concentration					
2.5%	533	4.1	790	4.9	1
4–5%	226	5.8	68	2.9	0.57 (0.18, 1.83)
Irrigation solution					
NaOCl alone	533	4.1	493	5.9	1
NaOCl combined + other[a]	226	5.8	365	3.3	0.88 (0.52, 1.51)
Additional use of iodine					
No	695	4.9	666	5.3	1
Yes	64	1.6	192	3.1	0.52 (0.24, 1.15)
Additional use of CHX					
No	728	4.7	771	5.1	1
Yes	31	3.2	87	2.3	0.57 (0.18, 1.85)
Additional use of EDTA					
No	572	4.0	630	4.8	1
Yes	187	6.4	228	4.8	1.34 (0.79, 2.27)
Inter-appointment pain					
No	724	3.9	724	4.8	1
Yes	85	9.4	134	4.5	1.48 (0.80, 2.75)
Inter-appointment swelling					
No	736	4.5	835	4.8	1
Yes	23	4.4	23	4.3	0.92 (0.22, 3.86)
Extrusion of root filling					
No	646	3.7	758	4.6	1
Yes	113	9.7	100	6.0	1.85 (1.10, 3.10)
Extrusion of sealer					
No	508	4.5	536	5.2	1
Yes	251	4.8	322	4.0	0.86 (0.52, 1.42)

[a]Confidence interval for hazard ratio (HR) estimated using robust standard error to allow for clustering within patients.
[b]Other irrigation solutions included 10% povidone iodine (Betadine; Seton Health Care PLC, Oldham, UK), 0.2% chlorhexidine gluconate (Adam Health Care Ltd, UK), 17% ethylene-diamine-tetra-acetic acid (EDTA) (AnalaR® grade; Merck BDH, Poole, UK).

Table 6 Effects of post-treatment restorative factors and additional endodontic treatment adjusted for type of treatment using Cox regression analysis

Factors	1°RCT No. of teeth	1°RCT Loss (%)	2°RCT No. of teeth	2°RCT Loss (%)	HR adjusted for type of treatment (95% CI)[a]
Core material					$P < 0.0001$[b]
Amalgam	389	3.6	486	4.1	1
Composite	234	2.6	142	2.1	0.62 (0.30, 1.30)
Glass–ionomer cement	57	12.3	89	7.9	2.43 (1.22, 4.84)
IRM®	12	33.3	17	29.4	10.08 (4.54, 22.36)
Post and amalgam	21	0.0	47	4.3	0.87 (0.21, 3.62)
Cast post and core	46	8.7	77	5.2	1.57 (0.72, 3.42)
Post present					
No	692	4.5	734	4.8	1
Yes	67	6.0	124	4.8	1.11 (0.51, 2.40)
Core lining used					$P = 0.02$[b]
None	353	6.8	453	6.2	1
Glass–ionomer cement	83	4.8	69	1.5	0.51 (0.20, 1.27)
IRM®	323	2.2	336	3.6	0.48 (0.27, 0.86)
Type of restoration					
Cast restoration					
No	397	5.8	319	7.5	1
Yes	362	3.3	539	3.2	0.44 (0.27, 0.71)
Temporary restoration					
No	752	4.3	845	4.3	1
Yes	7	42.9	13	38.5	13.60 (5.97, 31.04)
Used as abutment					$P = 0.6$[b]
No	706	4.5	817	4.5	1
Bridge	43	4.7	35	11.4	1.61 (0.64, 4.04)
Denture	10	10.0	6	0.0	1.46 (0.22, 9.87)
No	706	4.5	817	4.5	1
Yes (any type)	53	5.7	41	9.8	1.58 (0.68, 3.70)
Number of proximal contacts					$P = 0.007$[b]
None	24	12.5	26	3.9	1
One	162	6.2	177	9.6	1.02 (0.35, 2.94)
Two	573	3.8	655	3.5	0.49 (0.18, 1.35)
Two proximal contacts					
No	186	7.0	203	8.9	1
Yes	573	3.8	655	3.5	0.48 (0.31, 0.96)
Terminal tooth					
No	643	4.0	756	4.1	1
Yes	116	7.8	102	9.8	2.07 (1.24, 3.46)
Additional endodontic treatment					
No	745	4.4	828	5.0	1
Yes	14	14.3	30	0.0	0.92 (0.22, 3.84)
Non-surgical retreatment	1	–	2	–	–
Endodontic surgery	13	–	28	–	–

[a]Confidence interval for hazard ratio (HR) estimated using robust standard error to allow for clustering within patients.
[b]P value of test for heterogeneity for categorical factors.

Table 7 Potential prognostic factors for tooth loss after primary or secondary root canal treatment

General patient factors	Intra-operative factors
1. Diabetes systemic	1. Patency at canal terminus
2. Steroid therapy	2. Blockage of any canal
3. Thyroxine therapy	3. Crown or root perforation
Pre-operative factors	4. Extrusion of root filling into the periapical tissue
1. Pain	Post-operative restorative factors
2. Sinus	1. Cast post and core
3. Periodontal probing depth	2. Type of coronal restoration
4. Presence of fractured instruments	3. Number of proximal contacts
5. Fate of foreign material	4. Terminal tooth

post-operative temporary restoration had wide confidence interval, indicating that the corresponding estimated HR was imprecise.

There was, however, evidence that the proportional hazards assumption (i.e. the effect of the prognostic factors on tooth survival should remain the same through out the study period) had been violated (Global test: $P = 0.008$) for some of the prognostic factors in both of the penultimate models 1 and 2. Three factors (pre-operative pain, patency at the apical foramen and extrusion of gutta-percha root filling) had clearly violated the proportional hazards assumptions (Table 8). A single HR describing the effect of each of these factors is therefore inappropriate. The scaled Schoenfeld residuals over time were plotted for each of the three factors. The effect of pre-operative pain on hazard seems to stay the same until *about 22 months* and then declined thereafter, whilst the effect of patency at the apical terminus seems to increase after *about 19 months* post-operatively. Similarly, having extrusion of gutta-percha root filling did not have an effect on the hazard until *about 20–22 months* post-treatment; the hazard then increased thereafter.

Table 8 Test of proportional hazards assumption for model 1 and model 2

Factors	Model 1 *P value	Model 2 *P value
Type of treatment	0.9	0.8
Diabetic	0.9	0.9
Systemic steroid therapy	0.6	0.9
Pre-operative periodontal probing depth	0.2	0.3
Pre-operative pain	0.001	0.0005
Pre-operative sinus	0.06	0.05
Pre- or intra-operative perforation	0.7	0.9
Patency at apical terminus	0.006	0.01
Extrusion of gutta-percha root filling	0.02	0.02
Cast post and core	0.5	0.4
Post-operative temporary restoration present	0.5	0.4
Post-operative cast restoration present	0.8	0.6
Two proximal contacts	1.0	–
Terminal tooth	–	0.4
Global test	0.008	0.008

*P value for testing for trend.

All three prognostic factors had an effect on hazard of tooth loss that changed at about the same time after completion of treatment. The record for each observation was therefore split into two episodes at 22 months post-operatively, and interaction terms between the time-band and the prognostic factors were included in the new Cox models 1 and 2 (Table 9a,b). The number of failures was about the same in the two time-bands. These models no longer violated the proportional assumptions (global test: $P = 0.5$ and $P = 0.4$ for model 1 and model 2, respectively); therefore, the two models were considered as definitive (Table 9a,b). In summary, two prognostic models, using Cox regressions, were developed to describe the effects of prognostic factors on the survival of teeth after treatment.

The type of treatment did not have a significant effect on tooth loss (HR = 1.3; 95% CI 0.8, 2.1). The respective confidence interval was, however, very wide and indicative of a range between 20% less to 110% more tooth loss following 2°RCTx.

In total, thirteen significant prognostic factors were identified for 1°RCTx and 2°RCTx. Two of them were related to the patients' medical condition. Patients suffering from diabetes (HR = 3.2–3.4; $P \le 0.01$) or undergoing systemic steroid therapy (HR = 3.0–3.4, $P < 0.05$) were associated with threefold more tooth loss than their healthy counterparts.

Five significant pre-operative prognostic factors were identified. Pre-operative periodontal probing depths deeper than 5 mm were associated with twofold more tooth loss (HR = 2.0–2.4; $P = 0.04–0.1$). However, the confidence interval for the HR was wide, representing a

Table 9 (a,b) Definitive models 1 and 2 presenting the effects of 'pre-operative pain', 'patency at the apical foramen' and 'extrusion of gutta-percha root filling' before and after 22 months post-treatment

	(a) Model 1			(b) Model 2		
Factors	HR	95% CI for HR[a]	*P* value	HR	95% CI for HR[a]	*P* value
Type of treatment						
Primary root canal treatment	1			1		
Secondary root canal treatment	1.33	0.85, 2.11	0.2	1.31	0.83, 2.08	0.2
Diabetic						
No	1			1		
Yes	3.21	1.27, 8.10	0.01	3.46	1.43, 8.36	0.006
Systemic steroid therapy						
No	1			1		
Yes	2.96	1.09, 8.19	0.03	3.40	1.25, 9.30	0.02
Pre-operative periodontal probing depth						
<5mm	1			1		
≥5mm (narrow defects)	2.04	0.86, 4.83	0.1	2.35	1.01, 5.45	0.04
Pre-operative pain						
No	1			1		
Yes (within 22 months)	3.12	1.56, 6.25	0.001	3.10	1.53, 6.29	0.002
Yes (beyond 22 months)	2.46	1.22, 4.94	0.01	2.39	1.19, 4.82	0.02
Pre-operative sinus						
No	1			1		
Yes	2.22	1.29, 3.81	0.004	2.22	1.29, 3.82	0.004
Pre- or intra-operative perforation						
No	1			1		
Yes	3.68	1.62, 8.35	0.002	3.77	1.65, 8.60	0.002
Patency at canal terminus						
No	1			1		
Yes (within 22 months)	0.29	0.13, 0.65	0.002	0.31	0.14, 0.70	0.005
Yes (beyond 22 months)	1.65	0.23, 11.88	0.6	1.65	0.22, 12.20	0.6
Extrusion of gutta-percha root filling						
No	1	1		1		
Yes (within 22 months)	1.09	0.42, 2.81	0.2	1.05	0.41, 2.72	0.9
Yes (beyond 22 months)	2.98	1.45, 6.09	0.003	2.84	1.39, 5.82	0.004
Cast post and core						
No	1			1		
Yes	2.58	1.13, 5.87	0.02	2.60	1.16, 5.74	0.02
Post-operative temporary restoration present						
No	1			1		
Yes	7.53	3.31, 17.09	<0.001	8.26	3.58, 19.03	<0.001
Post-operative cast restoration present						
No	1			1		
Yes	0.38	0.22, 0.64	<0.001	0.43	0.25, 0.72	0.001
Two proximal contacts						
No	1			–	–	–
Yes	0.47	0.29, 0.76	0.002			
Terminal tooth						
No	–	–	–	1		
Yes				1.93	1.13, 3.31	0.02

[a]Confidence interval for hazard ratio (HR) estimated using robust standard error to allow for clustering within patients.

range between 14% reduction to 440% increase in hazard. The presence of pre-operative pain had a profound effect on tooth loss within the first 22 months after treatment (HR = 3.1; 95% CI 1.5, 6.3) with a lesser effect beyond 22 months (HR = 2.4; 95% CI 1.2, 4.9), post-operatively. The presence of a pre-operative sinus increased the hazard of tooth loss by 120% (HR = 2.2; $P = 0.004$) with a corresponding narrow confidence interval for the HR. The presence of pre- or intra-operative perforation increased tooth loss by nearly 300% (HR = 3.7; $P = 0.002$).

The effects of the other two intra-operative factors, patency at the apical terminus and extrusion of gutta-percha root filling material, had different effects on the hazard of tooth loss before and beyond 22 months post-operatively. Patency at the apical terminus reduced tooth loss (HR = 0.3; $P < 0.01$) within the first 22 months after treatment but had no significant effect on tooth survival beyond 22 months post-operatively. During the first 22-month period, there was upto 70% less tooth loss if patency at the apical terminus had been achieved.

Extrusion of gutta-percha root filling did not have any effect on tooth survival (HR = 1.1; 95% CI 0.4, 2.8) within the first 22 months but significantly increased the hazard of tooth loss by almost 200% beyond 22 months (HR = 3.0; 95% CI 1.5, 6.1) post-operatively.

Five significant post-operative restorative factors were identified. Teeth restored with temporary restorations were seven to eight times (HR = 7.5–8.3; $P < 0.001$) more likely to be extracted after treatment than their counterparts. On the other hand, teeth restored with a cast restoration after treatment reduced tooth loss by approximately 60% (HR = 0.4; $P < 0.001$). Teeth with restorations retained with a cast post and core were 2.6 times more likely to be extracted (HR = 2.6; $P = 0.02$). Teeth with two proximal contacts had 50% (HR = 0.5; $P = 0.002$) lower hazard of tooth loss after treatment than those teeth with none or one proximal contact, whereas terminal teeth were associated with almost 96% more (HR = 1.9; $P = 0.02$) tooth loss than those that were not located distal-most in the arch.

Discussion

Investigation into prognostic factors for tooth survival following root canal treatment was compromised by the low event rate with some combination of factors not present in the study cohort; only a small proportion of the study teeth were extracted during the study period. A larger sample size or a longer follow-up after treatment to achieve a higher event rate may have improved statistical power. The latter strategy may, however, have to be counterbalanced by a larger drop-out rate at recall. In the present data set, three of the prognostic factors (pre-operative pain, patency at apical foramen and extrusion of gutta-percha) did not remain constant over the study period, resulting in the penultimate prognostic model violating the proportional hazards assumption. If the hazards cannot be assumed proportional, then more advanced analytical methods exist, the simplest being to stratify the analysis for the factor that violates proportionality (Collett 2003); however, the effect of these factors then cannot be estimated. The present study therefore adopted a more complicated approach, which splits the data set at the time-point(s) when the effect of these factors changed, estimated as 22 month post-operatively. The new model included the modified effects of each factor by introducing interaction terms between the factor with time-bands into the final model (Cleves *et al.* 2004).

The present prospective study found that some prognostic factors for tooth survival were common with those for periapical healing, including 'sinus tract', 'absence of pre- and intra-operative tooth perforation', 'achievement of patency at canal terminus' and 'absence of root filling extrusion'. This suggests that lack of periapical healing affects tooth survival, consistent with the finding that an endodontic problem is one of the most common reasons for tooth extraction following treatment (Chen *et al.* 2008).

Teeth in patients suffering from diabetes or receiving systemic steroid therapy were found to have a higher chance of being extracted after treatment. The negative influence of diabetes on tooth survival was consistent with the report by Mindiola *et al.* (2006), whilst the influence of steroid therapy does not appear to have been reported previously. It may be argued that patients suffering from diabetes were more susceptible to periodontal disease (Genco & Löe 1993) or had a lower chance of periapical healing following root canal treatment (Fouad & Burleson 2003), which in turn could be the reason for tooth extraction. However, patients suffering from diabetes or receiving systemic steroid therapy *were not* associated with a lower chance of periapical healing but *were* associated with a higher hazard of tooth loss after RCTx. Both factors were found to have a significant influence on tooth survival even when they were entered simultaneously with pre-operative periodontal probing defect into a multivariable Cox regression model. The results may infer that diabetes increases the risk of tooth loss for reasons other than periodontal problems. Closer inspection of the data revealed that over 50% of such teeth were extracted because of persistent pain, which may be explained by the presence of neuropathy, a debilitating painful complication of diabetes (Edwards *et al.* 2008). It is further interesting to note that systemic steroid therapy is often prescribed to control such chronic pain (Colman *et al.* 2008, DePalma & Slipman 2008, Kalichman & Hunter 2008). In fact, arthritis was the reason for prescribing systemic steroid for the cases in the present study. This explanation is consistent with the finding that presence of pre-operative pain significantly increased the hazard of tooth loss.

Tooth morphological types may vary in their susceptibility to tooth fracture (Eakle *et al.* 1986, Lagouvardos *et al.* 1989), a common reason for tooth loss after treatment. Although a previous meta-analysis (Ng *et al.* 2010) had revealed that molar teeth had a higher chance of being extracted after treatment than other teeth, the present study found that tooth *type* had no significant influence on survival. Maxillary premolars and mandibular molars were found to have the highest frequency of extraction with tooth fracture being the most common reason in the present study. This observation was consistent with previous reports on higher prevalence of fracture of maxillary premolars and mandibular molars (Eakle *et al.* 1986, Lagouvardos *et al.* 1989). The factors, 'proximal contacts' and 'terminal teeth', were found to affect tooth survival significantly in the present study but were significantly correlated with 'molar teeth'. These findings concurred with the results from the previous meta-analysis (Ng *et al.* 2010) and the report by Tan *et al.* (2006). Of the extracted terminal teeth, 68% were fractured, whilst of the extracted non-terminal teeth, only 38% were fractured. Similarly, tooth fracture was the reason for extraction in 58% of teeth with one or less proximal contact, compared with 38% of extracted teeth with two proximal contacts. These results could be explained by the unfavourable distribution of occlusal force and higher non-axial stress on terminal teeth and those with less than two proximal contacts. Other reasons to explain their higher rate of loss are as follows: (i) failure of root canal treatment on a terminal tooth may be accepted more willingly as a reason for extraction as these teeth have little perceived aesthetic value and (ii) clinicians may be less likely to offer further surgical endodontic treatment on terminal molar teeth owing to access problems.

The presence of pre-operative periapical lesions was found to have no significant influence on tooth survival, consistent with the findings from a meta-analysis of pooled data from three studies (Ng *et al.* 2010). On the other hand, pre-operative periodontal probing defects of endodontic origin, pre-operative sinus and pre-operative pain which have the potential to persist after treatment were found to reduce tooth survival. The aforementioned observations were consistent with a previous report that the mere presence of a periapical lesion was not a sufficient reason for dentists and patients to opt for active treatment (Reit & Gröndahl 1988).

The pre-operative prognostic factor, 'periodontal probing defect', was consistent with that of an endodontic origin, as it fitted the probing profile of being deep, narrow and localized. Closer inspection of the data on this category revealed that approximately 70% of such teeth were extracted owing to root fracture. It may therefore be speculated that many of the teeth with such periodontal probing profiles were associated with an undiagnosed crack pre-operatively. Diagnostic tools such as 3D cone-beam tomography may be useful for detecting such problems earlier during management to allow appropriate treatment decisions.

Interestingly, the influence of pre-operative pain on tooth survival changed over time as its effect declined at around 22 months following treatment. This finding may be explained by the fact that pre-operative pain is a predictor for post-operative (Yesilsoy *et al.* 1988, Albashaireh & Alnegrish 1998) and chronic persistent (Polycarpou *et al.* 2005) pain after root canal treatment. The persistent pain may prompt patients to seek further endodontic treatment or tooth extraction sooner rather than later after treatment. The negative impact of pre-operative pain on tooth survival highlights the importance of accurate pain diagnosis. In some instances, the pain may be of non-endodontic origin and therefore persist after root canal treatment (Polycarpou *et al.* 2005). In other instances, pre-operative pain of endodontic origin may persist following treatment, as a result of peripheral or central sensitization (List *et al.* 2008). Therefore, effective pain diagnosis and management for patients presenting with pre-operative pain or the aforementioned medical conditions is crucial. The investigation into the influence of nature of pre-operative pain on tooth survival was beyond the scope of the present study; it would require detailed recording of the full characteristics of pain in future studies.

Amongst all intra-operative factors, 'no patency at apical foramen' and 'extrusion of gutta-percha root filling' were found to reduce tooth survival. Extraction of teeth with these conditions was more likely to be due to persistent periradicular problems as both of them were also prognostic factors for treatment success based on periapical healing. In the presence of persistent problems and knowing that the treatment objective of cleaning to the canal terminus could not be achieved, patients and dentists may be more likely to opt for extraction sooner than later. Although speculative, this practice might explain the interesting observation that 'patency at canal terminus' *only reduced tooth loss within 22 months* after treatment but not afterwards. In contrast, 'extrusion of root filling' did not influence tooth survival until after 22 months post-operatively, although this factor was also a significant prognostic factor for periapical healing. It may be speculated that dentists were more inclined to advise patients to adopt the 'wait and see' strategy if the root canal system had been perceived to be effectively cleaned to the apical terminus to allow sufficient time to judge periapical healing following root canal treatment. Another possible explanation is that root filling extrusion may result from excessive forces during compaction of gutta-percha resulting in minor cracks in the root. In time, these cracks may propagate with occlusal loading (Kishen 2005), resulting in re-infection or even root fracture. Such late failures may explain the delayed effect of 'extrusion of gutta-percha root filling'.

Part one of this study (Ng *et al.* 2011) showed that protection of teeth with crowns or cast restorations did not influence treatment success based on periapical healing as long as there was no sign of coronal leakage. In contrast, placement of crowns or cast restorations *was* found to improve tooth survival, consistent with the findings of the meta-analyses (Ng *et al.* 2010). However, neither the meta-analyses nor the present analysis had investigated the inter-relationship between tooth morphological type, the amount coronal tooth structure lost after treatment and the type of final restoration. In addition, it should be noted that the type of final coronal restoration was not randomly selected in the present study. Although the intuitive clinical inference from the result is that cast restorations should preferably be placed on all teeth after root canal treatment, this is probably a gross exaggeration of the true need. Fabrication of a full-coverage cast restoration requires further removal of tooth tissue from an already weakened tooth. On the basis of the findings from two previous studies (Reeh *et al.* 1989, Nagasiri & Chitmongkolsuk 2005), as well as the present findings, posterior teeth with compromised marginal ridges (mesially and/or distally), together with evidence of heavy occusal loading evidenced by faceting and/or cracks in the enamel, may benefit from cast cuspal coverage restorations. The restoration design should attempt to preserve as much remaining tooth tissue as possible; the implication is that the so-called non-aesthetic and technically demanding partial veneer onlays and partial coverage crowns would be the restorations of choice for root-treated teeth. In anterior teeth, the missing tooth tissue may often be replaced with plastic adhesive restorative material. A full crown is functionally only indicated when some form of intra-radicular retention aid is indicated to supplement the remaining tooth structure, as much of which as possible, should be preserved.

Pradoxically, the use of a cast post and core for retention of a restoration was found to reduce tooth survival, in contrast with the results of the meta-analysis (Ng *et al.* 2010) on previous data (Caplan & Weintraub 1997, Aquilino & Caplan 2002, Caplan *et al.* 2002, Salehrabi & Rotstein 2004), which found that retention posts had no significant influence on tooth survival. However, the analysis was not stratified by the type of post and core material. It may be speculated that the presence of posts had different effects on anterior and posterior teeth as they are subjected to different directions and magnitudes of occlusal force. However, the present survival data set did not have sufficient power to test interactive effects between factors because of the small number of failure events. Nevertheless, only 12% of the extracted teeth with cast post and core were incisor or canine teeth. Therefore, the use of such retention aids is perhaps better avoided in premolar and molar teeth. Alternative treatment options should be considered for severely broken down molar or premolar teeth. When restoring molar teeth, those with one or no adjacent teeth and terminal teeth, it is important to ensure favourable distribution of occlusal forces when designing restorations. If possible, root-treated teeth should be avoided as abutments for prostheses or for provision of occlusal guidance in excursive movements. Consistent with the report from a previous meta-analysis (Ng *et al.* 2010) which revealed that teeth functioning as prosthetic abutments had poorer survival, the present study also found a similar trend but the number of teeth ($n = 94$) functioning as abutments was too small to demonstrate a statistically significant effect. This finding may be related to the excessive and unfavourable distribution of occlusal stresses on abutment teeth.

Conclusion

The 4-year survival rate of root-treated teeth after 1°RCT or 2°RCTx was 95% (95% CI 94%, 96%) with no difference between the two types of treatment. In total, 13 significant prognostic factors were identified for tooth survival after RCTx. Amongst these 13 factors, 'pre-operative pain', 'canal terminus patency' and 'extruded root filling' had different effects on survival before and after 22 months post-treatment. Conditions found to improve tooth survival following 1°RCT or 2°RCTx were patients not suffering from diabetes or receiving systemic steroid therapy; absence of pre-operative deep periodontal probing defects, pain and sinus tract; absence of pre- and intra-operative tooth perforation; achievement of patency at canal terminus; absence of root filling extrusion; teeth with cast restoration after treatment; teeth with both mesial and distal adjacent teeth present; and teeth not requiring cast post and core for support and retention of restoration.

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References

Albashaireh ZSM, Alnegrish AS (1998) Postobturation pain after single- and multiple-visit endodontic therapy. A prospective study. *Journal of Dentistry* **26**, 227–32.

Aquilino SA, Caplan DJ (2002) Relationship between crown placement and the survival of endodontically treated teeth. *Journal of Prosthetic Dentistry* **87**, 256–63.

Caplan DJ, Weintraub JA (1997) Factors related to loss of root canal filled teeth. *Journal of Public Health in Dentistry* **57**, 31–9.

Caplan DJ, Kolker J, Rivera EM, Walton RE (2002) Relationship between number of proximal contacts and survival of root canal treated teeth. *International Endodontic Journal* **35**, 193–9.

Chen S-C, Chueb L-H, Hsiao CK, Wu H-P, Chiang C-P (2008) First untoward events and reasons for tooth extraction after nonsurgical endodontic treatment in Taiwan. *Journal of Endodontics* **34**, 671–4.

Cleves MA, Gould WW, Gutierrez RG (2004) *An Introduction to Survival Analysis Using Stata*, 2nd edn. College Station, Texas: Stata Press Publication, Stata Corporation.

Collett D (2003) *Modelling Survival Data in Medical Research*, 2nd edn. Florida, USA: Chapman & Hall/CRC.

Colman I, Friedman BW, Brown MD *et al.* (2008) Parenteral dexamethasone for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence. *British Medical Journal* **336**, 1359–61.

DePalma MJ, Slipman CW (2008) Evidence-informed management of chronic low back pain with epidural steroid injections. *The Spine Journal* **8**, 45–55.

Eakle ES, Maxwell EH, Braly BV (1986) Fracture of posterior teeth in adults. *Journal of American Dental Association* **112**, 215–8.

Edwards JL, Vincent AM, Cheng HL, Feldman EL (2008) Diabetic neuropathy: mechanisms to management. *Pharmacology and Therapeutics*, doi:10.1016/j.pharmthera.2008.05.005.

Fouad AF, Burleson J (2003) The effect of diabetes mellitus on endodontic treatment outcome: data from an electronic patient record. *Journal of American Dental Association* **134**, 43–51.

Genco RJ, Löe H (1993) The role of systemic conditions and disorders in periodontal disease. *Periodontology* **2000**(2), 98–116.

Gulabivala K (2004) Restoration of the root-treated tooth. In: Stock C, Walker R, Gulabivala K, eds. *Endodontics*, 3rd edn. Oxford, UK: Elsevier Mosby, pp. 279–306.

Kalichman L, Hunter DJ (2008) Diagnosis and conservative management of degenerative lumbar spondylolisthesis. *European Spine Journal* **17**, 327–35.

Kishen A (2005) Periapical biomechanics and the role of cyclic biting force in apical retrograde fluid movement. *International Endodontic Journal* **38**, 597–603.

Lagouvardos P, Sourai P, Douvitsas G (1989) Coronal fracture of posterior teeth. *Operative Dentistry* **14**, 28–32.

List T, Leijon G, Svensson P (2008) Somatosensory abnormalities in atypical odontalgia: a case-control study. *Pain* **139**, 333–41.

Mindiola MJ, Mickel AK, Sami C, Jones JJ, Lalumandier JA, Nelson SS (2006) Endodontic treatment in an American Indian population: a 10-year retrospective study. *Journal of Endodontics* **32**, 828–32.

Nagasiri R, Chitmongkolsuk S (2005) Long-term survival of endodontically treated molars without crown coverage: a retrospective cohort study. *Journal of Prosthetic Dentistry* **93**, 164–70.

Ng Y-L, Mann V, Gulabivala K (2010) Tooth survival following non-surgical root canal treatment: a systematic review of the literature. *International Endodontic Journal* **43**, 171–89.

Ng Y-L, Mann V, Gulabivala K (2011) A prospective study of the factors affecting outcomes of non-surgical root canal treatment: part 1: periapical health. *International Endodontic Journal* in press (doi:10.1111/j.1365-2591.2011.01872.x).

Polycarpou N, Ng Y-L, Moles DR, Canavan D, Gulabivala K (2005) Prevalence of and factors influencing persistent pain after endodontic treatment and complete periapical healing. *International Endodontic Journal* **38**, 169–78.

Reeh ES, Messer HH, Douglas WH (1989) Reduction in tooth stiffness as a result of endodontic and restorative procedures. *Journal of Endodontics* **15**, 512–6.

Reit C, Gröndahl HG (1988) Endodontic retreatment decision making among a group of general practitioners. *Scandinavian Journal of Dental Research* **96**, 112–7.

Rogers WH (1993) Regression standard errors in clustered samples. *Stata Technical Bulletin* **13**, 19–23. Reprinted in *Stata Technical Bulletin Reprints* **3**, 88–94.

Salehrabi R, Rotstein I (2004) Endodontic treatment outcomes in a large patient population in the USA: an epidemiological study. *Journal of Endodontics* **30**, 846–50.

Tan L, Chen NN, Poon CY, Wong HB (2006) Survival of root filled cracked teeth in a tertiary institution. *International Endodontic Journal* **39**, 886–9.

Yesilsoy C, Korzen LZ, Morse DR, Rankow H, Bolanos OR, Furst ML (1988) Post-endodontic obturation pain: a comparative evaluation. *Quintessence International* **19**, 431–8.