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Interventions for promoting the eruption of palatally displaced permanent canine teeth, without the need for surgical exposure, in children aged 9 to 14 years (Review)

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[Intervention Review]

Interventions for promoting the eruption of palatally displaced permanent canine teeth, without the need for surgical exposure, in children aged 9 to 14 years

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ABSTRACT

Background

A permanent upper (maxillary) canine tooth that grows into the roof of the mouth and frequently does not appear (erupt) is called a palatally displaced canine (PDC). The reported prevalence of PDC in the population varies between 1% and 3%. Management of the unerupted PDC can be lengthy, involving surgery to uncover the tooth and prolonged orthodontic (brace) treatment to straighten it; therefore, various procedures have been suggested to encourage a PDC to erupt without the need for surgical intervention.

Objectives

To assess the efficacy, safety and cost-effectiveness of any interceptive procedure to promote the eruption of a PDC compared to no treatment or other interceptive procedures in young people aged 9 to 14 years old.

Search methods

An information specialist searched four bibliographic databases up to 3 February 2021 and used additional search methods to identify published, unpublished and ongoing studies.

Selection criteria

We included randomised controlled trials (RCT) involving at least 80% of children aged between 9 and 14 years, who were diagnosed with an upper PDC and undergoing an intervention to enable the successful eruption of the unerupted PDC, which was compared with an untreated control group or another intervention.

Data collection and analysis

Two review authors, independently and in duplicate, examined titles, keywords, abstracts, full articles, extracted data and assessed risk of bias using the Cochrane Risk of Bias 1 tool (RoB1). The primary outcome was summarised with risk ratios (RR) and 95% confidence intervals (CI). We reported an intention-to-treat (ITT) analysis when data were available and a modified intention-to-treat (mITT) analysis if not. We also undertook several sensitivity analyses. We used summary of findings tables to present the main findings and our assessment of the certainty of the evidence.

Main results

We included four studies, involving 199 randomised participants (164 analysed), 108 girls and 91 boys, 82 of whom were diagnosed with unilateral PDC and 117 with bilateral PDC. The participants were aged between 8 and 13 years at recruitment. The certainty of the evidence was very low and future research may change our conclusions.

One study (randomised 67 participants, 89 teeth) found that extracting the primary canine may increase the proportion of PDCs that successfully erupt into the mouth at 12 months compared with no extraction (RR 2.87, 95% CI 0.90 to 9.23; 45 participants, 45 PDCs analysed; very low-certainty evidence), but the CI included the possibility of no difference; therefore the evidence was uncertain. There was no evidence that extraction of the primary canine reduced the number of young people with a PDC referred for surgery at 12 months (RR 0.61 (95% CI 0.29 to 1.28).

Three studies (randomised 132 participants, 227 teeth) found no difference in the proportion of successfully erupted PDCs at 18 months with a double primary tooth extraction compared with extraction of a single primary canine (RR 0.68, 95% CI 0.35 to 1.31; 119 participants analysed, 203 PDCs; mITT; very low-certainty evidence). Two of these studies found no difference in the proportions referred for surgical exposure between the single and the double primary extraction groups data at 48 months (RR 0.31, 95% CI 0.06 to 1.45).

There are some descriptive data suggesting that the more severe the displacement of the PDC towards the midline, the lower the proportion of successfully erupted PDCs with or without intervention.

Authors' conclusions

The evidence that extraction of the primary canine in a young person aged between 9 and 14 years diagnosed with a PDC may increase the proportion of erupted PDCs, without surgical intervention, is very uncertain. There is no evidence that double extraction of primary teeth increases the proportion of erupted PDC compared with a single primary tooth extraction at 18 months or the proportion referred for surgery by 48 months. Because we have only low to very low certainty in these findings, future research is necessary to help us know for sure the best way to deal with upper permanent teeth that are not erupting as expected.

PLAIN LANGUAGE SUMMARY

Interventions to encourage eruption of eye teeth buried under the gum or growing upwards, without the need for surgery, in children aged 9 to 14 years

What is the health problem?

Upper permanent canine teeth (commonly known as eye teeth or fang teeth) are positioned in the upper jaw, one on the right and one on the left. In around 1% to 3% of children, they may not erupt (appear from behind the gum and into the mouth) into their correct position. The permanent canine tooth or teeth may grow towards the palate (roof of the mouth) and remain unerupted (buried under the gum). This is known as a palatally displaced canine (PDC). If the permanent canine tooth remains displaced and unerupted, it can damage or change the position of neighbouring teeth, and occasionally it can lead to a cyst.

What are the treatments?

Management of a PDC can take a long time, involving surgery to uncover the tooth and prolonged orthodontic (brace) treatment to straighten it. Various quicker or easier alternatives have been suggested to encourage the tooth or teeth to erupt. These include extraction (taking out) of the primary (baby) canine, extraction of the primary canine and primary first molar (also called double primary tooth extraction), or using braces to create space in children's mouths.

What did we want to find out?

We wanted to find out if any of these treatment alternatives were successful for children aged 9 to 14 years, in terms of encouraging PDCs to erupt without using surgery.

What did we do?

We searched for studies that assessed the effectiveness of different ways to deal with palatally displaced canines up to 3 February 2021.

Where studies measured the same thing in the same or similar ways, we combined the results to give us a clearer idea about the effects of the treatment. We assessed whether the individual studies were at risk of being biased and we judged the overall reliability of the evidence we found.

What were the main findings?

We found four studies involving 199 children (195 analysed).

There is very weak evidence that extraction of the primary canine in children aged between 9 and 14 years may increase the probability that the PDC will successfully erupt into the mouth without the need for surgery by 12 months. There is no evidence it reduces the number of children needing surgery to correct their PDC.

There is no evidence that double extraction of primary teeth increases the proportion of erupted PDCs compared with a single primary tooth extraction by 18 months after treatment or that it reduces the number of children needing surgery to correct the PDC by 48 months.

There is some limited evidence suggesting that the severity of the displacement of the PDC towards the midline may be important in deciding whether or not to intervene. If it is very far from the midline, it may be less likely to be successful.

What does this mean?

The review authors found the reliability of the evidence to be very low so future research is necessary to help us know for sure the best way to deal with upper permanent canines that are not erupting as expected.

SUMMARY OF FINDINGS

Summary of findings 1. Primary canine extraction versus no extraction

Primary canine extraction versus no extraction

Population: young people aged 9–14 years
Setting: public dental clinics in Sweden. Participants were recruited, consented, randomised and followed up in a dental teaching hospital orthodontic department (University Clinics of Odontology, Gothenburg)
Intervention: single primary tooth (canine) extraction
Comparison: control (no extraction)

Outcomes	Anticipated absolute effects* (95% CI)			Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Without single primary tooth (canine) extraction	With single primary tooth (canine) extraction	Difference				
Eruption of PDC at 12 months Assessed by clinical observation	13.6%	39.1% (12.3 to 100)	25.5% more (1.4 fewer to 112.2 more)	RR 2.87 (0.90 to 9.23)	45 (1 RCT)	⊕⊖⊖⊖ **Very low**[a,b]	The evidence is uncertain about whether extraction of a single primary canine tooth has any effect on the proportions of successfully erupted PDCs at 12 months compared with no primary canine tooth extraction.
Referral for surgical exposure of PDC at 12 months Assessed by clinical observation	50.0%	32.0% (14.5 to 70)	18.0% fewer (35.5 fewer to 20 more)	RR 0.61 (0.29 to 1.28)	45 (1 RCT)	⊕⊖⊖⊖ **Very low**[a,b]	There is no evidence that extraction of a single primary canine tooth has an effect on the proportion of young people with a PDC referred for surgery at 12 months compared with no primary canine tooth extraction.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **PDC:** palatally displaced canine; **RCT:** randomised controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for indirectness as there was limited generalisability from one study in one centre.
[b]Downgraded two levels for imprecision as the evidence was from only one small study, with very few events.

Summary of findings 2. Double primary (canine and first molar) extractions versus single primary (canine) tooth extraction

Double primary (canine and first molar) extractions versus single primary (canine) tooth extraction

Population: young people aged 9–14 years
Setting: 2 studies in a dental teaching hospital in Italy (Department of Orthodontics, University of Bologna) and 1 study in 2 centres in Norway, 1 public (the Public Dental Health Competence Centre of Northern Norway, Tromsø) and 1 private (Bryne, Norway)
Intervention: double primary tooth (canine and molar) extractions
Comparison: single primary tooth (canine) extraction

Outcomes	Anticipated absolute effects* (95% CI)			Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	What happens
	Without double primary tooth (canine and molar) extractions	With double primary tooth (canine and molar) extractions	Difference				
Eruption of PDC at mean 18 months (mITT analysis) assessed by clinical observation	27.6%	18.8% (9.7 to 36.1)	8.8% fewer (17.9 fewer to 8.6 more)	RR 0.68 (0.35 to 1.31)	119 (3 RCTs)	⊕⊖⊖⊖ **Very low**[a,b]	There is no evidence that double primary teeth (canine and molar) extraction increases te proportion of successfully erupted PDCs at mean 18 months compared with single primary tooth (canine) extraction.
Referred for surgical exposure of the unerupted PDC by maximum 48 months (mITT analysis) assessed by clinical observation	8.7%	2.7% (0.5 to 12.6)	6.0% fewer (8.2 fewer to 3.9 more)	RR 0.31 (0.06 to 1.45)	96 (2 RCTs)	⊕⊖⊖⊖ **Very low**[a,c,d]	There is no evidence that double primary tooth (canine and molar) extractions results in a smaller proportion of participants being referred for surgical exposure of an unerupted PDC by maximum 48 months (ITT analysis) compared with single primary tooth extraction.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **mITT:** modified intention-to-treat; **PDC:** palatally displaced canine; **RCT:** randomised controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

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[a]Downgraded one level for imprecision as the sample sizes are small and mostly cross the line of no difference.
[b]Downgraded two levels for indirectness. Two studies were at high risk of bias due to concerns with how representative the samples were of people with PDC and in particular the very high prevalence of participants judged to have bilateral PDCs (unilateral:bilateral PDC ratio 1:3.8) (Bonetti 2010; Bonetti 2011).
[c]Downgraded one level for indirectness. Some clinicians would consider 48 months too long to observe a patient before intervening.
[d]Downgraded one level for indirectness. Two studies had a high proportion of the canines (85%) judged to be either in sector 1 (37 participants) or sector 2 (110 participants) (Bonetti 2010; Bonetti 2011). Not all clinicians would consider these teeth to be palatally displaced, particularly considering how young some of the participants were at baseline.

BACKGROUND

Description of the condition

The permanent canine tooth in the upper (maxillary) jaw sometimes grows into the roof of the mouth and does not erupt into the dental arch at the appropriate age. This is called a palatally displaced canine or PDC. The reported prevalence of PDC in the population varies between 1% and 3% (Ericson 1987; Thilander 1973), and it is usually discovered during a clinical dental examination and then confirmed using dental radiographs. Clinical features of a PDC include the canine not being palpable in the buccal sulcus by the age of 10 to 11 years, an asymmetry being present in palpation between the left and right side of the upper jaw, and the lateral incisor being late to erupt or showing a significant buccal proclination (Husain 2016). Dental radiographs may then be used to identify the exact position of the unerupted canine, usually by taking two radiographs at varying angles to the tooth and utilising the principle of parallax to localise it (Husain 2016).

Sometimes an unerupted canine is positioned to the outside or buccal to the dental arch (buccally displaced canine or BDC). It was thought that the majority of unerupted canines are displaced palatally (85%); however, one computerised tomography (CT) study suggested that 50% were palatally displaced, with the remainder either being positioned buccally or in the line of the arch (Ericson 2000).

The aetiology of PDC is thought to be multifactorial (Jacoby 1983). There is much speculation within the literature about whether it is caused by a disturbance in the local environment as the tooth erupts (e.g. guidance theory) (Becker 1995) or by genes (e.g. genetic theory) (Peck 1994). Disturbances in the local environment may include diminutive or absent lateral incisors (Brin 1986), retained primary (baby) canines (Thilander 1968), and crowding or delayed eruptive pathways (Moss 1972; Thilander 1968). There is thought to be a strong genetic component due to the co-occurrence with other dental anomalies, such as hypodontia, enamel hypoplasia, microdontia (Rutledge 2010), familial occurrence (Zilberman 1990), and racial variation (Becker 2015).

BDCs probably have a different aetiology to PDC and are usually caused by a lack of space within the dental arch. Most BDCs will eventually erupt into the mouth without intervention; however, PDCs often require surgery to uncover or expose them and then straightening with an orthodontic appliance or brace.

Unerupted permanent canines can lead to root resorption of the adjacent teeth. Root resorption (a pathological or physiological process that results in the loss of cementum, dentine or pulp) is common, particularly in females with enlarged dental follicles (Chaushu 2015). In the CT study by Ericson and colleagues, root resorption occurred in 38% of lateral incisor teeth and 9% of central incisor teeth (Ericson 2000). Rarely, ectopic canines can lead to cyst formation, infection or referred pain (Shetty 2004).

The management of PDC can be lengthy and time consuming. Leaving a PDC in situ might be considered to avoid complicated treatment with surgery and fixed braces. This is a reasonable option if the primary canine has a good-sized crown and root; however, even in these favourable circumstances, the primary canine will eventually be lost and the timing of this loss is unpredictable. Loss may occur early on in teenage years or as late as the sixth or seventh decade of life. The outcome is often an unsightly gap, leading to replacement of the canine with a denture, dental bridge or implant.

Therefore, it is generally recommended to align PDCs in young people if the displacement is not too severe and treatment with fixed braces is suitable. Alignment often involves a surgical procedure under general anaesthetic to uncover the buried tooth with either an open or closed exposure procedure (Parkin 2017a), followed by over two years of fixed brace treatment to move the canine into the correct position (Iramaneerat 1998).

Other treatment options include surgical removal of the PDC and, rarely, surgical transplantation of the PDC into the correct position within the dental arch.

Description of the intervention

Several interceptive (treating malocclusions as soon as they are detected) interventions designed to correct the direction and encourage the eruption of a PDC have been proposed.

In the past, the mainstay of these interventions was extraction of the primary canine in children aged 10 to 13 years old with normal space conditions. The main evidence offered to support this practice arose from a study by Ericson and Kurol (Ericson 1988). This prospective case series, with no control group, followed a group of children aged 10 to 13 years receiving the intervention (i.e. extraction of the primary canine). Royal College of Surgeons of England guidelines (Husain 2016) support the practice of extracting the primary canine based on evidence provided by this uncontrolled study (Ericson 1988) and one randomised controlled trial (RCT) (Naoumova 2015).

Alternative interceptive interventions to encourage the eruption of PDCs have been proposed and investigated in a number of studies, including some RCTs. Most of these interventions involved some form of space creation with either transverse expansion using rapid maxillary expansion (RME), a quadhelix (QH) or a transpalatal arch (Baccetti 2009; Baccetti 2011), or anteroposterior expansion using headgear (Silvola 2009), or a fixed orthodontic appliance (Olive 2002; Olive 2005).

Whereas most orthodontists would currently suggest interception for a PDC between the ages 9 and 13 years, Olive 2002 reported some improvement in the position of unerupted PDCs when creating space with fixed appliances in 15-year-olds, so we suggest 14 years as an upper age for intervention.

There are several time points that are relevant in terms of measuring the success of an intervention. At four to six months, clinicians would generally be considering a follow-up radiograph to detect signs of improvement in the position of the unerupted canine. If the canine has not erupted after one year, most clinicians would consider it appropriate to explore further treatment options including surgical exposure. These timings are based on the work of Ericson and Kurol (Ericson 1988). The mean length of treatment with fixed orthodontic appliances is 20 months (Tsichlaki 2016). Prolonged wearing of orthodontic appliances can have adverse effects, including poor gingival health, demineralisation and root resorption (Brown 2016).

How the intervention might work

It has been suggested that delayed loss of the primary canine might cause the unerupted permanent canine to be displaced, hence the idea of extracting the primary canine as an early intervention (Lappin 1951). Others have suggested that young people with a narrower than average upper jaw are more likely to have a PDC, hence the idea of creating more space for the unerupted tooth (Schindel 2007).

Why it is important to do this review

If an interceptive treatment leads to successful eruption of the PDC, this will prevent the need for a further more-invasive procedure, commonly performed under general anaesthetic, to uncover or expose the PDC canine and possibly prolonged treatment with orthodontic fixed braces. Fixed braces can lead to damage of the crowns of the teeth if not kept clean, and shortening of the roots of the adjacent teeth, as the canine is brought into alignment. If the PDC is severely displaced then braces may be required for more than three years, which is costly both to the healthcare system and to the child in terms of time away from school.

Since the proposed interceptive interventions might be a young person's first experience of dental treatment, it is important that the effectiveness of the interventions in promoting the eruption of a PDC is investigated. If early treatment is shown to work, then this will help clinicians justify intervening to prevent more-invasive surgical treatment to uncover the buried tooth later. In addition, it is important to investigate whether there are any differences in the success rates or adverse effects of different interceptive interventions that could inform clinical practice.

A Cochrane Review on this topic was first published in 2009 and updated in 2012 (Parkin 2009; Parkin 2012). We wrote and published a new protocol for this review, which widens the scope of that review to incorporate interceptive interventions other than extraction of primary teeth, as these are now being used more routinely to encourage and normalise the eruption of a PDC (Parkin 2017b). We also widened the age range to incorporate interceptive interventions that start earlier and continue later to give more time for the canine to erupt.

OBJECTIVES

To assess the efficacy, safety and cost-effectiveness of any interceptive procedure to promote the eruption of a maxillary permanent canine, which is palatally displaced (PDC) compared to no treatment or other interceptive procedures in young people aged 9 to 14 years old.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs with a non-intervention control group or an alternative intervention group. The minimum period for participant follow-up was six months after intervention or recruitment for the non-intervention controls. We included studies employing a parallel-group design that recruited participants judged to have a unilateral PDC or participants judged to have bilateral PDC, or both.

We included studies that combined data from participants judged to have a unilateral PDC with data from participants judged to have bilateral PDC, if both sides of the dental arch were allocated and received the same intervention/non-intervention. We realise that by excluding some participants from studies where the two sides of the same arch were separately randomised and received a different intervention/non-intervention this will potentially compromise the study randomisation and the effects of this decision are included in the results.

Types of participants

Inclusion criteria

- Studies with children diagnosed as having one or both permanent maxillary canines palatally displaced, where the definition of PDC was clear and likely to be valid (see Table 1: Bazargani 2013 was our preferred definition).
- Studies with at least 80% of participants in the age range 9 to 14 years.

Exclusion criteria

- If the authors of a report stated that participants with craniofacial anomalies or participants with a history of previous orthodontic treatment or participants were still in active orthodontic treatment, then we excluded the study unless the data from these participants could be clearly identified and excluded, either from the article or by contacting the authors.

Types of interventions

Any interceptive intervention, including the following.

- Extraction of the primary canine (single extraction) or primary canine and first molar (double extraction).
- Creation of space by widening the upper dental arch, using RME, QH or other technique.
- Creation of space by lengthening the upper dental arch, using headgear, mini-implants or other technique.
- Creation of space by widening the space within the dental arch, using a fixed orthodontic appliance or other technique.

Types of outcome measures

Primary outcomes

- Incidence of eruption of the PDC into the mouth. Successful eruption was defined as sufficient tooth showing to allow bonding of an orthodontic attachment without the need for surgery to uncover the tooth.

Secondary outcomes

Treatment efficacy

- Incidence of successfully erupted PDC that were favourably positioned, where this was defined as requiring no further active treatment to straighten the PDC using orthodontic appliances.
- Reported number of participants referred for surgical exposure of the PDC following the intervention.
- Reported time point of participants referred for surgical exposure of the PDC following the intervention.
- Time taken for the canine to erupt into the mouth following the intervention.

- Overall treatment time wearing orthodontic appliances.
- Any patient-reported outcomes (PROs), including the impact of the intervention assessed using measures of health-related quality of life or pain (or both) experienced.

Adverse events

- Reported incidence, prevalence, severity, or combination of on root resorption of the impacted canine or the adjacent incisors and first premolars (or both canine and incisors and first premolars), where root resorption was assessed using an ordinal index or the amount measured in millimetres.
- Any other adverse effects of the interventions, such as incidence and severity of gingival disease and demineralisation.

Cost-effectiveness

- Costs, including those of materials, facilities and the time of children, parents and clinicians.

We also examined:

- the effect that severity of PDC displacement towards the midline had on the proportion of successful spontaneous PDC eruptions with and without intervention.

We assessed outcomes for each included study at more than one time point. Clinically relevant time points were about four to six months, 12 months and 18 months following the completion of the intervention.

Search methods for identification of studies

Electronic searches

Cochrane Oral Health's Information Specialist conducted systematic searches in the following databases for RCTs and controlled clinical trials. Due to the Cochrane Centralised Search project to identify all clinical trials on the database and add them to CENTRAL, we only searched recent years of the Embase database. Please see the searching page on the Cochrane Oral Health website for more information. We did not place any other restrictions on the language or date of publication when searching the electronic databases:

- Cochrane Oral Health's Trials Register (searched 3 February 2021) (Appendix 1);
- Cochrane Central Register of Controlled Trials (CENTRAL; 2021, Issue 1) in the Cochrane Library (searched 3 February 2021) (Appendix 2);
- MEDLINE Ovid (1946 to 3 February 2021) (Appendix 3);
- Embase Ovid (8 May 2017 to 3 February 2021) (Appendix 4).

Subject strategies were modelled on the search strategy designed for MEDLINE Ovid. Where appropriate, they were combined with subject strategy adaptations of the highly sensitive search strategies designed by Cochrane for identifying RCTs and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2020)).

Searching other resources

We searched the following trial registries for ongoing studies (see Appendix 5 for the search strategies):

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov; searched 3 February 2021);
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch; searched 3 February 2021).

We checked the bibliographies of included studies and any relevant systematic reviews identified for further references to relevant trials.

We did not perform a separate search for adverse effects of interventions. We considered adverse effects described in included studies only.

We sent letters and emails to corresponding authors of relevant studies to identify unpublished trials or to clarify data.

We checked that none of the included studies in this review were retracted due to error or fraud.

Data collection and analysis

Selection of studies

The search was designed to be sensitive and include controlled clinical trials, these were filtered out early in the selection process if they were not randomised. A minimum of two review authors, independently and in duplicate, examined the titles, keywords and abstracts of reports identified from the search strategy for evidence of the following criteria.

- Is this an RCT?
- Are the participants 9 to 14 years of age?
- Is an intervention employed to encourage eruption of an unerupted palatally displaced maxillary permanent canine?

If the report fulfilled these three criteria, or if one or both review authors were unable to assess this from the title, keywords or abstract, we obtained the full article. All review authors were involved in screening the titles and abstracts. Disagreements were resolved through discussion between all the review authors.

Data extraction and management

Two review authors, both independently and in duplicate, extracted data from the included studies using a standardised data extraction form. Data extracted included the flow of participants in the study (e.g. number eligible, randomised and analysed), the characteristics and methodology of the study, and the prespecified primary and secondary outcomes of the review. We also recorded the method of assessment, units/scales of measurements and time(s) used in the studies to collect outcome data. Where possible, review authors contacted trial authors to request any missing data/information.

Assessment of risk of bias in included studies

A minimum of two review authors, independently and in duplicate, assessed the risk of bias in the included studies using version 1 of the Cochrane risk-of-bias tool for RCTs (RoB1). This tool is structured into a fixed set of domains related to different aspects of trial design, conduct and reporting leading to a judgement of a 'low', 'high' or 'unclear risk of bias, which are supported using written justifications. The overall risk of bias was the least favourable assessment across all domains. All the review authors

were involved in data extraction. Disagreements were resolved through discussion between all the review authors.

Measures of treatment effect

We assessed the primary outcome, namely the incidence of successful eruption of the PDC, using dichotomous data (i.e. 'yes' if the PDC successfully erupted and 'no' if it did not). We used risk ratio (RR) with 95% confidence interval (CI) as the summary measure.

For secondary outcomes with dichotomous data, such as the incidence of successfully erupted PDC that were favourably positioned, the incidence of young people requiring surgery to uncover the PDC and some root resorption data, we summarised data using RR with 95% CI. For secondary outcomes with continuous data, such time points for referral for surgery, time taken for the PDC to erupt, some PROs, adverse effects and cost-effectiveness outcome, when available, we summarised data using mean differences (MD) and 95% CI.

We examined and interpreted the outcome examining the effect of severity of PDC displacement towards the midline on the proportion of successfully erupted PDCs through narrative description.

We considered the most important time point for analysis to be 12 months; as Ericson and Kurol suggested there was no further improvement in the position of the PDC after this time (Ericson 1988). However, Olive observed that some PDCs successfully erupted up to 27 months following the start of active treatment to open space (Olive 2002). Therefore, we assessed outcomes at several time points to determine if there was any evidence of further change in the outcomes and if this was likely to be due to the intervention. We examined the effect of time point on the primary outcome and interpreted it through narrative description.

Unit of analysis issues

The unit of analysis for most outcomes was the individual participant, not teeth. The data for individual teeth are reported for the prevalence of root resorption at 12 months following extraction of the primary canine compared with no extraction. Individual tooth data are also provided for the outcome examining the relationship between the severity of displacement towards the midline and the prevalence of successful PDC eruption.

Where reports of included studies had sufficient information, we planned to use an aggregate data approach for meta-analysis. However, for each study we had to contact the authors for further information, particularly concerning the primary outcome of the review. All the authors responded to requests for further information and, although they did not provide us with individual participant data, we were able to complete the analysis using this additional information.

For the primary outcome and most secondary outcomes, we included data from participants judged to have a unilateral PDC, who received the intervention and the outcomes assessed on only the affected side. Some secondary outcomes concerning adverse events (root resorption, gingival diseases and demineralisation) could involve comparisons with the untreated contralateral canine.

We included the data from those participants judged to have bilateral PDCs and the participant was the unit of randomisation (i.e. both right and left sides were allocated to the same intervention or control). When the outcomes on the two sides were the same and favourable (i.e. both teeth erupted successfully) we recorded this. When the outcomes on the two sides differed, then we included the data from the PDC with the least favourable outcomes in the analysis (i.e. if a tooth on one side of a participant's mouth erupted, but the tooth on the other side of the mouth did not erupt, then we included the data from the unerupted tooth in the analysis). Therefore, only one outcome was recorded for each participant.

For the studies that randomised one side to intervention and the contralateral side to control, we only included data from the PDC that was allocated to the intervention for reasons of confounding outlined earlier.

For the studies that randomised the two sides separately, we only used the data for participants where the two teeth were allocated to the same on both sides (both teeth received the same intervention or both teeth were control teeth). In this situation, we included the data from the tooth with the worst outcome in the analysis.

Dealing with missing data

When possible, we investigated the effect of assignment to intervention using a full intention-to-treat (ITT) analysis. This requires that participants be analysed in the groups to which they were allocated, regardless of whether they received their allocated intervention (or non-intervention) or switched groups, and that outcome data from all randomized participants are included in the analysis. We contacted the authors of all the included studies to request additional and missing data and to clarify any inconsistencies in their reports. If the authors reported that participants dropped out or withdrew and no data were collected, when possible, we undertook a full ITT analysis employing the last observation carried forward (LOCF) method (White 2011). For the primary outcome of successful eruption of the PDC, this made the assumption that if the tooth was not erupted at the observation before withdrawal, then it was still unerupted at the missing observation.

Assessment of heterogeneity

We were able to undertake meta-analyses for one comparison, single versus double primary tooth extraction. We assessed clinical and methodological heterogeneity by examining the types of participants, interventions and outcomes in each study.

We assessed statistical heterogeneity by inspection of a graphical display of the estimated treatment effects from the included studies by performing Cochran's Q (derived from a Chi^2 test) and calculating the I^2 statistic (which describes the percentage of variability due to heterogeneity rather than to chance and ranges from 0% to 100%).

With regards to the I^2 statistic, low values indicate little or no heterogeneity and high values indicate considerable heterogeneity. The percentage value of the I^2 statistic can be interpreted as indicating that heterogeneity might not be important (0 to 40%), or may be moderate (30% to 60%), substantial (50% to 90%) or considerable (75% to 100%), as per the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2020).

The importance of the observed value of the I^2 statistic depends on the magnitude and direction of effects, and the strength of evidence for heterogeneity (e.g. P value from the Chi^2 test or the CI for the I^2 statistic) (Higgins 2020).

Assessment of reporting biases

Reporting bias arises when the reporting of research findings is influenced by the nature and direction of the findings of the research. To minimise potential reporting biases, we conducted a sensitive search of multiple sources with no restriction on language or completion of the trial. If there were more than 10 studies for one outcome, we planned to construct a funnel plot and examine it for asymmetry, which is evidence of potential publication bias. Only four studies are included in this review, therefore we were unable to construct a funnel plot.

Data synthesis

The primary outcome of the review was dichotomous (yes the PDC successfully erupted or no the PDC did not successfully erupt) and assessed using RR with 95% CI. The secondary outcome summarising the incidence of successfully erupted PDC that were favourably positioned was also dichotomous and similarly assessed using RRs with CIs. The secondary outcomes for efficiency (time taken for the canine to erupt, overall treatment time, PROs), some adverse events (severity of root resorption in millimetre) and cost-effectiveness were continuous outcomes and were assessed using MD with 95% CIs. The remaining efficiency outcomes (reported number of participants referred for surgery, reported time points for referral), adverse event outcomes (incidence/prevalence and severity of root resorption, gingival disease and demineralisation) were ordinal data, but were too infrequently reported for a formal statistical analysis. The effect that severity of PDC displacement towards the midline has on the proportion of successful spontaneous PDC eruptions with and without intervention was analysed descriptively with no formal statistical analysis.

The study design and in particular the method of within-person allocation for some studies was taken into account as described previously (Unit of analysis issues) to avoid potential unit of analysis error.

Subgroup analysis and investigation of heterogeneity

We performed no formal subgroup analyses. We discussed differences in the successful eruption of PDCs that were initially mild, moderate or severely displaced towards the midline at the level of a descriptive analysis.

Sensitivity analysis

We undertook descriptive sensitivity analyses to investigate the effect of excluding the data from participants diagnosed with bilateral PDCs on the comparison extraction of the primary canine versus no extraction. We examined the investigator supplied data for the primary outcome and the secondary outcome referred for surgical exposure at 12 months.

We also undertook sensitivity analyses to compare a full ITT analysis employing the LOCF method with a 'modified intention-to-treat' (mITT) analysis using only the available reported participant data to investigate the potential effect of attrition bias on the findings. We also investigated the effect of excluding one study for the comparison single versus double primary tooth extraction (Hadler-Olsen 2020). In this study, some participants judged to have a bilateral PDC were excluded from our analysis, as the two sides of the same arch were randomised separately and received different interventions/non-interventions. We examined the outcomes successful eruption of the PDC at 18 and 48 months, as well as the referral for surgical exposure at 48 months.

Summary of findings and assessment of the certainty of the evidence

We developed summary of findings tables for the comparisons and outcomes that we considered most important for patients and clinicians using GRADEpro GDT software (GRADEpro GDT). The primary outcome was the successful eruption of the PDC, such that it no longer required surgical exposure either under local or general anaesthetic. We also included the outcome referred for surgical exposure, which we believe is relevant for patients and clinicians. This outcome is not necessarily the inverse of the primary outcome (i.e. if the PDC remains unerupted the patient is referred for surgical exposure). On examination of the patient's radiograph, the clinician might consider the position of the PDC to have improved and, therefore, may decide to review the patient again in a few months to see if the PDC will erupt. We would certainly consider this to be appropriate at the 12-month review.

Unfortunately, the outcomes were assessed at different time points for the two comparisons. For the comparison of primary canine extraction versus no extraction, there were data for both outcomes at 12 months and we included these data in the summary of findings table. For the comparison of single versus double primary tooth extraction, we used the 18-month data in the summary of findings table as we believe this to be the most appropriate time point, as outlined in the Discussion. Data for surgical exposure referral were only available at 48 months and we have summarised these in the summary of findings table.

We assessed the level of certainty in the findings with reference to the risk of bias assessments, directness of the evidence, consistency of the results, precision of the estimates and risk of publication bias. We categorised the level of certainty for each of the comparisons as high, moderate, low or very low.

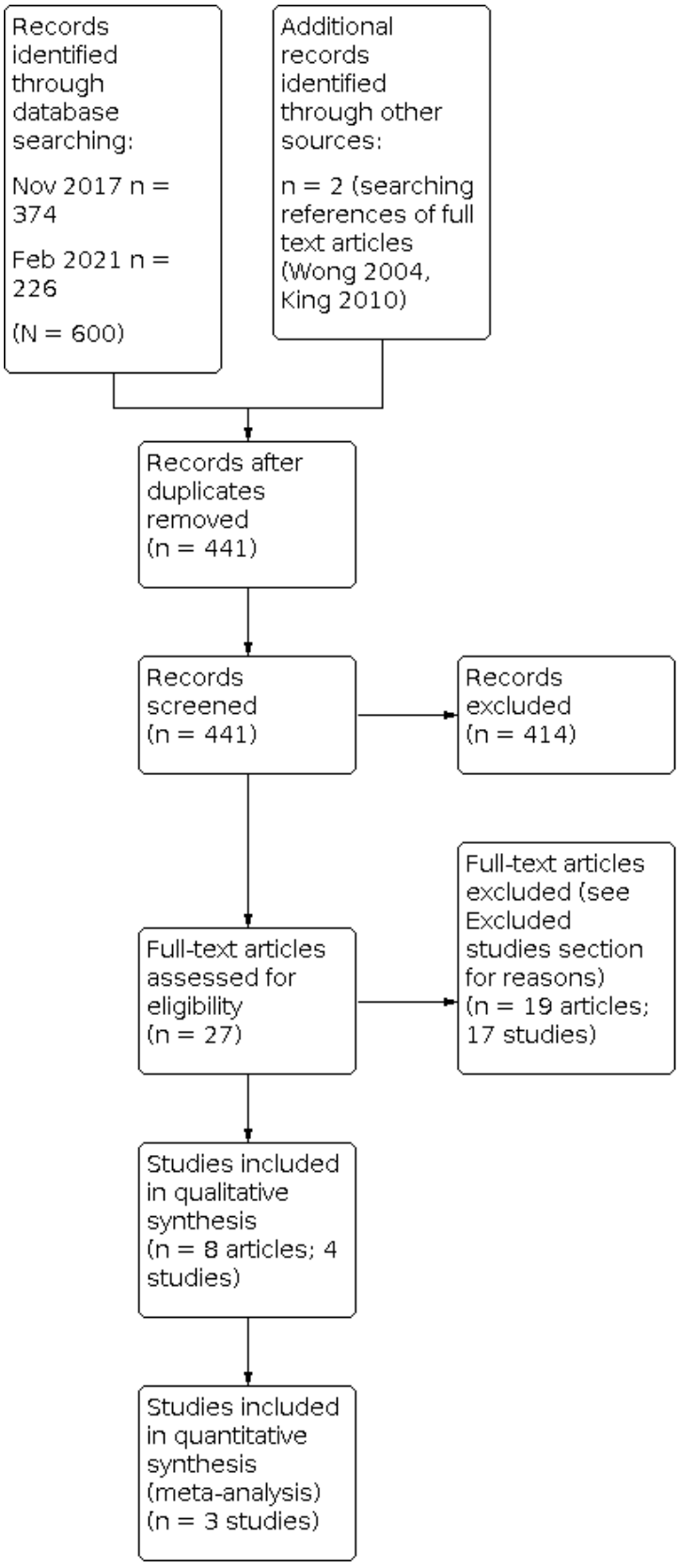
RESULTS

Description of studies

Results of the search

The results of the searches are shown in a flow diagram (Figure 1). Searches undertaken up to 3 February 2021 identified 600 articles. A search of these references identified two further articles giving a total of 602 references. This was reduced to 441 when duplicates were removed. Following screening of titles and abstracts, we discarded 414 records and obtained the full articles for the remaining 27 records. On examination of the full articles, we excluded 19 articles (17 studies), leaving eight articles (four studies) for inclusion in the review. Three studies were described in three articles (Bonetti 2010; Bonetti 2011; Hadler-Olsen 2020), and one study was described across five articles (Naoumova 2015).

Figure 1.



Characteristics of the trial participants and settings

The four studies involved 199 randomised participants (164 analysed), 108 girls and 91 boys, 82 diagnosed with unilateral PDC and 117 with bilateral PDC. The participants were aged between 8 and 13 years at recruitment.

All studies were undertaken in Europe, two in Italy (Bonetti 2010; Bonetti 2011), one in Sweden (Naoumova 2015), and one in Norway (Hadler-Olsen 2020). Two studies screened, recruited, delivered the intervention and followed up participants in a single centre dental teaching hospital (Department of Orthodontics, University of Bologna, Italy) (Bonetti 2010; Bonetti 2011). One study screened participants in one of 15 public dental clinics in or around Gothenburg, Sweden (Naoumova 2015). Eligible participants were invited to take part, then recruited, consented, randomised and followed up in one dental teaching hospital orthodontic department (University Clinics of Odontology, Gothenburg), where any intervention was provided by one operator. In the fourth study, participants were screened, invited and any intervention and follow-up was delivered in one of two centres, one public (the Public Dental Health Competence Centre of Northern Norway, Tromsø) and one private provider (Bryne, Norway) (Hadler-Olsen 2020).

Characteristics of the interventions

One study, involving 67 participants, compared the extraction of the upper primary canine versus non-extraction of the primary canine (Naoumova 2015). The study randomised 45 participants with suspected unilateral PDC to one of two parallel groups, either to have the extraction of the primary canine on the side of the suspected PDC (23 participants) or a non-intervention, no extraction control (22 participants). After 12 months, if the PDC had not erupted in control participants then the primary canine was extracted.

The study randomly allocated 22 participants with a suspected bilateral PDC using a within-person (or split mouth) technique to either have their upper primary canine removed on the participant's right or left upper dental arch, with the suspected PDC on the opposite side used as a non-extraction control. Again we have an issue with this approach because there is risk, with such small numbers, that potential confounders, such as the severity of PDC displacement, will not be accounted for in the randomisation process. Two reports from this study indicated that the severity of displacement of a PDC does affect whether the tooth will erupt or not (Naoumova 2015; Naoumova 2018); therefore, we decided to exclude data from the non-intervention control side of those with bilateral PDC and only include the data from the intervention side.

Three studies, involving 132 participants, compared single upper primary canine extraction versus double upper primary canine and first molar extraction (Bonetti 2010; Bonetti 2011; Hadler-Olsen 2020). Two studies randomly allocated participants to one of two parallel groups (single extraction of the upper primary canine versus double extraction of the upper primary canine and first molar) (Bonetti 2010; Bonetti 2011). If participants were diagnosed with a unilateral PDC (21 participants, 21 teeth; 19 analysed) then the intervention was delivered to only the side of the upper dental arch where the succeeding permanent canine was suspected to be 'centrally or palatally displaced'. If the participant was diagnosed with bilateral PDC (79 participants, 158 teeth; 77 analysed, 154 teeth), then the same allocated intervention was delivered to both sides.

One study randomly allocated 16 participants diagnosed with unilateral PDC to one of two intervention groups (single extraction of the upper primary canine versus double extraction of the upper primary canine and first molar) on the side of the dental arch with the suspected unilateral PDC (Hadler-Olsen 2020); however in 16 participants diagnosed with bilateral PDC a within-person study was employed and the two sides were randomly allocated to groups separately. We decided to include the data for the 16 participants with unilateral PDC, who were randomised to either single extraction of primary canine or double extraction of both primary canine and primary first molar and those participants with bilateral PDC who received the same intervention on both sides (both sides single extraction of primary canine only or both sides double extraction of both primary canine and primary first molar; seven participants). We decided to exclude data for our primary outcome (successful eruption of the PDC) for nine participants in this study who had bilateral PDC and who received different interventions on the two sides. The reason for this is because of the risk of potential confounding factors (i.e. one side could have been in a more severe position than the other, which would explain why it did not erupt and not the intervention). We do not believe that randomisation of such a small number will account for potential confounding factors such as the severity of PDC displacement.

Characteristics of the outcomes

Two studies did not have an explicit statement of their prespecified primary outcome of most interest or when it was to be assessed, as required by the CONSORT guidelines (Bonetti 2010; Bonetti 2011). One of these failed to report a sample size calculation from which the primary outcome could be inferred (Bonetti 2010). The other indicated that the sample size was based on 'a pilot sampling of canines' and detecting a difference between the two groups of 10 degrees in the alpha-angle of the canine (alpha-angle as described by Ericson 1988), which would require "a minimum of 26 canines … for each group", thereby ignoring the potential effect of clustering of teeth within the mouth (Bonetti 2011).

Naoumova 2015 stated that the primary outcome was the successful eruption of the PDC by 24 months; however, the authors go on to use a different outcome for their sample size calculation, based on "detecting a difference of 5 degrees (SD [standard deviation] 6.38) of angle measured in the frontal and sagittal views between the extraction and the CG [control group]". This is contrary to the CONSORT guidelines, which suggest that the justification for the sample size should be based on the primary outcome.

Similarly, Hadler-Olsen 2020 stated two primary outcomes in the report (emergence of the maxillary canine into the oral cavity and emergence of the maxillary canine into a favourable position), but not the most important time point these outcomes would be assessed. However, the sample size was justified on the basis of an improvement in the alpha-angle. When questioned on this, the corresponding author confirmed that the primary outcome in the protocol was change in the alpha-angle and, therefore, was different to that in the report.

In terms of secondary outcomes, two of the studies do not provide an explicit declaration of what these were and when they were to be assessed (Bonetti 2010; Bonetti 2011). The third

study reported these as various radiographic positional changes of the PDC over time and root resorption of the adjacent teeth (Naoumova 2015). Hadler-Olsen 2020 explicitly described various secondary outcomes in their report, including the alpha-angle, which, according to the authors, was the primary outcome in the protocol.

The studies were all implicitly investigating the superiority of one intervention either over a no treatment control (Naoumova 2015), or over an alternative intervention (Bonetti 2010; Bonetti 2011; Hadler-Olsen 2020).

Excluded studies

The details and reasons for exclusion of 17 studies are outlined in the Characteristics of excluded studies table.

Studies awaiting classification

We found no studies awaiting classification.

Ongoing studies

One study is ongoing (NCT03684525; see Characteristics of ongoing studies table).

Risk of bias in included studies

The risk of bias assessments are summarised in Figure 2 and Figure 3, and details provided in the risk of bias sections of the Characteristics of included studies table). Overall, we assessed two studies at high risk of bias (Bonetti 2010; Bonetti 2011), and two at unclear risk of bias (Hadler-Olsen 2020; Naoumova 2015).

Figure 2.

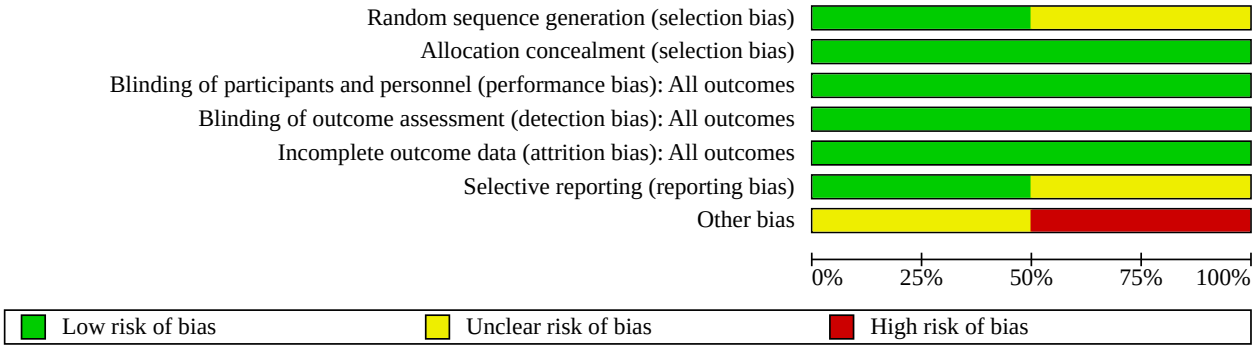
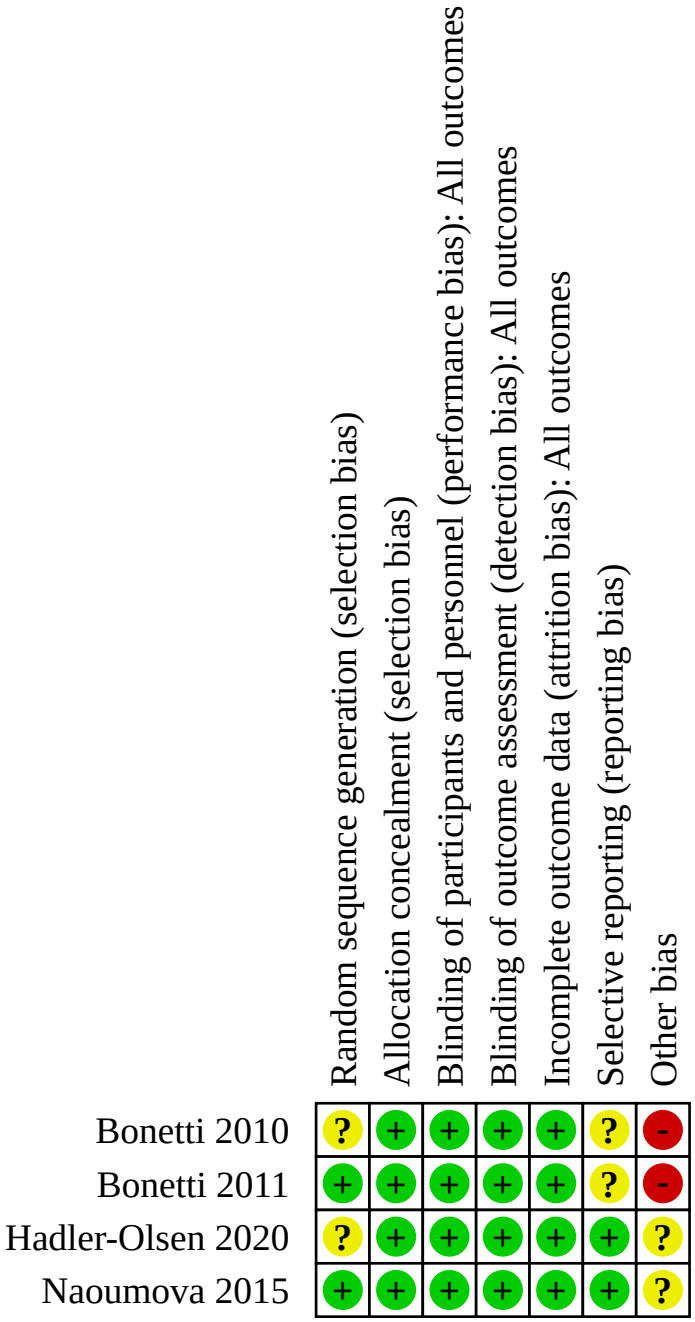


Figure 3.



Allocation

Following further clarification from all the corresponding authors about their random sequence generation and allocation concealment, we assessed two studies at low risk of selection bias (Bonetti 2011; Naoumova 2015). Allocation concealment was at low risk of bias for the remaining study (Bonetti 2010; Hadler-Olsen 2020); however, the random sequence generation was assessed as an unclear risk of bias. There was an apparent imbalance in the severity of PDC displacement between the two groups at baseline. Severity of PDC displacement is a potential confounding factor, that

could have a significant effect on the outcome of the intervention. The fact that the randomisation process apparently did not account for this confounder indicates to us that this should be considered an unclear risk of bias.

Blinding

It was not possible to blind either participants or clinicians to the participants' assigned intervention throughout the trial; however, the review authors do not consider that this knowledge would affect the primary outcome of the review (i.e. whether the permanent canine would erupt into the mouth or not), so the risks of either performance or detection bias (or both) were low. Neither was there evidence that the group assignment led to a failure to implement the intervention as intended, or to trial participants not agreeing to their assigned intervention.

Incomplete outcome data

There were very few withdrawals and dropouts from any study and they were all judged at low risk of attrition bias.

Selective reporting

We assessed two studies at unclear risk of selective reporting bias, as they did not report registration of the studies in a publicly available database or availability of a study protocol prior to recruitment starting and there is little indication that data were analysed in accordance with a prespecified analysis plan that was finalised before unblinded outcome data were available for analysis (Bonetti 2010; Bonetti 2011).

One study reported that the trial was registered (www.fou.nu/is/sverige; reg nos: 40921), but we were unable to access this register to confirm when registration occurred (Naoumova 2015). The study authors stated that the protocol was not published before trial commencement and, as previously stated, the primary outcome did not match the outcome used to justify the sample size. The fact that the primary outcome changed between the protocol and the study report does not necessarily indicate that a study is at a higher risk of bias. Although the author did not explain why this change had occurred, she was forthcoming with all the information we requested and we therefore judged the study at low risk of bias in this domain.

The fourth included study also reported that it was registered in an open-access clinical trials database and all the important outcomes were reported, except pain/discomfort from the intervention (Hadler-Olsen 2020). However, the stated primary outcome in the database did not match the two primary outcomes in the report and the corresponding author confirmed that the primary outcome was changed between the protocol and the report. Although the author did not explain why this change had occurred, he was forthcoming with all the information we requested and we therefore judged the study at low risk of bias in this domain.

Other potential sources of bias

There were several areas of potential high risk of bias from other sources. We considered two studies at high risk of bias due to concerns as to how representative the samples were of people with PDC, and in particular, the very high prevalence of participants judged to have bilateral PDCs (Bonetti 2010; Bonetti 2011). We also have some concerns regarding the validity of diagnosing PDCs in the younger age ranges included in the study. Peck 2011 also expressed this concern (see 'Age when a PDC can be reliably identified' under Overall completeness and applicability of evidence). There were issues with the other two studies and we judged these at an unclear risk of bias (Naoumova 2015; Hadler-Olsen 2020).

Effects of interventions

See: **Summary of findings 1** Primary canine extraction versus no extraction; **Summary of findings 2** Double primary (canine and first molar) extractions versus single primary (canine) tooth extraction

The four studies in this review investigated two comparisons: extraction of the primary canine compared with no extraction and extraction of the primary canine (single primary extraction) compared with the extraction of the primary canine and primary first primary molar (double primary extraction).

Extraction of the primary canine versus no extraction

One study, involving 67 participants, compared extraction of the primary canine with no extraction (Naoumova 2015). For the reasons explained previously (see 'Characteristics of the interventions' under Included studies), we only included data from those participants judged to have a unilateral PDC and were therefore randomly allocated to parallel intervention or no-intervention groups (45 participants).

Primary outcome

Incidence of eruption of the palatally displaced canine into the mouth

These data for the primary outcome of successful eruption of the PDC at 12 months following the intervention/start of observation are shown in Table 2. In 9/23 (39%) participants who had extraction of the primary canine, the PDC successfully erupted at 12 months. This compares to 3/22 (14%) participants in whom the PDC successfully erupted when the primary canine was not extracted. According to these data, extracting the primary canine increases the proportion of PDCs that successfully erupt into the mouth within a 12-month period by 2.87 (risk or prevalence ratio), but the 95% CIs are wide (0.90 to 9.23) and include the possibility that there is no difference between extraction and no extraction. The effect of excluding the data from the participants judged to have bilateral PDCs is described in the sensitivity analysis below.

Secondary outcomes

Treatment efficacy

Eighteen of 45 (40%) participants diagnosed with a unilateral PDC were referred for surgical exposure at 12 months because either the position of the PDC had not improved or worsened on radiographs (Table 3: 7/23 in the extraction group, 11/22 in the no-extraction group). The RR was 0.61 (95% CI 0.29 to 1.28), and the CIs indicate that there was no difference in actual surgical referral between the two groups.

Table 4 shows that the probability that PDC would successfully erupt depends on how displaced the PDC was when diagnosed. Those teeth with a relatively minor displacement towards the midline (sector 2) were much more likely to erupt (14/19 teeth; 74%) compared with those in sector 4 (0/10 teeth).

In terms of PROs, Naoumova 2015 published one article investigating pain, discomfort and use of analgesics following the extraction of primary canines (Naoumova 2012). The article included data from 44 young people who had extraction of one primary canine, which we presumed consisted of the 22 participants in the RCT diagnosed with bilateral PDCs (who had a single primary canine extraction) and 22/23 participants diagnosed with a unilateral PDC. However, the reports stated that a much higher proportion of young people with bilateral PDC were screened and invited to take part in the study (37 with bilateral PDC, 20 with unilateral PDC) and 54 were randomised (three young people or parents with bilateral PDCs declined to participate and those randomised to non-extraction were excluded). The extraction group were compared with a similar group of young people who were not taking part in the RCT; these data are outside the scope of this review. Self-reported pre–post visual analogue scale (VAS) pain data were collected the evening after the extraction and one week later. This showed that the pain and discomfort from the extraction of the primary canine was low both during and after the procedure, although the injection was more painful than the extraction in girls. Pain and discomfort were mostly not present at one week. They found that 35% of the boys and 50% of the girls took one dose of analgesia the evening following the extraction, although the prevalences of other impacts were low.

Adverse events

Naoumova 2015 assessed root resorption of the adjacent permanent teeth caused by the PDC during the study using cone beam computerised tomography (CBCT) radiographs obtained at 0, 6 and 12 months and graded as per the Ericson 2000 classification of root resorption: 1. no resorption, intact root surfaces and the cementum layer may be lost; 2. slight resorption, resorption up to half of the dentine thickness to the pulp; 3. moderate resorption, resorption midway to the pulp or more, the pulp lining being unbroken and 4. severe resorption, the pulp is exposed by the resorption. An exclusion criterion for this study was grade 3 or 4 resorption of adjacent permanent teeth caused by the PDC, but no participants were excluded for this reason either at the start or during the study. The reason for this was to prevent participants with severe root resorption being randomised to control/no treatment as this was deemed unethical. Table 5 shows the proportion of participants with root resorption of their adjacent permanent teeth caused by the PDC at 12 months. The data shows no difference between the two groups with an RR of 0.60 (95% CI 0.28 to 1.31).

Cost-effectiveness

The study did not report cost-effectiveness.

Effect severity of PDC displacement towards the midline had on the proportion of successful spontaneous PDC eruptions

The study did not report the effect severity of PDC displacement towards the midline had on the proportion of successful spontaneous PDC eruptions.

Sensitivity analyses

To determine if inclusion of data from the participants diagnosed with bilateral PDCs might influence the results, we asked the corresponding author for further information about the primary outcome of our review. The author replied that at 12 months, 3/22 participants diagnosed with bilateral PDCs had both canines erupted (two participants had eruption on the extraction side after eight months and the non-extraction side after 12 months and one participant had eruption on both sides after 12 months) and that there were no other eruptions at this time point. Therefore, these data indicate that equal numbers of extraction and non-extraction side PDCs had erupted in participants with bilateral PDCs at 12 months. We have not included them in the formal analysis as we did not believe it would change the findings.

We also asked the corresponding author for more information concerning the secondary outcome, referral for surgical exposure. The response was that the number of participants with bilateral PDCs who had surgical exposure due to the intervention PDC not erupting was seven and the number of participants who had surgical exposure due to control side PDC not erupting was 16. This makes a total of 23, which is one larger than the total number of participants judged to have bilateral PDCs in the trial. This shows that at least one individual had surgical exposure on both sides and demonstrates that interpreting the data from participants with bilateral PDCs for this outcome could be problematic. It is possible that, for practical reasons, surgery was undertaken on both sides to avoid participants undergoing a second procedure at a future date if the contralateral PDC did not erupt. Again, we did not include these data in the formal analysis.

Single versus double primary tooth extraction

Three studies, involving 132 participants (119 analysed), compared extraction of a single primary (canine) tooth with double primary (canine and molar) extraction (Bonetti 2010; Bonetti 2011; Hadler-Olsen 2020).

Primary outcome

Incidence of eruption of the palatally displaced canine into the mouth

All three studies assessed the primary outcome of successful eruption of the PDC at 18 months (or a mean of 18 months) following the intervention. The results suggest that there is no difference in the successful eruption of the PDC at 18 months with a double primary tooth extraction versus extraction of the primary canine only (RR 0.68, 95% CI 0.35 to 1.31; mITT; Analysis 1.1).

Hadler-Olsen 2020 also had data for successful eruption of the PDC at 12 months (23 participants; Table 6) and 24 months (23 participants; Table 7). Neither of these tables showed a difference in the successful eruption of the PDC following extraction of two primary teeth compared with extraction of only the primary canine (RR at 12 months: 0.27, 95% CI 0.04 to 2.08; Table 6; RR at 24 months: 0.61, 95% CI 0.29 to 1.25; Table 7). In this study, all participants received their allocated intervention and there were no withdrawals or dropouts; however, we excluded some participants because they received different treatment on the two sides of their mouth. Therefore, we have categorised our analysis as mITT and we were unable to perform a true ITT analysis. The study observed an increase in the number of PDCs erupting between 12 and 18 months in both groups (extraction of canine only from four to eight; extraction of canine and molar from one to four), but little change in the number erupting between 18 and 24 months (extraction of canine only from eight to nine; extraction of canine and molar from four to five). This suggests that 18 months is a suitable period to observe the eruption of the PDC and if the tooth is not through then, clinicians should consider further intervention.

Two studies also had data for successful eruption of the PDC a maximum of 48 months after the intervention (Bonetti 2010; Bonetti 2011). This suggests that there was a slightly higher prevalence of eruption of the PDC with a double primary extraction compared to a single primary extraction (RR 1.28, 95% CI 1.06 to 1.54; mITT; Analysis 1.2). These two studies observed a large increase in the number of PDCs erupting between 18 and 48 months in both groups (extraction of canine only from 8 to 34; extraction of canine and molar from 7 to 47) and we discuss possible reasons for this below.

Secondary outcomes

Treatment efficacy

Hadler-Olsen 2020 reported emergence of the PDC into a favourable position (they stated this was a primary outcome although this was not stated as such in their protocol). The study defines a favourable position as "maxillary canines erupted in sector I in clinically normal buccopalatal relationship with occluding teeth in the mandible". The data for this outcome at 12, 18 and 24 months are summarised in Table 8, Table 9, and Table 10. These show that very few of the PDCs that erupted into the mouth were in a favourable position (at 24 months, only 5/14 erupted PDCs were in a favourable position) and orthodontic alignment was still required.

Two studies, from the same university clinic in Italy, had data for surgical exposure after a maximum observation period of 48 months (Bonetti 2010; Bonetti 2011). There was no difference in the proportions referred for surgical exposure between the single and the double primary extraction groups data at 48 months (RR 0.31, 95% CI 0.06 to 1.45, mITT; Analysis 1.3). This finding is unexpected. If, as suggested by the previous finding, there was a slightly higher proportion of participants in the double extraction group with successfully erupted PDCs at 48 months, then there should be a lower proportion referred for surgical exposure, because it is very unlikely that the tooth will erupt so long after the intervention and clinicians should be referring for surgery. We investigated this further using a sensitivity analysis, which is reported below.

Hadler-Olsen 2020 reported that nine participants required surgical exposure at various stages throughout the study as the PDC was judged to have worsened on the review radiograph. Five participants at 12 months (in single extraction group, 4 in double extraction group), one at 18 months (double extraction group) and three at 24 months (2 in single extraction group, 1 in double extraction group).

Adverse events

The studies did not report adverse events.

Cost-effectiveness

The studies did not report cost-effectiveness.

Effect severity of PDC displacement towards the midline had on the proportion of successful spontaneous PDC eruptions

Data from Hadler-Olsen 2020 on the effect of severity of displacement towards the midline and proportion of successfully erupted PDC at 12, 18 and 24 months are shown in Table 11, Table 12, Table 13. There were no withdrawals or dropouts. These tables include data for all teeth, including the nine participants diagnosed with bilateral PDC who were excluded from other analyses as they had different interventions on the two sides, as the potential confounding effect of severity of PDC displacement would be examined in this analysis. These demonstrate that the proportion of successfully erupted PDCs increases between 12 and 18 months, but there is little change between 18 and 24 months. This again would suggest that 18 months is a suitable observation period following an intervention. The data also show a partial relationship between severity of medial displacement and proportion of successfully erupted PDCs with 5/7 teeth starting in sector 2 erupted at 18 months (no change at 24 months), whereas only 9/18 teeth that started in sector 3 had erupted at 18 months (slightly improved to 8/18 at 24 months). However, 4/5 teeth starting in sector 4 had erupted at 18 months and this increased to 5/5 at 24 months, which does not support the hypothesis that the more towards the midline the tooth is, the less likely the success of any intervention.

Table 14 and Table 15 show data for the effect of severity of displacement towards the midline on the proportion of successfully erupted PDCs at a mean of 18 months and a maximum of 48 months for Bonetti 2010 and Bonetti 2011 combined. A striking feature of these tables is that 33 teeth were judged to be in sector 1, which we would consider to be a normal position for an undisplaced canine. Why these were included in the study is not clear. The majority of the teeth were judged to be in sector 2 (75/132, 57%), which, again in a young child with an immature lateral incisor would be considered to be a normal position for an undisplaced canine. The data at 18 months show a relationship between medial displacement and proportion of successfully erupted PDC with 17/75 (23%) starting in sector 2 being erupted compared with 1/17 (6%) starting in sector 3 and 1/7 (14%) in sector 4. A relationship between medial position and proportion of successfully erupted PDCs is not supported by the data at 48 months with 54/79 (68%) PDCs starting in sector 2 erupted, 13/15 (87%) starting in sector 3 and 6/7 (86%) in sector 4.

Sensitivity analyses

We conducted sensitivity analyses to investigate the effect of potential attrition bias on the outcomes by comparing the data from a mITT analysis with that of an ITT analysis calculated using LOCF. For the primary outcome, this assumed the worst-case scenario for the missing participants was that the PDC remained unerupted. This showed no difference in the successful eruption of the PDC at 18 months between the two analyses (mITT: RR 0.68, 95% CI 0.35 to 1.31; Analysis 1.1; ITT: RR 0.71, 95% CI 0.37 to 1.37; Table 16).

Two studies also had data for successful eruption of the PDC at a maximum of 48 months after the intervention (Bonetti 2010; Bonetti 2011). Both analyses showed a slightly higher proportion of participants in the double extraction group successfully erupted than in the single extraction group (mITT: RR 1.28, 95% CI 1.06 to 1.54; Analysis 1.2; ITT: RR 1.38, 95% CI 1.13 to 1.69; Table 17). However, for the secondary outcome of referred for surgical exposure by 48 months, whereas the mITT analysis suggested there were no differences in this outcome at 48 months (mITT: RR 0.31, 95% CI 0.06 to 1.45; Analysis 1.3), the ITT analysis suggested there was a slight difference in favour of double extraction (ITT: RR 0.20, 95% CI 0.05 to 0.87; Table 18). This would be expected if there was higher ratio of successfully erupted PDCs at 48 months in the double extraction group compared with the single extraction group, as it is very unlikely that a PDC will successfully erupt so long after the intervention and clinicians should be referring for

surgery. The 48-month observation timepoint is further examined in the Discussion section.

The sensitivity analyses examining the effect of excluding Hadler-Olsen 2020 where data from participants judged to have a bilateral PDC and randomly allocated to receive different interventions on the two sides were excluded for the primary outcome demonstrated minimal differences in the risk or prevalence ratios for either the mITT (with: RR 0.68, 95% CI 0.35 to 1.31; without: RR 0.80, 95% CI 0.31 to 2.07) or ITT analyses (with: RR 0.71, 95% CI 0.37 to 1.37; without: RR 0.88, 95% CI 0.34 to 2.25).

DISCUSSION

Summary of main results

The extraction of the primary canine when a clinician suspects that the permanent canine is displaced has become accepted clinical practice (Short 2009). For many clinicians, this appears to be on the basis of one report of a series of 35 children who received the intervention but who were not compared with an untreated control group (Ericson 1988). This review has found that the proportion of PDCs that were successfully erupted at 12 months was higher following the extraction of the primary canine compared with not extracting the primary canine, but the CIs were wide and included the possibility that there was no difference. The certainty of the evidence was very low, because the results were based on one small study in a single centre and with unclear risk of bias. There was some evidence that successful eruption was dependent upon how displaced towards the midline the PDC was when diagnosed, with PDCs that were relatively mildly displaced towards the midline (sector 2) more likely to erupt with or without intervention than those more displaced towards the midline (sector 4).

The evidence for the effectiveness of double extraction of primary teeth compared with single extraction was mixed and the certainty of the evidence was very low. There was no evidence that double extraction of primary teeth (primary canine and first molar) led to a higher proportion of successfully erupted PDCs compared with a single extraction of the primary canine at 18 months. There was some evidence from two studies, judged at high risk of bias, that there was a higher proportion of successfully erupted PDCs in participants who received the double extraction of primary teeth and were observed for a mean of 48 months (Bonetti 2010; Bonetti 2011). However, this observation period is much longer than most clinicians would usually observe patients before intervening and is likely to be a reflection of the very young age of the participants when they were recruited to the trial. The potential problems with these two studies are discussed further below (see 'Age when a palatally displaced canine can be reliably identified' under Overall completeness and applicability of evidence).

Overall completeness and applicability of evidence

We will consider two issues about designing a study to investigate whether an intervention might improve the probability that a PDC will erupt without the need for surgical intervention.

- Definition of a PDC.
- Age when a PDC can be reliably identified.

Definition of a palatally displaced canine

Various definitions have been used previously, ranging from the very vague to the slightly more precise (Table 1). Most studies used the criteria outlined by Ericson and Kurol (or variations) for the judgement of the position of the maxillary canine (Ericson 1988). This includes the assessment of three criteria:

- medial position of the canine crown classified into five sectors;
- angulation of the long axis of canine to a vertical line drawn between the central incisors;
- vertical distance of the canine cusp tip to the occlusal plane.

Medial position of the canine crown

In the much quoted article by Ericson and Kurol advocating the extraction of the primary canine (Ericson 1988), the prevalence of displaced canines requiring surgical intervention was just 4%. However, canines lying in sectors 1 and 2 were included in this 4% figure. If only canines lying in sectors 3 and 4 were included, then prevalence is considerably higher at 36%.

Lindauer and colleagues examined the OPT radiographs of 28 participants with PDC (15 unilateral, 13 bilateral; mean age 12 years 1 month, SD 11 months) and compared this with a control sample of 28 participants with normal eruption of the maxillary canine (mean age 11 years 8 months, SD 19 months) (Lindauer 1992). The prevalence of PDC if the cusp tip (note Ericson and Kurol only refer to the canine crown not the cusp tip, so Lindauer and colleagues might be using slightly different criteria) was located in sector 1 was 12%, if in sector 2 the prevalence of PDC was 83%. None of the non-PDC group teeth were located in sectors 3 and 4 (defined as any position mesial to anterior surface of the root of the lateral incisor, so includes sector 5 of Ericson and Kurol) therefore the prevalence of PDC when the cusp-tip was in these sectors was 100%. They identified a younger age subset of this group (mean age 9 years 6 months, SD 10 months) and found 92% of non-PDC teeth were in sector 1.

Warford and colleagues examined the OPT radiographs of 82 orthodontic patients whose chronological age was less than 12 years with 35 PDC (unclear how many were unilateral and how many bilateral) (Warford 2003). They found that the sector in which the canine was placed (according to the criteria described in Lindauer 1992, i.e. no sector 5) is a better predictor of future displacement than angle. The odds ratios of a maxillary canine in each sector being eventually diagnosed as palatally displaced were 0.99 in sector 4, 0.80 in sector 3; 0.53 in sector 2 if the long axis of the canine was between 40 and 54 degrees to a line drawn through the nasal floor (i.e. was more mesially inclined); and 0.05 in sector 1. No CIs were quoted.

Fernandez and colleagues observed that the extent of root development of the lateral incisor was also an important factor to take into consideration (Fernandez 1998). They stated that "When the lateral incisor is not yet fully developed, panoramic radiographs more commonly show overlapping of the canine and lateral incisor. In contrast, when lateral incisor development is complete, such overlapping is rare; moreover, the few cases in which it is observed involve a greater mesial inclination of the canine". They went on to state that "the overlapping of the canine and lateral incisor in panoramic radiographs when the incisor has completed its development may be a sign of eruptive disorders

of the canine, suggesting the adoption of preventive measures to avoid impaction; for example, extraction of the primary canine. This is particularly applicable to patients in whom the cuspid bulge is not palpated in the vestibular aspect of the alveolar process after age 10 years, or when other dental development disorders are present, such as agenesis, ankylosis, dental malformations, or ectopic eruptions".

Angulation

Fernandez and colleagues examined the panoramic radiographs of 305 children aged 4 to 12 years taken in one paediatric dentistry practice (Fernandez 1998). They noted that "during eruption, the upper canine increases its inclination mesially, until a maximum angle is reached at approximately 9 years of age. From this inflexion point onwards, the tooth progressively straightens until it emerges above the gingival margin". They went on to state that "considerable individual variability exists as to the degree of canine inclination at a given point in the course of eruption, therefore the capacity to predict inclination at a given age is limited".

Warford and colleagues examined the OPT radiographs of 82 orthodontic patients whose chronological age was less than 12 years with 35 PDC (unclear how many were unilateral and how many bilateral) (Warford 2003). They found that the sector position was a better predictor of future displacement than the angle of the canine.

Vertical height of the canine crown

This has not been used in the definition of PDC.

Age when a palatally displaced canine can be reliably identified

We decided to exclude studies from this review that recruited a high proportion of participants (more than 20%) who were younger than nine years old. The reason for this was that we believe that the detection of a PDC before the age of 10 years is unreliable, as shown by several studies.

Ericson 1986a examined 505 children aged 8 to 12 years and carried out a radiological examination on 36 children with clinical indicators of a PDC (lack of palpation in the buccal sulcus; late eruption, displacement of lateral incisor). This article stated that "A difference in palpation of the canine positions, between the two sides (asymmetry), was a strong indication of aberrant eruption in children 10 years and older, but was an uncertain criterion in the age-groups 8 and 9". They go on to state "It is clear that younger children (below 10 years of age) with a potential for ectopic eruption, may later produce a correct eruption path. Early radiographic examination therefore does not always indicated (*sic*) the final path of eruption. Thus, it is not practical to use the findings from early radiographic investigations as an indicator of the prognosis of eruption. Also, the absence of complications with canine eruption in the age groups 8 and 9 years suggests that clinical supervision may be sufficient".

A second article outlining the clinical supervision of maxillary canine eruption in the same cohort of children stated that "The opinion that the maxillary canine is normally palpable at 8 or 9 yr [years] of age or at the latest at 9–9½ yr of age was not confirmed in this study. The individual variation in tooth development and eruption seems to be wide without implying any disturbances" (Ericson 1986b). They go on to state "In this study, both canines could be identified in 71% of the 10-yr-olds (Table 3). In cases of late dental development, the canines are too high up in the alveolar process to be palpable at this age. This was the case in 16% of the 10-yr-olds in this study. The absence of palpation findings in the latter cases does not necessitate radiographic examination but should be weighed against the general dental development". In a later article the same authors reiterate that "The optimal age for radiologic investigation is 10 to 13 years, depending on the individual child's somatic development" (Ericson 1987).

Some authors have suggested that radiographs can be used to predict when the maxillary canine is displaced earlier than 10 years of age. Sambataro and colleagues propose that a posterior-anterior radiograph can be used to detect a PDC at the age of eight years (Sambataro 2005). Their formula was based on the radiographs of just 12 children. The authors stated that two children were incorrectly diagnosed, but did not indicate whether these were children with a PDC, who were not diagnosed (false negative) or, more worryingly, children without a PDC who were incorrectly diagnosed with a PDC (false positive). These children would presumably then receive an unnecessary intervention.

Sajnani and colleagues also proposed that measurements from panoramic radiographs may be used to diagnose a PDC as early as eight years of age (Sajnani 2012). Again, this was based on a small number of children (14 below nine years of age with follow-up radiographs). The study included children with both buccal and palatal displacement and it is unclear how many false positives (and hence unnecessary interventions) would result.

In contrast, Coulter and Richardson examined the longitudinal records of 30 children from the Belfast growth study, who were examined annually from the age of 5 to 15 years (Coulter 1997). They stated that "Movement [of the maxillary permanent canine] in the lateral plane between 5 and 9 years of age was small and mainly in a palatal direction. Thereafter buccal movement occurred. This buccal movement was greatest between 10 and 12 years of age". They went on to state that "The findings of this study would support [the] assertion [of Ericson and Kurol] in that movement prior to age 9 years is still predominantly in a palatal direction, with movement after 9 years of age being buccal. The maxillary canine appears to move buccally from age 9 onwards, this movement being significant at the 1 per cent level in the year prior to eruption, at the 0.1 per cent in the year of eruption into the oral cavity and at the 5 per cent level in the year after eruption".

The eminent Professor Sheldon Peck, who has published extensively in this area, wrote a letter to a leading academic orthodontic journal regarding the age of participants in one study (Peck 2011). He stated that "many of the younger subjects in the Bonetti study [Bonetti 2011] sample may simply have had temporarily angled normally erupting canines". In response to Professor Peck's letter, the authors failed to adequately address his critique.

In addition to the potential risk of a false-positive finding (and hence unnecessary intervention) resulting from the use of radiographs to diagnose a PDC in young children, the proposal that routine use of radiographs (and hence increased exposure to ionising radiation) before any clinical signs of a PDC are apparent in all eight-year-old children, to detect a condition with a prevalence in the population of 1% to 3%, is unlikely to achieve widespread

acceptance. An age range of 9 to 13 years therefore appears justified.

Quality of the evidence

Two studies were assessed at unclear risk of bias (Naoumova 2015; Hadler-Olsen 2020), mainly because of doubts about whether the primary outcome in the final reports matched the original primary outcome in the protocol or a mismatch in the reported primary outcome and the outcome used to justify the sample size.

Two studies were considered at a high potential risk of bias for several reasons (Bonetti 2010; Bonetti 2011):

- participants as young as eight years were recruited to one of the studies (Bonetti 2011), which, in our opinion (and that of others, e.g. Peck 2011), is too young to accurately diagnose a PDC;
- a very high proportion of participants were judged to have bilateral PDC (unilateral:bilateral PDC ratios Bonetti 2010 = 1:4.5, Bonetti 2011 = 1:3);
- a high proportion of the canines (85%) were judged to be either in sector 1 (n = 37) or sector 2 (n = 110). A canine in sector 1 has no radiographic overlap between the unerupted PDC and the adjacent lateral incisors and we would not consider these teeth to be palatally displaced. A slight overlap between the canine crown and the lateral incisor root can be considered normal in young people before full development of the lateral incisor root (Fernandez 1998);
- follow-up time was very long (mean 48 months). This is probably a reflection of the young age that participants were recruited. Many clinicians would consider four years to be too long before considering further intervention for a PDC.

We contacted the corresponding author of Bonetti 2011 about the high proportion of participants diagnosed with bilateral PDCs and the response was similar to that supplied to the letter by Peck about the young age of the participants. The author's argument was that there is a high risk of root resorption with PDC. However, many of the PDCs in this study were not displaced. In addition, the data supplied by the corresponding author showed that in seven participants, the PDCs had not erupted at a mean of 48 months, but they were not sent for surgical exposure (Bonetti 2010: group 1 = 2, group 2 = 1; Bonetti 2011: group 1 = 4). When asked about this, the author responded, "In these participants the canines erupted, thus permitting bracket positioning for final arch alignment, beyond the end of the observation", so it was clear that some participants were followed up for even longer than 48 months and it was not clear how the decision to refer for surgical exposure was made.

We agreed to exclude studies that used a within-person or split-mouth design. This is quite an unusual design to use in studies outside of dentistry. It assumes that all variables are equal between the two sides of the mouth or that randomisation will account for confounding factors, such as the severity of displacement of the PDC. We were not sure that we could assume the former (does the extraction of the primary canine on one side of the mouth really have no effect on the other side of the mouth, e.g. by increasing the potential for a shift in the dental centreline?). Randomisation might take into account confounders, but only if the sample size is reasonably large. All the included studies had some participants with bilateral PDCs and managed the group allocation differently. Bonetti 2010 and Bonetti 2011 used a parallel design (which was confirmed by the corresponding author). This means that participants received the same intervention on the two sides. This makes the analysis simpler as it reduces the possible influence of confounding factors or an intervention on one side of the mouth affecting the other side of the mouth. In these participants, a positive primary outcome was defined as when both canines had erupted in the mouth and a negative outcome was when one or both canines did not erupt. Likewise, for the secondary outcomes, such as requirement for surgical exposure, a positive outcome is achieved when neither canine requires surgical exposure and a negative outcome when one or both canines required surgical exposure. This is the method we recommend using for future studies.

The other two included studies managed the group allocation of participants with bilateral PDC differently. Naoumova 2015 randomised right or left sides to either the intervention (extraction of the primary canine) or no treatment control, whereas Hadler-Olsen 2020 randomised the two sides separately, so they could be allocated to the same intervention or different interventions. We would not recommend either of these approaches for future studies for the reasons of confounding previously outlined.

In the study by Naoumova 2015 the authors stated that the primary canine was extracted in control participants if it was not showing signs of mobility at T2 (12 months). The rationale for this was that Ericson and Kurol observed that maximum improvement in the position of the canine, following extraction of the primary canine, occurred up to 12 months and if there was no improvement in the position of the PDC at 12 months then they suggested that an alternative treatment should be pursued (Ericson 1988); however, we are concerned that this might bias the outcome, as the results from other studies included in this review have found that the PDC can erupt beyond the 12-month observation time. Also, the authors stated that 'for ethical reasons' the primary canines were extracted after a period of 12 months, which implies a lack of equipoise for the possibility of eruption of the PDC after this date. According to data from three of the included studies (Bonetti 2010; Bonetti 2011; Hadler-Olsen 2020), the proportion of successfully erupting PDCs continued to increase up to 18 months, after which there was limited improvement.

We judged the certainty of the evidence to be very low for both comparisons due to a mix of indirectness, risk of bias, imprecision and inconsistency.

Potential biases in the review process

We undertook a search of several electronic sources, in addition to references lists, with no restrictions on language or publication status. We consider we identified all possible studies that might meet the inclusion criteria for this review. We contacted study authors whenever possible and we are very grateful to those who responded with further information and data.

Agreements and disagreements with other studies or reviews

Two earlier systematic reviews have examined evidence for the effectiveness of primary maxillary canine extraction, as an interceptive procedure, aiming to normalise the eruption of a palatally displaced maxillary permanent canine (Naoumova 2011;

Parkin 2012). Both reviews noted that the evidence for this intervention was weak and further research was required.

Since then, several further systematic reviews in this area have been carried out (Al Naqbi 2020; Almasoud 2017; Alyammahi 2018; Elangovan 2019). These reviews all concluded that the addition of orthodontic procedures to increase space in the arch or extraction of primary canines (or both) will lead to increased probability of eruption. However, all four of these systematic reviews have included studies that we consider at risk of bias and reporting errors. For this reason, their conclusions must be interpreted with caution.

The most recent systematic review was conducted by Grisar and colleagues (Grisar 2020). The authors had a slightly different research question in that they looked at the relationship of initial location of PDCs and treatment outcome. They included two RCTs and 15 non-RCTs. They concluded, along with other systematic reviews, that there is limited evidence that interceptive treatment for PDCs is effective. Furthermore, the interceptions are less successful if the alpha angle is high and PDCs are more displaced in both a vertical and a horizontal direction. They also concluded that further research should be based on larger samples and RCT designs to support the conclusions of the current literature. They also explained that since impacted maxillary canines are uncommon and different aspects, such as the position of the impacted canine, patient age, and patient's demands and expectations, must be considered, they felt that carrying out a well-designed RCT was not possible. They suggested future research should be done using high-quality observational studies with standardised outcome measures.

There is general agreement in all the systematic reviews we found in our search that there is some evidence, though limited, that extraction of primary canines can lead to eruption of PDCs. However, success is likely to be dependent upon the initial location of the PDC. There is also agreement that further research is needed with better designed RCTs with larger sample sizes and inclusion of different ethnic groups. The trials conducted to date have been with white populations.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence is uncertain that extraction of the primary canine in young people aged between 9 and 14 years with palatal displacement of the permanent canine will increase the probability that the palatally displaced canine (PDC) will erupt.

There is some evidence that the PDC displacement severity should be considered before any intervention. If the unerupted canine is minimally displaced towards the midline (overlap of less than half the width of the upper permanent lateral incisor on a plain view upper standard occlusal radiograph or equivalent) then it might be more successful.

There is no evidence that extraction of the primary canine reduces the number of young people with a PDC referred for surgery.

Extraction of two primary teeth (the primary canine and first molar) rather than the primary canine only may not increase the probability that the PDC will spontaneously erupt or reduce the number of young people referred for surgery.

From very limited evidence, it may be that the more an unerupted permanent canine is displaced towards the midline, the lower the probability that extraction of the primary canine will lead to successful eruption of the PDC (overlap of greater than half the width of the upper permanent lateral incisor on a plain view upper standard occlusal radiograph or equivalent). If the unerupted permanent canine is severely displaced towards the midline (overlap of greater than the full width of the upper permanent lateral incisor on a plain view upper standard occlusal radiograph or equivalent), it seems to be very unlikely that extraction of the primary canine or any intervention will improve the position of the PDC.

Where there is no overlap of the unerupted permanent canine on the upper permanent lateral incisor root on a plain view upper standard occlusal radiograph or equivalent, or there is overlap of less than half the width of the upper permanent lateral incisor and the lateral incisor is immature with an open apex, then the unerupted canine should not be considered to be in an aberrant position. If there is sufficient space within the dental arch then the tooth is likely to erupt without intervention and should be observed.

General dentists may find it helpful to seek the opinion of a specialist orthodontist if they suspect an upper permanent canine is palatally displaced in a young person after the age of nine years to determine whether intervention either in the form of extraction of the primary canine or space creation is appropriate.

If the unerupted PDC has not erupted by 18 months following any intervention then the probability of eruption may be low and alternative methods of management should be considered.

Implications for research

Further clinical trials are required to confirm if and when extraction of the primary canine increases the probability that a PDC will erupt into the mouth without surgical intervention.

The effectiveness of other interventions, such as creating space within the dental arch, to increase the probability that a PDC will erupt into the mouth without surgical intervention need to be investigated with well-designed clinical trials.

The primary outcome of these trials should be whether the PDC successfully erupts without surgical intervention. Measures of radiographic improvement are not useful if the PDC still requires surgical intervention.

Participants aged 9 to 14 years only should be recruited, as the authors of this review assert that it is unlikely that a PDC can be accurately diagnosed before the age of 9 years and intervention in young people over the age of 14 years is less likely to be effective.

Participants should only be recruited if there is reasonable evidence that the unerupted canine is palatally displaced (at least some overlap of the unerupted canine with the root of the upper permanent lateral incisor on a plain view upper standard occlusal radiograph or equivalent) and the lateral incisor is mature with a closed apex.

Participants with unerupted canines that are severely displaced towards the midline (overlap of greater than the full width of the upper permanent lateral incisor on a plain view upper standard

occlusal radiograph or equivalent) are unlikely to benefit from early intervention and should be excluded from these clinical trials. Researchers should consider stratifying participants according to the amount that their PDC is displaced towards the midline in their randomisation.

Clinical trials should ensure that the participant is the unit of randomisation, not the tooth. Participants with suspected bilateral PDC would therefore receive the same intervention on both sides. A successful primary outcome would be when both teeth erupt into the mouth.

The most appropriate time points for data collection are likely to be baseline and 18 months.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bonetti 2010

Study characteristics	
Methods	**Design:** RCT with 2 parallel groups. Not explicit that it is assessing superiority, but inferred **Setting:** 1 university clinic (Department of Orthodontics, University of Bologna, Italy) **Unit of randomisation:** participant **Recruitment dates:** not reported **Study duration:** not reported **Ethical approval:** yes
Participants	**Inclusion criteria:** Caucasian ancestry (known or assumed); presence of primary maxillary canines and primary first molars in the dental arch; and good-quality panoramic radiographs **Exclusion criteria:** previous orthodontic treatment; labially displaced PMC; aplasia or severe hypoplasia of the permanent maxillary lateral incisors crowns; odontomas; cysts; evidence of traumatic injuries to the permanent incisors or to the face; multiple or advanced caries of the maxillary teeth; and any systemic conditions that made children susceptible to PMC **Diagnosis PDC:**clinical – absence of palpation of the PMC bulges, PMC bulges palpable palatally, abnormal inclination or rotation (or both) of the adjacent permanent maxillary lateral incisor crown. Radiographic – PMCs inclination to the midline exceeding 25°; and overlapping of the PMC crowns with the permanent maxillary lateral incisor roots

Bonetti 2010 *(Continued)*

	Participants randomised: group 1 = 30 (girls = 14, boys = 16; PDCs = 53, unilateral = 7, bilateral = 23); group 2 = 30 (girls = 16, boys = 14; PDCs 56, unilateral = 4, bilateral = 26) **Participants analysed:** group 1 = 29 (girls = 13, boys = 16); PDCs = 52, unilateral 6, bilateral 23); group 2 = 30 (girls = 16, boys = 14; PDCs = 56, unilateral = 4, bilateral = 26) **Unilateral:bilateral PDC ratio:** 1:4.5 **Age at baseline:** group 1 = mean 10.1 (SD 1.1) years; group 2 = mean 10.2 (SD 0.9) years, range 9–13 years
Interventions	**Group 1:** extraction primary maxillary canine per upper dental quadrant where PDC diagnosed **Group 2:** extraction primary maxillary canine and primary maxillary molar per upper dental quadrant where PDC diagnosed No untreated control group
Outcomes	**Primary outcome:** not explicitly stated and no sample size calculation **Primary outcome endpoint:** not stated **Secondary outcomes:** not explicitly stated **Outcomes reported (in order):** PMCs inclination to the midline (alpha-angle); PMCs inclination to the long axis of the adjacent permanent maxillary lateral incisors (beta-angle); position of PMC crowns positions in regard to sectors 1–5; inclination of the permanent maxillary first premolars to the midline (pi-angle). Only data for teeth reported, which does not take into account possible clustering effect of teeth within the mouth. The authors also stated that a "successful outcome was defined, when surgical uncovering was not required, as the complete eruption of the PMCs into the dental arch within 48 months from the initial observation, thus permitting bracket positioning for final arch alignment when needed, according to Leonardi et al" (Leonardi 2004); however, no data were presented in the report for this outcome. Corresponding author was contacted and provided data. **Outcome endpoint:** no statement about a priori endpoint, but stated that "panoramic radiographs were taken at the initial observation (T0) and after an average period of 18 months (T1) from intervention" (author supplied data SD 0.5; range 18–20 months). An additional endpoint was reported at a maximum of 48 months (mean, SD and range requested but not supplied) from the initial observation, to determine if the tooth had erupted sufficient for placement of an orthodontic attachment, but as stated previously no data were presented in the report and the corresponding author was contacted and provided data.
Notes	**Funding source:** not reported **Trial registration:** not reported **Other:** authors confirmed that the participants in this study were different to those reported in Bonetti 2011.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The report provided some evidence that a random component was used in the sequence generation process using a computer. The investigators also stated they used a block design, presumably to get equal numbers in the 2 groups, but provided no details about block size. However, there do appear to be baseline differences between intervention groups suggesting there might have been a problem with the randomisation process. There was an imbalance in the severity of PDC displacement between the 2 groups, as judged by the mesial displacement of the canine crown (sector). At baseline, 2/52 PDCs in group 1 overlapped the adjacent lateral incisor by more than half the in-

Bonetti 2010 *(Continued)*

		cisor root width (sector 3 to sector 4) compared with 13/56 of PDCs in group 2, which, therefore, had a higher proportion of more severely displaced PDCs.
Allocation concealment (selection bias)	Low risk	The report provided evidence that the allocation sequence was concealed using consecutively numbered and sealed envelopes until participants were enrolled and assigned to intervention.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	It was not possible to blind either participants or clinicians to the participants' assigned intervention throughout the trial; however, we did not consider that this knowledge would affect the primary outcome of the review, i.e. whether the permanent canine would erupt into the mouth or not. Neither was there evidence that the group assignment led to a failure to implement the intervention as intended, or to trial participants not agreeing to their assigned intervention.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The method of assessing the primary outcome in this trial was appropriate and there was no evidence or reason to believe that the assessment of the primary outcome differed between intervention groups. The outcome assessors were probably aware of the intervention received by study participants, as double or single primary extractions would be visible both clinically and on panoramic radiographs until all primary displacements had been exfoliated; however, we believe it unlikely that the assessment of the primary outcome would have been influenced by knowledge of intervention received.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data were available for nearly all participants randomised. There was 1 dropout due to the participant's family moving away during the trial.
Selective reporting (reporting bias)	Unclear risk	Not clear if data were analysed in accordance with a prespecified analysis plan that was finalised before unblinded outcome data were available for analysis. There was no evidence in the report that the study was registered in an open-access clinical trials database before recruitment. Data are only presented for improvement in angles and sector positions of unerupted PDC on radiographs taken at T0 and T1 (mean 18 months apart). There were no data in the report on successful eruption of the PDC, but this was supplied by the authors. The authors stated that 7 PDCs (group 1 = 3; group 2 = 4) "required further radiographic observation (beyond 18 months *sic mean*) before treatment was considered a success", suggesting that all PDCs erupted successfully. However, in reply to an e-mail enquiry, the authors indicated that 5 participants (group 1 = 4; group 2 = 1) were referred for surgical exposure of the unerupted PDC after the 48-month observation period.
Other bias	High risk	We are concerned about the validity of diagnosing PDC in the younger age range included in this study (9 year-olds). There are some doubts about whether the sample is representative of individuals with PDC in the population. Sixty participants (30 girls and 30 boys) were recruited to the trial. First, it is generally considered that the prevalence of PDC is higher in girls than boys (Sacerdoti 2004 suggest girl:boy ratio of 1.65:1 for children with unilateral PDC and 4:1 for children with bilateral PDC), whereas the sample had a 1:1 girl:boy ratio. Also, the proportion of participants diagnosed with bilateral PDC was very high (unilateral:bilateral PDC ratio 1:4.5). It is generally considered that the prevalence of unilateral PDC in the population is higher than bilateral (Sacerdoti 2004 suggest a unilateral:bilateral ratio of 2:1). Data supplied by the author indicated of the 108 unerupted permanent canines (in the 59 participants analysed) that the investigators considered to be 'ectopic', 26 (24%) were in sector 1 (group 1 = 16; group 2 = 10) and 67 (62%) were in sector 2 (group 1 = 34; group 2 = 33). These would be considered either

Bonetti 2010 *(Continued)*

	not to be or only mildly displaced. The remaining teeth were either in sector 3 (12, 11%; group 1 = 2, group 2 = 10) or sector 4 (3, 3%; group 1 = 0, group 2 = 3). There were no teeth in sector 5. 1 justification for advocating the extraction of 2 primary teeth per quadrant was that a higher proportion of PDCs considered ectopic in the participants from this group (group 2) improved their sector position (27/56 (48%) improved by 1 sector, 9/56 (16%) by 2 sectors) compared with the PDC in the participants from the single primary extraction per quadrant group (group 1: 17/52 (32%) improved by 1 sector, 0/52 by 2 sectors). However, there were only 2 teeth in group1 that were in sector 3 or above and therefore could improve by 2 sectors (see comment about baseline discrepancies). In addition, 1 tooth in group 2 that the authors stated improved by 2 sectors, was in sector 2, so it was not possible for this tooth to improve by 2 sectors.

Bonetti 2011

Study characteristics	
Methods	**Design:** RCT, 2 parallel groups, not explicit that it was assessing superiority, but inferred **Setting:** university clinic (Department of Orthodontics, University of Bologna, Italy) **Unit of randomisation:** participant **Recruitment dates:** not reported **Study duration:** not reported **Ethical approval:** not reported
Participants	**Inclusion criteria:** 'White ancestry', aged 8–13 years, primary canines and first molars present in upper dental arch **Exclusion criteria:** previous or current orthodontic treatment, missing or small upper lateral incisors, evidence of trauma to incisors or face, advanced caries, cleft of lip or palate, or craniofacial syndrome or pathology (odontomes, cysts) **Diagnosis PDC:** not given in inclusion criteria, but later in report indicated. Clinical: absence of palpation of the PMC bulge, PMC bulge palpable palatally and 'no abnormal inclination or rotation of the adjacent lateral incisor crown' (different to Bonetti 2010). Radiographic: PMC inclination to the midline exceeding 25° and overlapping of the PMC crown with the root of the permanent lateral incisor. **Participants randomised:** intervention group 1 = 20 (girl:boy not reported; PDCs = 33, unilateral = 7, bilateral = 13); intervention group 2 = 20 (girls = 11, boys = 9; PDCs = 37, unilateral = 3, bilateral = 17); control (non-randomised) = 31 (girl:boy not reported; PDCs = 53, unilateral =9, bilateral = 22) **Participants analysed:** intervention group 1 = 17 (girls = 8, boys = 9; PDCs = 28, unilateral = 6, bilateral = 11); intervention group 2 = 20 (girls = 11, boys = 9; PDCs = 37, unilateral = 3, bilateral = 17); control (non-randomised) = 31 (girls:boys not reported; PDCs = 53, unilateral = 9, bilateral = 22) not included in flow diagram or described in text, but inferred from data in Table III, where data from 53 canines were included **Unilateral:bilateral PDC ratio:** 1:3 **Age at baseline:** intervention group 1: mean 9.8 years (SD not given); intervention group 2: mean 10.2 years (SD not given); control (non-randomised): mean 9.0 years (SD not given). Range 8–13 years
Interventions	**Intervention group 1:** extraction of primary canine per quadrant 'corresponding to' PDC

Bonetti 2011 *(Continued)*

	Intervention group 2: extraction of primary canine and primary first molar per quadrant 'corresponding to' PDC **Control (non-randomised):** observation only, but not randomised, judged not to be at risk of PDC or resorption of roots of adjacent teeth. Not clear who made this judgement and what criteria were used
Outcomes	**Primary outcome:** not explicitly stated. Sample size calculation based on an absolute difference in inclination to the midline (alpha-angle) of 10 (SD 13)° between the 2 groups (significance level = 0.05; power = 0.80), an estimated 26 canines required, but ignored clustering of teeth within the mouth **Primary outcome endpoint:** not stated **Secondary outcomes:** not explicitly stated **Outcomes reported (in order):** PMCs inclination to the midline (alpha-angle); position of PMC crowns in regard to sectors 1–5; influence of the stage of root development of the permanent canines on 'the final result'. Only data for teeth reported, which did not take into account possible clustering effect of teeth within the mouth. Proportions of 'successful outcomes' also reported, defined as "complete eruption of the permanent canine into the dental arch within 48 months from the initial observation, thus permitting bracket positioning for final arch alignment when needed". **Outcome endpoint:** no statement about a priori endpoint, but stated that "panoramic radiographs were taken at the initial observation (T0) and after an average period of 18 mths (T1) from intervention" (author supplied data SD 0.6; range 16–20 months). An additional endpoint is reported at a maximum of 48 months (mean, SD and range requested but not supplied) from the initial observation, to determine if the tooth had erupted sufficient for placement of an orthodontic attachment.
Notes	**Funding:** no information **Trial registration:** no information **Other:** authors confirmed that the participants in this study were different to the participants reported in Bonetti 2010.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The report provided some evidence that a random component was used in the sequence generation process using a computer. The investigators also stated that they used a block design presumably to get equal numbers in the 2 groups, but provided no details about block size. There was no information in the report about baseline differences between intervention groups that might suggest a problem with the randomisation process.
Allocation concealment (selection bias)	Low risk	The report provided evidence that the allocation sequence was concealed using consecutively numbered and sealed envelopes until participants were enrolled and assigned to intervention.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	It was not possible to blind either participants or clinicians to the participants' assigned intervention throughout the trial; however, the review authors did not consider that this knowledge would affect the primary outcome of the review, i.e. whether the permanent canine would erupt into the mouth or not. Neither was there evidence that the group assignment led to a failure to implement the intervention as intended, or to trial participants not agreeing to their assigned intervention.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The method of assessing the primary outcome in this trial was appropriate and there was no evidence or reason to believe that the assessment of the primary outcome differed between intervention groups. The outcome assessors were probably aware of the intervention received by study participants, as double

Bonetti 2011 *(Continued)*

		or single primary extractions would be visible both clinically and on panoramic radiographs until all primary displacements had been exfoliated; however, the review authors believe it unlikely that the assessment of the primary outcome would have been influenced by knowledge of intervention received.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data were available for nearly all participants randomised. 3 (15%) participants with 5 PDCs were not included in the analysis from group 1 (2 families moved away, 1 had a poor radiograph); 0 participants were lost to follow-up in group 2. The untreated control group was not included in the flow diagram and there was no explicit description about withdrawals and dropouts from this group, but it also appeared to be 0, the group consisted of 31 participants with 53 canines and data from 53 canines were included in Table II. This group did not appear to be randomised, so we did not include them in the analysis.
Selective reporting (reporting bias)	Unclear risk	Not clear if data were analysed in accordance with a prespecified analysis plan that was finalised before unblinded outcome data were available for analysis. There was no evidence in the report that the study was registered in an open-access clinical trials database before recruitment. Data were only presented for changes in angles and sector positions of unerupted PDC on radiographs taken at baseline and mean 18 months (Table III, Bonetti 2011). Data on successful eruption of these teeth were included in the report, but these did not appear to take into account possible clustering of data within individuals. We contacted the author who provided suitable data.
Other bias	High risk	There was no assessment of baseline equivalence between the groups. We are also concerned about the validity of diagnosing a PDC in the younger age ranges included in the study (8- to 9-year-old children). Peck 2011 also expressed this concern. There are some doubts about whether the sample was representative of children with PDC in the population. 40 participants (20 girls and 20 boys) were recruited to the trial. First, it is generally considered that the prevalence of PDC is higher in girls than boys (Sacerdoti 2004 suggest a girl:boy ratio of 1.65:1 for children with unilateral PDC and 4:1 for children with bilateral PDC), whereas the sample had a 1:1 gender ratio. Also, the proportion of participants diagnosed with bilateral PDC was very high (unilateral:bilateral PDC ratio 1:3). It is generally considered that the prevalence of unilateral PDC in the population is higher than bilateral (Sacerdoti 2004 suggest a unilateral:bilateral ratio of 2:1). Data supplied by the author indicates of the 65 unerupted permanent canines (in the 40 participants analysed) that the investigators considered to be 'ectopic', 11 (17%) were in sector 1 (group 1 = 5; group 2 = 6) and 44 (68%) were in sector 2 (group 1 = 20; group 2 = 24). These would be considered either not to be or only mildly displaced. The remaining teeth were either in sector 3 (6, 9%; group 1 = 2, group 2 = 4) or sector 4 (4, 6%; group 1 = 0, group 2 = 3). There were no teeth in sector 5.

Hadler-Olsen 2020

Study characteristics	
Methods	**Design:** RCT, parallel and within-group, not explicit that it was assessing superiority, but inferred **Setting:** 2 sites, Public Dental Health Competence Centre of Northern Norway and private clinic Bryne, Norway carried out all the procedures including screening, recruitment, delivering intervention and follow-up

Hadler-Olsen 2020 *(Continued)*

	Unit of randomisation: individual PDC, therefore in participants with bilateral PDC the 2 sides were randomised separately **Recruitment dates:** 2013–2018 **Study duration:** not reported **Ethical approval:** 'regional ethical committee of Northern Norway' (2012/623/REK Nord); approved June 2012
Participants	**Inclusion criteria:** dental age 9.5–10.5 years, primary canines and first molars present in upper dental arch, PDC in sectors 2, 3 or 4 with alpha-angle ≤ 25° on dental pantomogram **Exclusion criteria:** missing upper lateral incisors, previous orthodontic treatment, any condition preventing local anaesthetic or extraction, cleft of lip or palate, or craniofacial syndrome or pathology (odontomes, cysts) **Diagnosis PDC:**radiographic: 2 periapical radiographs using parallax **Participants randomised:** 32 (girls = 18, boys = 14; PDCs = 48, unilateral = 16, bilateral = 16) **Participants analysed:** 32 **Unilateral:bilateral PDC ratio:** 1:1 **Age at baseline:** girls = mean 10.7 (SD 0.7) years, boys = mean 11.2 (SD 1.0) years, range 9.5–13.5 years
Interventions	**Intervention group 1:** single extraction of primary canine only (12 participants, 10 unilateral PDC, 2 bilateral PDC; 14 teeth) **Intervention group 2:** double extraction of both primary canine and primary first molar (11 participants, 6 unilateral PDC, 5 bilateral PDC; 16 teeth) **Intervention group 3:** single extraction on 1 side and double extraction on the other (9 participants, 9 bilateral PDC; 18 teeth) No untreated control group
Outcomes	**Primary outcomes:** 2 stated primary outcomes, emergence of the PDC into the oral cavity (yes/no) and emergence of the PDC into a favourable position, i.e. sector 1 (yes/no); however, the justification of the sample size was based on the mean radiographic change in the position of the PDC relative to a vertical mid-maxillary line (alpha-angle), between baseline (T0) and 12 months (T1) of the 2 intervention groups, from a previous study (Bonetti 2010) **Primary outcome endpoint:** not stated. Data were collected at 12, 18 and 24 months **Secondary outcomes:** 4 stated secondary outcomes, radiographic angular changes in the position of the PDC relative to a bicondylar line, the adjacent lateral incisor and a vertical mid-maxillary line (alpha-angle), as well as radiographic change in the sector assessed using the criteria of Ericson and Kurol (Ericson 1988) **Secondary outcome endpoint:** not stated. Data were collected at 12, 18 and 24 months
Notes	**Funding:** authors stated that "no funding or other support was received to conduct this study". **Trial registration:** NCT02675036 on ClinicalTrials.gov

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	There is no information in the report on the method of random sequence generation, so we contacted the corresponding author who replied that "It was

Hadler-Olsen 2020 *(Continued)*

		generated using software at http://www.randomization.com". There was no stratification, e.g. that the 2 centres had an equal number of participants in each group; however, they did use a block randomisation, with block sizes varying randomly between 2, 4, 6 and 8, to ensure equal numbers of participants in the 2 intervention groups.
Allocation concealment (selection bias)	Low risk	There was no information in the report on the method of allocation concealment, but the corresponding author replied that they used 'sequentially numbered opaque envelopes'.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	It was not possible to blind either participants or clinicians to the participants' assigned intervention throughout the trial; however, we did not consider that this knowledge would affect the primary outcome of the review, i.e. whether the permanent canine would erupt into the mouth or not. Neither was there evidence that the group assignment led to a failure to implement the intervention as intended, or to trial participants not agreeing to their assigned intervention.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The method of assessing the primary outcome in the report of the trial (not the primary outcome in the protocol) was appropriate and there was no evidence or reason to believe that the assessment of the primary outcome differed between intervention groups. The outcome assessors were probably aware of the intervention received by study participants, as primary extractions would be visible both clinically and on panoramic radiographs until all primary canines had been exfoliated (the corresponding author confirmed that there was no blinding of radiographs); however, the review authors believe it unlikely that the assessment of the primary outcome would have been influenced by knowledge of intervention received.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data were available for all participants randomised.
Selective reporting (reporting bias)	Low risk	The study was registered in an open access clinical trials database (ClinicalTrials.gov NCT02675036); however, this was in February 2016, which appears to be after recruitment to the trial had started in September 2014. Data for all important outcomes are presented. The primary outcome in the database did not match the 2 stated primary outcomes in the report. When asked about this, the corresponding author replied that "The primary outcome in the protocol was to observe changes in the alpha angle", therefore, there seems to have been a change in the primary outcome between the protocol and the report. Although the author did not explain why this change had occurred, he was forthcoming with all the information we requested and we therefore judged the study to be a low risk of bias in this domain.
Other bias	Unclear risk	There were 2 other areas of concern with this study. There is some doubt about whether the sample is representative of individuals with PDC in the population. 32 participants (18 girls and 14 boys) were recruited to the trial. First, it is generally considered that the prevalence of PDC is higher in girls than boys (Sacerdoti 2004 suggest girl:boy ratio 1.65:1 for children with unilateral PDC and 4:1 for children with bilateral PDC), whereas the sample had only slightly higher proportion of girls to boys (1.29:1). Also, data were presented for 48 canines; therefore, 16 participants were diagnosed with unilateral maxillary PDC and 16 were diagnosed with bilateral maxillary PDCs. A unilateral:bilateral PDC ratio of 1:1 is high. It is generally considered that the prevalence of unilateral PDC in the population is higher than bilateral (Sacerdoti 2004 suggest a unilateral:bilateral ratio of 2:1). When asked about this the author speculated that there might be 2 reasons for this.

Hadler-Olsen 2020 *(Continued)*

- Definitions used for PDC. In our study, we had quite strict criterias to what we considered a PDC (sector 3, or sector 2 with an angle to the midline > 25 degrees) and no primary canine and primary molars lost. Therefore, our sample may include different cases than other studies. Perhaps we have more of the genetically determined PDCs and not as many PDCs caused by physical barriers.
- Whether PDC cases with space deficiency are included in the sample or not. Several studies do not include cases with space deficiency – e.g. Naoumova et al. (extraction of the deciduous canine as an interceptive treatment in children with PDCs, 2015). We know that the chance for space deficiency is increased with bilateral PDCs, as the absence of permanent canines causes a narrower maxillary arch (Saiar et al. 2006). Our study included cases with space deficiency – so again – the sample may be different due to the selection criteria.

It was not clear from the report how the intervention for the participants with bilateral PDCs was undertaken, i.e. were they randomised once and both canines treated with the same allocated intervention or was the PDC on each side randomised separately, so that a patient with bilateral PDC could have different treatments on each side of the mouth? The author responded that the PDC on each side was randomised separately so they could have had different interventions. This is a within-person or split-mouth design, which we believe is problematic in this area.

Naoumova 2015

Study characteristics	
Methods	**Design:** RCT, 2 parallel and 1 within-person groups, not explicit that it was assessing superiority, but inferred **Settings:** recruited from 15 public dental clinics, Gothenburg, Västra Götaland County Council, Sweden, treated and followed up in 1 centre (Department of Orthodontics, Institute of Odontology, Gothenburg, Sweden) **Unit of randomisation:** both participant (unilateral PDC) and side of dental arch (bilateral PDC) **Recruitment period:** September 2008 to January 2011 **Study duration:** not stated **Ethical approval:** yes – Sahlgrenska Academy Research Ethics Committee (Dnr 578-08)
Participants	**Inclusion criteria:** Caucasian (believed to be white people), aged 10–13 years, unilateral or bilateral PDC in upper dental arch, retained primary canines and no previous orthodontic treatment **Exclusion criteria:** crowding in upper dental arch > 2 mm, severe root resorption of adjacent teeth (grades 3 and 4), cleft of lip or palate, or craniofacial syndrome or pathology (odontomes, cysts) **Diagnosis of PDC:** maxillary permanent canine non-palpable and ≥ 2 intra-oral radiographs confirming palatal position, using principle of parallax Intervention groups were: group 1 (unilateral PDC allocated to extraction of the primary canine), unilateral control (unilateral PDC allocated to observation only), group 2 (bilateral PDC allocated to extraction of either the right or left canine) **Participants randomised:**intervention group 1 (unilateral PDCs only) = 23; unilateral control = 22 (girls = 29, boys = 16; PDCs = 45); intervention group 2 (bilateral PDCs only) = 22 (girls = 11, boys = 11; PDCs = 44)

Naoumova 2015 *(Continued)*

	Participants analysed: T1 (6 months): intervention group 1 = 23; unilateral control = 22; intervention group 2 = 22 T2 (12 months): authors stated that "Fifteen out of the 67 patients (3 bilateral PDC and 12 unilateral PDC [3 from the CG and 9 from the EG]) did not have a radiographic examination at the 12 month control because the canines had emerged through the gingiva and were under eruption, i.e. clinically visible between T1 and T2. Imputation values were used in these cases [for radiographic analysis]". Flow chart stated that 89 out of original 99 PDCs were included in the analysis at 12 months. T3 (24 mths): Author query: the flow diagram had numbers of individual teeth, rather than participants. There were no dropouts at 12 months, but some at 24 months, i.e. 18 teeth, but how many participants and in which groups? Author reply: "Surgical exposure and orthodontic treatment were done on 41 PDCs while 30 PDCs were continued to follow up with clinical examination and X-ray if needed, total observation period 24 months. Out of these 30 PDCs: 20 erupted in the EG [experimental group] (11 patients in the unilateral group, 10 patients in the bilateral group) and 10 in the CG [control group] (6 patients in the unilateral group, 3 patients in the bilateral group)". **Unilateral:bilateral PDC ratio:** 2:1 **Age at baseline:** intervention group 1 = mean 11.2 (SD 1.1) years; unilateral control = mean 11.3 (SD 1.1) years;intervention group 2 = mean 11.6 (SD 1.0) years; range 10–13 years
Interventions	**Intervention group 1:** participants with unilateral PDC allocated to extraction of primary canine **Intervention group 2:** participants with bilateral PDC, allocated to extraction of either right or left primary canine **Unilateral control group:** participants with unilateral PDC allocated to observation only (no treatment)
Outcomes	**Primary outcome:** stated primary outcome 'eruption of the permanent canine' (presumably difference between the proportions of intervention and control group participants who demonstrated successful eruption of the PDC defined as 'emerged through the gingiva (during the total observation time i.e. 24 months'; however, sample size calculation based on 'detecting a difference of 5 degrees (SD 6.38) of angle measured in the frontal and sagittal views', so stated primary outcome and primary outcome upon which the sample size calculation was based did not match. Author reply: "Yes, the sample size was based on 5 degrees of difference between the EG and CG, but the primary outcome was eruption or not. I do agree, that looking at it now retrospective it seems very strange. But if the canine erupts significantly more in the EG then it also indirectly means that it had more than 5 degree of angular differences between the canine in the CG since it had erupted and became more uprighted". **Primary outcome endpoint:** 24 mths **Secondary outcomes:** positional changes in the PDC measured from the radiographs (mesial and sagittal angles, PDC cusp tip to dental arch plane, PDC root apex to dental arch plane and PDC cusp tip to midline) T1 to T0, T2 to T1. Root resorption of adjacent teeth **Secondary outcomes endpoint:** not stated **Observation and data collection points:** T0: baseline radiograph (CBCT) and if allocated to intervention then extraction was carried out on the same day, by 1 operator (JN); T1: 6 months after T0 (clinical examination and CBCT if permanent canine not clinically visible); T2: 12 months after T0 (individual treatment plans, if the PDC had improved position continued to review, PDC no change or worse position referred for surgical exposure or if in the control group the primary canine was extracted. Author query: you state that the primary canine was extracted in the control group at T2 (12 months) if it was not mobile, but was this true even if the unerupted PDC had improved in position?

Naoumova 2015 *(Continued)*

	Author reply: the PDC with an improved position at T2 had mobile deciduous canines due to the uprighted position of the permanent canine; T3: 24 months end of observation period.
Notes	**Funding:** the Local Research and Development Board for Gothenburg and Södra Bohuslän; the Health & Medical Care Committee of the Regional Executive Board, Västra Götaland Region; the Gothenburg Dental Society **Trial registration:** FoUiSverige (www.fou.nu/is/sverige) Registration Nos: 40921 **Other:** author confirmed that data from these publications were from the same cohort of participants. A further article has been published including data from participants in this study, but the outcomes are not relevant to this review: therefore, it has not been included (Naoumova J, Alfaro GE, Peck S. Space conditions, palatal vault height, and tooth size in patients with and without palatally displaced canines: a prospective cohort study. *Angle Orthodontist* 2018;88(6):726-32. DOI: 10.2319/120717-843.1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The report provided evidence that the allocation sequence was randomly generated, as it stated "permuted block randomisation". Author clarified that the random sequence was generated with a computer and it was stratified on whether the participant had a unilateral or bilateral PDC. There was some evidence of minor baseline differences between intervention groups, in that there were slightly different numbers of right (13) and left (9) PDCs allocated to extraction of the deciduous canine in the 22 participants with bilateral PDCs. The author believed this was due to the size of the blocks, so there was no serious evidence of a problem with the randomisation process.
Allocation concealment (selection bias)	Low risk	The report provided evidence that the allocation sequence was concealed until participants were enrolled and assigned to interventions, by stating that "sequentially numbered, sealed opaque envelopes opened by a dental nurse after written consent obtained".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	It was not possible to blind either participants or clinicians to the participants' assigned intervention throughout the trial; however, we did not consider that this knowledge would affect the primary outcome of the review, i.e. whether the permanent canine would erupt into the mouth or not. Neither was there evidence that the group assignment led to a failure to implement the intervention as intended, or to trial participants not agreeing to their assigned intervention.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The method of assessing the primary outcome in this trial was appropriate and there was no evidence or reason to believe that the assessment of the primary outcome differed between intervention groups. The outcome assessors were probably aware of the intervention received by study participants, as primary extractions would be visible both clinically and on panoramic radiographs until all primary canines had been exfoliated; however, we believe it unlikely that the assessment of the primary outcome would have been influenced by knowledge of intervention received.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There did not appear to be any withdrawals and dropouts of participants at T2 (12 months), but the number of teeth in the flowchart (89) did not match the number of teeth at T0 (99). The authors stated that at T2 "Fifteen out of the 67 patients (3 bilateral PDC and 12 unilateral PDC [3 from the CG [control group] and 9 from the EG] [experimental group]) did not have a radiographic examination … because the canines had emerged through the gingiva and were under eruption". They go on to state that that "imputation values were used in these cases" [for the radiographic analysis].

Naoumova 2015 *(Continued)*

		T3 (24 mths): Author query: the flow diagram has numbers of individual teeth, rather than participants. There were no dropouts at 12 months, but some at 24 months, i.e. 18 teeth, but how many participants and in which groups? Author reply: "Surgical exposure and orthodontic treatment were done on 41 PDCs while 30 PDCs were continued to follow up with clinical examination and X-ray if needed, total observation period 24 months. Out of these 30 PDCs: 20 erupted in the EG (11 patients in the unilateral group, 10 patients in the bilateral group) and 10 in the CG (6 patients in the unilateral group, 3 patients in the bilateral group)".
Selective reporting (reporting bias)	Low risk	The trial was registered (www.fou.nu/is/sverige; reg nos: 40921), but authors stated that the protocol was not published before trial commencement. The stated primary outcome did not match the outcome used to justify the sample size. Although the author could not explain why this change had occurred, she was forthcoming with all the information we requested and we therefore judged the study at low risk of bias in this domain.
Other bias	Unclear risk	This study had both a girl:boy ratio of participants (1.48:1) and unilateral:bilateral PDC ratio (2:1) consistent with the prevalence of the condition in the literature. The authors stated that the primary canine was extracted in control participants if it was not showing signs of mobility at T2 (12 months). The rationale for this was that Ericson and Kurol observed that maximum improvement in the position of the canine, following extraction of the primary canine, occurred up to 12 months and if there was no improvement in the position of the PDC at 12 months then they suggested that an alternative treatment should be pursued (Ericson 1988); however, we are concerned that this might bias the outcome, as other studies have found that the PDC can erupt beyond the 12 month observation time.

CBCT: cone beam computerised tomography; PDC: palatally displaced canine; PMC: permanent maxillary canine; RCT: randomised controlled trial; SD: standard deviation.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Armi 2011	Study included participants who were younger than the inclusion criteria for this review (see the Discussion).
Arnautska 2015	Retrospective study design.
Baccetti 2008	Study included participants who were younger than the inclusion criteria for this review (see the Discussion).
Baccetti 2009	Participants were very young at the start of the study (mean ages 8.8 (SD 9) months in the treatment group and 8.4 (SD 12) months in the non-treatment group; range 7.6–9.6 years). PDC diagnosed from PA radiographs using a technique described by Sambataro 2005, who have suggested that a PA radiograph can be used to diagnose a PDC from the age of 8 years. Their formula was based on the radiographs of just 12 individuals. The authors stated that 2 children were incorrectly diagnosed, but did not indicate whether these were children with a PDC, who were not diagnosed (false negative) or more worryingly children without a PDC who were incorrectly diagnosed with a PDC (false positive). These children would presumably then receive an unnecessary intervention. Sajnani 2012 have also suggested that measurements from panoramic radiographs may be

Study	Reason for exclusion
	used to diagnose a displaced maxillary permanent canine, as early as 8 years of age. Again this was based on a small number of individuals (14 children aged < 9 years with follow-up radiographs). The study included children with both buccal and palatal displacement and it is not clear how many false positives (and hence unnecessary interventions) would result. There was a difference in the numbers between the 2 groups at baseline (treatment group 35; no treatment control 25) and it was not clear what proportion of participants in each group were considered to have unilateral and bilateral PDCs. There are no details of the methods of random sequence generation or allocation concealment. Withdrawals and dropouts were accounted for, but the study was considered at high risk of bias.
Baccetti 2011	Study was described as randomised; however, the recruitment period was very long (1991–2009) and we were unable to determine whether the participants in this study were different people from those included in other studies from this research group.
Barros 2018	Prospective, longitudinal study with non-random allocation.
Bazargani 2013	Employed a within-person (split-mouth) study design and we were unable to use the data for the purposes of this review.
Caprioglio 2020	Retrospective study design.
Fleming 2012	Commentary on Armi 2011.
Hadler-Olsen 2018	Not an RCT, but a secondary analysis of data from 2 previous studies investigating the early treatment of children with class II malocclusion (Pirttiniemi 2005; Silvola 2009). Participants younger than review inclusion criteria (mean 7.6 years) and include both buccal and palatal maxillary canines.
King 2010	Retrospective cohort study for all types of interceptive treatment, not specific to PDC and no useful information.
Leonardi 2004	No information provided about the methods of generating the random sequence or allocation concealment. Groups very imbalanced at baseline with many more participants with bilateral PDC in the extraction plus headgear group compared to the other groups. Numbers of withdrawals and dropouts incomplete and inconsistent. The report stated that 50 participants were recruited to the trial and 7 participants did not complete; however, they provided data for 46 participants with 62 PDCs (extraction only 11; extraction plus headgear 21; untreated control group 14). Attempts to clarify this information with the authors were unsuccessful. The study was judged at high risk of bias.
Maspero 2016	Abstract reported the groups were 'randomly' divided, whereas methods mentions selecting participants from a sample of 2500 in active treatment, 10 'accepting treatment proposed' and 10 'refusing treatment'. Subject of interest maxillary canine-first premolar transposition.
O'Neill 2010	Commentary on Baccetti 2009.
Sigler 2011	Not an RCT. Compared 1 group of 40 participants receiving rapid maxillary expansion and extraction of primary canine in Michigan (US), with a control group of 30 untreated individuals in Florence (Italy). The control group was the same as in other publications by the same authors (Baccetti 2011).
Silvola 2009	Participants started treatment with headgear aged 7 years, which is much younger than our inclusion criteria of 9–14 years. Control group received a variety of interventions (38% extraction of primary canines, 19% interdental stripping, 39% extraction of lower primary canines), which makes analysis complicated. Although participants were followed up to 16 years, the authors provided no data about successful eruption of canines only on the angulation of the upper canine during eruption.

Study	Reason for exclusion
Wong 2004	Non-systematic narrative review.

PA: posterior-anterior; PDC: palatally displaced canine; RCT: randomised controlled trial; SD: standard deviation.

Characteristics of ongoing studies *[ordered by study ID]*

NCT03684525

Study name	Assessment of extraction of primary canines in treating mesioangular displaced permanent canines
Methods	Randomised, 2 parallel groups, 'factorial assignment', single site, single investigator
Participants	43 young people aged 9–13 years with unilateral 'mesioangular displaced' maxillary canines
Interventions	Extraction of both maxillary canines vs untreated control group
Outcomes	Primary: successful eruption of maxillary permanent canines into the dental arch (time frame: 12 months) Secondary: successful improvement of permanent canine position radiographically (time frame: 12 months) using cone beam computerised tomography
Starting date	November 2017
Contact information	Najlaa M Alamoudi: nalamoudi@kau.edu.sa; Reem K Naaman: dr.reem.naaman@hotmail.com
Notes	Authors contacted by e-mail on 2 March 2021 for an update on the progress of the study. Replied 3 March 2021 "The study is complete. We are now in the process of writing up the manuscript and publishing".

DATA AND ANALYSES

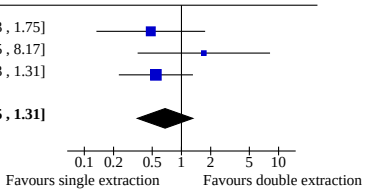
Comparison 1. Single versus double primary tooth extraction

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Eruption of palatally displaced canine (PDC) at mean 18 months (modified intention-to-treat (mITT))	3	119	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.35, 1.31]
1.2 Eruption of PDC by 48 months (mITT)	2	96	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [1.06, 1.54]
1.3 Number of participants referred for surgical exposure of the unerupted PDC by 48 months (mITT analysis)	2	96	Risk Ratio (M-H, Fixed, 95% CI)	0.31 [0.06, 1.45]

Analysis 1.1. Comparison 1: Single versus double primary tooth extraction, Outcome 1: Eruption of palatally displaced canine (PDC) at mean 18 months (modified intention-to-treat (mITT))

Study or Subgroup	Double primary extraction (canine &d) Events	Total	Single primary extraction (canine) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bonetti 2010 (1)	3	30	6	29	38.3%	0.48 [0.13 , 1.75]
Bonetti 2011 (2)	4	20	2	17	13.6%	1.70 [0.35 , 8.17]
Hadler-Olsen 2020 (3)	4	11	8	12	48.1%	0.55 [0.23 , 1.31]
Total (95% CI)		**61**		**58**	**100.0%**	**0.68 [0.35 , 1.31]**
Total events:	11		16			

Heterogeneity: Chi² = 1.82, df = 2 (P = 0.40); I² = 0%
Test for overall effect: Z = 1.16 (P = 0.25)
Test for subgroup differences: Not applicable

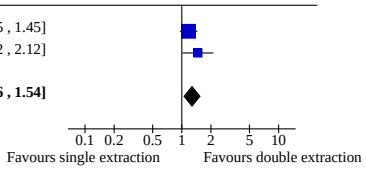


Footnotes
(1) One dropout from the extraction of canine only group (family moved away).
(2) Two dropouts (family moved away) and one withdrawal (inadequate radiograph) from extraction of canine only group.
(3) No withdrawals or dropouts. Included all participants diagnosed with unilateral PDC and those diagnosed with bilateral PDCs who had the same intervention on the two sides.

Analysis 1.2. Comparison 1: Single versus double primary tooth extraction, Outcome 2: Eruption of PDC by 48 months (mITT)

Study or Subgroup	Double primary extraction (canine & d) Events	Total	Single primary extraction (canine) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bonetti 2010 (1)	28	30	23	29	66.3%	1.18 [0.95 , 1.45]
Bonetti 2011 (2)	19	20	11	17	33.7%	1.47 [1.02 , 2.12]
Total (95% CI)		**50**		**46**	**100.0%**	**1.28 [1.06 , 1.54]**
Total events:	47		34			

Heterogeneity: Chi² = 1.14, df = 1 (P = 0.29); I² = 12%
Test for overall effect: Z = 2.54 (P = 0.01)
Test for subgroup differences: Not applicable

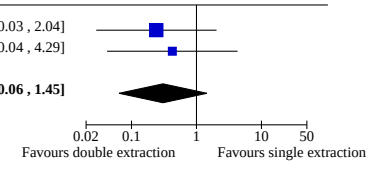


Footnotes
(1) One dropout from the extraction of canine only group (family moved away).
(2) Two dropouts (family moved away) and one withdrawal (inadequate radiograph) from extraction of canine only group.

Analysis 1.3. Comparison 1: Single versus double primary tooth extraction, Outcome 3: Number of participants referred for surgical exposure of the unerupted PDC by 48 months (mITT analysis)

Study or Subgroup	Double primary extraction (canine and molar) Events	Total	Single primary extraction (canine) Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bonetti 2010 (1)	1	30	4	29	65.3%	0.24 [0.03 , 2.04]
Bonetti 2011 (2)	1	20	2	17	34.7%	0.42 [0.04 , 4.29]
Total (95% CI)		**50**		**46**	**100.0%**	**0.31 [0.06 , 1.45]**
Total events:	2		6			

Heterogeneity: Chi² = 0.12, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 1.49 (P = 0.14)
Test for subgroup differences: Not applicable



Footnotes
(1) One dropout from the extraction of canine only group (family moved away).
(2) Two dropouts (family moved away) and one withdrawal (inadequate radiograph) from extraction of canine only group.

ADDITIONAL TABLES

Table 1. Definitions of palatally displaced permanent maxillary canine teeth from interventional PDC studies

Reference	Definition of PDC	Unilateral or bilateral
Leonardi 2004	"Intaosseous palatal position of the maxillary permanent canines from panoramic radiographs and periapical radiographs".	Either

Table 1. Definitions of palatally displaced permanent maxillary canine teeth from interventional PDC studies *(Continued)*

Baccetti 2008	"PDC were diagnosed as an intraosseous palatal position of the maxillary permanent canines from panoramic and periapical radiographs. The displacement of the upper canine to the palatal side was checked by means of double determination of the periapical radiographs".	Either
Baccetti 2009	"Prediction of canine palatal impaction derived from analysis of PA films by Sambataro 2005".[a]	Either
Silvola 2009	"Inclusion criteria were the need for orthodontic treatment due to moderate crowding and a Class II tendency"; therefore, no definition of displaced canine.	—
Bonetti 2010	Absence of palpation of PMC bulges; PMC bulges palatally; abnormal inclination and/or rotation of adjacent permanent maxillary lateral incisor crown; PMCs inclination to the midline > 25°; and overlapping of the PMC crowns with the permanent maxillary lateral incisor roots.	Either
Armi 2011	"PDC was diagnosed as intraosseous palatal position of the maxillary permanent canines from panoramic radiographs and periapical radiographs. The displacement of the upper canine to the palatal side was checked by means of double- determination periapical radiographs".	Either
Baccetti 2011	"Diagnosis of intraosseous malposition of the upper permanent canine(s) derived from the analysis of panoramic radiographs according to the method by- Ericson 1987 by means of alpha angle, d distance, and sector measurements.[b] PDCs showing an alpha angle greater than or equal to 15 degrees were included in the trial (milder forms of PDC were not enrolled). 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. Such PDCs either were unilateral or bilateral".	Either
Bonetti 2011	Absence of palpation of canine bulge; canine bulge palpable palatally; no[c] abnormal inclination and/or rotation of adjacent permanent maxillary lateral incisor crown; inclination of canine to vertical line passing through midline >25 deg; and overlapping of the PMC crowns with the permanent maxillary lateral incisor roots.	Either
Sigler 2011	"Diagnosis of intraosseous malposition of the upper permanent canine(s) derived from the analysis of panoramic radiographs according to the method by- Ericson 1987 by means of alpha angle, d distance, and sector measurements.[b] PDCs showing an alpha angle greater than or equal to 15 degrees were included in the trial (milder forms of PDC were not enrolled). 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. Such PDCs either were unilateral or bilateral".	Either
Bazargani 2013	"A canine within sectors 2–5, and intraosseous position within the palate as observed on the patients corresponding intraoral occlusal radiographs".	Bilateral
Naoumova 2015	"The canine was considered palatally displaced when clinical palpation of a labial canine bulge was absent and when the canine crown was diagnosed on intraoral radiographs as palatally positioned using Clark's rule".	—
Hadler-Olsen 2020	"Palatal position of the canine verified by taking two periapical radiographs and by using the Same Lingual Opposite Buccal (SLOB) rule."	—

PA: posterior-anterior; PDC: palatally displaced canine; PMC: permanent maxillary canine.

[a]This was based on measurements carried out on the PA radiographs of 12 individuals who eventually were diagnosed with a unilateral PDC and compared with 31 who did not develop a PDC. The *mean* age when the first radiograph was taken was 8 years and 5 months (no indication of the variability).
[b]Approximately 2/3 were in sectors 1 and 2.
[c]This is different to Bonetti 2010 where the word 'no' was not included.

Table 2. Extraction of canine versus no extraction: outcome: eruption of PDC at 12 months (ITT analysis)

	Ext C	No ext	Total
Yes	9	3	12
No	14	19	33
Total	23	22	45
RR 2.87 (95% CI 0.90 to 9.23)			

C: canine; CI: confidence interval; ext: extraction; ITT: intention to treat; NNTB: number needed to treat for an additional beneficial outcome; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by corresponding author of Naoumova 2015. No withdrawals or dropouts. Includes only participants with unilateral PDC (45 children).

Table 3. Extraction of canine versus no extraction: outcome: referred for surgical exposure of PDC at 12 months (ITT analysis)

	Ext C	No ext	Total
Yes	7	11	18
No	16	11	17
Total	23	22	45
RR 0.61 (95% CI 0.29 to 1.28)			

C: canine; CI: confidence interval; ext: extraction; ITT: intention to treat; NNTB: number needed to treat for an additional beneficial outcome; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by corresponding author of Naoumova 2015. No withdrawals or dropouts. Includes only participants with unilateral PDC (45 children).

Table 4. Extraction versus no extraction: outcome: eruption of PDC at 12 months by sector (mITT analysis)

Successful eruption of PDC	Baseline sector						Totals
	2		3		4		
	Ext C	No ext	Ext C	No ext	Ext C	No ext	
Yes	8	6	4	0	0	0	18
No	2	3	13	13	6	4	41
Total	10	9	17	13	6	4	59

C: canine; ext: extraction; mITT: modified intention to treat; PDC: palatally displaced canine.
Data supplied by corresponding author of Naoumova 2015. No withdrawals or dropouts. The author explained why the number of canines in this table was 59 and not 89 (total numbers of PDCs in the study), hence mITT: quote: "We followed the patients that had a favourable eruption path after 12 months. The table is correct since we have only 18 PDC that erupted at T2: 12 in the EG [experimental group] and 6 in the CG [control group]. 41 PDC were decided at T2 that they would need exposure: 14 from the EG and 27 from the CG. After T2: 30 PDC erupted: 20 PDC in the EG and 10 in the CG. In total 89 PDCs".

Table 5. Extraction of canine versus no extraction: outcome: root resorption of adjacent permanent teeth caused by the PDC at 12 months

Root resorption	Ext C	No ext	Total
Yes	8	13	21
No	37	31	68
Total	45	44	89
RR 0.60 (95% CI 0.28 to 1.31)			

C: canine; CI: confidence interval; ext: extraction; PDC: palatally displaced canine; RR: risk ratio.
Data obtained from scientific paper as reported in Naoumova 2015 and refer to individual teeth rather than participants. Root resorption graded as per Ericson and Kurol classification (Ericson 2000): 1. no resorption, intact root surfaces, and the cementum layer may be lost; 2. slight resorption, resorption up to half of the dentine thickness to the pulp; 3. moderate resorption, resorption midway to the pulp or more, the pulp lining being unbroken and 4. severe resorption, the pulp is exposed by the resorption. Participants with resorption of the adjacent teeth grades 3 and 4 were to be excluded, but no participants were excluded for this reason at the start of, or during, the study.
Ext C and grade 1 (no resorption) = 37 participants
Ext C and grade 2 (resorption) = 8 participants
No ext C and grade 1 (no resorption) = 31 participants
No ext C and grade 2 (resorption) = 13 participants

Table 6. Single versus double primary tooth extraction: outcome: eruption of PDC at 12 months (mITT analysis)

Number of participants with both canines in the mouth	Ext C only	Ext C and D	Total
Yes	4	1	5
No	8	10	18
Total	12	11	23
RR 0.27 (95% CI 0.04 to 2.08)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; mITT: modified intention to treat; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by corresponding author of Hadler-Olsen 2020.
32 participants entered the study. 9 participants with bilateral PDC excluded as they had different interventions on the two sides, hence mITT analysis. Of the remaining 23 participants:

- number of participants with unilateral PDC = 16; successful eruption refers only to the side diagnosed as a PDC, as it was assumed that the ipsilateral canine, not diagnosed as a PDC, will have erupted;
- number of participants with a bilateral PDC = 7; successful eruption defined as those who had the same intervention on both sides and in whom both canines successfully erupted;
- 5 participants included in unsuccessful 'No' row received surgical intervention at 12 months because their PDC had worsened on their radiograph (single ext group = 1; double ext group = 4).

Table 7. Single versus double primary tooth extraction: outcome: eruption of PDC at 24 months (mITT analysis)

Number of participants with both canines in the mouth	Ext C only	Ext C and D	Total
Yes	9	5	14
No	3	6	9

Table 7. Single versus double primary tooth extraction: outcome: eruption of PDC at 24 months (mITT analysis) *(Continued)*

Total	12	11	23
RR 0.61 (95% CI 0.29 to 1.25)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; mITT: modified intention to treat; NNTB: number needed to treat for an additional beneficial outcome; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by corresponding author of Hadler-Olsen 2020.
32 participants entered the study. 9 participants with bilateral PDC excluded as they had different interventions on the 2 sides, hence mITT analysis. Of the remaining 23 participants:

- number of participants with unilateral PDC = 16; successful eruption refers only to the side diagnosed as a PDC, as it is assumed that the ipsilateral canine, not diagnosed as a PDC, will have erupted;
- number of participants with a bilateral PDC = 7; successful eruption defined as those who had the same intervention on both sides and in whom both canines successfully erupted;
- all participants included in unsuccessful 'No' row received surgical intervention at 24 months because their PDC had worsened on their radiograph.

Table 8. Single versus double primary tooth extraction: outcome: eruption of PDC into a favourable position at 12 months (mITT analysis)

Number of participants with both canines in the mouth	Ext C only	Ext C and D	Total
Yes	1	1	2
No	11	10	21
Total	12	11	23
RR 1.09 (95% CI 0.08 to 15.42)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; mITT: modified intention to treat; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by corresponding author of Hadler-Olsen 2020.
Number of participants with unilateral PDC = 16; successful eruption refers only to the side diagnosed as a PDC, as it is assumed that the ipsilateral canine, not diagnosed as a PDC, will have erupted.
Number of participants with a bilateral PDC = 7; successful eruption defined as those who had the same intervention on both sides and in whom both canines successfully erupted, hence mITT analysis.
Nine participants with bilateral PDC from study excluded as they had different interventions on the two sides.

Table 9. Single versus double primary tooth extraction: outcome: eruption of PDC into a favourable position at 18 months (mITT analysis)

Number of participants with both canines in the mouth	Ext C only	Ext C and D	Total
Yes	2	3	5
No	10	8	18
Total	12	11	23
RR 1.64 (95% CI 0.33 to 8.03)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; mITT: modified intention to treat; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by corresponding author of Hadler-Olsen 2020. No withdrawals or dropouts.

Number of participants with unilateral PDC = 16; successful eruption refers only to the side diagnosed as a PDC, as it is assumed that the ipsilateral canine, not diagnosed as a PDC, will have erupted.
Number of participants with a bilateral PDC = 7; successful eruption defined as those who had the same intervention on both sides and in whom both canines successfully erupted, hence mITT analysis.

Table 10. Single versus double primary tooth extraction: outcome: eruption of PDC into a favourable position at 24 months (mITT analysis)

Number of participants with both canines in the mouth	Ext C only	Ext C and D	Total
Yes	2	3	5
No	10	8	18
Total	12	11	23
RR 1.64 (95% CI 0.33 to 8.03)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; mITT: modified intention to treat; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by corresponding author of Hadler-Olsen 2020.
Number of participants with unilateral PDC = 16; successful eruption refers only to the side diagnosed as a PDC, as it is assumed that the ipsilateral canine, not diagnosed as a PDC, will have erupted.
Number of participants with a bilateral PDC = 7; successful eruption defined as those who had the same intervention on both sides and in whom both canines successfully erupted, hence mITT analysis.
Nine participants with bilateral PDC from study excluded as they had different interventions on the two sides.

Table 11. Single versus double primary tooth extraction: outcome: eruption of PDC at 12 months by sector (ITT analysis)

Successful eruption of PDC	Baseline sector						Totals
	2		3		4		
	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	
Yes	0	0	8	4	0	2	14
No	6	3	5	15	4	1	34
Total	6	3	13	19	4	3	48

C: canine; D: primary first molar; ext: extraction; ITT: intention to treat; PDC: palatally displaced canine.
Data supplied by corresponding author of Hadler-Olsen 2020.
No withdrawals or dropouts. Data related to all teeth in the study (not participants), including those from the nine participants diagnosed with bilateral PDC who were excluded from other analyses, as they had different interventions on the two sides, hence ITT analysis.

Table 12. Single versus double primary tooth extraction: outcome: eruption of PDC at 18 months by sector (ITT analysis)

Successful eruption of PDC	Baseline sector						Totals
	2		3		4		
	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	
Yes	4	3	11	10	2	2	32
No	2	0	2	9	2	1	16
Total	6	3	13	19	4	3	48

C: canine; D: primary first molar; ext: extraction; ITT: intention to treat; PDC: palatally displaced canine.
Data supplied by corresponding author of Hadler-Olsen 2020.
No withdrawals or dropouts. Data related to all teeth in the study (not participants), including those from the nine participants diagnosed with bilateral PDC who were excluded from other analyses, as they had different interventions on the two sides, hence ITT analysis.

Table 13. Single versus double primary tooth extraction: outcome: eruption of PDC at 24 months by sector (ITT analysis)

Successful eruption of PDC	Baseline sector	Totals

Table 13. Single versus double primary tooth extraction: outcome: eruption of PDC at 24 months by sector (ITT analysis) *(Continued)*

	2		3		4		
	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	
Yes	4	3	11	11	3	2	34
No	2	0	2	8	1	1	14
Total	6	3	13	19	4	3	48

C: canine; D: primary first molar; ext: extraction; ITT: intention to treat; PDC: palatally displaced canine.
Data supplied by corresponding author of Hadler-Olsen 2020.
No withdrawals or dropouts. Data related to all teeth in the study (not participants), including those from the nine participants diagnosed with bilateral PDC who were excluded from other analyses, as they had different interventions on the two sides, hence ITT analysis.

Table 14. Single versus double primary tooth extraction: outcome: eruption of PDC at mean 18 months by sector (ITT analysis)

Successful eruption of PDC	Baseline sector										Totals
	1		2		3		4		5		
	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	
Yes	7	4	6	15	0	0	0	1	0	0	33
No	14	12	48	41	4	15	1	5	0	0	140
Totals	21	16	54	56	4	15	1	6	0	0	173

C: canine; D: primary first molar; ext: extraction; ITT: intention to treat; PDC: palatally displaced canine.
Data supplied by corresponding author for Bonetti 2010; Bonetti 2011. Data related to all teeth in the study (not participants), hence ITT analysis.

Table 15. Single versus double primary tooth extraction: outcome: eruption of PDC at maximum 48 months by sector (ITT analysis)

Successful eruption of PDC	Baseline sector					Totals
	1	2	3	4	5	

Table 15. Single versus double primary tooth extraction: outcome: eruption of PDC at maximum 48 months by sector (ITT analysis) *(Continued)*

	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	Ext C only	Ext C and D	
Yes	20	14	45	55	1	15	0	6	0	0	156
No	1	2	9	1	3	0	1	0	0	0	17
Totals	21	16	54	56	4	15	1	6	0	0	173

C: canine; D: primary first molar; ext: extraction; ITT: intention to treat; PDC: palatally displaced canine.
Data supplied by corresponding author for Bonetti 2010; Bonetti 2011. Data related to all teeth in the study (not participants), hence ITT analysis.

Table 16. Single versus double primary tooth extraction: outcome: eruption of PDC at 18 months (ITT analysis)

Number of participants with both canines in the mouth	Ext C only	Ext C and D	Total
Yes	16	11	27
No	46	50	96
Total	62	61	123
RR 0.71 (95% CI 0.37 to 1.37)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; ITT: intention to treat; LOCF: last observation carried forward; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by Bonetti 2010[a], Bonetti 2011[b] and Hadler-Olsen 2020[c].
[a]One withdrawal/dropout from the ext C only group (ITT analysis using LOCF).
[b]Three withdrawals/dropouts from ext C only group (ITT analysis using LOCF).
[c]No withdrawals and dropouts. Included all participants diagnosed with unilateral PDC and those diagnosed with bilateral PDCs who had the same intervention on the two sides.

Table 17. Eruption of PDC by 48 months (ITT analysis)

Number of participants with both canines in the mouth	Ext C only	Ext C and D	Total
Yes	34	47	81
No	16	3	19
Total	50	50	100
RR 1.38 (95% CI 1.13 to 1.69)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; ITT: intention to treat; LOCF: last observation carried forward; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by Bonetti 2010[a]; Bonetti 2011[b].
[a]One withdrawal/dropout from the ext C only group (ITT analysis using LOCF).
[b]Three withdrawals/dropouts from ext C only group (ITT analysis using LOCF).

Table 18. Number of participants referred for surgical exposure of the unerupted PDC by 48 months (ITT analysis)

	Ext C only	Ext C and D	Total
Yes	10	2	12
No	40	48	88
Total	50	50	100
RR 0.20 (95% CI 0.05 to 0.87)			

C: canine; CI: confidence interval; D: primary first molar; ext: extraction; ITT: intention to treat; LOCF: last observation carried forward; PDC: palatally displaced canine; RR: risk ratio.
Data supplied by Bonetti 2010[a]; Bonetti 2011[b].
[a]One withdrawal/dropout from the ext C only group (ITT analysis using LOCF).

[b]Three withdrawals/dropouts from ext C only group (ITT analysis using LOCF).

APPENDICES

Appendix 1. Cochrane Oral Health's Trials Register search strategy

Cochrane Oral Health's Trials Register is available via the Cochrane Register of Studies. For information on how the register is compiled, see https://oralhealth.cochrane.org/trials

1 MESH DESCRIPTOR Cuspid AND INREGISTER
2 (canine* or cuspid* or "eye tooth" or "eye teeth") AND INREGISTER
3 #1 or #2
4 MESH DESCRIPTOR Tooth, Impacted AND INREGISTER
5 MESH DESCRIPTOR Tooth, Unerupted AND INREGISTER
6 MESH DESCRIPTOR Tooth Eruption, Ectopic AND INREGISTER 23
7 ((tooth or teeth or canine* or cuspid*) near5 (impact* or unerupt* or erupt* or displac* or ectopic*)) AND INREGISTER
8 #4 or #5 or #6 or #7
9 MESH DESCRIPTOR Maxilla AND INREGISTER
10 MESH DESCRIPTOR Palate AND INREGISTER
11 (maxilla* or palat* or (upper NEAR1 jaw*) or (roof NEAR2 mouth)) AND INREGISTER
12 #9 or #10 or #11
13 #3 AND #8 AND #12

Appendix 2. Cochrane Central Register of Controlled Clinical Trials (CENTRAL) search strategy

1 MESH DESCRIPTOR cuspid
2 (canine* or cuspid* or "eye tooth" or "eye teeth")
3 #1 or #2
4 MESH DESCRIPTOR Tooth, Impacted
5 MESH DESCRIPTOR Tooth, Unerupted
6 MESH DESCRIPTOR Tooth Eruption, Ectopic
7 ((tooth or teeth or canine* or cuspid*) near5 (impact* or unerupt* or erupt* or displac* or ectopic*))
8 #4 or #5 or #6 or #7
9 MESH DESCRIPTOR Maxilla
10 MESH DESCRIPTOR Palate
11 (maxilla* or palat* or (upper NEAR1 jaw*) or (roof NEAR2 mouth))
12 #9 or #10 or #11
13 #3 AND #8 AND #12

Appendix 3. MEDLINE Ovid search strategy

1. Cuspid/
2. (canine$ or cuspid$ or "eye tooth" or "eye teeth").mp.
3. or/1-2
4. Tooth, impacted/
5. Tooth, unerupted/
6. Tooth eruption, ectopic/
7. ((tooth or teeth or canine$ or cuspid$) adj5 (impact$ or unerupt$ or erupt$ or displac$ or ectopic$)).mp.
8. or/4-7
9. Maxilla/
10. Palate/
11. (maxilla$ or palat$ or (upper adj jaw$) or (roof adj2 mouth)).mp.
12. or/9-11
13. 3 and 8 and 12

The above subject search was linked with the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials in MEDLINE (as described in Lefebvre 2020, box 3b).

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.

5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/ not humans.sh.
11. 9 not 10

Appendix 4. Embase Ovid search strategy

1. Canine tooth/
2. (canine$ or cuspid$ or "eye tooth" or "eye teeth").mp.
3. or/1-2
4. Tooth, unerupted/
5. Tooth eruption/
6. ((tooth or teeth or canine$ or cuspid$) adj5 (impact$ or unerupt$ or erupt$ or displac$ or ectopic$)).mp.
7. or/4-6
8. Maxilla/
9. Palate/
10. (maxilla$ or palat$ or (upper adj jaw$) or (roof adj2 mouth)).mp.
11. or/8-10
12. 3 and 7 and 11

The above subject search was linked with the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials in Embase (as described in Lefebvre 2020, box 3e).

1. Randomized controlled trial/
2. Controlled clinical study/
3. random$.ti,ab.
4. randomization/
5. intermethod comparison/
6. placebo.ti,ab.
7. (compare or compared or comparison).ti.
8. ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.
9. (open adj label).ti,ab.
10. ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.
11. double blind procedure/
12. parallel group$1.ti,ab.
13. (crossover or cross over).ti,ab.
14. ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant $1)).ti,ab.
15. (assigned or allocated).ti,ab.
16. (controlled adj7 (study or design or trial)).ti,ab.
17. (volunteer or volunteers).ti,ab.
18. human experiment/
19. trial.ti.
20. or/1-19
21. random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.)
22. Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.)
23. (((case adj control$) and random$) not randomi?ed controlled).ti,ab.
24. (Systematic review not (trial or study)).ti.
25. (nonrandom$ not random$).ti,ab.
26. "Random field$".ti,ab.
27. (random cluster adj3 sampl$).ti,ab.
28. (review.ab. and review.pt.) not trial.ti.
29. "we searched".ab. and (review.ti. or review.pt.)

30."update review".ab.
31.(databases adj4 searched).ab.
32.(rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/
33.Animal experiment/ not (human experiment/ or human/)
34.or/21-33
35.20 not 34

Appendix 5. Trials registry search strategies

US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) search strategy

Expert search interface:
((canine OR canines OR cuspid OR cuspids OR "eye tooth" OR "eye teeth") AND (impacted OR unerupted OR displaced OR ectopic))

World Health Organization International Clinical Trials Registry Platform search strategy

canine* AND impacted OR canine* AND unerupted OR canine* AND displaced OR canine* AND ectopic OR cuspid* AND impacted OR cuspid* AND unerupted OR cuspid* AND displaced OR cuspid* AND ectopic OR "eye tooth" AND impacted OR "eye tooth" AND unerupted OR "eye tooth" AND displaced OR "eye tooth" AND ectopic OR "eye teeth" AND impacted OR "eye teeth" AND unerupted OR "eye teeth" AND displaced OR "eye teeth" AND ectopic

WHAT'S NEW

Date	Event	Description
4 January 2022	Amended	Minor edits

HISTORY

Protocol first published: Issue 10, 2017
Review first published: Issue 12, 2021

CONTRIBUTIONS OF AUTHORS

NP, FB, PB and AA contributed to the development of the protocol.

NP, FB, PB and AA screened search records, extracted and analysed data, and assessed risk of bias.

NP, FB, PB, AA and BT contributed to the writing of the review and the conclusions.

DECLARATIONS OF INTEREST

PB: none.

AA: none.

FB: none.

NP: none.

BT: none.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol, we stated that we would include both parallel-group and split-mouth studies. However, during the review process we altered this to: 'The minimum period for participant follow-up was six months after intervention or recruitment for the non-intervention controls. We included studies employing a parallel-group design that recruited participants judged to have a unilateral PDC or participants judged to have bilateral PDC, or both'. The reason for this difference is that we believe that interpretation of data from participants judged to have bilateral PDC recruited to studies involving a within-person (or split mouth) design is problematic (Hujoel 1998). This design of study allocates an intervention to one side of the dental arch and untreated control to the other side (or two different interventions to the two sides of the dental arch). We consider there to be two potential problems with this approach. First, it assumes that all confounding pretreatment factors, in particular the severity of PDC displacement (i.e. sector, height from occlusal plane and angulation) are similar between the two sides. It is possible that randomisation might account for some of these confounding factors, but only if the sample size is large (i.e. many 10s, if not 100s of participants). Second, it assumes that an intervention on one side of the dental arch has no effect on the opposite side. For these reasons we decided to exclude studies employing a within-person (or split mouth) design that exclusively recruited participants judged to have bilateral PDC and who were allocated to different interventions on the two sides.

In the protocol, we stated that we would include the secondary outcome measure of reported improvement in the medial, vertical or angular position of the PDC, as measured from radiographs. However, the review was designed to determine the success of interceptive interventions (treating malocclusions as soon as they are detected) designed to promote the eruption of a PDC. Therefore, even if the PDC did improve in position, but still remained unerupted, the patient would still require a surgery to expose/brace treatment to align the PDC. Therefore, this outcome could not be used to inform a clinician when deciding whether to undertake an interceptive intervention to promote the eruption of a PDC to avoid the need for a surgical exposure. However, we do acknowledge that any improvement in the position of the PDC could potentially affect, following surgical exposure, time to align the PDC and therefore time in braces.

In the review, we added a secondary outcome of reported number and time point of patients referred for surgical exposure of the PDC following the intervention. This secondary outcome was reported by all the included studies and provides information with regards to follow-up periods and effectiveness of the interventions.

For types of participants, in our protocol, we stated we would include 'studies with children diagnosed as having one or both permanent maxillary canines palatally displaced', but in the review we added 'where the definition of PDC was clear and likely to be valid' for the reasons discussed later in the review.

NOTES

The protocol for this review was an expanded update of a previously published review: Parkin N, Furness S, Shah A, Thind B, Marshman Z, Glenroy G, Dyer F, Benson PE. Extraction of primary (baby) teeth for unerupted palatally displaced permanent canine teeth in children. Cochrane Database of Systematic Reviews 2012, Issue 12.