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Systematic review

Effectiveness of extraction of primary canines for interceptive management of palatally displaced permanent canines: a systematic review and meta-analysis

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Summary

Background: Although extraction of primary canines in the mixed dentition has been suggested as a measure to prevent impaction of palatally displaced permanent canines (PDCs), the relevant evidence has been inconclusive.

Objective: To assess the effectiveness of this practice and investigate the quality of the evidence.

Search methods: Search without restrictions in 15 databases and hand searching until April 2017.

Selection criteria: Randomized clinical trials comparing extraction of primary canines in the mixed dentition to no treatment.

Data collection and analysis: Following study retrieval and selection, data extraction, and individual study risk of bias assessment using the Cochrane Risk of Bias Tool, the random effects method of combining treatment effects was used. The overall quality of the available evidence was assessed with the Grades of Recommendation, Assessment, Development, and Evaluation approach.

Results: Finally 5 studies were identified involving 214 individuals, followed for up to 48 months post-intervention. Two studies were at low and the rest at high risk of bias. Although at the 12-month evaluation, extraction of the primary canine did not result in a statistically significant difference [risk ratio (RR): 1.537; 95% confidence interval (CI): 0.656–3.601, $P = 0.323$; 1 study, $n = 67$ individuals], beyond 12 months a benefit was noted (RR: 1.784; 95% CI: 1.376–2.314, $P = 0.000$; 5 studies, $n = 214$ individuals; $I^2 = 0\%$). Analysis of the studies at low risk of bias confirmed the above-mentioned result (RR: 1.713; 95% CI: 1.226–2.394, $P = 0.002$; 2 studies, $n = 91$ individuals; $I^2 = 0\%$; moderate quality evidence). No difference was observed regarding root resorption of adjacent permanent teeth (RR: 0.602; 95% CI: 0.277–1.308, $P = 0.200$; 1 study; $n = 67$ individuals; moderate quality evidence).

Conclusions: Extraction of primary canines in the mixed dentition may increase the chance of subsequent successful eruption of PDC in the long term. However, better study standardization is necessary.

Introduction

Rationale

Maxillary permanent canine impaction occurs quite commonly ([1]). Its prevalence ranges approximately between 1 and 3 per cent in Caucasian populations ([2–4]) and more frequently affects females than males ([3–6]). Many studies report that the palatal direction of displacement is very common ([4–8]) and that displaced canines are associated with adverse effects, such as an increased risk of root resorption to the neighbouring teeth and on rare occasions cyst formation or infection ([9–14]).

Impacted maxillary permanent canines usually require intervention in the form of surgical exposure and subsequent orthodontic traction. Such comprehensive management may necessitate significant commitment and costs from the patient and the healthcare provider. Moreover, it may involve risks and complications, if the prognosis, treatment planning, and biomechanics are not thoroughly considered ([1]). The interceptive extraction of the deciduous canines in cases of palatally displaced permanent canines has been suggested since the 1930s ([15]). In such cases, provided that space conditions are normal, extraction of the primary canine is supposed to lead to a change in the path of the eruption of the permanent and ultimately guide it into the dental arch. This practice was later investigated in case series studies ([16,17]). However, the evidence from studies up to 2012 has been inconclusive ([18,19]).

Objectives

The objective of the present systematic review was to systematically investigate and appraise the quality of the most up to date evidence currently available from Randomized Clinical Trials regarding the effectiveness of the extraction of primary canine(s) in patients in the mixed dentition, as a measure to facilitate the successful eruption of palatally displaced canines in the permanent dentition.

Materials and methods

Protocol and registration

The present review was based on a specific protocol developed and piloted following the guidelines outlined in the PRISMA-P statement ([20]) and registered in PROSPERO (CRD42015029130). Furthermore conduct and reporting followed the Cochrane Handbook for Systematic Reviews of Interventions ([21]) and the PRISMA statement ([22]), respectively.

Eligibility criteria

The eligibility criteria were based on the Participants, Intervention, Comparison, Outcomes, Study design (PICOS) acronym, and randomized clinical trials (RCTs) were considered, involving individuals in the mixed dentition with unilateral or bilateral palatally displaced permanent canine(s). The studies should compare the outcomes of the extraction, compared to no treatment or delayed treatment, after at least 12 months of observation. Non-comparative studies (case reports and case series), systematic reviews, and meta-analyses were excluded (Supplementary Table 1).

Information sources and search strategy

Overall, 15 databases were searched until April 15th, 2017. One author (ASA) developed detailed search strategies for each database. They were based on the strategy developed for MEDLINE but revised appropriately for each database to take account of the differences in controlled vocabulary and syntax rules (Supplementary Table 2). Moreover, reference lists in other reviews, guidelines, included or excluded studies, as well as other related articles were searched for additional studies.

No restriction was placed on the language, date, or status of publication. In addition, efforts to obtain additional or ongoing trials were made and the reference lists of all eligible studies, as well as relevant reviews, were searched. The authors of ongoing studies were to be contacted in order to provide additional data for the review if available.

Study selection

Two authors (ASA and EGK) assessed electronically the retrieved records for inclusion independently. They were not blinded to the identity of the authors, their institution, or the results of the research. Subsequently, they obtained and assessed, again independently, the full report of records considered by either reviewer to meet the inclusion criteria. Disagreements were resolved by discussion or consultation with the third author (AEA).

Data collection and data items

The same two authors performed data extraction independently and any disagreements were again resolved by discussion or consultation with the third author. Predetermined and pre-piloted data collection forms were used to record the following information: bibliographic details of the study; details on study design, duration of the observation period, and verification of study eligibility; participant characteristics (where available number, age, gender) at the beginning and at each point of data analysis (if patient attrition was observed the respective reasons were noted); intervention characteristics; proportion of successful eruption of permanent maxillary canines in each arm of the study; proportion of root resorption of adjacent teeth and other adverse effects; where available, length of time until eruption, data on patient-reported outcomes (pain, patient satisfaction etc.), economic evaluation data, and additional information like *a priori* sample size calculation, baseline comparability of the groups (regarding age, gender, maxillary canine position, space availability in the arch, and malocclusion), and reliability of the method of assessment (Supplementary Table 1).

Risk of bias in individual studies

Two authors (ASA and EGK) assessed the risk of bias in individual studies, independently and in duplicate, using The Cochrane Collaboration's Risk of Bias assessment tool for RCTs ([21]). The Risk of Bias assessment tool includes the domains of random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), Blinding of outcome assessors (detection bias), incomplete outcome data (attrition bias), Selective outcome reporting (reporting bias), and other sources of bias. Any disagreements were resolved by discussion or consultation with the third author (AEA).

Summary measures and synthesis of results

Data on the successful eruption of the permanent maxillary canine in the dental arch and root resorption of adjacent permanent teeth are dichotomous and were expressed as risk ratios (RR) together with the relevant 95 per cent confidence intervals (CI). In order to have a measure of the absolute effect on the proportions of individuals with the desired outcome, data were also expressed as risk difference (RD) together with the relevant 95 per cent CI.

The random effects method for meta-analysis was used to combine data, since they were expected to differ across studies due to diversity, in terms of population groups, settings, procedures, and follow-up (23,24). To identify the presence and extent of between-study heterogeneity, the overlap of the 95 per cent CI for the results of individual studies was inspected graphically and the I^2 statistic was calculated (21).

All analyses were done with comprehensive meta-analysis software 2.2.046 (©2007 Biostat Inc.). Significance (a) was set at 0.05, except for the 0.10 used for the heterogeneity tests (25).

Risk of bias across studies and additional analyses

If a sufficient number of studies were identified, analyses were planned for 'small-study effects' and publication bias (21). If deemed possible, exploratory subgroup analyses were planned according to participant characteristics, such as gender, or the position of the displaced canine. In addition, results were investigated after exclusion of studies at high risk of bias. Moreover, additional analyses were conducted in order to investigate the potential effects from the inclusion in the retrieved studies of patients with bilateral palatally displaced canines (assuming correlations of 0, 0.25, and 0.50). Furthermore, as in studies that it was not available otherwise, data expressed on subject basis were considered as unilateral cases, additional analyses were conducted. Finally, the quality of evidence at longest follow up available was assessed based on the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach (26).

Results

Study selection

The flow of records through the reviewing process is shown in Figure 1. We initially identified 2193 references, and excluded 1078 as duplicates and 1106 more on the basis of their title and abstract. From the nine records that remained and were assessed for eligibility, four studies were excluded because they investigated or compared with different interventions (Supplementary Table 3). Finally, five full-text trial reports were included in the systematic review (27–31).

Study characteristics

The characteristics of the studies included in the present systematic review are presented in Tables 1 and 2. The papers were published between 2004 and 2015, and investigated in 214 patients the extraction of primary maxillary canine(s) to no treatment. Patients were followed for a period of up to 48 months. One study presented data also for the 12-month evaluation (27).

Three studies reported *a priori* calculation of sample size (27–29), and one made reference to the power of the study but it was not specified if the power was calculated *a priori* or *post hoc* (29). In addition, all five included studies, considered examining the reliability of the measurements carried out in some way and included reference to baseline comparability.

Risk of bias within studies

Table 3 presents a summary of findings regarding the risk of bias assessment for the included studies and more details can be found in Supplementary Table 4.

Two studies were classified as being at low risk of bias (27,28). The rest were considered to be at high risk of bias mainly because of problems regarding the domains of random sequence generation
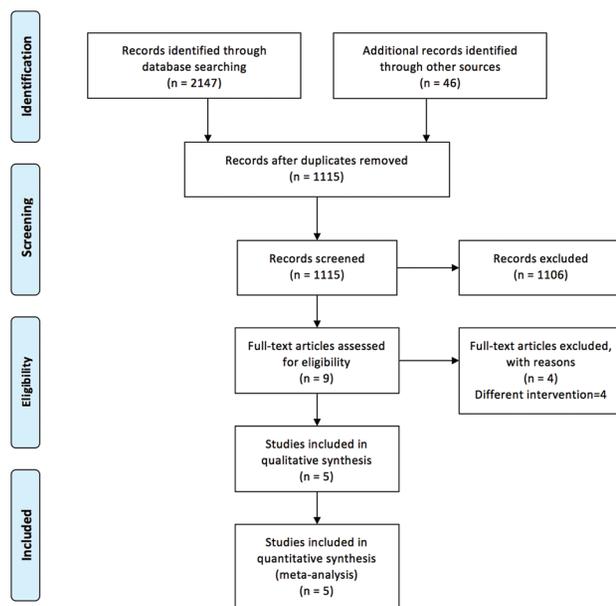

Figure 1. Flow of records through the reviewing process.

and allocation concealment. Regarding the rest of the considered domains, blinding of the participants, and the personnel providing the instructions was not possible. However, in the context of the present research design, there was no reason to believe that bias could be introduced because of absence of blinding in these cases. On the contrary, blinding of the outcome assessment could possibly involve risk of bias because it is not possible to blind the extracted canine and only baseline assessments could be blinded. As the reporting of some of the included studies presented general deficiencies, it is not clear how these could have affected the appraisal of the outcomes included in the present systematic review. Moreover, the risk from incomplete outcome data because of the existence of dropouts was unclear in two out of five studies considered.

Results of individual studies and synthesis of results

All five studies provided data on the prevalence of successful canine eruption after the extraction of the primary canine(s). The proportion of successful eruption in the extraction group was reported to be between 50 and 69 per cent (Baccetti *et al.* (29): 65.2 per cent at 18 months; Baccetti *et al.* (30): 62.5 per cent at 26 months; Bazargani *et al.* (28): 67 per cent at 18 months; Leonardi *et al.* (31): 50 per cent at 48 months; Naoumova *et al.* (27): 69 per cent with the mean eruption time of 15.6 months).

At the 12-month evaluation, extraction of the primary canine did not result in a statistically significant benefit on the proportion of successful canine eruption [RR: 1.537, 95% CI: 0.656–3.601, $P = 0.323$; RD: 0.085, 95% CI: –0.080 to 0.251, $P = 0.313$; $n = 67$ participants] (27). Beyond 12 months, overall, extraction of the primary canine proved beneficial [RR: 1.784, 95 per cent CI: 1.376–2.314, $P = 0.000$; RD: 0.287, 95% CI: 0.172–0.403, $P = 0.000$; 5 studies, $n = 214$ participants; $I^2 = 0\%$] (27–31) (Figure 2).

Only one study reported on the effect of primary canine extraction on root resorption of adjacent permanent teeth (27). No statistically significant benefit was observed [RR: 0.602, 95% CI: 0.277–1.308, $P = 0.200$; RD: –0.118, 95% CI: –0.293 to 0.057; $P = 0.188$; $n = 67$ participants]. One study reported a significant

Table 1. General characteristics of the studies included in the systematic review.

Study	Total observation period and outcomes	Additional information
Baccetti *et al.* (29) [2008—Italy]	Total observation period: 18 months for both groups Definition of successful eruption and assessment: Full eruption of the tooth, permitting bracket positioning for final arch alignment when needed; unsuccessful outcome represented by the lack of eruption of the permanent canine at the completion of the clinical observation period (18 months after the initial observation)	*A priori* sample calculation: Reference that (… The power … was greater than 0.85. …) Baseline group comparability: Reference that (… The severity of canine displacement was similar…) Measurement reliability considered: Yes
Baccetti *et al.* (30) [2011—Italy]	Total observation period: Until subjects had an early permanent dentition and a post-pubertal stage of cervical vertebral maturation (CS 5 or CS 6) (32). Extraction group ($\bar{x} \pm$ SD): 26 ± 10 months; control group ($\bar{x} \pm$ SD): 37 ± 14 months; $P > 0.05$. Definition of successful eruption and assessment: Full eruption of the tooth, permitting bracket positioning for final arch alignment when needed; unsuccessful outcome represented by the lack of eruption of the permanent canine at the completion of the clinical observation period [a time point when the subjects had an early permanent dentition and a CS 5 or CS 6 (32)	*A priori* sample calculation: Yes Baseline group comparability: Yes [age; gender ratio; d (mm), α (°), sector (14); CS (40), Unilateral PDC/Bilateral PDCs, Root development of PDC (33)] Measurement reliability considered: Yes
Bazargani *et al.* (28) [2014—Sweden]	Total observation period: 18 months for both groups Definition of successful eruption and assessment: Eruption above the gingival margin in an aesthetically acceptable location in the dental arch after 18 months (assessment at baseline and at 18 months) Other outcomes: Midline of the upper dental arch (mm) (Study casts and visual inspection; assessment at baseline and 18 months); Space between distal contact points of 2s and distal contact point of Cs (mm) (Study casts measured with digital caliper in the dental arch; after the extraction of the Cs the mesial contact points of either the Ds or the 4s were considered; assessment at baseline, 6, 12, 18 months)	*A priori* sample calculation: Yes Baseline group comparability: Yes [d (mm), α (°), sector (16); age/gender within the split mouth design] Measurement reliability considered: Yes
Leonardi *et al.* (31) [2004—Italy]	Total observation period: 48 months for both groups Definition of successful eruption and assessment: Full eruption of the tooth, permitting bracket positioning for final arch alignment when needed; unsuccessful outcome represented by the lack of eruption of the permanent canine at the completion of the clinical observation period (48 months after the initial observation)	*A priori* sample calculation: NR Baseline group comparability: Yes [age, gender distribution]; Reference that […Severity of canine displacement was similar…] Measurement reliability considered: Yes
Naoumova *et al.* (27) [2015—Sweden]	Total observation period: 24 months for both groups Definition of successful eruption and assessment: Canine emerged through the gingiva (assessment at baseline, 12 and 24 months) Other outcomes: Length of time until eruption (in months); Root resorption of adjacent teeth; Harms	*A priori* sample calculation: Yes Baseline group comparability: Yes [gender; mesioangular angle (°), sagittal angle (°), vertical position (mm), canine cusp tip-dental arch plane (mm), canine root apex-dental arch plane (mm), canine cusp tip-midline (mm); root resorption (12)] Measurement reliability considered: Yes

PDC, palatally displaced canine; NR, not reported; RCT, randomized controlled trial.

decrease in the primary canine region space at the extraction site, but no midline shift toward the extraction side (28). No other harms were observed (27). In the extraction group, the mean eruption time was 15.6 ± 5.6 months, whereas in the control group 18.8 ± 5.8 months (27). No information on patient reported outcomes or economic evaluation data could be retrieved.

Risk of bias across studies and additional analyses

Because it was not possible to retrieve a sufficient number of trials and relevant data, we were not able to conduct analyses for 'small-study effects' and publication bias (21), nor the exploratory subgroup analyses.

Analysis of the retrieved data focusing on the studies at low risk of bias, confirmed that extraction of the primary canine provides a statistically significant benefit on the proportion of successful canine eruption [RR: 1.713, 95% CI: 1.226–2.394, $P = 0.002$; RD: 0.303, 95% CI: 0.168–0.438, $P = 0.000$; 2 studies, $n = 91$ participants; $I^2 = 0\%$] (27,28) (Figure 3). The additional analyses provided corroborating data (Supplementary Tables 5 and 6).

Overall, the quality of evidence based on the studies at low risk of bias, for the latter comparison, as well as for the effect of primary canine extraction on root resorption of adjacent permanent teeth was considered as moderate (Table 4).

Table 2. Participant characteristics of the studies included in the systematic review.

Study	Inclusion and exclusion criteria	Number of patients and PDCs included and analyzed
Baccetti *et al.* (29)	Inclusion criteria: Caucasians; unilateral, or bilateral PDCs; dental age at baseline 8–13 years (34); skeletal age at baseline showing active phases of skeletal growth before CS 3 (32) Exclusion criteria: Previous orthodontic treatment; craniofacial syndromes, odontomas, cysts, cleft lip and/or palate, sequelae of traumatic injuries to the face, or multiple or advanced caries; crowding at the upper arch as evaluated by means of intraoral inspection; aplasia or severe hypoplasia of the crowns of the upper lateral incisors Diagnostic criteria for PDCs: Intra-osseous palatal position of the maxillary permanent canines from panoramic radiographs and periapical radiographs (displacement of the upper canine to the palatal side was checked by means of double determination from periapical radiographs)	Group 1: extraction of the deciduous canine Analyzed: 23 subjects (8 M, 15 F); 25 PDCs Age ($\overline{x}$): 11.7 years Group 2: non-extraction of the deciduous canine Analyzed: 22 subjects (9 M, 26 F); 26 PDCs Age ($\overline{x}$): 11.6 years
Baccetti *et al.* (30)	Inclusion criteria: Caucasians; unilateral or bilateral PDCs, age at baseline 9.5–13 years; late mixed dentition stage; skeletal age at baseline showing active phases of skeletal growth before CS 4 (32); presence of Class II or Class III tendency or mild tooth-size/arch-size discrepancy Exclusion criteria: Previous orthodontic treatment; craniofacial syndromes, supernumerary teeth, odontomas, cysts, sequelae of traumatic injuries Diagnostic criteria for PDCs: Intra-osseous palatal position of the maxillary permanent canines from panoramic radiographs [PDCs showing α angle equal to or greater than 15° (14)]; palatal displacement of the canine(s) was confirmed by evaluating the position of the canine on the lateral cephalogram, and, when necessary, by means of Clark's tube shift rule using multiple intraoral radiographs of the canine region.	Group 1: extraction of the deciduous canine Included: 25 subjects (11 M, 14 F) Analyzed: 24 subjects (10 M, 14 F); 34 PDCs Age ($\overline{x}$ ± SD): 11.1 ± 0.9 years Group 2: non-extraction of the deciduous canine Included: 30 subjects (12 M, 18 F), Analyzed: 29 subjects (11 M, 18 F); 42 PDCs Age ($\overline{x}$ ± SD): 10.4 ± 0.8 years
Bazargani *et al.* (28)	Inclusion criteria: Inability to locate the canines by digital palpation, bilateral PDCs identified on the panoramic and intraoral occlusal radiographs, age at diagnosis between 10 and 14 years, with dental stage in the late mixed dentition Exclusion criteria: Patients with previous or ongoing orthodontic treatment, aplasia of the upper lateral incisors, moderate to severe crowding in the upper arch (>3 mm) and/or craniofacial syndromes, odontomas, cysts or cleft lip and/or palate Diagnostic criteria for PDCs: Non palpable canine bulge in the alveolar process, canine within sectors 2–5, in an intraosseous position within the palate, and exceeding the long axis of the upper lateral incisors on an intraoral occlusal radiograph (16)	Included: 24 subjects (8 M, 16 F); 48 PDCs Age ($\overline{x}$ ± SD): 11.6 ± 1.2 years Group 1: extraction of the deciduous canine Included: 24 subjects; 24 PDCs Analyzed: 24 subjects; 24 PDCs Group 2: non-extraction of the deciduous canine Included: same 24 subjects; 24 contralateral side PDCs Analyzed: same 24 subjects; 24 contralateral side PDCs
Leonardi *et al.* (31)	Inclusion criteria: Caucasians; unilateral of bilateral PDC; dental age at baseline 8–13 years according (34); skeletal age at baseline showing active phases of skeletal growth (before CVMS IV, 32) Exclusion criteria: Previous orthodontic treatment; craniofacial syndromes, odontomas and/or cysts, cleft lip and/or palate, sequelae of traumatic injuries to the face, multiple or advanced caries (or both); crowding at the upper arch; aplasia or severe hypoplasia of the crown of upper lateral incisors Diagnostic criteria for PDCs: Intraosseous palatal position of the maxillary permanent canines from panoramic radiographs and periapical radiographs	Group 1: extraction of the deciduous canine Analyzed: 11 subjects (5 M, 6 F); 14 PDCs Age ($\overline{x}$): 11.6 years Group 2: non-extraction of the deciduous canine Analyzed: 14 subjects (4 M, 10 F); 16 PDCs Age ($\overline{x}$): 11.6 years
Naoumova *et al.* (27)	Inclusion criteria: Caucasians at age 10–13 years with either maxillary unilateral or bilateral PDC, persisting deciduous canine, no previous experience of orthodontic treatment Exclusion criteria: Crowding in the maxilla exceeding 2 mm, ongoing orthodontic treatment, resorption of the adjacent teeth, grades 3 and 4 according to Ericson and Kurol (12), either at the start or during the trial caused by the displaced canine, craniofacial syndromes, odontomas and/or cysts, cleft lip, and/or palate Diagnostic criteria for PDCs: Non palpable canine bulge in the alveolar process, canine crown diagnosed on intraoral radiographs as palatally positioned using Clark's rule	67 subjects, age ($\overline{x}$ ± SD): 11.4 ± 1.0 years 27 M, age ($\overline{x}$ ± SD): 11.4 ± 0.9 years 16 F, age ($\overline{x}$ ± SD): 11.3 ± 1.1 years Group 1: extraction of the deciduous canine 45 PDCs (45 analyzed following intention-to-treat analysis) Group 2: non-extraction of the deciduous canine 44 PDCs (44 analyzed following intention-to-treat analysis)

M, males; F, females; PDC, palatally displaced canine.

Table 3. Summary of the risk of bias assessment. [Domains examined: 1: Random sequence generation; 2: Allocation concealment; 3: Blinding of participants and personnel; 4: Blinding of outcome assessment; 5: Incomplete outcome data; 6: Selective outcome reporting; 7: Other potential threats to validity]

Domain	Study				
	Baccetti *et al.* (29)	Baccetti *et al.* (30)	Bazargani *et al.* (28)	Leonardi *et al.* (31)	Naoumova *et al.* (27)
1	Unclear	Unclear	Low	Unclear	Low
2	High	High	Low	High	Low
3	Low	Low	Low	Low	Low
4	Unclear	Unclear	Low	Unclear	Low
5	Unclear	Low	Low	Unclear	Low
6	High	High	Low	High	Low
7	Unclear	Unclear	Low	Unclear	Low
Summary	High	High	Low	High	Low

Study name	Statistics for each study					Risk ratio and 95% CI
	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	
[2004] Leonardi et al	1,500	0,576	3,903	0,831	0,406	
[2008] Baccetti et al	1,793	0,957	3,361	1,823	0,068	
[2011] Baccetti et al	2,266	1,164	4,411	2,406	0,016	
[2014] Bazargani et al	1,600	0,922	2,777	1,670	0,095	
[2015] Naoumova et al	1,783	1,170	2,716	2,692	0,007	
	1,784	1,376	2,314	4,367	0,000	

0,1 0,2 0,5 1 2 5 10

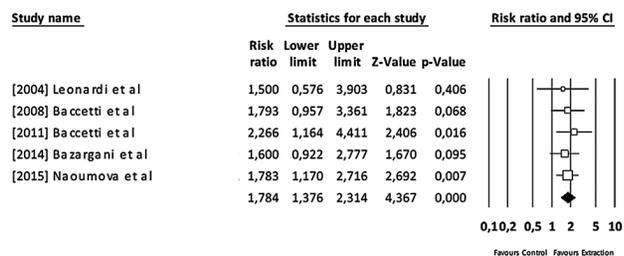Favours Control   Favours Extraction

Figure 2. Successful eruption of palatally displaced permanent maxillary canine after extraction of the corresponding primary. [Observation beyond 12 months–all studies].
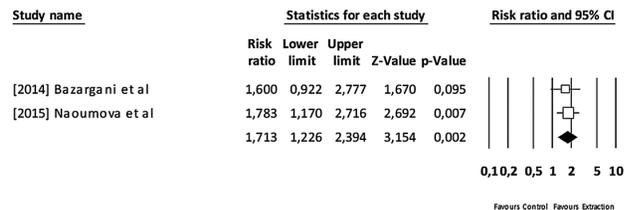
Study name	Statistics for each study					Risk ratio and 95% CI
	Risk ratio	Lower limit	Upper limit	Z-Value	p-Value	
[2014] Bazargani et al	1,600	0,922	2,777	1,670	0,095	
[2015] Naoumova et al	1,783	1,170	2,716	2,692	0,007	
	1,713	1,226	2,394	3,154	0,002	

0,1 0,2 0,5 1 2 5 10

Favours Control   Favours Extraction

Figure 3. Successful eruption of palatally displaced permanent maxillary canine after extraction of the corresponding primary. [Observation beyond 12 months–low risk of bias studies].

Discussion

Summary of evidence

Overall, based on the information provided from the studies eligible for inclusion in the present review, at the assessments conducted over 1 year, the extraction of the primary maxillary canine resulted in more permanent canines successfully erupting compared to no treatment. The proportion of successful eruption in the extraction group was reported to be between 50 and 69%. The aforementioned data add on the information provided in earlier systematic reviews, which concluded that the scientific evidence was weak and inconclusive to fully evaluate the effect the extraction of the primary canines for the interceptive management of palatally displaced canines (18,19). Moreover, a significant decrease in the primary canine region space at the extraction site was noted, possibly underlying the usefulness of space maintainers during the observation period (28). Finally, regarding root resorption of the adjacent permanent teeth, no significant differences were noted. The quality of evidence

was considered as moderate, giving an insight on the strength of the relevant recommendations.

The small number of studies retrieved reflects on the scarcity of relevant research at the top of the widely accepted hierarchy of scientific evidence, although it is widely accepted that well-designed and properly executed RCTs provide the best evidence on the efficacy of health care interventions (35,36). The consequent lack of extensive data with high-evidence-based potential is rather surprising bearing in mind not only the prevalence of the problem (2–5), but also the fact that the management of impacted permanent maxillary canines necessitates a comprehensive approach potentially requiring significant commitment and costs from the patient and healthcare provider (19). This management may also involve risks and complications, if prognosis, treatment planning, and the orthodontic biomechanics are not thoroughly considered (1). Thus, relevant, evidence-based information on possible interceptive management of the condition would be beneficial in supporting the care provided in these cases.

Despite the scarcity of evidence-based information exploratory quantitative data synthesis was attempted where applicable. The I^2 statistic obtained from the meta-analytic calculations suggested a relatively insignificant degree of heterogeneity. Generally, in the context of the present review, heterogeneity can arise from diversity in terms of the characteristics of population groups, settings, procedures, and follow-up (i.e. ethnic origin, dental and skeletal age, differences in the employed diagnostic criteria, and definition of successful eruption and assessment) and was incorporated into a justifiable random effects model. The risk of bias was assessed by considering the various possible sources of bias for randomized controlled trials, and it was classified as low for two studies (27,28). However, several problems were located in the other three eligible trials mainly because of problems regarding the domains of random sequence generation and allocation concealment. Moreover, because of the general shortcomings in their reporting it is not clear how the difficulties in assessment blinding could have affected the appraisal of the outcomes included in the present systematic review. Moreover, in two out five studies considered, dropouts were not explained to an adequate extent regarding each arm of the study. Finally, in the outcomes considered, the overall quality of evidence was downgraded because of problems related to imprecision. The numbers of patients analyzed were limited, creating serious problems regarding the precision of the results obtained.

Strengths and limitations

The strengths of the present review include the methodology that followed well-established guidelines and the fact that it focused exclusively on randomized controlled trials. In addition, an attempt was made to summarize the quality of available evidence and thus provide an insight into the strength of the relevant recommendations based on the GRADE approach (26). Moreover, the search strategy employed was exhaustive, covering electronic, manual, and gray literature material up to April 2017, and comprehensive, including every available randomized controlled trial comparing extraction of the primary canine to no treatment, irrespective of language, date, and status of publication, in accordance with the recommendation that 'systematic reviews of interventions' require a thorough, objective and reproducible search of a range of sources to identify as many relevant studies as possible (21). Every effort to decrease bias in the methodology employed was made. Screening, verification of eligibility, abstraction of information, assessment of risk of bias, and of the quality of evidence were performed in duplicate, and any disagreement was resolved by discussion or consultation with the thesis

Table 4. Quality of available evidence.

Quality assessment						Effect	Quality
Studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Relative (95% CI)	
Successful eruption of the permanent (studies at low risk of bias)							
2	Not serious	Not serious	Not serious	Serious[a]	None	RR 1.713 (1.226 lower to 2.394 higher) $P = 0.002$	⊕⊕⊕○ Moderate
Root resorption of adjacent permanent teeth							
1	Not serious	Not serious	Not serious	Serious[a]	None	RR 0.602 (0.277 lower to 1.308 higher) $P = 0.200$	⊕⊕⊕○ Moderate
Space change at the primary canine region							
1	Not serious	Not serious	Not serious	Serious[a]	None	−1.0 mm (−1.9 to −0.2) $P = 0.010$	⊕⊕⊕○ Moderate

CI, confidence interval; RR, risk ratio.
[a]The number of cases analyzed was limited.

supervisor until a final consensus was achieved. Finally, the random effects model was employed during exploratory quantitative data synthesis to incorporate any observed heterogeneity (37).

There are also limitations to the present review, mainly arising from the nature and characteristics of the data retrieved during the review process. The scarcity of relevant information from low risk of bias RCTs rendered quantitative syntheses exploratory until additional research becomes available. However, current concepts support that data from as few as two studies can be combined, provided that these can be meaningfully pooled (38), as all other summarizing techniques are less transparent and/or are less likely to be valid (39). Furthermore, exploratory subgroup analyses and analyses for 'small-study effects' and publication bias (21), could not be carried out even though they were incorporated as possibilities according to the review protocol. Moreover, limitations may arise from the incorporation in the retrieved studies of patients with bilateral displaced canines. Of the five studies included in the quantitative synthesis, two incorporated or discussed relevant statistical adjustments (27, 28). In one of them, finally, it was decided to analyze the whole material and not only the unilateral group as two independent observations because there was no difference in the correlation between extraction and successful outcome between independent observations and dependent paired observations in the bilateral group (27). Meta-analysis of these studies would ideally require knowledge of a measure of the correlation of the data (40). Such a measure was not reported and would have warranted the retrieval of the entire data set for each trial, but that was not attempted. However, additional analyses, taking into account the nature of the data (40), provided corroborating results. Another limitation of the data retrieved in this study stems from the small number of cases finally analyzed resulting in subsequent problems regarding the precision of the effect estimates. Also, it has to be acknowledged that the results of this review relate mostly to patients from the specific ethnic backgrounds of the patients under study. Bearing in mind the reported racial differences in the prevalence of the phenomenon of palatally displaced canines (41), the generalizability of the available evidence may be curtailed.

Recommendations for future research

Since canine impaction is a relatively common phenomenon, and its management potentially complex and challenging, the need for well-designed RCTs with better standardization and appropriate reporting depending on the research design could be useful (42). It would also be beneficial to have future RCTs examining different

groups from ethnic backgrounds other than Caucasian to find if any differences exist. Moreover, to more fully understanding the effect of these strategies, further investigation of the possible predictors of success; inclusion in the analyses of patient-reported outcomes like quality of life; analyses of costs, and benefits in the socioeconomic context, as well as further investigation of any possible adverse effects should be carried out.

Conclusions

The present systematic review and meta-analysis highlights the fact that extraction of the primary canines in the mixed dentition may increase the probability of the subsequent successful eruption of palatally displaced canines in the long term. However, more low risk of bias studies with sufficient sample sizes, are needed in order to enrich the available evidence, increase the precision of the observed effect estimates, and unequivocally guide clinical decisions.

Supplementary material

Supplementary data are available at *European Journal of Orthodontics* online.

Conflict of interest

None to declare.

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