

Meta-Analysis
Oral Surgery

Treatments for intrusive luxation in permanent teeth: a systematic review and meta-analysis

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L.A. Costa, C.C.C. Ribeiro, L.M. Cantanhede, J.F. Santiago Júnior, M.R. de Mendonça, A.L.P. Pereira: Treatments for intrusive luxation in permanent teeth: a systematic review and meta-analysis. *Int. J. Oral Maxillofac. Surg.* 2017; 46: 214–229. © 2016 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

Abstract. Intrusive luxation is a severe form of dental trauma and there is no consensus regarding its management for permanent teeth. A systematic review and meta-analysis was performed to identify the appropriate treatment for teeth with intrusive luxation. The PubMed/MEDLINE, Embase, US Clinical Trials, and ISRCTN Registry electronic databases were used to search for articles in English and unpublished studies without a date limit. Eligible studies evaluated periodontal results (root resorption as the primary outcome; marginal bone defects and/or pulpal changes as secondary outcomes) after spontaneous re-eruption (SRE), orthodontic repositioning (ORP), or surgical repositioning (SRP) for patients with one or more traumatically intruded permanent teeth. Risk ratios with 95% confidence intervals were used to compare treatments. The meta-analysis revealed no significant difference ($P > 0.05$) between SRP and SRE for root resorption. For secondary outcomes, SRE was significantly better than SRP and ORP ($P < 0.05$). Subgroup analyses showed no significant differences among treatments in teeth with completely formed roots ($P > 0.05$) and a better prognosis when SRE was performed in teeth with incompletely formed roots ($P < 0.05$). The available evidence does not allow us to conclude on the best treatment for traumatically intruded teeth. More reliable evidence is needed.

Key words: tooth injuries; dental trauma; dentition; permanent; meta-analysis.

Accepted for publication 31 August 2016
Available online 17 September 2016

Dental trauma is a significant problem that affects approximately 25% of school-age children, and its incidence can exceed those of dental caries and periodontal disease in this population.^{1–3} Moreover,

approximately 33% of adults suffer trauma in the permanent dentition.²

Intrusive luxation is a severe form of dental trauma, accounting for 0.5–2% of traumas affecting the permanent

dentition.⁴ Its low incidence makes it difficult to perform research involving a large number of participants,⁵ and makes treatment strictly empirical, even at major trauma centres.²

Intrusive luxation is defined as the axial dislocation of a tooth in its alveolus.^{3,6-9} The injury is so severe because the root surface of the intruded tooth remains in intimate contact with the alveolar bone, resulting in the destruction of most fibres of the periodontal ligament and the cementum of the root surface.^{9,10} Vascular compression of the periodontium and pulpal complex causes ischemia.¹⁰ As a result of these characteristics, healing following intrusive luxation is associated with several complications, such as inflammatory and replacement root resorption.^{9,10}

Currently, three treatments are available for intrusive luxation: spontaneous re-eruption, orthodontic repositioning, and surgical repositioning. However, the published evidence provides conflicting prognoses for these three treatment types.⁵

The protocols used by the International Association of Dental Traumatology (IADT)³ and by the UK National Clinical Guidelines in Paediatric Dentistry¹¹ were developed based on literature reviews and consensus meetings. In addition, the treatment decision considers the degree of intrusion and the degree of root formation, which are important confounding variables related to the treatment outcome.¹⁰

In 2014, a systematic review concluded that spontaneous eruption yields the least complications in immature teeth, regardless of the degree of intrusion, and observed no significant differences between active treatments (surgical and orthodontic).¹² These conclusions were based exclusively on the results of the articles included in the review, without statistical analyses. Therefore, a further study including the statistical analysis of primary studies could produce a single estimate result and an overall conclusion, providing the best available evidence to guide the selection of the optimal treatment methods in the future.¹³

A systematic review and meta-analysis of interventional and observational studies—both prospective and retrospective—was thus performed to assess the periodontal effects (inflammatory and/or substitution root resorption) of the three treatments, spontaneous re-eruption, orthodontic repositioning, and surgical repositioning, used to manage patients with one or more permanent teeth that have suffered intrusive luxation.

Materials and methods

This systematic review and meta-analysis was performed in accordance with the criteria established in the PRISMA 2009 guidelines.¹⁴ It is registered in the

PROSPERO database (National Institute for Health Research) under registration number CRD42015025334.

Selection criteria

The PICO (population, intervention, comparison, and outcomes) method was used to define the research question and to optimize the search strategy¹⁵: (1) Population: only studies on humans with one or more traumatically intruded permanent teeth were included. (2) Intervention: spontaneous re-eruption, orthodontic repositioning, or surgical repositioning of the intruded tooth/teeth were evaluated. (3) Comparison: comparisons between orthodontic and surgical repositioning, between one of the two types of repositioning and no repositioning, and between the two types of repositioning and no repositioning were evaluated. (4) Outcome: root resorption was the primary outcome evaluated, and marginal bone defects and pulpal changes were the secondary outcomes. All studies that evaluated at least one type of periodontal parameter were included.

Search strategy to identify studies

The search strategy was developed for PubMed/MEDLINE and revised for other databases. Search terms were related to the types and populations of the studies (Fig. 1). The searches were performed systematically in April 2015 using the online databases Embase and PubMed/MEDLINE. Studies published in English were selected, without restriction on year of publication. The references of pre-selected articles were also reviewed.

- #1 Search cohort study
- #2 Search prospective study
- #3 Search clinical study
- #4 Search retrospective study
- #5 Search intervention study
- #6 Search observational study
- #7 Search treatment
- #8 Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
- #9 Search intrusive luxation
- #10 Search intrusion
- #11 Search permanent tooth
- #12 Search permanent teeth
- #13 Search #9 OR #10
- #14 Search #11 OR #12
- #15 Search #8 AND #13 AND #14

Fig. 1. Search strategy.

Articles that were not available online were obtained using a bibliographic commutation program (Comut; Programa de Comutação Bibliográfica do Instituto Brasileiro de Informação em Ciência e Tecnologia). The US Clinical Trials (<http://www.clinicaltrials.gov>) and ISRCTN Registry (<http://www.isrctn.com>) websites were searched for unpublished literature (records of clinical trials) using only the term 'dental trauma', because 'intrusion' and 'intrusive luxation' did not present any results.

Two independent reviewers (LAC and LMC) identified and evaluated the titles and abstracts of the articles. When the information in the title and abstract was insufficient, the entire article was read. The two reviewers met to finalize the article selection. When there was disagreement, a third reviewer (CCCR) decided on the article inclusion. The articles included in this review had to report at least 6 months of follow-up.

Evaluation of study quality

The quality of each study was evaluated on the basis of the risk of bias using the criteria recommended in the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0.¹⁵ The following criteria were applied: (1) random sequence generation to form intervention groups; (2) allocation concealment before grouping; (3) blinding of participants and healthcare providers; (4) blinding of the outcome evaluators; (5) incomplete outcome data (i.e., reasons for losses not reported or no corresponding data from the text and tables); (6) selective reporting (i.e., possibility of

establishing a connection between diagnosis, treatment, and outcome); and (7) other biases (mainly related to the study design).

Using these criteria, the articles were classified as having a low risk of bias (improbable that bias directly affected the results) if all criteria were followed, as having a moderate risk of bias (bias leaving some doubt about the validity of the results) if one or more criteria were partially followed and judged as having an indeterminate risk of bias, or as having a high risk of bias (bias that severely weakened the reliability of the results) if one or more criteria were not followed.

The studies covered by this research normally followed some type of protocol for choosing the treatment type according to the degree of intrusion and the degree of root formation, which are important confounding variables. Therefore, a second selection was performed, wherein only studies that reported the primary (periodontal) and/or secondary (bone and pulp) outcomes to treatments and/or the diagnosis (degree of intrusion and degree of root formation) were retained. When the pre-selected studies did not meet these criteria, the corresponding authors were e-mailed for additional information. Papers were excluded if the authors did not reply.

Three reviewers (LAC, LMC, CCCR) independently evaluated the quality of the pre-selected studies, and a kappa test was performed to assess the agreement between the reviewers. Disagreements were resolved by discussion until consensus was reached.

Data extraction

Two reviewers (LAC and LMC), who were not blinded to the title of the journal or the authors, extracted the following data from the articles: the collection period, country of study, sample size, sample characteristics, degree of intrusion, degree of root formation, treatments performed, and outcomes. All data were stored in a Microsoft Excel 2007 spreadsheet.

Summary measures

To compare the presence or absence of periodontal and pulpal outcomes after treatment, risk ratios (RR) with 95% confidence intervals (CI) were used; the standard deviation of each group was also analyzed. A meta-analysis was performed only when the comparison of at least three studies was possible.

Values of $P < 0.05$ were considered significant for all of the analyses

performed. A software program was used for the meta-analysis, as well as to produce the forest plots (Review Manager, RevMan version 5.3; The Nordic Cochrane Centre, Copenhagen, Denmark; The Cochrane Collaboration, 2014).

Risk of bias in the studies

The fixed-effects model was used when there was no statistically significant difference and the random-effects model when there was a statistically significant difference, i.e., a high level of heterogeneity, between trials (this was considered significant at $P < 0.1$). Heterogeneity was assessed using the Q method (χ^2), and the value of I^2 was calculated.¹⁶ The statistical value of I^2 was used to analyze heterogeneity, where I^2 of 50–75% indicated moderate heterogeneity and I^2 above 75% indicated significant heterogeneity.¹⁷

Additional analyses

To analyze the sensitivity of the tests employed, a subgroup analysis to identify any potential causes of heterogeneity was performed. Specifically, subgroup analyses based on the degree of root formation and the degree of intrusion were performed.

Results

The electronic search yielded 294 unique titles. After evaluating all of the titles and abstracts, and reading 17 full articles, seven studies were eligible on the basis of the inclusion criteria.^{5–8,10,18,19} No unpublished study met the eligibility criteria.

A search of the references revealed 16 additional studies of interest that had not been identified in the original search. After searching for and reading the full-texts of these articles, three of them were eligible for inclusion in this review.^{9,20,21} Finally, a total of 10 articles met the inclusion criteria and were included (Fig. 2).

The 10 eligible articles were assessed for their individual quality and risk of bias. After this step, two articles were excluded. The reasons for exclusion are presented in Table 1.

The risk of bias did not influence the exclusion of the articles, but it did affect the interpretation of the data obtained. The kappa test for agreement among the reviewers was 0.84 (95% CI 0.63–1.0).

Characteristics of selected articles

Initially, only five of the 10 eligible articles were included in this review, as they

presented data on the correlations between the treatments and outcomes.^{5,6,8,18,20} The corresponding authors of the remaining studies were contacted by e-mail for additional information, and three authors responded.^{7,10,21} With the additional data provided, these three studies were included in the review, yielding eight articles that appropriately addressed the research questions.^{5–8,10,18,20,21}

The studies included in this review reported 6 months to 5 years of follow-up. The outcomes presented in these studies are reported without establishing relationships with the follow-up period shown.

Table 2 presents the key information from these eight selected articles. Only one study included cases from two centres,⁸ and only one study reported financing using outside funds.⁵

Characteristics of participants

The participants ranged in age from 6 to 67 years. Some patients had more than one tooth that had been traumatically intruded. None of the studies had a control group or employed randomization. In all studies, the patients were allocated to the different interventions based on the clinician's decision.

Intervention characteristics

Two studies did not include orthodontic repositioning among the interventions.^{6,20} One study, whose title indicated that it had only involved surgical repositioning and spontaneous re-eruption, reported having performed a single orthodontic repositioning.¹⁸ One study divided the treatments into surgical and non-surgical procedures, where orthodontic repositioning and re-eruption were grouped together.²¹

Reporting of diagnostic characteristics (degree of intrusion and degree of root formation)

The degree of root formation was reported according to the maturity of the apex, root canal walls, Nolla's classification,²² Moorrees et al.,²³ and Andreasen and Pedersen.⁹ The classification of the degree of root formation varied drastically (Table 2).

Reported outcomes

All of the articles reported the primary outcome (inflammatory or replacement root resorption). Two studies did not report on the secondary outcome of marginal

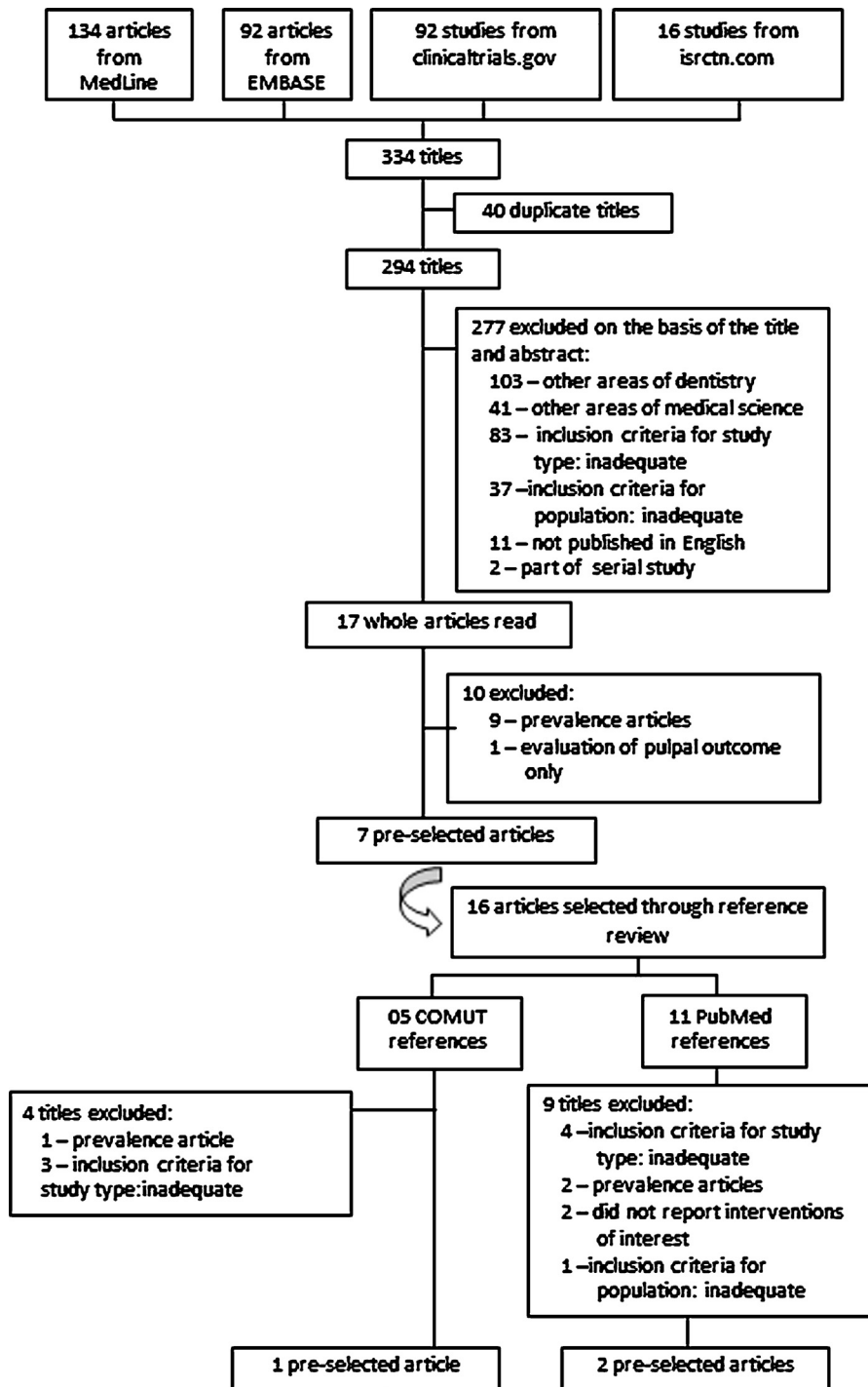


Fig. 2. Flow chart of the screening and selection process.

Table 1. Studies excluded from the analysis.

Studies excluded	Reasons for exclusion
Andreasen and Pedersen, 1985 ⁹	It was not possible to establish a relationship between the outcome and levels of root formation and intrusion, or between the outcome and treatment
Tsilingaridis et al., 2012 ¹⁹	It was possible to establish a relationship between the diagnosis and treatment, but not between these and the outcomes

Table 2. Main characteristics of the selected studies.

Study	Country	n	Age (years), mean (range), or mean \pm SD	Follow-up	Antibiotics	Local disinfection	Post-surgical splint
Kinirons and Sutcliffe, 1991 ²⁰	Northern Ireland	29	9.55 (7–12)	2 years total	NR	NR	Removable splint 4–7 days
Ebeleseder et al., 2000 ¹⁸	Austria	58	11.1 \pm 5.21 (medium-term) 11.7 \pm 4.25 (short-term)	Medium-term group: mean 40 months Short-term group: mean 9 months	Cephalosporin, penicillin, or erythromycin for 8 days	Chlorhexidine mouth rinse 3 times daily for 2 weeks	Held in place with thread and resin for 3–4 weeks
Andreasen et al., 2006 ⁵	Denmark	140	8 \pm 11.41 6–11, n = 73 12–17, n = 30 18–67, n = 37	\geq 1 year	1 g penicillin immediately and 500 mg 4 times daily for 4 days	NR	Rigid, semi-rigid, or flexible for 6–8 weeks
Wigen et al., 2008 ⁸	Norway	51	6–11, 45 teeth 12–17, 6 teeth	Mean 4 years, range 1–12 years	Penicillin prescribed to 15 patients (from table) and nine patients (from text)	0.1% chlorhexidine mouth rinse 2 \times daily	Held in place with wire and resin for 2–6 weeks
Moreira Neto et al., 2009 ⁶	Brazil	15	8.9 (7–14.8)	Minimum 6 months, mean 26.6 months	NR	NR	NR
Stewart et al., 2009 ⁷	Ireland	55	9.3 \pm 1.99	2.3 \pm 1.6 years	21 patients, posology NR	NR	NR
Al-Badri et al., 2002 ²¹	Northern Ireland and North East England	61	9.3 \pm 1.94	Mean 2.9 years	NR	NR	NR
Humphrey et al., 2003 ¹⁰	Canada	31	9.3 \pm 2.7	Minimum 6 months, mean 26.6 months	Penicillin (50 mg/kg) prescribed to all patients for 7 days	0.1% chlorhexidine gluconate mouth rinse	Passive non-rigid splint of 0.014 or 0.016 inch stainless steel orthodontic wire
Study	Losses	Treatment time	Degree of intrusion	Classification of root development	Treatment	Correlation possible	
Kinirons and Sutcliffe, 1991 ²⁰	9 teeth: 6 SRE, 3 SRP	SRE: NR SRP: >24 h, 9 teeth; <24 h, 10 teeth	<4 mm: 14 teeth \geq 5 mm: 15 teeth	Root canal and apex features	SRE: 10 teeth SRP: 19 teeth	Outcome/treatment	
Ebeleseder et al., 2000 ¹⁸	2 teeth in medium-term and 1 tooth in short- term follow-up; due to epithelial invagination (1), longitudinal fracture (1), a new trauma (1)	Emergency	1–2 mm: 12 teeth 3–4 mm: 15 teeth 5–mm: 14 teeth >9 mm: 16 teeth NR: 1 tooth	Root, root canal, and apex features	SRE: 9 teeth SRP: 48 teeth ORP: 1 tooth	Outcome/degree of intrusion; outcome/degree of root formation; outcome/treatment	
Andreasen et al., 2006 ⁵	28 teeth: by root resorption (17), spontaneous root fracture after endodontic treatment (4), due to poor prognosis (7)	\leq 24 h: 58 teeth \geq 24 h: 11 teeth SRE: 38 teeth NR: 33 teeth	1–3 mm: 30 teeth 4–5 mm: 54 teeth 6–7 mm: 24 teeth 8–9 mm: 18 teeth 10–16 mm: 14 teeth	Root and apex features	SRE: 38 teeth ORP: 29 teeth SRP: 73 teeth	Degree of intrusion/ treatment/outcome; degree of root formation/ treatment/outcome	

Table 2 (Continued)

Study	Losses	Treatment time	Degree of intrusion	Classification of root development	Treatment	Correlation possible
Wigen et al., 2008 ⁸	7 teeth: due to ankylosis (2), immature teeth with necrotic pulp (4), extracted for orthodontic reasons (1)	NR	Incisor almost invisible; 21 teeth >2 mm; 22 teeth <2 mm; 8 teeth	Root and apex features	SRE: 37 teeth ORP: 7 teeth SRP: 7 teeth	Outcome/degree of intrusion; outcome/degree of root formation; Outcome/treatment
Moreira Neto et al., 2009 ⁶	2 teeth: due to inflammatory root resorption (1), replacement root resorption (1)	NR	All >6 mm	Nolla's classification	SRE: 5 teeth SRP: 10 teeth	Degree of intrusion/degree of root formation/treatment/outcome
Stewart et al., 2009 ⁷	5 teeth: 1 tooth SRE, with incomplete apex; 4 teeth ORP with incomplete apex	NR	<3 mm: 4 teeth 3–6 mm: 10 teeth >6 mm: 11 teeth NR: 30 teeth	Root and apex features	SRE: 19 teeth ORP: 22 teeth SRP: 14 teeth	Degree of root formation/treatment/outcome
Al-Badri et al., 2002 ²¹	13 teeth: submitted treatment NR	NR	0–2 mm: 7 teeth 3–5 mm: 27 teeth >5 mm: 27 teeth	According to apex features	SRP: 35 teeth NSRP: 26 teeth	Degree of root formation/treatment/outcome
Humphrey et al., 2003 ¹⁰	5 teeth: reasons NR	NR	<3 mm: 8 teeth 3–6 mm: 12 teeth >6 mm: 11 teeth	Root and apex features	SRE: 11 teeth ORP: 6 teeth SRP: 14 teeth	Degree of intrusion/degree of root formation/treatment/outcome

NR, not reported; NSRP, no surgical repositioning (spontaneous re-eruption or orthodontic repositioning); ORP, orthodontic repositioning; SRE, spontaneous re-eruption; SRP, surgical repositioning.

bone defects.^{8,21} Seven studies reported on the secondary outcome of pulpal changes^{5–8,10,18,20}; however one of them did not provide sufficient information for this outcome.²⁰ Table 3 presents the outcomes according to the diagnosis and treatment reported in the selected articles.

Risk of bias

All of the studies were considered to have a high risk of bias based on the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0¹⁵ (Table 4).

Meta-analysis results

All of the included articles were considered for meta-analysis. However, statistical analysis required a similar approach for categorizing the degree of intrusion, degree of root formation, and the treatment performed. Therefore, the two types of root resorption (inflammatory root resorption and replacement root resorption) were grouped to perform the meta-analysis. The articles that reported these two types of root resorption without specifying whether the affected tooth suffered both were excluded from this analysis. The inclusion of these articles could have interfered with the results, as these teeth could have been counted twice thereby overestimating the results.^{24,25}

Treatment vs. outcome—primary outcome

The primary outcome was analyzed to identify the treatment with the better prognosis for the periodontal effect (root resorption). This analysis could only be performed with surgical repositioning and spontaneous re-eruption.

The results from four articles were analyzed, and no significant difference was observed (RR 1.30, 95% CI 0.90–1.88; *P* = 0.16).^{5–7,20} The χ^2 for heterogeneity was 2.68 (*P* = 0.44; *I*² = 0%) (Fig. 3).

Secondary outcomes

The secondary outcomes were analyzed to identify the treatment with the better prognosis for bone and pulpal effects (marginal bone defects and pulpal changes). The analyses included surgical repositioning vs. spontaneous re-eruption, orthodontic repositioning vs. spontaneous re-eruption, and surgical repositioning vs. orthodontic repositioning.

Five studies were included in the analysis of surgical repositioning vs. spontaneous re-eruption with regard to marginal

Table 3. Outcomes related to diagnoses and/or treatment.

Study		Outcome			
Kinirons and Sutcliffe, 1991 ²⁰	Treatment	Inflammatory root resorption, number of teeth (%) SRE: 4/10 (40%) SRP: 7/19 (36.8%)	Replacement root resorption, number of teeth (%) NR	Marginal bone defects, number of teeth (%) SRE: 5/10 (50%) SRP: 2/19 (10.5%)	Pulpal changes, number of teeth (%) NR
	Diagnosis	Inflammatory root resorption, number of teeth (%) NR	Replacement root resorption, number of teeth (%) Degree of intrusion: 1–2 mm: 0/12 (0%) 3–4 mm: 4/15 (26.7%) 5–9 mm: 5/14 (35.7%) >9 mm: 5/16 (31.2%) Degree of root formation: Incomplete: 11/48 (22.9%) Complete: 3/10 (30%)	Marginal bone defects, number of teeth (%) Degree of intrusion: 1–2 mm: 1/12 (8.3%) 3–4 mm: 6/15 (40%) 5–9 mm: 5/14 (35.7%) >9 mm: 8/16 (50%) Degree of root formation: Incomplete: 13/48 (27.1%) Complete: 7/10 (70%)	Pulpal changes, number of teeth (%) Degree of intrusion: 1–2 mm: 4/12 (33.3%) 3–4 mm: 9/15 (60%) 5–9 mm: 12/14 (85.7%) >9 mm: 11/16 (68.7%) Degree of root formation: Incomplete: 29/48 (60.4%) Complete: 7/10 (70%)
Ebeleseder et al., 2000 ¹⁸	Treatment	NR	ORP + SRE: 0/10 (0%) SRP: 14/48 (29.2%)	ORP + SRE: 2/10 (20%) SRP: 18/48 (37.5%)	ORP + SRE: 4/10 (40%) SRP: 32/48 (66.7%)
	Diagnosis and treatment	Inflammatory root resorption, number of teeth (%)	Root resorption (inflammatory + replacement), number of teeth (%) Degree of intrusion: ≤3 mm: SRE: 3/12 (25%) ORP: 2/7 (28.6%) SRP: 3/11 (27.3%) >3 and ≤7 mm: SRE: 7/21 (33.3%) ORP: 6/14 (42.8%) SRP: 27/43 (62.8%) >7 mm: SRE: 3/5 (60%) ORP: 5/8 (62.5%) SRP: 11/19 (57.9%) Root formation: Incomplete: SRE: 10/28 (35.7%) ORP: 4/8 (50%) SRP: 4/7 (57.1%) Complete: SRE: 3/10 (30%) ORP: 9/21 (42.8%) SRP: 37/66 (56.1%)	Marginal bone defects, number of teeth (%) Degree of intrusion: ≤3 mm: SRE: 0/12 (0%) ORP: 2/7 (28.6%) SRP: 5/11 (45.4%) >3 to ≤7 mm: SRE: 0/21 (0.0%) ORP: 5/14 (35.7%) SRP: 19/43 (44.2%) >7 mm: SRE: 0/5 (0%) ORP: 2/8 (25%) SRP: 12/19 (63.1%) Root formation: Incomplete: SRE: 0/28 (0%) ORP: 1/8 (12.5%) SRP: 1/7 (14.3%) Complete: SRE: 0/10 (0%) ORP: 8/70 ^b (11.4%) SRP: 35/66 (53.0%)	Pulpal changes, number of teeth (%) Degree of intrusion: ≤3 mm: SRE: 8/12 (66.7%) ORP: 6/7 (85.7%) SRP: 11/11 (100%) >3 to ≤7 mm: SRE: 16/21 (76.2%) ORP: 13/14 (92.8%) SRP: 39/43 (90.7%) >7 mm: SRE: 5/5 (100%) ORP: 8/8 (100%) SRP: 18/19 (94.7%) Root formation: Incomplete: SRE: 20/28 (71.4%) ORP: 6/9 ^b (66.7%) SRP: 3/7 (42.8%) Complete: SRE: 9/10 (90%) ORP: 21/21 (100%) SRP: 65/66 (98.5%)
Andreasen et al., 2006 ⁵	Diagnosis and treatment	Inflammatory root resorption, number of teeth (%)	Replacement root resorption, number of teeth (%)	Marginal bone defects, number of teeth (%)	Pulpal changes, number of teeth (%)

Table 3 (Continued)

Study		Outcome			
Wigen et al., 2008 ⁸	Diagnosis	Root formation: Immature: 6/31 (19.3%) Mature: 7/20 (35%) Degree of intrusion: Complete: 6/21 (28.6%) Partial: 23/30 (76.7%)	Root formation: Immature: 2/31 (6.4%) Mature: 4/20 (20%) Degree of intrusion: Complete: 5/21 (23.8%) Partial: 1/30 (3.3%)	NR	Root formation: Immature: 14/31 (45.2%) Mature: 15/20 (75%) Degree of intrusion: Complete: 15/21 (71.4%) Partial: 14/30 (46.7%)
	Treatment	SRE: 7/37 (18.9%) ORP: 4/7 (57.1%) SRP: 2/7 (28.6%)	SRE: 2/37 (5.4%) ORP: 2/7 (28.6%) SRP: 2/7 (28.6%)	NR	SRE: 18/37 (48.6%) ORP: 6/7 (85.7%) SRP: 5/7 (71.4%)
Moreira Neto et al., 2009 ⁶	Diagnosis + treatment	Inflammatory root resorption, number of teeth (%) Degree of intrusion >6 mm Incomplete root formation (<i>n</i> = 7): SRE: 1/3 (33.3%) SRP: 0/4 (0%) Complete root formation (<i>n</i> = 8): SRE: 1/2 (50%) SRP: 4/6 (66.7%)	Replacement root resorption, number of teeth (%) Degree of intrusion >6 mm Incomplete root formation (<i>n</i> = 7): SRE: 0/3 (0%) SRP: 0/4 (0%) Complete root formation (<i>n</i> = 8): SRE: 0/2 (0%) SRP: 3/6 (50%)	Marginal bone defects, number of teeth (%) Degree of intrusion >6 mm Incomplete root formation (<i>n</i> = 7): SRE: 1/3 (33.3%) SRP: 2/4 (50%) Complete root formation (<i>n</i> = 8): SRE: 0/2 (0%) SRP: 6/6 (100%)	Pulpal changes, number of teeth (%) Degree of intrusion >6 mm Incomplete root formation (<i>n</i> = 7): SRE: 3/3 (100%) SRP: 4/4 (100%) Complete root formation (<i>n</i> = 8): SRE: 2/2 (100%) SRP: 6/6 (100%)
		Root resorption, number of teeth (%) Apex incomplete (<i>n</i> = 34): SRE: 4/16 (25%) ORP: 4/15 (26.7%) SRP: 1/3 (33.3%) Apex complete (<i>n</i> = 21): SRE: 2/3 (66.7%) ORP: 3/7 (42.8%) SRP: 3/11 (27.3%)		Marginal bone defects, number of teeth (%) Apex incomplete (<i>n</i> = 34): SRE: 1/16 (6.2%) ORP: 6/15 (40%) SRP: 0/3 (0%) Apex complete (<i>n</i> = 21): SRE: 0/3 (0%) ORP: 2/7 (28.6%) SRP: 1/11 (9.1%)	Pulpal changes, number of teeth (%) Apex incomplete (<i>n</i> = 34): SRE: 4/16 (25%) ORP: 6/15 (40%) SRP: 1/3 (33.3%) Apex complete (<i>n</i> = 21): SRE: 2/3 (66.7%) ORP: 5/7 (71.4%) SRP: 7/11 (63.6%)
Al-Badri et al., 2002 ^{21 a}	Diagnosis (root formation) + treatment	Root resorption, number of teeth (%) Apex divergent (<i>n</i> = 23): SRE + ORP: 7/18 (38.9%) SRP: 1/5 (20%) Apex parallel (<i>n</i> = 10): NR Apex closed (<i>n</i> = 28): SRE + ORP: 4/4 (100%) SRP: 20/24 (83.3%)		Marginal bone defects, number of teeth (%) NR	Pulpal changes, number of teeth (%) NR
		Inflammatory root resorption, number of teeth (%)	Replacement root resorption, number of teeth (%)	Marginal bone defects, number of teeth (%)	Pulpal changes, number of teeth (%)

Table 3 (Continued)

Study	Diagnosis + treatment	Outcome										
		Degree of intrusion <3 mm Immature apex (n = 6): SRE: 2/4 (50%) ORP: 1/1 (100%) SRP: 1/1 (100%) Mature apex (n = 2): SRE: 0/0 (0%) ORP: 0/0 (0%) SRP: 2/2 (100%)	Degree of intrusion 3–6 mm Immature apex (n = 7): SRE: 2/3 (66.7%) ORP: 1/2 (50%) SRP: 2/2 (100%) Mature apex (n = 5): SRE: 3/3 (100%) ORP: 1/1 (100%) SRP: 1/1 (100%)	Degree of intrusion >6 mm Immature apex (n = 4): SRE: 1/1 (100%) ORP: 0/0 (0%) SRP: 3/3 (100%) Mature apex (n = 7): SRE: 0/0 (0%) ORP: 2/2 (100%) SRP: 2/5 (40%)	Degree of intrusion <3 mm Immature apex (n = 6): SRE: 0/4 (0%) ORP: 0/1 (0%) SRP: 1/1 (100%) Mature apex (n = 2): SRE: 0/0 (0%) ORP: 0/0 (0%) SRP: 0/2 (0%)	Degree of intrusion 3–6 mm Immature apex (n = 7): SRE: 0/3 (0%) ORP: 2/2 (100%) SRP: 0/2 (0%) Mature apex (n = 5): SRE: 0/3 (0%) ORP: 0/1 (0%) SRP: 0/1 (0%)	Degree of intrusion >6 mm Immature apex (n = 4): SRE: 1/1 (100%) ORP: 0/0 (0%) SRP: 0/3 (0%) Mature apex (n = 7): SRE: 0/0 (0%) ORP: 2/2 (100%) SRP: 1/5 (20%)	Degree of intrusion <3 mm Immature apex (n = 6): SRE: 1/4 (25.0%) ORP: 1/1 (100%) SRP: 1/1 (100%) Mature apex (n = 2): SRE: 0/0 (0%) ORP: 0/0 (0%) SRP: 1/2 (50%)	Degree of intrusion 3–6 mm Immature apex (n = 7): SRE: 0/3 (0%) ORP: 2/2 (100%) SRP: 1/2 (50%) Mature apex (n = 5): SRE: 2/3 (66.7%) ORP: 1/1 (100%) SRP: 0/1 (0%)	Degree of intrusion >6 mm Immature apex (n = 4): SRE: 0/1 (0%) ORP: 0/0 (0%) SRP: 3/3 (100%) Mature apex (n = 7): SRE: 0/0 (0%) ORP: 0/2 (0%) SRP: 3/5 (60%)	Degree of intrusion <3 mm Immature apex (n = 6): SRE: 1/4 (25.0%) ORP: 1/1 (100%) SRP: 1/1 (100%) Mature apex (n = 2): SRE: 0/0 (0%) ORP: 0/0 (0%) SRP: 1/2 (50%)	Degree of intrusion 3–6 mm Immature apex (n = 7): SRE: 0/3 (0%) ORP: 2/2 (100%) SRP: 1/2 (50%) Mature apex (n = 5): SRE: 2/3 (66.7%) ORP: 1/1 (100%) SRP: 0/1 (0%)
Humphrey et al., 2003 ^{10 a}												

NR, not reported; ORP, orthodontic repositioning; SRE, spontaneous re-eruption; SRP, surgical repositioning.

^aInformation provided by the authors.

^bInformation published in Table 6 of the referenced article.

bone defects.^{5–7,10,20} A significant difference favouring spontaneous re-eruption was observed (RR 3.15, 95% CI 1.68–5.89; $P = 0.0003$), with significant heterogeneity. The χ^2 for heterogeneity was 17.52 ($P = 0.002$; $I^2 = 77%$) (Fig. 4A).

Three studies were included in the analysis of orthodontic repositioning vs. spontaneous re-eruption with regard to marginal bone defects.^{5,7,10} A significant difference favouring spontaneous re-eruption was observed (RR 0.19, 95% CI 0.06–0.54; $P = 0.002$), with moderate heterogeneity. The χ^2 for heterogeneity was 5.59 ($P = 0.06$; $I^2 = 64%$) (Fig. 4B).

Three studies were included in the analysis of surgical repositioning vs. orthodontic repositioning with regard to marginal bone defects.^{5,7,10} No significant difference was observed (RR 1.29, 95% CI 0.77–2.16; $P = 0.33$). The heterogeneity was moderate. The χ^2 for heterogeneity was 5.07 ($P = 0.08$; $I^2 = 61%$) (Fig. 4C).

Five studies were included in the analysis of surgical repositioning vs. spontaneous re-eruption with regard to pulpal changes.^{5–8,10} A significant difference favouring spontaneous re-eruption was observed (RR 1.35, 95% CI 1.14–1.60; $P = 0.0005$), with moderate heterogeneity. The χ^2 for heterogeneity was 8.19 ($P = 0.08$; $I^2 = 51%$) (Fig. 5A).

Four studies were included in the analysis of orthodontic repositioning vs. spontaneous re-eruption with regard to pulpal changes.^{5,7,8,10} A significant difference favouring spontaneous re-eruption was observed (RR 0.69, 95% CI 0.56–0.84; $P = 0.0003$). The χ^2 for heterogeneity was 5.55 ($P = 0.14$; $I^2 = 46%$) (Fig. 5B).

Four studies were included in the analysis of surgical repositioning vs. orthodontic repositioning with regard to pulpal changes.^{5,7,8,10} No significant difference was observed (RR 0.99, 95% CI 0.87–1.13; $P = 0.87$). The χ^2 for heterogeneity was 1.00 ($P = 0.80$; $I^2 = 0%$) (Fig. 5C).

Subgroup analyses

Subgroups analyses were performed considering the confounding variable of ‘degree of root formation’ only for surgical repositioning vs. spontaneous re-eruption. An analysis that considered the degree of intrusion could not be performed.

Four studies were included in the analysis of incomplete root formation vs. complete root formation with regard to root resorption.^{5,6,18,21} Teeth with complete root formation suffered significantly more root resorption than teeth with incomplete root formation (RR 0.40, 95% CI 0.18–0.90; $P = 0.03$). Heterogeneity was

Table 4. Summary of the risk of bias for the studies selected.

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Kinirons and Sutcliffe, 1991 ²⁰	High	High	High	High	High	Moderate	High
Ebeleseder et al., 2000 ¹⁸	High	High	High	High	Low	Moderate	High
Andreasen et al., 2006 ⁵	High	High	High	High	High	Moderate	High
Wigen et al., 2008 ⁸	High	High	High	High	Moderate	Moderate	High
Moreira Neto et al., 2009 ⁶	High	High	High	High	High	Low	High
Stewart et al., 2009 ⁷	High	High	High	Moderate	High	High	High
Al-Badri et al., 2002 ²¹	High	High	High	High	High	Moderate	High
Humphrey et al., 2003 ¹⁰	High	High	High	High	Low	High	High

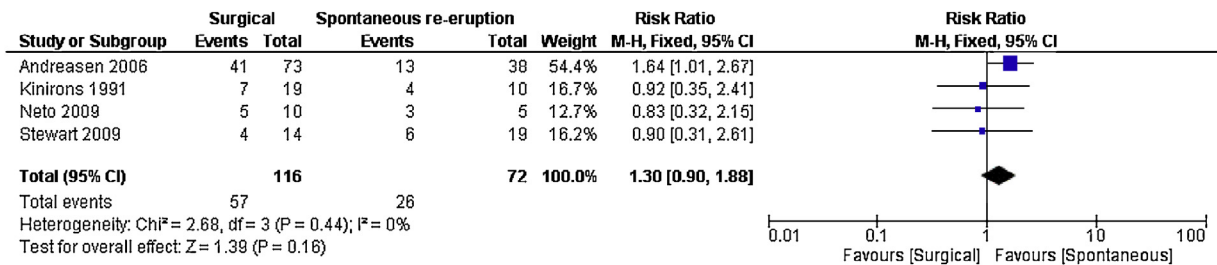


Fig. 3. Forest plot for the comparison of surgical repositioning vs. spontaneous re-eruption with regard to the outcome 'root resorption'.

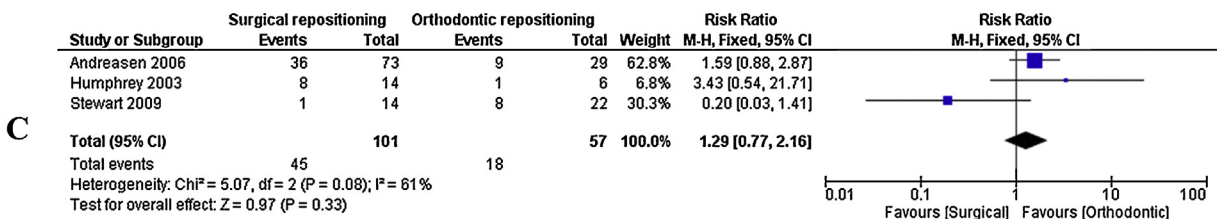
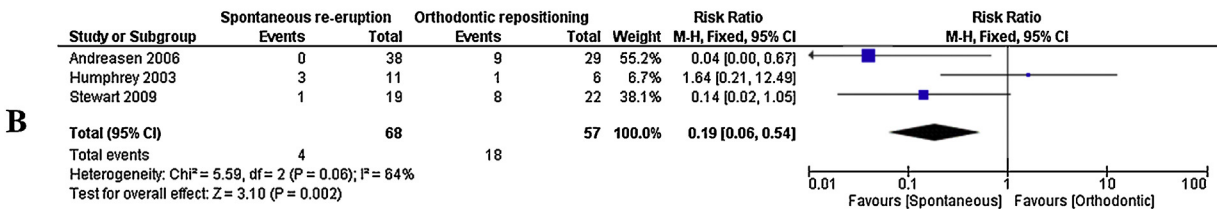
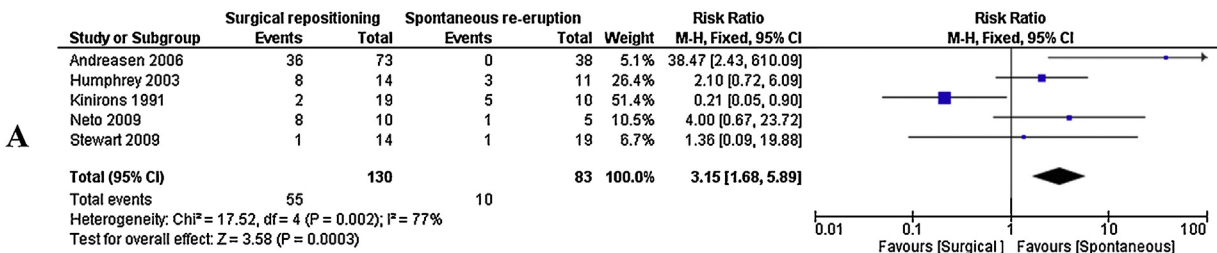


Fig. 4. Forest plots for the comparison of repositioning methods with regard to the outcome 'marginal bone defects': (A) surgical repositioning vs. spontaneous re-eruption; (B) orthodontic repositioning vs. spontaneous re-eruption; (C) surgical repositioning vs. orthodontic repositioning.

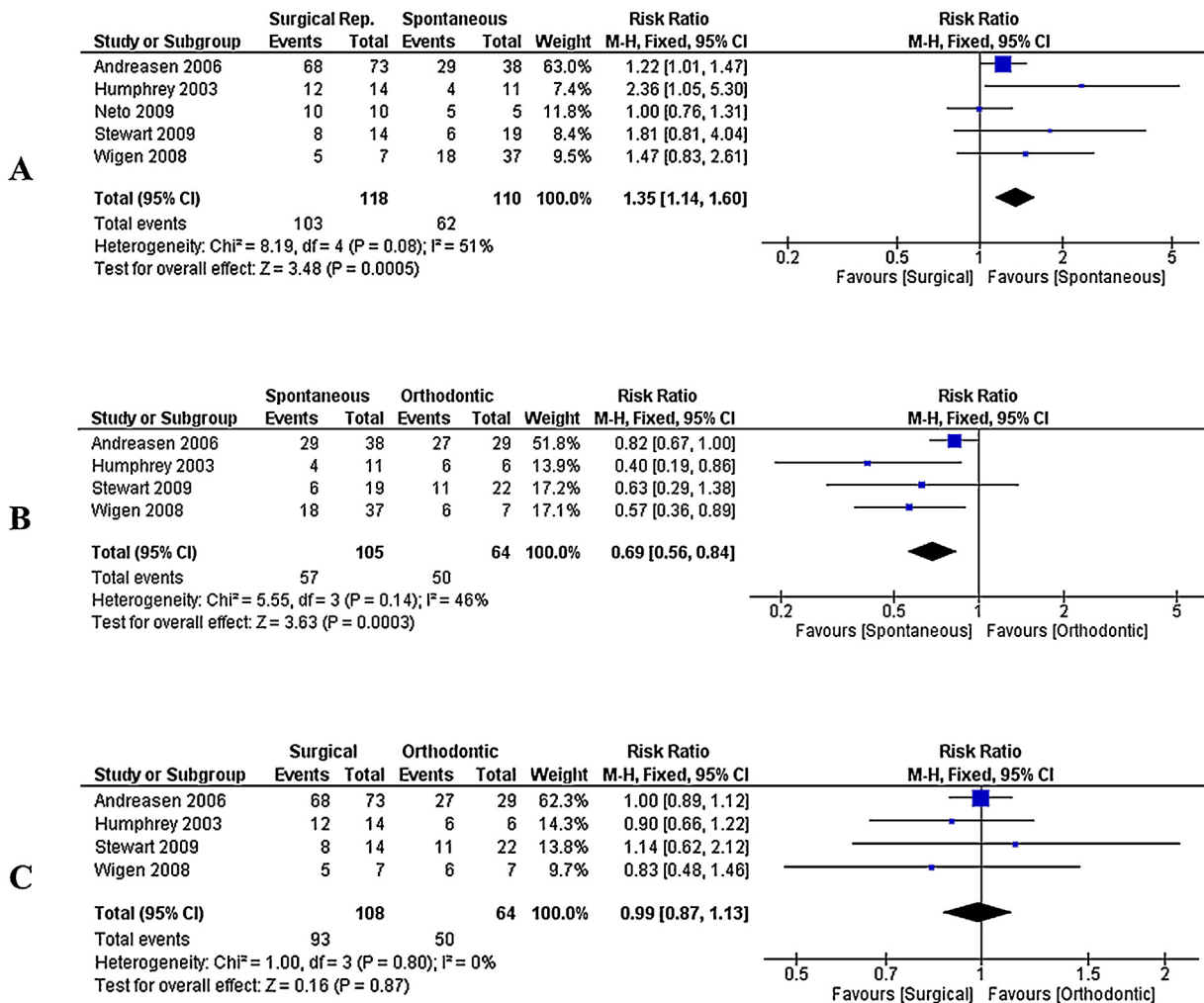


Fig. 5. Forest plots for the comparison of repositioning methods with regard to the outcome ‘pulpal changes’: (A) surgical repositioning vs. spontaneous re-eruption; (B) orthodontic repositioning vs. spontaneous re-eruption; (C) surgical repositioning vs. orthodontic repositioning.

moderate. The χ^2 for heterogeneity was 9.75 ($P = 0.02$; $I^2 = 69\%$) (Fig. 6A).

Four studies were included in the analysis of incomplete root formation vs. complete root formation with regard to marginal bone defects.^{5,6,10,18} No significant difference was observed (RR 0.78, 95% CI 0.57–1.05; $P = 0.10$). Heterogeneity was moderate. The χ^2 for heterogeneity was 5.80 ($P = 0.12$; $I^2 = 48\%$) (Fig. 6B).

Five studies were included in the analysis of incomplete root formation vs. complete root formation with regard to pulpal changes.^{5,6,8,10,18} Teeth with complete root formation suffered significantly more pulpal changes than teeth with incomplete root formation (RR 0.76, 95% CI 0.63–0.92; $P = 0.004$). Heterogeneity was moderate. The χ^2 for heterogeneity was 5.78 ($P = 0.22$; $I^2 = 31\%$) (Fig. 6C).

The degree of root formation + treatment (surgical repositioning and spontaneous re-eruption) was analyzed with regard to the outcomes. It was not possible

to compare the treatments in teeth with incomplete root formation for the outcome ‘root resorption’.

Three studies were included in the analysis of incomplete root formation + surgical repositioning vs. spontaneous re-eruption with regard to marginal bone defects.^{5,6,10} A significant difference favouring spontaneous re-eruption was observed (RR 4.88, 95% CI 1.49–15.95; $P = 0.009$). The χ^2 for heterogeneity was 0.72 ($P = 0.70$; $I^2 = 0\%$) (Fig. 7A).

Three studies were included in the analysis of incomplete root formation + surgical repositioning vs. spontaneous re-eruption with regard to pulpal changes.^{5,6,10} A significant difference favouring spontaneous re-eruption was observed (RR 1.69, 95% CI 1.10–2.60; $P = 0.02$), with significant heterogeneity. The χ^2 for heterogeneity was 10.26 ($P = 0.006$; $I^2 = 81\%$) (Fig. 7B).

Three studies were included in the analysis of complete root formation + surgical

repositioning vs. spontaneous re-eruption with regard to root resorption.^{5,6,21} No significant difference was observed (RR 1.24, 95% CI 0.78–1.97; $P = 0.36$). The heterogeneity was moderate. The χ^2 for heterogeneity was 4.24 ($P = 0.12$; $I^2 = 53\%$) (Fig. 8A).

Three studies were included in the analysis of complete root formation + surgical repositioning vs. spontaneous re-eruption with regard to marginal bone defects.^{5,6,10} No significant difference was observed (RR 3.15, 95% CI 1.02–9.79; $P = 0.05$), with significant heterogeneity. The χ^2 for heterogeneity was 8.82 ($P = 0.01$; $I^2 = 77\%$) (Fig. 8B).

Three studies were included in the analysis of complete root formation + surgical repositioning vs. spontaneous re-eruption with regard to pulpal changes.^{5,6,10} No significant difference was observed (RR 1.12, 95% CI 0.90–1.39; $P = 0.33$). The χ^2 for heterogeneity was 0.24 ($P = 0.89$; $I^2 = 0\%$) (Fig. 8C).

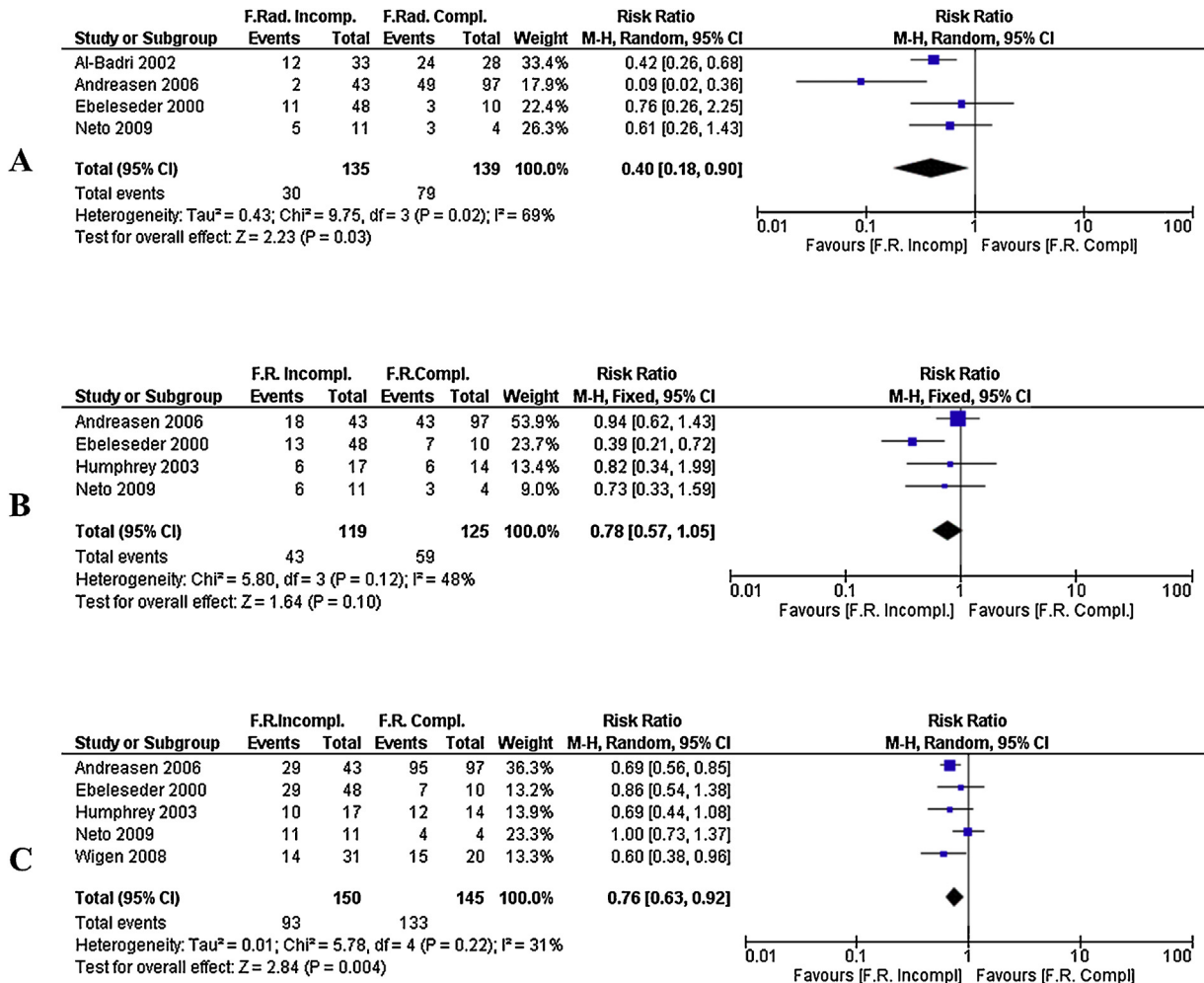


Fig. 6. Forest plots for the comparison of the degree of root formation with the outcomes (A) root resorption, (B) marginal bone defects, and (C) pulpal changes.

A summary of the meta-analysis results can be seen in Table 5.

Discussion

Spontaneous re-eruption appears to have the best prognosis in comparison to active repositioning (orthodontic and surgical repositioning) for marginal bone defects and pulpal changes. The degree of root formation may be an important characteristic to consider, as the subgroup analysis revealed a better prognosis for incomplete root formation for all outcomes compared with complete root formation.

The subgroup analysis did not show differences between the treatments performed when the roots were completely formed. Overall, these results need to be evaluated with caution because of the high heterogeneity that accompanied most of the analyses and the high risk of bias of the individual studies, which weakens

confidence in the results. Moreover, no clinical trials were identified in this research and all of the articles included were case series, a design that limits the weight of the evidence because of the lack of blinding, randomization, and a control group.

There was no significant difference between surgical repositioning and spontaneous re-eruption for the primary outcome of root resorption, possibly because the degree of root formation was not considered in this analysis. However, for the secondary outcomes of marginal bone loss and pulp necrosis, spontaneous re-eruption yielded a significantly better prognosis in comparison with orthodontic repositioning and surgical repositioning.

These findings could be explained by the traction force applied by orthodontic or surgical methods, which could lead to additional damage to traumatically intruded teeth and may disrupt the remaining

periodontal ligament¹⁸ and apical neurovascular bundle that has already been damaged by crushing.¹⁰ This may cause healing complications,⁴ whereas spontaneous re-eruption would be a more physiological way for the tooth to return to its position.

However, these results should be evaluated carefully because this analysis did not take into account the degree of root formation and intrusion, two important confounding variables that could impact the treatment outcomes.^{6,10}

Teeth with incomplete root formation submitted to spontaneous re-eruption were associated with better secondary outcomes than teeth treated with surgical repositioning. This result may be explained by the presence of incompletely formed teeth in the analysis, as a subgroup analysis performed only with teeth with complete root formation did not yield differences between the treatments for any of the

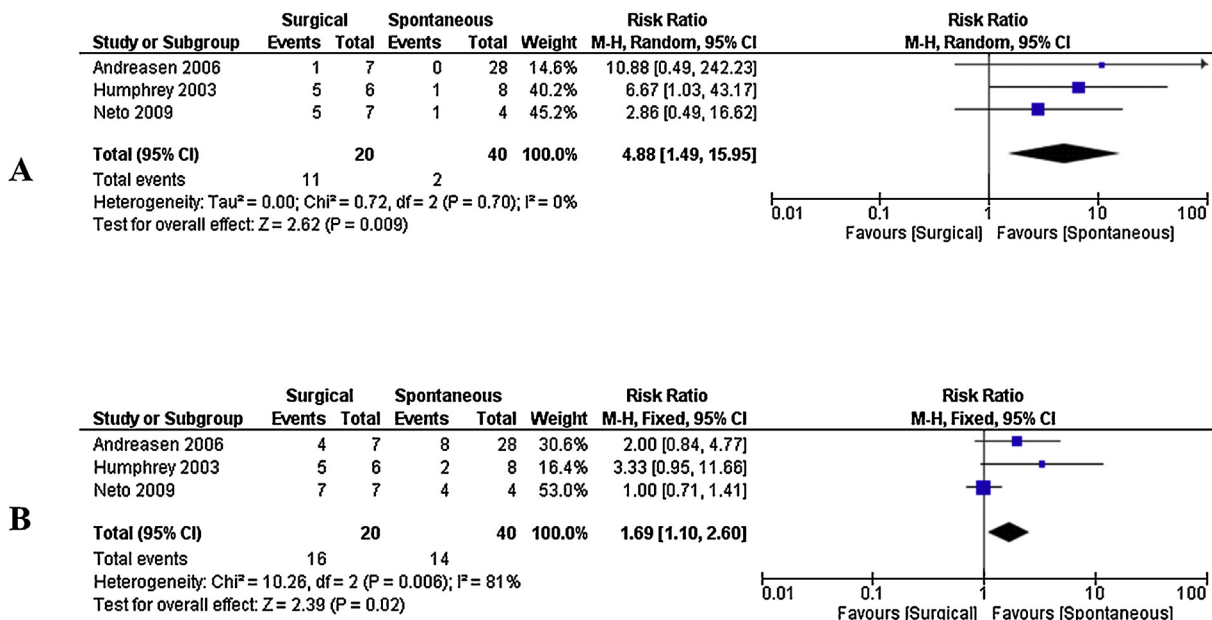


Fig. 7. Forest plots for the comparison of the degree of root formation and repositioning methods (incomplete root formation + surgical repositioning vs. spontaneous re-eruption) for the outcomes (A) marginal bone defects, and (B) pulpal changes.

outcomes evaluated. The better prognosis associated with re-eruption and the recovery of teeth with incompletely formed roots has been observed previously.^{4,9,18,26,27}

The present results suggest that the degree of root formation is essential for the treatment prognosis. Moreover, future studies that aim to compare these treatment choices should divide their analysis into two categories—teeth with complete root formation and teeth with incomplete root formation—as this is a variable that directly impacts the outcomes in an independent way. The clinician needs to assume the degree of root formation as a predictor for treatment success and consider it when making treatment decisions.

The findings of this research suggest that the prognosis is defined at the moment of the accident based on the aspects of the tooth before trauma, as proposed by Andreasen and Pedersen.⁹ The results observed in this review also suggest that spontaneous re-eruption is the superior treatment in cases of incomplete root formation, as these teeth exhibited the best prognosis.

A higher degree of intrusion was observed to be associated with a more severe injury, due to the higher compression and ischaemia of the periodontal ligament, which may increase the chance of root resorption.^{10,21} Thus, the degree of intrusion appears to be another variable that could be considered in defining the prognosis. However, it was not possible to include this variable in the present

meta-analysis due to the lack of standardization among the studies in categorizing the degree of intrusion.

Clinical trials investigating dental trauma are unlikely to have the level of blinding that is recommended by Cochrane (patient and dentist). Therefore, it becomes difficult to determine the extent to which the lack of blinding influences the results already obtained for this type of experiment. However, it is possible to blind the investigator analysing the radiographs, but this was not done in any of the studies included and, thus, can be considered an important source of bias.¹⁵

Additionally, the studies were not randomized, which can introduce a serious selection bias that produces unevenness in the prognostic factors.¹⁵ In the studies included in this review, patients were allocated to the different treatment groups according to a pre-established protocol^{6–8,20,21} that took into account the degree of intrusion and root formation,^{5,10,18} which are two important confounding variables.¹⁰ Randomization is difficult to perform in dental trauma studies due to its low incidence, emergency nature, and the fact that it requires a multi-professional treatment approach in many cases.^{21,28} The absence of randomization in these studies elicits other problems. The protocols differed not only from one study to another, but also, and without explanation, within the same study, where a treatment group that should have been homogeneous was not.

Furthermore, the lack of standardization in the use of antibiotic therapy, type of

post-surgical splint, local disinfection, and the timing of orthodontic repositioning (immediate or late) may have significantly interfered with the results, which makes a comparison of the articles difficult. Moreover, most articles did not explain their losses, which increases the risk of reporting bias. Still, there were observable differences between the numbers presented in the text and in the tables and difficulties in establishing a relationship between the diagnoses (the degree of intrusion and root formation), treatments, and outcomes. These discrepancies and difficulties resulted in the exclusion of two of the pre-selected articles.^{9,19}

Unfortunately, the poor quality of the studies included is not a finding unique to this review. As early as 1985, Andreasen and Andreasen reported concerns regarding the quality of studies on dental trauma.²⁹ In 2010, a new study by Andreasen et al. also reported this concern.³⁰ Two systematic reviews published in 2013 and 2014 also highlighted this problem.^{12,28}

This systematic review and meta-analysis is important because intrusive luxation, although rare, has consequences that often lead to dental loss. However, the limitations of this research include the search method (only electronic) and language (only publications in English were included).

In conclusion, based on the methodology applied, the available evidence does not allow us to definitively identify the best treatment for traumatically intruded teeth. More reliable evidence, with a minimal

Table 5. Summary of meta-analysis results.

Comparison	Outcomes	Spontaneous re-eruption	Surgical repositioning	Orthodontic repositioning	Incomplete root formation	Complete root formation
Outcomes vs. treatments	Root resorption	Not different	Not different			
	Marginal bone defects	Better prognosis ^b	Worse prognosis ^b			
	Marginal bone defects	Better prognosis ^a		Worse prognosis ^a		
	Marginal bone defects		Not different ^a	Not different ^a		
	Pulpal changes	Better prognosis ^a	Worse prognosis ^a			
	Pulpal changes	Better prognosis		Worse prognosis		
	Pulpal changes		Not different	Not different		
Outcomes vs. degree of root formation	Root resorption				Better prognosis ^a	Worse prognosis ^a
	Marginal bone defects				Not different ^a	Not different ^a
	Pulpal changes				Better prognosis ^a	Worse prognosis ^a
Incomplete root formation + treatment vs. outcomes	Marginal bone defects	Better prognosis	Worse prognosis			
	Pulpal changes	Better prognosis ^b	Worse prognosis ^b			
Complete root formation + treatment vs. outcomes	Root resorption	Not different ^a	Not different ^a			
	Marginal bone defects	Not different ^b	Not different ^b			
	Pulpal changes	Not different	Not different			

Notes: Shaded cells correspond to the characteristics (treatment or degree of root formation) compared. Treatments were considered better or worse only when a statistically significant difference was found ($P < 0.05$); statistically insignificant differences ($P > 0.05$) were considered not different.

^a Moderate heterogeneity ($I^2 = 50-75\%$).

^b Significant heterogeneity ($I^2 > 75\%$).

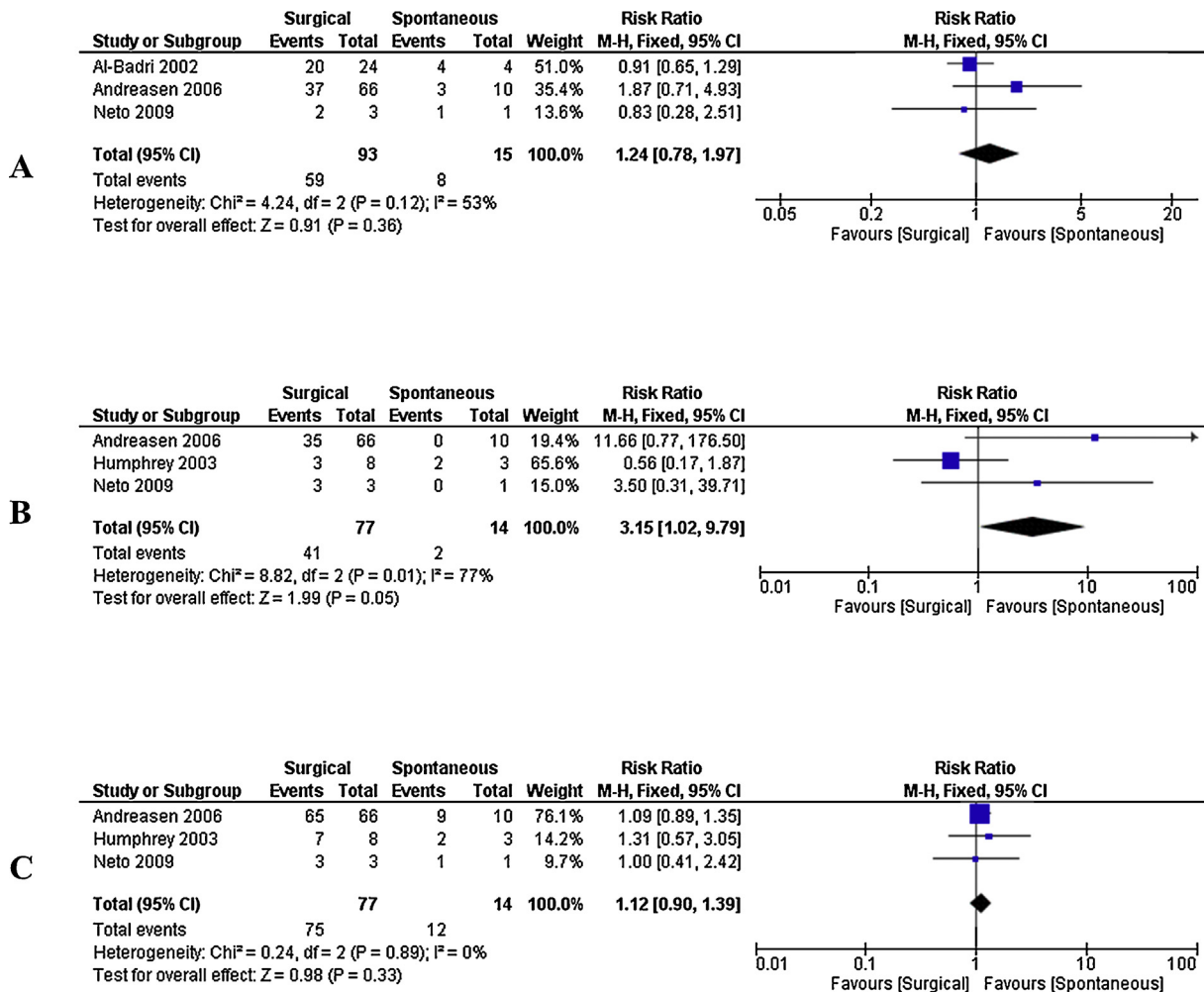


Fig. 8. Forest plots for the comparison of the degree of root formation and repositioning methods (complete root formation + surgical repositioning vs. spontaneous re-eruption) for the outcomes (A) root resorption, (B) marginal bone defects, and (C) pulpal changes.

risk of bias and standardized clinical protocols, is needed.

The results of this systematic review and meta-analysis suggest that, whenever possible, spontaneous re-eruption should be the treatment of choice. When spontaneous re-eruption is not indicated, there is no difference between orthodontic and surgical repositioning in terms of the positive outcome rates. The degree of root formation is important to the prognosis of the teeth, where teeth with incomplete root formation display a better prognosis.

Funding

Fundação de Amparo a Pesquisa do Maranhão (FAPEMA; No. 09/2014).

Competing interests

The authors report no conflicts of interest related to this study.

Ethical approval

Not required.

Patient consent

Not required.

Acknowledgement. We thank the Fundação de Amparo a Pesquisa do Maranhão (FAPEMA) for support and funding.

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