DO THE VARIOUS INTERCEPTIVE INTERVENTIONS IMPROVE THE POSITION OF PALATALLY DISPLACED PERMANENT CANINES?
A META-ANALYSIS

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ABSTRACT

Do the various interceptive interventions improve the position of palatally displaced permanent canines? A meta-analysis

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Background: Extraction of maxillary primary canines (Cs) and other interceptive interventions in the mixed dentition have been suggested to increase the rate of normal eruption of palatally displaced permanent canines (PDCs). However, the information on the overall effect on PDCs position has not been yet summarized in an evidence-based manner.

Objective: To assess whether this practice improves the position of PDCs and to investigate the quality of the evidence.

Search methods: Unrestricted searches in 8 databases and manual searching of the reference lists in relevant studies were performed up to March 2021 (Medline via PubMed, CENTRAL, Cochrane Database of Systematic Reviews, Scopus, Web of Science, Arab World Research, ClinicalTrials.gov, ProQuest Dissertations and Theses Global).

Selection criteria: We looked for data on the positional changes of PDCs (mesial inclination, vertical position, canine crown cusp tip to midline) from randomized controlled trials, assessing the various interceptive interventions.

Data collection and analysis: Following study retrieval and selection, relevant data were extracted, and the risk of bias was assessed using the Cochrane Risk of Bias 2 Tool. Exploratory synthesis and meta-regression were carried out using the random effects model, and the overall quality of the available evidence was assessed with the Grades of Recommendation, Assessment, Development, and Evaluation approach.

Results: Five studies (3 at low risk of bias) were identified, involving 238 individuals, followed for up to 18 months post-intervention with orthopantomograms or cone beam computed tomography. Exploratory data synthesis showed that PDCs' position improved more in the extraction sites compared to non-extraction. Analysis of the studies at low risk confirmed the above observations (6 and 12 months). Improvements were observed in patients using headgear after extraction of the Cs compared to extraction alone, but not in patients with double extraction of Cs and first molars. The quality of available evidence was rated as moderate at best.

Conclusions: Interceptive interventions in the mixed dentition may improve the position of PDCs. However, further studies are warranted in order to determine the clinical significance of the changes.

DEDICATION

To start with, most of all, thanks to Allah (God) without whom I would not have what I am thankful for now. I would also like to dedicate my Master Dissertation to my parents and husband for their continuous support and motivation throughout the years.

DECLARATION

I declare that all the content of the thesis is my own work. There is no conflict of interest with any other entity or organization.

Name: Ahlam Habib

Signature:

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1. INTRODUCTION

Tooth impaction constitutes one of the most important problems encountered in orthodontic practice. The maxillary permanent canines are considered to be the most commonly impacted teeth after the third molars, with a prevalence rate of up to 9% (Hou et al., 2010; Fardi et al., 2011; Mercuri et al., 2013; Herrera-Atoche et al., 2017). The maxillary canine remains mainly impacted palatally to the dental arch (Mercuri et al., 2013) and is found more often in females than males, at a ratio of 2:1 (Mercuri et al., 2013). Maxillary canines can remain impacted either unilaterally or bilaterally, which appear in 8-10% of impaction cases (Herrera-Atoche, et al., 2017).

Multiple complications and side effects have been associated with maxillary permanent canine impaction, such as cyst formation, root resorption of the adjacent teeth (Rafflenbeul et al., 2019; Guarnieri et al., 2016; Husain et al., 2016), complex orthodontic mechanics (Manne et al., 2012), as well as an increase in treatment cost and time (Mavreas and Athanasiou, 2008). In adults, resorption of the crown of the impacted canine has also been observed (Azaz and Shteyer, 1978). Therefore, early interceptive management of the palatally displaced permanent canines (PDCs) could be beneficial in order to mitigate such risks and complications (Manne et al., 2012).

Several approaches have been described for the interceptive management of the PDCs, such as extraction of the primary canines alone (Counihan et al., 2013; Husain et al., 2016), or in combination with orthodontic procedures, like trans-palatal arches, rapid maxillary expansion, or cervical-pull headgear (Hadler-Olsen et al., 2018; Leonardi et al., 2004; Baccetti et al., 2008; 2009; 2011; Armi et al., 2011). It has been reported that these approaches are effective in promoting the successful spontaneous eruption of the PDCs compared to non-extraction (Alyammahi et al., 2018; Al Naqbi et al., 2020), however, the information regarding the positional changes has not been summarized in an evidence-based manner. Even in the case that the PDC does not finally erupt spontaneously, an interceptive procedure would be beneficial if it results in an improvement in its position, that will make subsequent surgical and orthodontic intervention more straightforward and predictable.

The aim of this dissertation is to assess whether the practice of extraction of the deciduous canines and other interceptive interventions in the mixed dentition improve the position of PDCs and investigate the quality of the evidence.

2. REVIEW OF THE LITERATURE

A tooth which fails to erupt at its expected site in the dental arch within its normal duration of eruption (accompanied by clinical or radiographic evidence in which further eruption is not expected) is considered an impacted tooth (Kokich and Mathews, 1993). Displacement of the maxillary permanent canines, and especially palatally displaced maxillary canines, results in impaction (Baccetti et al., 2008). PDCs are considered a developmental disturbance of the maxillary permanent canines, and, without treatment, might result in the need for surgical exposure and orthodontic traction (Peck et al., 1996).

The permanent maxillary canine, which has the longest duration of development and the most complex path of eruption, originates from the deepest area of the maxilla (Dewel, 1949). Its tooth bud is situated in the corner amidst the orbit, the nasal cavity, and the frontal wall of the maxillary sinus (Jacoby, 1983). The calcification process of the permanent maxillary canine begins at 4 to 5 months after birth, while the enamel formation is completed by the age of 6 to 7 years (Counihan et al., 2013). The timing of canine eruption in the oral cavity, which differs between genders, usually occurs at the mean of age 11.5 years, while root completion takes place between 13 and 15 years of age (Wedl et al., 2004). Due to the late eruption of the permanent maxillary canine, there is a big risk of exposure to undesirable developmental influences (Becker, 2012). Moreover, during its extended development, maxillary canine movement occurs in all three planes of space (Richardson and Coulter, 1997). It shifts almost 22 mm between 5 and 15 years age, resulting in the longest eruption path among the permanent teeth (Richardson and Coulter, 1997).

The maxillary canine crown is critically positioned adjacent to the lateral incisor roots

(Bishara, 1992). Consequently, resorption of the root of the lateral incisors is considered a major danger during the eruption or traction of the permanent maxillary canine (Broadbent, 1941).

2.1. Epidemiology of palatal displacement of the maxillary permanent canines

Palatal impaction of permanent maxillary canines has been observed in the skulls of humans dating far back as six hundred years BCE (Baccetti et al., 1995; Iseri et al., 1993). Many studies have noted that permanent canines are more likely to erupt palatally in Caucasian populations (Walker et al., 2005), yet in Asian populations, a canine is more likely to erupt buccally (Oliver et al., 1989). Although the prevalence of palatal impaction of maxillary canines appears generally to be low, it often differs based on the ethnic group (Becker, 2012). European populations have shown five times higher rates of palatal impaction in comparison to Asians (Peck et al., 1994). While Japan has the lowest prevalence of palatally impacted canines with only 0.3% (Takahama and Aiyama, 1982), the Portuguese population has a reported a prevalence of 4.5% (Moreira et al., 2015). A highest rate (6.8%) has been reported in Italians (Mercuri et al., 2013). Recently, based on CBCT scans, it has been observed that the Chinese and European populations have 45% of canine impaction cases positioned labially, 40% located palatally, and 15% positioned in the center of the alveolar process (Alqerban et al., 2011; 2014, Liu et al., 2008).

2.2. Related anomalies

Palatally displaced canines often appear to be associated with other dental anomalies (Mercuri et al., 2013, Naoumova and Kjellberg, 2018). Such anomalies include congenitally missing teeth (like the permanent maxillary laterals), abnormal tooth morphology (peg shaped lateral crowns, general underdevelopment of the dentition), and tooth transposition (Mercuri et al., 2013, Naoumova and Kjellberg, 2018). Palatally impacted canines have been associated with aplasia in at least one tooth, particularly the third molars (Naumova and Kjellberg, 2018). Unilaterally palatally impacted canines occur mainly in conjunction with aplasia of the maxillary laterals. However, bilateral palatally impacted canines have been related with absent third molars (Sacerdoti and Baccetti, 2004). Family relatives of patients with palatally impacted canines can be also affected by similar conditions (Ziberman et al., 1990). Patients with palatally displaced canines rarely have dental crowding (Peck et al., 1994). PDCs have also been associated with vertical hypodivergent skeletal relationships and deep bite (Leifert and Jonas, 2003; Sacerdoti and Baccetti, 2004).

2.3. Etiology of the palatal displacement of maxillary permanent canines

Generally, PDCs are believed to be a multifactorial condition that cannot be attributed to a specific cause. Although they are mainly caused by local factors, general factors can also contribute (Bishara, 1992).

2.3.1. General factors

Though several studies have blamed genetics for being the cause of palatally impacted canines (Peck et al., 1994), this association has not been unequivocally established (Becker and Chaushu, 2015).

The following observations are believed to be evidence supporting the genetic theory for the etiology of impacted canines (Becker and Chaushu, 2015):

- Existence of different dental abnormalities with genetic causes linked to palatally impacted canines (aplasia or hypoplasia of 2nd premolars, absence or deformities of the maxillary laterals, primary molars in infra-occlusion, hypoplasia of the enamel and tooth transposition).
- The bilateral incidence of PDCs.
- The differing prevalence of PDCs in different populations.
- The existence of sexual dimorphism in the prevalence of PDCs.
- The existence of familial tendency in the prevalence of PDCs.

However, several lines of evidence do not support the proposed genetic theory (Becker and Chaushu, 2015).

a) In genetics, bilateralism is the rule and not the exception. Therefore, bilateral impaction should be more common than unilateralism.

b) Monozygous twins should exhibit higher prevalence of impacted canines in comparison to dizygous twins (Camilleri et al., 2008).

c) Canine impaction should be corelated more with congenitally missing laterals in the other quadrant, which is a more potent genetic trait than anomalous laterals (Becker et al., 1999).

A special situation involving canine impaction, that can be considered of a genetic cause, is the misposition of the apices of the maxillary canines bilaterally, where both canines' apices are dislodged palatally and distally to the premolars (Becker and Chaushu, 2015).

Moreover, multiple diseases and conditions have been associated with dental impaction, such as irradiation, endocrine deficiencies, and febrile disorders (Bishara, 1992). Furthermore, multiple impacted teeth are very common in Gardner syndrome or Familial Adenomatous Polyposis. The frequency of impacted teeth ranges from 4% to 38% in Familial Adenomatous Polyposis cases, which is nearly ten times the rate of the normal population (Wijn et al., 2007; de Oliveira Ribas et al., 2009). Impacted teeth are also found to be associated with Yunis-Varon syndrome, Down syndrome and cleidocranial dysplasia (Gorlin et al., 2001).

2.3.2. Local factors

The local etiological factors of canine impaction can be categorized as follows (Becker and Chaushu, 2015):

a) Soft tissue obstructions or lesions.

b) Obstructions from hard tissues.

c) Developmental disorders of the maxillary permanent incisors.

Deflection or impediment to the path of eruption of the maxillary permanent canine can happen because of soft tissue lesions, like radicular cysts, tumors, periapical granulomas or dentigerous cysts (Becker and Chaushu, 2015). These lesions can be exacerbated by the existence of prolonged retained and inflamed primary canines (Becker and Chaushu, 2015).

Furthermore, hard tissue lesions, such as supernumerary teeth and odontomas, as well as the primary canine over-retention, could act as an obstacle for the normal development and emergence of the maxillary permanent canine through the gingiva (Becker and Chaushu, 2015).

Dense overlying bone or palatal thickening of the mucosa could also drive palatally the maxillary canine, giving rise to eruption difficulties and causing canine impaction (Alkadhimi et al., 2017).

The fact that the development of the maxillary permanent canines happens close to the lateral is also quite important (Chaushu, 2015). Their normal root morphology is of particular importance, as it guides the canine into a favorable eruption path (Becker et al., 1981; Jacoby, 1983; Bishara, 1992). The presence of sufficient space and normal development of the permanent maxillary canine do not guarantee successful eruption, like in cases of central incisors impactions. Such circumstances will cause tipping of the crown of the lateral in the mesial direction and the root apex in the distal direction, leading to deflection on the path of eruption of the permanent canine (Becker and Chaushu, 2015).

Traumas to the maxilla may cause canine dilacerations which can lead to impaction (do Espírito Santo Jácomo and Campos, 2009; de Amorim et al., 2018).

2.4. Consequences from impacted permanent maxillary canines

Aesthetics, function, and occlusal protection are all provided by the permanent maxillary canine, making it one of the most important teeth in the maxillary arch (Thiruvenkatachari et al., 2017; Pokorny, 2008). Regular clinical examination and follow up must be carried out so as to avoid the adverse effects that might arise from its displacement or impaction.

Root resorption of the permanent maxillary lateral incisor is a complication caused by impacted maxillary canines (Ericson and Kurol, 2000; Walker et al., 2005; Kalavritinos et al., 2020; Wang et al., 2020). It is observed most frequently between the ages of 11 and 12 (Ericson and Kurol, 2000) and more often in females than in males (Bjerklin and Ericson, 2006). Walker et al. (2005) observed that in 66.7% of impacted maxillary canine cases, root resorption would occur in the adjacent lateral incisor, and only in 11.1% of the cases would the central incisors or the first premolar be affected. Loss of vitality of the incisors has been observed due to severe resorption as well.

The most severe complication in cases of extensive root resorption is the need to extract the affected teeth, which increases treatment complexity, duration, and costs (Manne et al., 2012). The crowns of the impacted teeth can also be affected by resorption, mainly in adults (Azaz and Shteyer, 1978). Although this does not occur frequently (about 14% of the impacted maxillary crowns), the crown of the impacted teeth can still be subject to resorption as a result of inflammatory processes that damage the enamel epithelium (Azaz and Shteyer, 1978).

Another potential outcome is the loss of the permanent canine's space in the dental arch due to its impaction. In this case, the adjacent teeth migrate in its space, causing loss of dental arch perimeter and length (Manne et al., 2012).

Dentigerous cysts have also been observed arising from maxillary impacted canines, due to cystic modifications in the follicular sac (Becker and Chaushu, 2015; Manne et al., 2012). The events mentioned above can also occur in combination (Manne et al., 2012).

2.5. Determination of the position of displaced maxillary permanent canines

During routine patient examination, the dentist must regularly check for canine displacement, as signs like a palatal bulge, prolonged retention of the primary canines, or drifting of the laterals do not usually make patients request dental help. Therefore, clinical examination and radiographic follow-up at the right time is crucial to aid in the correct management of any displacement or impaction. These steps will assist in identifying the problem at an early period, as well as in detecting other hidden complications that are usually associated with displaced maxillary canines (Sacerdoti and Baccetti, 2004). Thus, inspection, palpation and radiographic examination are important to reach an optimum diagnosis (verification of the position of the impacted tooth and its condition) and to mitigate any problems in the adjacent structures.

2.5.1. Inspection and palpation

Displaced or impacted maxillary permanent canines can be identified through multiple signs and symptoms during clinical inspection. When the primary canine is retained in position past its exfoliation time, or when there is an excessive delay in the eruption of the permanent maxillary canine, it should be considered as indications of canine impaction or displacement (Power and Short and, 1993; Bishara, 1992).

The absence of a labial canine bulge between 10 and 12 years age is considered a sign of canine impaction. However, this is not an absolute indication, and one would require an X-ray to evaluate the position and the eruption path of the permanent maxillary canine (Bishara, 1992). In addition, asymmetric features regarding the development of the labial canine bulges, the primary canine's exfoliation and the permanent canine's eruption must not be ignored in clinical evaluation (Bishara, 1992; Shapira and Kuftinec 1998). Features of the neighboring teeth must also be inspected, including tooth mobility, the available keratinized gingiva, loss of attachment's signs and periodontal health (Chapokas et al., 2012).

The unerupted permanent canines' position could be predicted from the angulation of the adjacent lateral incisor (Counihan et al., 2013; Chapokas et al., 2012). The unerupted canine is mainly found in a labial position when the lateral is inclined mesially or tipped labially, and it is expected to be situated palatally when the lateral incisor root is palpable labially (Becker, 2012; Counihan et al., 2013; Chapokas et al., 2012). Furthermore, if the "Ugly Duckling" stage continues past the age of 11, then it can suggest that the eruption of the canine may be problematic (Becker, 2012; Chaushu and Becker, 2015).

Clinical inspection of the region also includes an assessment of the mobility of the corresponding primary canine if present, as well as the palpation of the alveolar process, the mucosa of the palate and the buccal sulcus (Counihan et al., 2013; Husain et al., 2016). This routine process must start early, approximately around 8 to 9 years of age (Short and Power, 1993).

2.5.2. Radiography

Radiographic evaluation, in conjunction with clinical examination, is essential in determining the position and the eruption path of displaced maxillary permanent canines (Ericson and Kurol, 1986a; 1986b). The indicated radiographs should not be performed prior to the age of 10, as they will not provide any important information at this stage (Ericson and Kurol, 1986b; 1987a). Furthermore, it would be too early, at that age, for any complications of the permanent maxillary impacted canine to be observed (Olow-Nordenram and Anneroth, 1982).

The panoramic, as well as the lateral cephalometric x-rays, that are used extensively in dentistry and orthodontics, cannot provide much information about the location of the canine, or even the resorption of the root of the adjacent tooth due to structure superimposition (Chapokas et al., 2012). The periapical radiograph is one of the most useful ways to evaluate the position of the canine (Bishara, 1992). The vertical and mesiodistal canine position can be ascertained by one periapical radiograph. However, a second one should be taken at a different angle, to provide information on the bucco-lingual positioning of the crown (Bishara, 1992). This radiographic technique is named the parallax technique (Husain et al., 2016). The parallax technique can be performed in a vertical or a horizontal way, depending on the positioning of the x-ray tube (Southall and Gravely, 1989). The horizontal parallax is more reliable in locating impacted canines (Armstrong et al., 2003).

Cone beam computer tomography (CBCT) is, presently, considered the most precise technique to locate an impacted canine and verify the presence and severity of possible resorption in the adjacent teeth (Doğramaci et al., 2015; Naoumova et al., 2014; Walker et al., 2005). However, the overuse of CBCT is not recommended (Isaacson et al., 2015; Halazonetis, 2012) due to the higher radiation doses when compared to other radiographic tools. To mitigate this problem, a minimum field of view must be utilized when taking a CBCT, in order to only visualize the impacted canine area (European Commission Radiation Protection Series, ECRP, 2012).

2.6. Management of impacted maxillary permanent canines

In the cases of impacted canines, it is usually needed to have a group of professionals from various specialties to evaluate, diagnose, and formulate a treatment plan. The team has to include an orthodontist, an oral surgeon, a periodontist, a general dentist and a pediatric dentist (Alkadhimi et al., 2017). Specific cases might not need any interference, and normal observation will prove sufficient (Husain et al., 2016). These cases involve displaced teeth that are located away from the rest of the dentition, normal roots of the adjacent teeth, lack of complications and a primary canine with good prognosis (Husain et al., 2016).

Several approaches are available to deal with displaced canines, such as the removal of any obstacles, surgical exposure and orthodontic traction, as well as, albeit rarely, the extraction of the impacted tooth with or without auto-transplantation (Alkadhimi et al., 2017).

2.6.1. Surgical interventions

Guiding the canine to its ideal location in the arch is usually performed through a combination of orthodontic treatment and surgical intervention (Bishara, 1992). Multiple surgical techniques are available to manage impacted canines, and the most appropriate one is to be chosen based on several factors, such as radiographic and clinical parameters, as well as the orthodontist's and surgeon's proficiencies and skills (Fleming et al., 2010; Alkadhimi et al., 2017). Exposure of the impacted canines with surgery is usually required when the patient is older than the average age to qualify for interceptive interventions (Husain et al., 2012).

Prior to the exposure of the canine, space availability is essential; this is the reason why surgical procedure is usually done between 6 to 9 months after the initial alignment of the dentition (Fleming et al., 2010).

Resorption of the root, ankylosis of the canine, poor esthetic outcomes and periodontal problems might be considered complications encountered during surgical exposure and orthodontic traction of the maxillary canine (Chapokas et al., 2012).

There are two major techniques to expose a palatally impacted canine; the closed and the open technique (Alkadhimi et al, 2017). However, currently, there is insufficient evidence to judge which one of the two methods constitutes the best option (Alkadhimi et al., 2017; Parkin et al., 2008).

A full thickness palatal mucoperiosteal flap must be raised when using the closed exposure method. Then, the canine's crown has to be uncovered by removing the overlying osseous tissue (Hunt, 1977), followed by the bonding of a bracket, with a gold or a metallic chain, on the canine's crown. Following this procedure, the flap can be sutured back into position, with the chain passing through an incision in the margin of the gingiva (Alkadhimi et al., 2017).

Open exposure can be performed either by excising the mucosa covering the crown of the impacted canine, or by raising a complete mucoperiosteal flap and removing enough amount of bone in order to facilitate the placement of an attachment. This is followed by flap repositioning and the creation of a hole in the mucosa that is filled with a surgical pack (Alkadhimi et al., 2017). The open exposure method can be combined with or without mechanical traction, depending on the developmental stage of the adjacent roots and the inclination of the impacted canine (Alkadhimi et al., 2017).

Normal eruption by open surgical exposure without traction can be expected when the canine is in normal axial position and the root is still not completely formed, although this would take a longer time compared to orthodontic traction (Kokich, 2004). Using this technique would minimize the stage of active treatment. However, if gingiva hypertrophy is present, re-exposure would be required (Alkadhimi et al., 2017; Kokich, 2004).

The open surgical exposure technique combined with traction has to be utilized to direct

the impacted canine toward the right place in the arch, especially once root development is complete and the canine is improperly inclined (Bishara, 1998; Kokich, 2004). This technique has two variations, depending on the time of the placement of the orthodontic attachment and force application (Bishara, 1998). In the first variation, the placement of the attachment is performed on the same day as the surgery, and the traction force is applied immediately. The second variation is a two-step procedure, that is used when bonding of the attachment cannot be performed due to bleeding. In such conditions, positioning of the attachment could be postponed until the surgical trauma starts to heal (Lewis, 1971). Both techniques can be used in the case of palatally impacted canines, as the mucosa is highly keratinized, thick and well attached (Alkadhimi et al., 2017).
Open surgical exposure for the impacted canines must not be done when there is severe root resorption of the adjacent incisors, as it may endanger tooth vitality (Walker et al., 2005). Moreover, this technique must not be performed when there is a deep impaction of the maxillary canine, as in such cases, the patient might not feel comfortable (Alkadhimi et al., 2017).

During canine exposure, it is very important to reduce the amount of the removed bone and to avoid exposing of cementoenamel junction (Alkadhimi et al., 2017). Safe orthodontic practices, as well as accurate control of the force's direction, are necessary during active tooth eruption to prevent undesired movement of the tooth, resorption of the root of the adjacent teeth, and failure to successfully reposition the displaced canine (Arriola-Guillén et al., 2018). That is why careful controlling of the initial movement of the tooth is necessary, and may require a combination of two different forces in distal and occlusal directions prior to alignment of the tooth buccally into the natural location in the maxillary arch (Fleming et al., 2010).

Failure in tooth movement could result from remaining bone around the crown of the impacted canine, tooth ankylosis, or poor orthodontic traction technique (Kokich and Mathews, 1993). Mechanical injury from the use of the low-speed bur and chemical trauma from phosphoric acid in the cervical area might cause deterioration to the root's cementum or the periodontal ligament and lead to ankylosis (Alkadhimi et al., 2017; Koutzoglou and Kostaki, 2013).

Esthetic problems in the treatment of impacted canines have been associated with inadequate root torque, deficient band of attached gingiva or gingival recession, and the lack of occlusal wear (Schmidt and Kokich, 2007).

An alternative surgical procedure, which can be performed if other options are not indicated, is the transplantation of the tooth if the formation of the apex has not been completed (Husain et al., 2016). Adequate alveolar bone thickness and dental arch space are required to support the transplanted tooth with minimum trauma and are crucial for the final outcome (Husain et al., 2016).

Another treatment option could be the surgical extraction of the palatally impacted canine. This may be performed in cases of extreme impaction (Husain et al., 2016).

2.7. Interceptive procedures for palatally positioned permanent canines

Interceptive treatment is considered important to mitigate the complications related to impacted maxillary permanent canines and their treatment. This type of management was first mentioned in the literature in 1930s, by Buchner (1936). He was considered a pioneer in his field, proposing the use of a lingual appliance in the maxilla and the extraction of the primary maxillary canines.

A study by Ericsson and Kurol (1988) demonstrated that once extraction of the correspondent primary canines at the indicated time has been performed, a favorable direction in the eruption path of the palatally displaced permanent canines occurred in 78% of the cases. In addition, Power and Short (1993) noted that natural eruption of the palatal displaced canines occurred in 62% of the cases, while 19% exhibited clear improvement of the eruption path following the removal of the corresponding primary canines. A recent systematic review showed that the removal of the related primary canine may increase the chance of spontaneous eruption of the displaced canines in the long-term (Alyammahi et al., 2018). Moreover, it has been shown that the use of rapid palatal expansion, transpalatal arches and headgear can improve the chances for normal eruption of the palatally displaced canines in comparison to non-intervention; however, in comparison to extraction, no overall differences were noted (Al Naqbi et al., 2020). Even in the cases that a displaced canine does not erupt spontaneously, this type of interceptive procedure would be beneficial if it resulted in an overall improvement in the position of the impacted tooth, making subsequent surgical and orthodontic procedures more straightforward, predictable and less risky. However, until now, the relevant information has not been summarized in an evidence-based manner.

3. AIM

3.1. Aim

To investigate the effect of various interceptive management approaches in the position of palatally displaced canines.

3.2. Objectives

To quantitively summarize the effect of various interceptive management approaches in the mesial inclination position of palatally displaced canines.
To quantitively summarize the effect of various interceptive management approaches in the vertical position of palatally displaced canines.
To quantitively summarize the effect of various interceptive management approaches in the canine cusp tip to midline position of palatally displaced canines.

4. MATERIALS AND METHODS

4.1 Protocol and registration

The present review was based on a broader protocol developed, registered, carried out and reported following relevant methodological guidelines (Shamseer et al., 2015; Moher et al., 2015; Page et al., 2021; Beller et al., 2013; Higgins et al., 2019) (PROSPERO: CRD42015029130). As the present study is a systematic review, ethical approval was not required.

4.2 Eligibility criteria

The eligibility criteria were based on the PICOS (Participants, Intervention, Comparison, Outcomes, Study design) acronym (Appendix 1) (Higgins et al., 2019). We looked for Randomized Clinical Trials (RCTs), involving individuals in the mixed dentition, with unilateral or bilateral palatally displaced permanent canine(s). Moreover, we included individuals of any gender and racial background. The studies should investigate the outcomes of the extraction of the primary canine(s) and other primary teeth, as well as various interceptive orthodontic procedures (such as, but not limited to: rapid maxillary expansion, transpalatal arches, headgear, etc.) combined with or without extraction. The outcomes considered should be relevant to the changes in the position of the PDCs over time as assessed in orthopantomograms (OPG) or CBCT (changes in mesial inclination, i.e., alpha angle, etc.; changes in vertical position, i.e., distance D from the dental arch, distance from the palatal plane, etc.; changes in canine cusp tip to midline position, i.e., sectors, distance in mm, etc.). The comparator could be no treatment, extraction of the primary canine only, other alternative or adjunctive orthodontic procedures, or delayed treatment in case of worsening or lack of improvement. Finally, we did not consider animal, in vitro, ex-vivo or in silico studies; non-randomized studies, non-comparative studies (case reports and case series), systematic reviews and meta-analyses.

4.3 Information sources and search strategy

The principal supervisor developed the detailed search strategies for each of the databases that we searched until March 25th 2021 (Medline [PubMed], CENTRAL [Cochrane Library; includes records from Embase, CINAHL, ClinicalTrials.gov, WHO's ICTRP, KoreaMed, Cochrane Review Groups' Specialized Registers, and records identified by handsearching], Cochrane Database of Systematic Reviews [Cochrane Library], Scopus, Web of Knowledge [including Web of Science Core Collection, KCI Korean Journal Database, Russian Science Citation Index, SciELO Citation Index and Zoological Record], Arab World Research [EBSCOhost], ClinicalTrials.gov [U.S. National Library of Medicine] and ProQuest Dissertation and Theses [ProQuest]) (Appendix 2). We did not impose any restrictions on the language or date of publication. Duplicates were removed using EndNote's duplicate identification strategy (EndNote X9™, Clarivate™, Philadelphia, PA, USA) and then manually by the principal supervisor. We also manually searched the reference lists in relevant articles to identify additional studies (AH and EGK).

4.4 Study selection, data collection and data items

Two authors (AH and EGK) assessed the retrieved records for inclusion independently. If the abstract was unclear, the full paper was accessed to determine eligibility for inclusion. From the finally eligible studies, the following information was extracted in predetermined forms: bibliographic details of the study; details on study design and verification of study eligibility; inclusion and exclusion criteria; participant characteristics (where available number, age, gender) at the beginning and at each point of data analysis (if patient attrition was observed the respective reasons were noted); intervention characteristics; duration of the observation period; outcomes measured for the positional changes of the PDCs over time as assessed in OPG or CBCT (changes in mesial inclination, i.e. alpha angle, etc.; changes in vertical position, i.e. distance D from the dental arch, distance from the palatal plane, etc.; changes in canine cusp tip to midline position, i.e. sectors, distance in mm, etc.); additional information like a priori sample size calculation, baseline comparability of the groups; reliability of the method of assessment; numerical results and information regarding the risk of bias assessment domains. If clarifications were needed regarding the published data, or additional material was required, then attempts to contact the corresponding authors through email were made.

4.5 Risk of bias in individual studies

The risk of bias in individual studies was assessed by two authors (AH and EGK) independently with the RoB2 tool for RCTs (Higgins et al., 2019). Assessments were subsequently entered into the Risk-of-bias VISualization (robvis) web application (McGuinness and Higgins, 2020). In all the aforementioned processes, disagreements were settled by discussion with the AEA; following the relevant suggestions, kappa statistics were not calculated (Higgins et al., 2019).

4.6 Data synthesis

Data on the positional changes of the PDCs over time presented variety (mesial inclination: alpha angle, mesioangular angle; vertical position: distance D from the dental arch, distance from the palatal plane; canine cusp tip to midline position, sectors according to Ericsson and Kurol (1988) and Lindauer et al. (1992), distance in mm, etc.). In order for the summary measures to be comparable across studies, the differences in the changes between the various interventions were expressed using the standardised mean difference (SMD) in the form of Hedges's g (together with 95% Confidence Interval - CI) (Higgins et al., 2019; Hedges, 1981; Hedges and Olkin, 1985). The magnitude of the effect size was appraised according to Sawilowsky (2009). In order to facilitate the interpretation of the positional changes' SMDs, those were re-expressed into mesial inclination, vertical position and canine cusp tip to midline position units, based on the CBCT information from the Naoumova (2014) study. Ordinal scales were summarized using methods for continuous data (Higgins et al., 2019). Due to the lack of an adequate number of retrieved studies, it was not possible to calculate the corresponding 95% prediction intervals (Higgins et al., 2019).

To identify the presence and the extent of heterogeneity between studies, the overlap of 95% confidence interval for the results of individual studies was inspected graphically, and the I^2 statistic was calculated (Higgins et al., 2019). All analyses were carried out with Comprehensive Meta-Analysis Software version 3 (©2014 Biostat Inc., Englewood, New Jersey, USA). Significance (a) was set at 0.05, except for 0.10 used for Q tests (Ioannidis, 2008).

4.7 Risk of bias across studies and additional analyses

As per protocol, analyses were to be carried out for “small-study effects” and publication bias. However, they were not finally performed, due to the lack of an adequate number of studies (Higgins et al., 2019). We used meta-regression to explore whether the duration of follow-up modified the results. Finally, despite the lack of extensive information for some outcomes, the quality of the available evidence regarding differences in the PDCs changes in position after 12 months of observation was assessed (Guyatt et al., 2011) in order to adopt a structured and transparent approach in formulating an interpretation of the evidence. The 12-month post-intervention period has been suggested to be an appropriate time point to review the treatment plan for patients with still unerupted PDCs after an interceptive intervention (Naoumova, 2014; Hadler-Olsen, 2019).

5. RESULTS

5.1 Study selection

Following database searches, we collected 2895 records, and 2 more manually. Eight hundred forty-six records were identified as duplicates, and a further 2035 were excluded on the basis of their title and abstract. Subsequently, 16 papers were assessed for eligibility, and 11 records were excluded for the following reasons: 3 did not include follow-up data (Bacetti et al., 2009; Baccetti et al., 2011; Naoumova and Kjellberg, 2018); 2 did not report on the outcomes of interest (Armi et al., 2011; Naumova et al., 2015); 2 did not focus on palatally displaced canines (Alessandri Bonetti et al., 2010; 2011), 2 were records of dissertations, based on which, a paper was later published (Naumova, 2014; Hadler-Olsen, 2019), one was a record of study protocol, with results published later (ClinicalTrials.gov Identifier: NCT02675036), and another one was a study protocol without published results (ClinicalTrials.gov Identifier: NCT0368452; authors contacted for results but no response received) (Appendix 3).

Finally, 5 papers were included in the review (Figure 1) (Leonardi et al., 2004; Baccetti et al., 2008; Bazargani et al., 2014; Naoumova et al., 2015; Hadler-Olsen et al., 2020). Two of these papers were a part of dissertation projects that were checked whether they included useful information additional to that in the published article (Naumova, 2014; Hadler-Olsen, 2019).

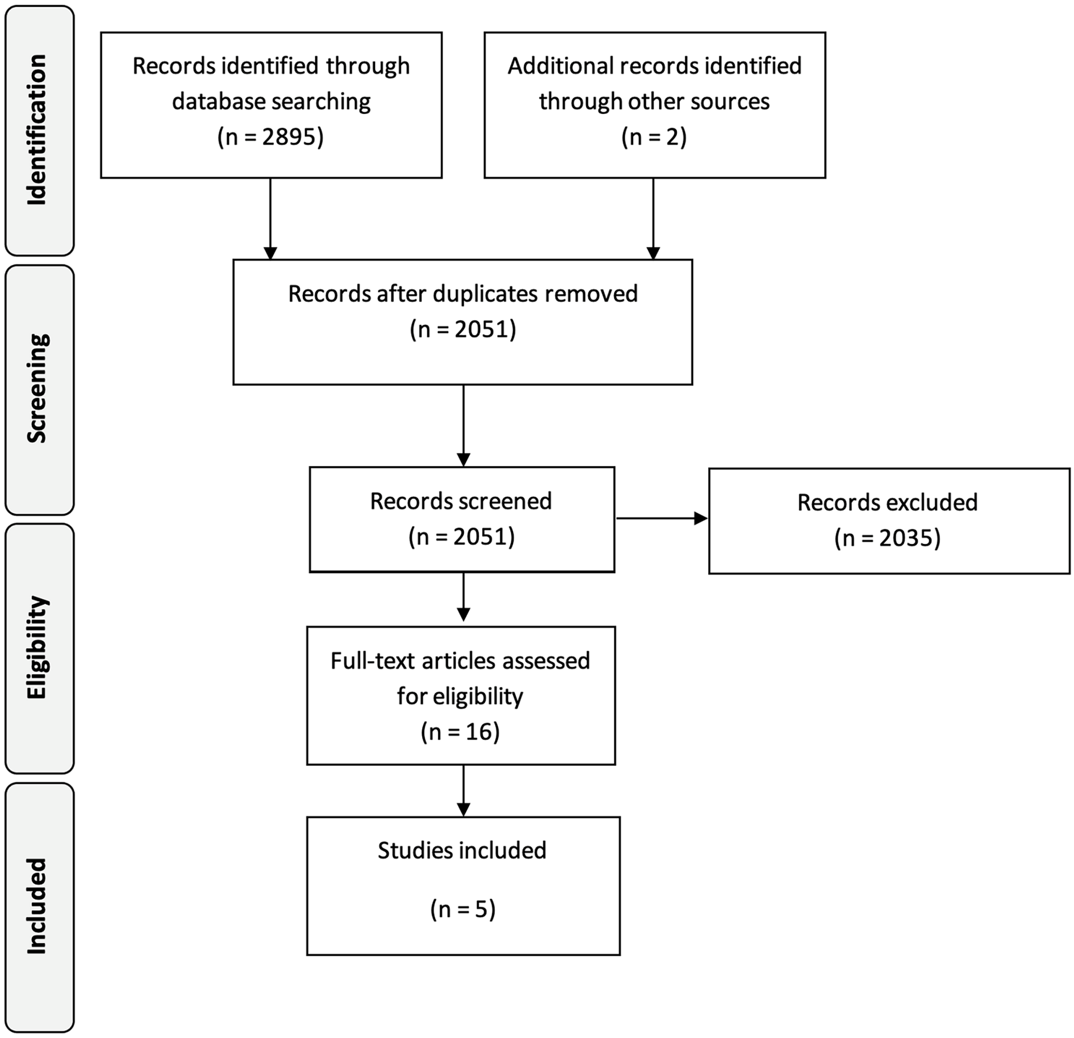


Figure 1. Flowchart of records.

5.2 Study characteristics

The characteristics of the studies included in the present systematic review are presented in Tables 1 and 2. The papers were published between 2004 and 2020, & investigated, in a total of 238 patients, the extraction of primary maxillary canine(s) compared to no intervention (Leonardi et al., 2004; Baccetti et al., 2008; Bazargani et al., 2014; Naoumova et al., 2015), the additional use of head-gear (Leonardi et al., 2004; Baccetti et al., 2008) & the supplementary extraction of the first primary molars (Hadler-Olsen et al., 2020). Patients were followed for a period of up to 18 months.

The positional changes of the PDCs were followed using OPG (Leonardi et al., 2004; Baccetti et al., 2008; Bazargani et al., 2014; Hadler-Olsen et al., 2020) & CBCT (Naoumova et al., 2015). The PDCs mesial inclination was assessed using Ericsson and Kurol's (1988) alpha angle (Leonardi et al., 2004; Baccetti et al., 2008; Bazargani et al., 2014; Hadler-Olsen et al., 2020) & mesionagular angle (Naoumova et al., 2015). The PDCs vertical position was assessed using Ericsson and Kurol's (1988) d-distance of the canine cusp tip from the occlusal plane (Leonardi et al., 2004; Baccetti et al., 2008; Bazargani et al., 2014) & the distance from the ANS-PNS reference plane (Naoumova et al., 2015). The PDCs crown to midline position was categorized into sectors according to Ericsson & Kurol (1988) (Leonardi et al., 2004; Baccetti et al., 2008; Bazargani et al., 2014) or Lindauer et al. (1992) (Hadler-Olsen et al., 2020), or was measured in mm from the midline (Naoumova et al., 2015).

Three studies reported *a priori* calculation of sample size (Bazargani et al., 2014; Naoumova et al., 2015; Hadler-Olsen et al., 2020), & one made reference to the power of the study, but it was not specified if the power was calculated *a priori* or *post hoc* (Baccetti et al., 2008). In addition, all five included studies, considered examining the reliability of the measurements carried out in some way, & included reference to baseline comparability.

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

Study	Inclusion and exclusion criteria Diagnostic criteria for PDCs	Number of subjects and PDCs analyzed [gender, age (mean ±SD)]
Baccetti et al. [2008 - Italy]	**Inclusion criteria:** Caucasians; unilateral or bilateral PDCs; dental age 8 – 13y (Becker and Chaushu, 2000); skeletal age before CVMS 3 (Baccetti et al., 2005) **Exclusion criteria:** Previous orthodontic Tx; craniofacial syndromes, odontomas, cysts, cleft lip and/or palate, sequelae of trauma to the face, multiple/advanced caries; clinical Mx crowding; aplasia or severe hypoplasia of the crowns of the Mx 2(s) **Diagnostic criteria for PDCs:** Intraosseous palatal position of the Mx 3(s) from OPG and PA radiographs using Clark's rule	**HG+ExC:** 24 subjects; 35 PDCs [10M, 14F; 11.9y] **ExC:** 23 subjects; 25 PDCs [8M, 15F; 11.7y] **No intervention:** 22 subjects; 26 PDCs [9M, 13F; 11.6y]
Bazargani et al. [2014 - Sweden]	**Inclusion criteria:** Inability to locate the 3(s) by digital palpation; bilateral PDCs identified on the OPG and occlusal radiographs; age at diagnosis 10 - 14y; late mixed dentition **Exclusion criteria:** Previous/ongoing orthodontic Tx, aplasia of Mx 2(s), Mx crowding >3 mm; craniofacial syndromes, odontomas, cysts, cleft lip and/or palate **Diagnostic criteria for PDCs:** Non-palpable bulge; 3(s) within sectors 2–5, in an intraosseous position within the palate, and exceeding the long axis of the upper lateral incisors on an IO occlusal radiograph (Ericsson and Kurol, 1988)	**Split mouth study** 24 subjects; 48 PDCs [8M, 16F; 11.6 ±1.2y] **ExC:** 24 PDCs **No intervention:** 24 contralateral PDCs
Hadler-Olsen et al. [2020 – Norway]	**Inclusion criteria:** 9.5–13.5y; dental age of 9.5-10.5y (AlQahtani et al., 2014); unilateral or bilateral PDCs; both Mx Cs and Ds **Exclusion criteria:** Agenesis of Mx 2(s); previous orthodontic Tx; any disease preventing local anaesthesia or extraction; craniofacial syndromes, cleft lip/palate, odontomas, cysts **Diagnostic criteria for PDCs:** palatal position of the 3(s) verified by Clark's rule; eruption in sectors III/IV (Lindauer et al., 1992) or sector II with an angle between the long axis of 3 and the facial midline >25º (Hadler-Olsen et al., 2015) assessed on OPG	32 subjects, 48 PDCs [14M, 11.2 ±1.0y; 18F, 10.7 ±0.7y] **ExC:** 23 PDCs [11.0 ±1.1y] **ExC+D:** 25 PDCs [10.8 ±0.7]
Leonardi et al. [2004 - Italy]	**Inclusion criteria:** Caucasians; unilateral of bilateral PDC; dental age at baseline 8 – 13y (Becker and Chaushu, 2000); skeletal age before CVMS 4 (Baccetti et al., 2005) **Exclusion criteria:** Previous orthodontic Tx; craniofacial syndromes, odontomas, cysts, cleft lip and/or palate, sequelae of traumatic injuries to the face, multiple or advanced caries (or both); Mx crowding; aplasia or severe hypoplasia of the Mx 2(s) **Diagnostic criteria for PDCs:** Intraosseous palatal position of the Mx 3(s) from OPG and PA radiographs	**HG+ExC:** 21 subjects; 32 PDCs [7M, 14F; 12.2y] **ExC:** 11 subjects; 14 PDCs [5M, 6F; 11.6y] **No intervention**: 14 subjects; 16 PDCs [4M, 10F; 11.6y]
Naoumova et al. [2015 - Sweden]	**Inclusion criteria:** Caucasians; 10–13y; unilateral or bilateral PDC; persisting Cs; no previous experience of orthodontic Tx **Exclusion criteria:** Mx crowding >2 mm, ongoing orthodontic Tx, grades 3/4 resorption of the adjacent teeth at the start or during Tx (Ericson and Kurol, 2000); craniofacial syndromes; odontomas, cysts, cleft lip and/or palate **Diagnostic criteria for PDCs:** Non palpable bulge; crown of 3(s) palatally positioned (Clark's rule)	67 subjects, 89 PDCs [27M, 11.4 ±0.9y; 16F, 11.3 ±1.1y] **ExC:** 45 PDCs[a] **No intervention**: 44 PDCs[a]

C: primary canine; CS: Cervical Stage; ExC: Extraction of the primary canine; D: primary first molar; F: Female; HG: cervical-pull headgear; IO: intraoral; M: Male; PA: periapical; PDCs: Mx: maxillary; Palatally Displaced Canines; OPG: orthopantomogram; SD: Standard Deviation; Tx: treatment; y: years; 2(s): permanent lateral incisor(s); 3(s): permanent canine(s)
[a] Analyzed following Intention-to-treat principle.

Table 2. Radiographic examination, outcomes measured and additional information.

Study	Radiographic examination and Outcomes	Additional information
Baccetti et al. [2008 - Italy]	**Radiographic examination:** OPG at baseline and after an average period of 18m **Mesial inclination:** alpha angle (º) (Ericson and Kurol, 1988) **Vertical position:** d distance (mm) (Ericson and Kurol, 1988) **Canine crown to midline position:** Sectors (Ericson and Kurol, 1988)	**A priori sample calculation:** Reference that [The power … was greater than 0.85. …] **Baseline group comparability:** Reference that […The severity of canine displacement was similar…] **Measurement reliability considered:** Yes
Bazargani et al. [2014 - Sweden]	**Radiographic examination:** OPG at baseline and at 6, 12 and 18m **Mesial inclination:** alpha angle (º) (Ericson and Kurol, 1988) **Vertical position:** d distance(mm) (Ericson and Kurol, 1988) **Canine crown to midline position:** Sectors (Ericson and Kurol, 1988)	**A priori sample calculation:** Yes **Baseline group comparability:** Yes [d distance, α angle, sector; age/gender within the split mouth design] **Measurement reliability considered:** Yes
Hadler-Olsen et al. [2020 – Norway]	**Radiographic examination:** OPG at baseline and every 6m until the canine erupted [a] **Mesial inclination:** alpha angle (º) (Ericson and Kurol, 1988) **Canine crown to midline position:** Sectors (Lindauer et al., 1992)	**A priori sample calculation:** Yes **Baseline group comparability:** Yes [age, dental age, alpha angle, sector] **Measurement reliability considered:** Yes (Hadler-Olser et al., 2018)
Leonardi et al. [2004 - Italy]	**Radiographic examination:** OPG at baseline and after an average period of 18m **Mesial inclination:** alpha angle (º) (Ericson and Kurol, 1988) **Vertical position:** d distance (mm) (Ericson and Kurol, 1988) **Canine crown to midline position:** Sectors (Ericson and Kurol, 1988)	**A priori sample calculation:** NR **Baseline group comparability:** Yes [age, gender distribution]; Reference that […Severity of canine displacement was similar…] **Measurement reliability considered:** Yes
Naoumova et al. [2015 - Sweden]	**Radiographic examination:** CBCT at baseline and at 6 and 12m **Mesial inclination:** mesioangular angle (º) (Naoumova et al., 2014) **Vertical position:** distance from the ANS-PNS refernce plane (mm) (Naoumova et al., 2014) **Canine crown to midline position:** canine cusp tip-midline distance (mm) (Naoumova et al., 2014)	**A priori sample calculation:** Yes **Baseline group comparability:** Yes [gender; mesioangular angle, vertical position, canine cusp tip-midline distance] **Measurement reliability considered:** Yes

CBCT: Cone Beam Computed Tomography; PDCs: Palatally Displaced Canines, m: months; NR: Not Reported; OPG: Orthopantomogram
[a] Mean: 14.8 months (range 6–24 months).

5.3 Risk of bias within studies

Figure 2 presents a summary of findings regarding the risk of bias assessment for the included studies. Three studies were classified as being at low risk of bias (Bazargani et al., 2014; Naoumova et al., 2015; Hadler-Olsen et al., 2020). The rest were considered to present some concerns, primarily because of problems regarding the domain of the randomization process. Regarding the remainder of the considered items, blinding of the participants and the personnel providing instructions was not possible. However, in the context of the present research design, there was no reason to believe that bias could be introduced because of absence of blinding in these cases. On the contrary, blinding of the outcome assessment could possibly involve risk of bias, because it is not possible to blind the extracted canine, and only baseline assessments could be blinded. As the reporting – and maybe the conduct – of some of the included studies presented general deficiencies, it is not clear how these could have affected the appraisal of the outcomes included in the present systematic review.

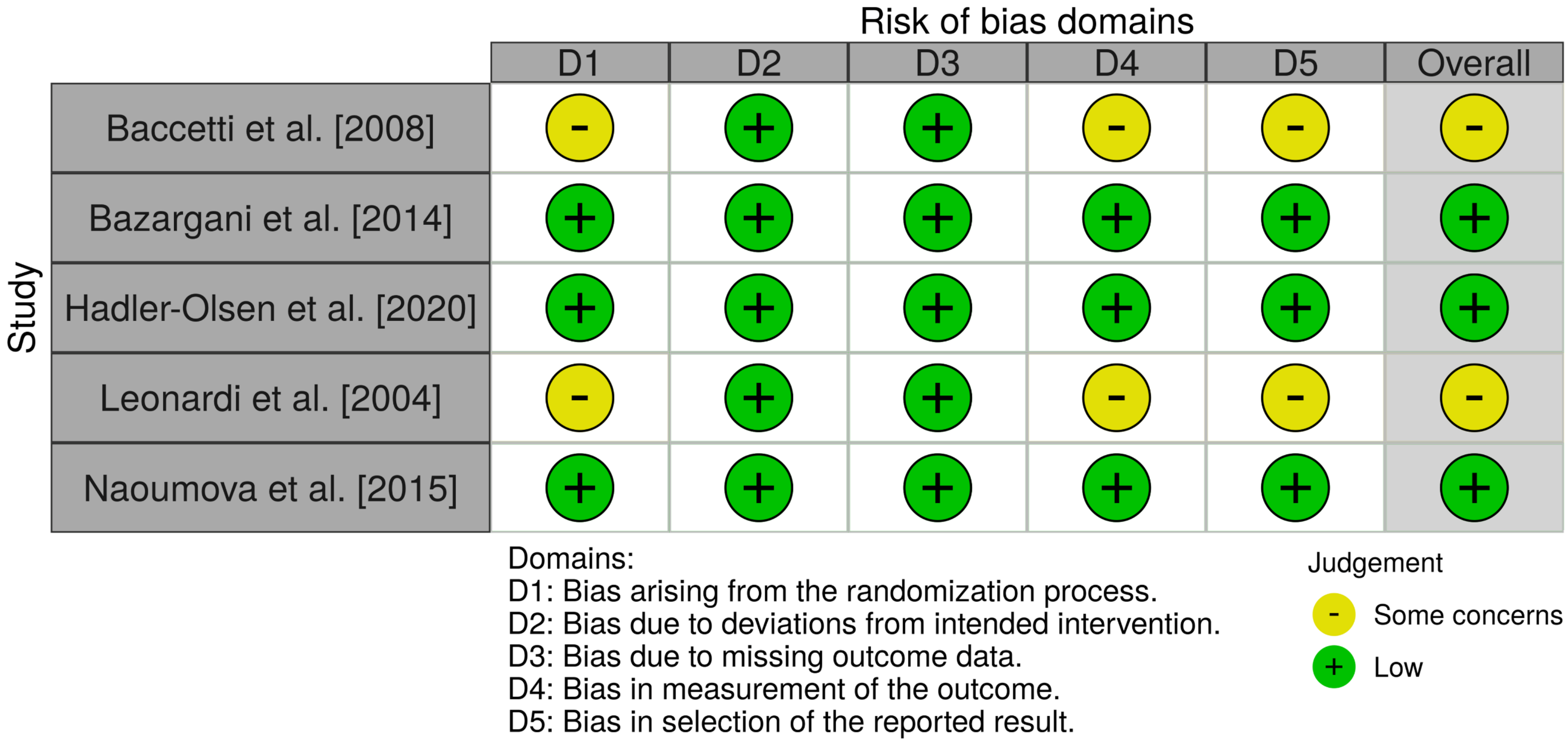


Figure 2. Risk of bias assessment.

5.4 Positional changes of the PDCs

On the whole, exploratory data synthesis showed that the position of the PDCs improved more in the extraction sites compared to the sites of no intervention at the 6-, 12- and 18-months follow-ups (Table 3, Figure 3). Only the assessment at 6 months of the PDCs crown position from the midline did not demonstrate any statistically significant benefit. At the 12-month post-intervention assessment, the magnitude of the effect was considered large (Sawilowsky, 2009) and corresponded to greater improvements in the extraction sites' CBCT measurements of approximately 2^{o} in the mesial inclination, 2.5 mm in the vertical position and 2 mm in the horizontal position of the canine cusp tip from the midline.

Analysis of the data focusing on the studies at low risk corroborated the above observations for the 6- and 12-month follow-ups (Table 4, Figure 4). In the series of exploratory meta-regressions for the differences in PDCs' positional changes that included the intercept and the length of follow-up (in months) as predictor, no statistically significant effects were observed (Table 5, Figure 5). The R^2 analog ranged from 0.00 to 0.42.

The comparison of the changes between extraction of the primary canine and extraction plus headgear sites after 18 months of observation showed statistically significant improvements in the position of the PDCs for the patients using headgear additionally, with regard to the mesial inclination and the crown to midline position (Table 6, Figure 6). The magnitude of the effects ranged from small to medium (Sawilowsky, 2009).

The comparison of the changes between sites with extraction of the primary canines, compared to the additional extraction of the primary first molars, after 14.8 months of follow-up, did not reveal any statistically significant differences in the mesial inclination ($p=0.203$) or the PDC crown to midline position ($p>0.05$).

Regarding the differences in the PDCs changes in position, the quality of available evidence was rated as moderate at best (Guyatt et al., 2011) (Table 7).

Table 3. Positional changes of PDCs [Comparisons between extraction and non-extraction sites – All studies].

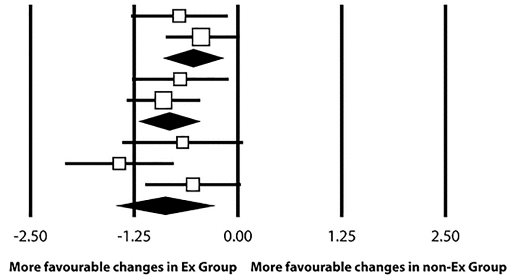
			Effect size and 95% confidence interval [a]					
		No of studies	**Hedges' g [b]**	**SE**	**LL**	**UL**	**P-value**	**I^2 (%)**
PDC mesial inclination	**6 months - baseline**	2	-0.53	0.17	-0.87	-0.20	**0.002**	0.00
	12 months - baseline	2	-0.82	0.18	-1.17	-0.48	**0.000**	0.00
	18 months - baseline	3	-0.87	0.28	-1.43	-0.32	**0.002**	55.29
PDC vertical position	**6 months - baseline**	2	-0.70	0.17	-1.04	-0.36	**0.000**	0.00
	12 months - baseline	2	-1.09	0.29	-1.65	-0.53	**0.000**	57.01
	18 months - baseline	3	-0.69	0.20	-1.08	-0.31	**0.000**	12.40
PDC crown to midline position	**6 months - baseline**	2	-0.66	0.35	-1.34	0.02	0.057	72.91
	12 months - baseline	2	-0.88	0.44	-1.74	-0.01	**0.046**	82.45
	18 months - baseline	3	-0.40	0.18	-0.75	-0.05	**0.024**	0.00

LL: Lower limit; MD: mesiodistal; PDCs: palatally displaced canines; SE: Standard Error; UL: Upper limit
[a] Statistically significant differences in bold; [b] Negative values denote more favorable changes in the extraction sites.

A.

Statistics for each study

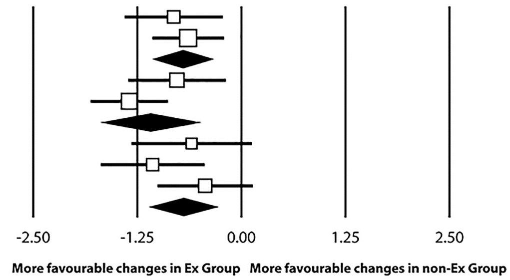
		Hedges's g	Standard error	Lower limit	Upper limit	p-Value
6 months	[2014] Bazargani et al.	-0.71	0.29	-1.28	-0.13	0.016
	[2015] Naoumova et al.	-0.44	0.21	-0.86	-0.03	0.037
		-0.53	0.17	-0.87	-0.20	0.002
12 months	[2014] Bazargani et al.	-0.69	0.29	-1.27	-0.12	0.018
	[2015] Naoumova et al.	-0.90	0.22	-1.33	-0.46	0.000
		-0.82	0.18	-1.17	-0.48	0.000
18 months	[2004] Leonardi et al.	-0.67	0.37	-1.38	0.05	0.069
	[2008] Baccetti et al.	-1.43	0.33	-2.07	-0.78	0.000
	[2014] Bazargani et al.	-0.54	0.29	-1.11	0.03	0.062
		-0.87	0.28	-1.43	-0.32	0.002



B.

Statistics for each study

		Hedges's g	Standard error	Lower limit	Upper limit	p-Value
6 months	[2014] Bazargani et al.	-0.81	0.30	-1.39	-0.23	0.006
	[2015] Naoumova et al.	-0.64	0.22	-1.06	-0.22	0.003
		-0.70	0.17	-1.04	-0.36	0.000
12 months	[2014] Bazargani et al.	-0.77	0.29	-1.35	-0.20	0.009
	[2015] Naoumova et al.	-1.35	0.23	-1.80	-0.89	0.000
		-1.09	0.29	-1.65	-0.53	0.000
18 months	[2004] Leonardi et al.	-0.60	0.36	-1.31	0.12	0.102
	[2008] Baccetti et al.	-1.06	0.31	-1.68	-0.45	0.001
	[2014] Bazargani et al.	-0.43	0.29	-1.00	0.13	0.131
		-0.69	0.20	-1.08	-0.31	0.000



C.

Statistics for each study

		Hedges's g	Standard error	Lower limit	Upper limit	p-Value
6 months	[2014] Bazargani et al.	-0.29	0.29	-0.85	0.27	0.310
	[2015] Naoumova et al.	-0.99	0.22	-1.42	-0.55	0.000
		-0.66	0.35	-1.34	0.02	0.057
12 months	[2014] Bazargani et al.	-0.42	0.29	-0.98	0.14	0.144
	[2015] Naoumova et al.	-1.30	0.23	-1.75	-0.85	0.000
		-0.88	0.44	-1.74	-0.01	0.046
18 months	[2004] Leonardi et al.	-0.42	0.36	-1.13	0.28	0.240
	[2008] Baccetti et al.	-0.47	0.30	-1.05	0.11	0.112
	[2014] Bazargani et al.	-0.33	0.29	-0.89	0.23	0.255
		-0.40	0.18	-0.75	-0.05	0.024

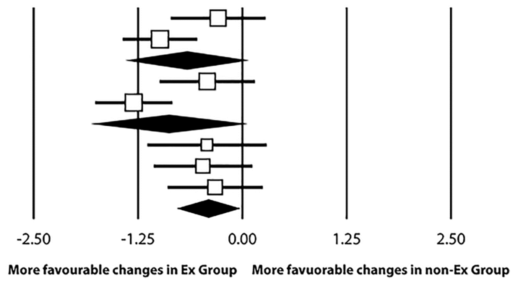


Figure 3. Positional changes of PDCs: Comparisons between extraction and non-extraction sites – All studies. A. Mesial inclination; B. Vertical position; C. Canine crown to midline position.

Table 4. Positional changes of PDCs [Comparisons between extraction and non-extraction sites – Low risk of bias studies].

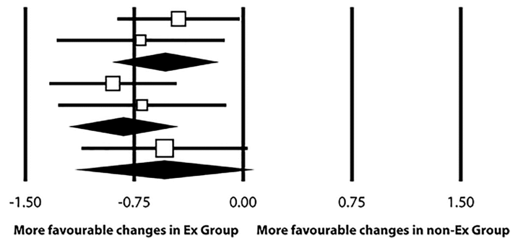
			Effect size and 95% confidence interval [a]					
		No of studies	**Hedges' g [b]**	**SE**	**LL**	**UL**	**P-value**	**I^2 (%)**
PDC mesial inclination	**6 months - baseline**	2	-0.53	0.17	-0.87	-0.20	**0.002**	0.00
	12 months - baseline	2	-0.82	0.18	-1.17	-0.48	**0.000**	0.00
	18 months - baseline	1	-0.54	0.29	-1.11	0.03	0.062	N/A
PDC vertical position	**6 months - baseline**	2	-0.70	0.17	-1.04	-0.36	**0.000**	0.00
	12 months - baseline	2	-1.09	0.29	-1.65	-0.53	**0.000**	57.01
	18 months - baseline	1	-0.43	0.29	-1.00	0.13	0.131	N/A
PDC crown to midline position	**6 months - baseline**	2	-0.66	0.35	-1.34	0.02	0.057	72.91
	12 months - baseline	2	-0.88	0.44	-1.74	-0.01	**0.046**	82.45
	18 months - baseline	1	-0.33	0.29	-0.89	0.23	0.255	N/A

LL: Lower limit; MD: mesiodistal; N/A: Not applicable; PDCs: palatally displaced canines; SE: Standard Error; UL: Upper limit
[a] Statistically significant differences in bold; [b] Negative values denote more favorable changes in the extraction sites.

A.

Statistics for each study

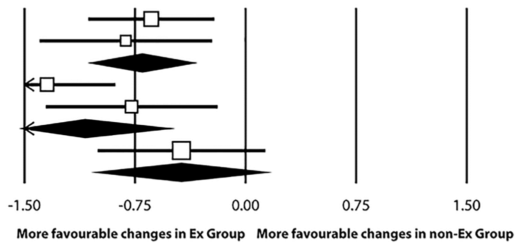
		Hedges's g	Standard error	Lower limit	Upper limit	p-Value
06 months	[2015] Naoumova et al.	-0.44	0.21	-0.86	-0.03	0.037
	[2014] Bazargani et al.	-0.71	0.29	-1.28	-0.13	0.016
		-0.53	0.17	-0.87	-0.20	0.002
12 months	[2015] Naoumova et al.	-0.90	0.22	-1.33	-0.46	0.000
	[2014] Bazargani et al.	-0.69	0.29	-1.27	-0.12	0.018
		-0.82	0.18	-1.17	-0.48	0.000
18 months	[2014] Bazargani et al.	-0.54	0.29	-1.11	0.03	0.062
		-0.54	0.29	-1.11	0.03	0.062



B.

Statistics for each study

		Hedges's g	Standard error	Lower limit	Upper limit	p-Value
6 months	[2015] Naoumova et al.	-0.64	0.22	-1.06	-0.22	0.003
	[2014] Bazargani et al.	-0.81	0.30	-1.39	-0.23	0.006
		-0.70	0.17	-1.04	-0.36	0.000
12 months	[2015] Naoumova et al.	-1.35	0.23	-1.80	-0.89	0.000
	[2014] Bazargani et al.	-0.77	0.29	-1.35	-0.20	0.009
		-1.09	0.29	-1.65	-0.53	0.000
18 months	[2014] Bazargani et al.	-0.43	0.29	-1.00	0.13	0.131
		-0.43	0.29	-1.00	0.13	0.131



C.

Statistics for each study

		Hedges's g	Standard error	Lower limit	Upper limit	p-Value
6 months	[2015] Naoumova et al.	-0.99	0.22	-1.42	-0.55	0.000
	[2014] Bazargani et al.	-0.29	0.29	-0.85	0.27	0.310
		-0.66	0.35	-1.34	0.02	0.057
12 months	[2015] Naoumova et al.	-1.30	0.23	-1.75	-0.85	0.000
	[2014] Bazargani et al.	-0.42	0.29	-0.98	0.14	0.144
		-0.88	0.44	-1.74	-0.01	0.046
18 months	[2014] Bazargani et al.	-0.33	0.29	-0.89	0.23	0.255
		-0.33	0.29	-0.89	0.23	0.255

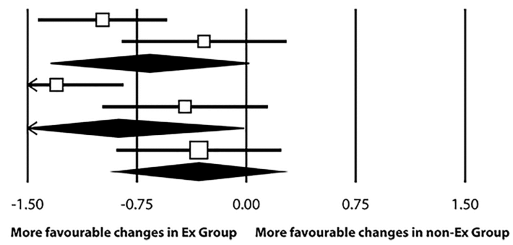


Figure 4. Positional changes of PDCs: Comparisons between extraction and non-extraction sites – Studies at low risk of bias. A. Mesial inclination; B. Vertical position; C. Canine crown to midline position.

Table 5. Meta-regression for the effect of the length of follow-up on the differences in PDCs' positional changes.

					Test of the model[1]			Goodness of fit			
	Coefficient	**SE**	**LL**	**UL**	**Q**	**df**	**p-value**	**Q**	**df**	**p-value**	**R^2 analog**
PDC mesial inclination	-0.027	0.022	-0.071	0.017	1.44	1	0.229	5.64	5	0.342	0.42
PDC vertical position	0.003	0.028	-0.052	0.057	0.01	1	0.922	8.59	5	0.126	0.00
PDC crown to midline position	0.0241	0.033	-0.041	0.089	0.52	1	0.472	12.69	8	0.026	0.00

PDCs: palatally displaced canines

[1] Random effects (Method of Moments), Z-Distribution

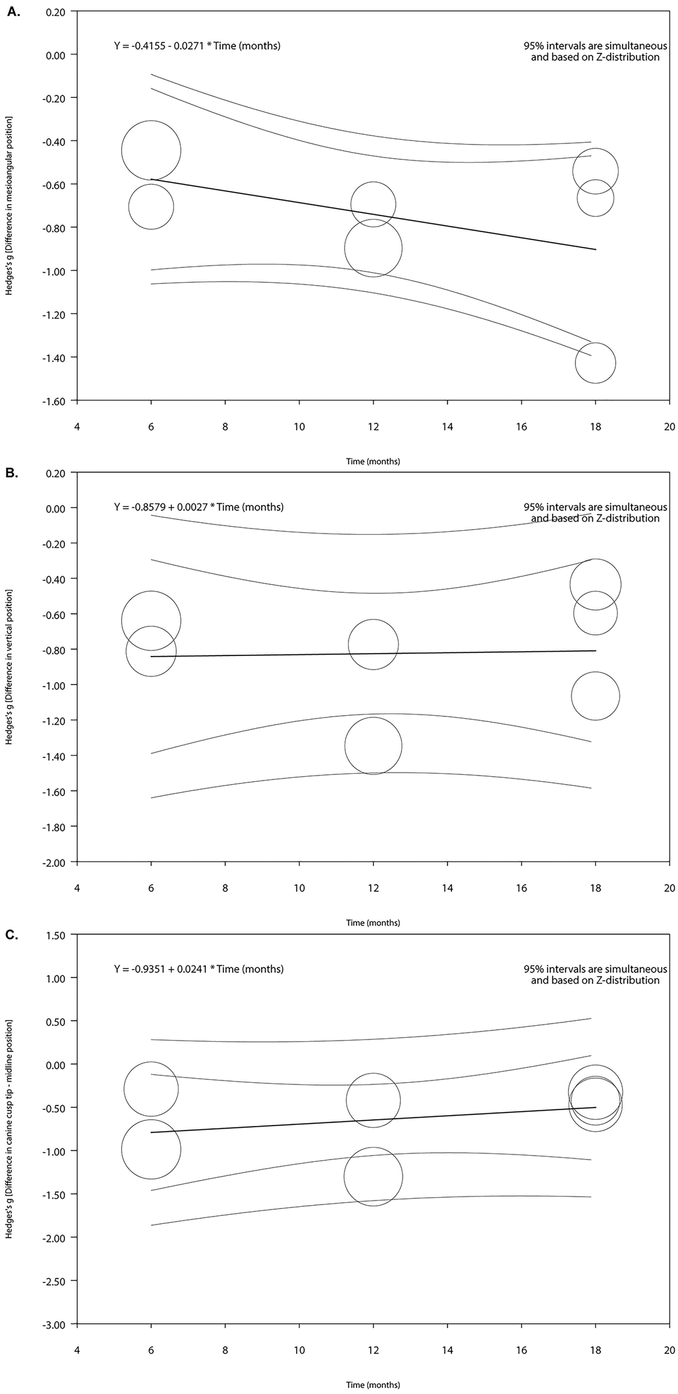


Figure 5. Regression scatter plots of the difference in Palatally Displaced Canines positional changes, on the predictor of length of follow-up (in months). A. Mesial inclination; B. Vertical position; C. Canine crown to midline position. Confidence intervals and prediction intervals are displayed (inner and outer lines around the regression line).

Table 6. Positional changes of PDCs [Comparisons between extraction and extraction plus headgear sites – All studies].

			Effect size and 95% confidence interval [a]					
		No of studies	**Hedges' g [b]**	**SE**	**LL**	**UL**	**P-value**	**I^2 (%)**
PDC mesial inclination	**18 months - baseline**	2	0.64	0.22	0.22	1.07	**0.003**	0.00
PDC vertical position	**18 months - baseline**	2	0.19	0.21	-0.23	0.60	0.382	0.00
PDC crown to midline position	**18 months - baseline**	2	0.43	0.22	0.01	0.85	**0.044**	0.00

LL: Lower limit; MD: mesiodistal; PDCs: palatally displaced canines; SE: Standard Error; UL: Upper limit

[a] Statistically significant differences in bold; [b] Negative values denote more favorable changes in the extraction sites.

Statistics for each study

Outcome	Study	Hedges's g	Standard error	Lower limit	Upper limit	p-Value
Mesial inclination	[2004] Leonardi et al.	0.81	0.33	0.17	1.44	0.013
	[2008] Baccetti et al.	0.51	0.29	-0.06	1.09	0.078
		0.64	0.22	0.22	1.07	0.003
Vertical position	[2004] Leonardi et al.	0.17	0.32	-0.45	0.79	0.584
	[2008] Baccetti et al.	0.20	0.29	-0.37	0.76	0.493
		0.19	0.21	-0.23	0.60	0.382
Crown tip to midline	[2004] Leonardi et al.	0.21	0.32	-0.41	0.82	0.516
	[2008] Baccetti et al.	0.63	0.29	0.05	1.21	0.032
		0.43	0.22	0.01	0.85	0.044

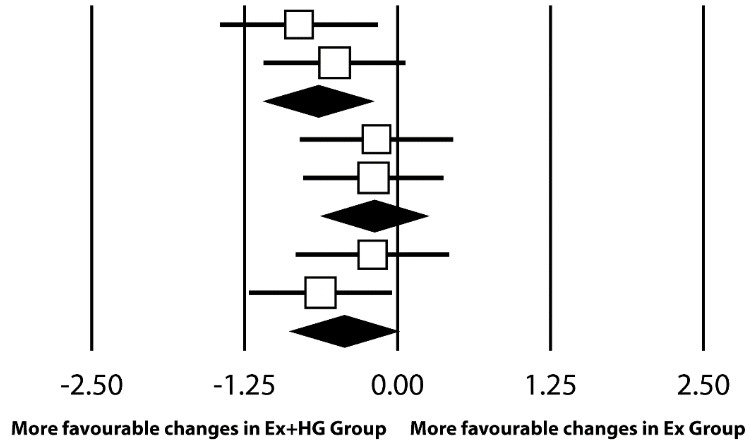


Figure 6. Positional changes of PDCs: Comparisons between extraction and extraction plus headgear sites – All studies.

Table 7. Quality of available evidence.

Quality assessment						Effect	Quality
Studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Hedges's g (95% CI)[a]	
PDC mesial inclination [12 months follow-up; studies at low risk of bias]							
2	Not serious	Not serious	Not serious	Serious[b]	None	**-0.82** (-1.17 to -0.48) **p=0.000**	⊕⊕⊕○ **MODERATE**
PDC vertical position [12 months follow-up; studies at low risk of bias]							
2	Not serious	Not serious	Not serious	Serious[b]	None	**-1.09** (-1.65 to -0.53) **p=0.000**	⊕⊕⊕○ **MODERATE**
PDC crown to midline position [12 months follow-up; studies at low risk of bias]							
2	Not serious	Serious[c]	Not serious	Serious[b]	None	**- 0.88** (-1.74 to -0.01) **p=0.024**	⊕⊕○○ **LOW**

CI: Confidence Interval; PDCs: palatally displaced canines

[a] Negative values denote more favorable changes in the extraction sites. [b] Results are based on studies with few patients. [c] Moderate heterogeneity may be present.

6. DISCUSSION

6.1. Summary of evidence

Bearing in mind the risks and potential complications of surgical exposure and orthodontic traction of PDCs, any interceptive approach that could help mitigate these problems would be desirable. Overall, based in the information reported in the studies eligible for inclusion, the extraction of the primary maxillary canine could, 12 months later, significantly improve the position of PDCs compared to no intervention. The quality of evidence was assessed to be moderate, implying that the true effect is probably close to the estimated effect, but more research is needed in order to determine the exact magnitude of benefit.

Additionally, using the HG after the extraction of the primary canines, compared to extracting alone, resulted in greater improvement in the position of PDCs. However, the comparison between single extraction and double extraction sites (primary canine vs. primary canine and molar) did not show any differences in position improvement. These results add to the information presented in previous systematic reviews regarding the effectiveness of the practice of extracting the primary canine in the spontaneous eruption of PDCs, alone or in combination with other orthodontic procedures (Alyammahi et al., 2018; Al Naqbi et al. 2020).

Even in the case that the PDC does not finally erupt spontaneously, an interceptive procedure would be beneficial if it results in a positional improvement that will make subsequent surgical and orthodontic intervention more straightforward and predictable. The canine crown position relative to the midline and the mesial inclination of the canine are the most important variables in predicting the treatment outcome (Grisar et al., 2021). In addition, the improvement of root parallelism, resulting from the decrease in the inclination to the midline and the lateral incisor long axis, together with movement of the crown to a more distal position, may alleviate the risk of root resorption of the adjacent teeth (Alessandri Bonetti et al., 2011). When orthodontic traction is considered for a canine that remains impacted, lower treatment times to alignment are expected when the eruption path is shorter (Schubert et al., 2018).

The total number of records originally identified were reduced to five RCTs. This result reflects the lack of relevant research at the top of the recognized hierarchy of scientific evidence, which provides the best evidence on the efficacy of health care interventions. The consequent lack of extensive information with high evidence-based potential is rather unexpected, considering the prevalence of the problem and that the management of impacted permanent maxillary canines requires a comprehensive approach, with a significant amount of commitment and expense from the patient and orthodontist (Parkin et al., 2012). Management of impacted canines might also include risks and complications if the diagnosis, treatment plan and biomechanics are not well evaluated (Becker, 2012). Subsequent root resorption can sometimes be detrimental (Rafflenbeul et al., 2019; Becker et al., 2005) and might be underestimated in the absence of appropriate and accurate diagnostic methods, such as cone-beam computed tomography (Alamadi et al., 2017). Therefore, relevant, evidence-based information on possible interceptive management of PDCs would be helpful in supporting the treatment carried out in such cases.

Despite the small number of available RCTs, exploratory quantitative data synthesis was attempted where applicable. The extraction of deciduous canines resulted in greater improvement in PDCs' position compared to no intervention. The magnitude of the effect was considered large and corresponded to greater improvements of approximately 2° in the mesial inclination, 2.5 mm in the vertical position, and 2 mm in the horizontal position of the canine cusp tip from the midline. The analyses of studies at low risk of bias provided corroborating evidence, and the overall quality of evidence from these studies regarding PDCs' positional changes after 12 months of observation was assessed to be moderate, thus strengthening the relevant recommendations. The 12-month post-intervention period has been suggested to be an appropriate time point to review the treatment plan for patients with still unerupted PDCs after an interceptive intervention (Naoumova, 2014; Hadler-Olsen, 2019). Primary reports from Ericson and Kurol (1988) demonstrated that extraction of the related primary canines at the correct time may improve the path of eruption of the palatally displaced canines in 78% of cases.

The comparisons between extraction and extraction plus headgear sites showed improvements in PDCs' position for the patients using headgear, regarding the mesial inclination (p=0.003), and the crown to midline position (p=0.044). In this case, the magnitude of the effects ranged from small to medium. It is important to bear in mind that an individual's skeletal pattern and occlusal relations should always be assessed in all three planes of space when deciding on the use of such intervention as headgear.

The extraction of deciduous canines and first molars resulted in no difference in PDCs' changes compared to extracting only the canine after 14.8 months of follow-up for the mesial inclination (p=0.203) or the PDC crown to midline position (p>0.05). This is contrary to two previous studies of similar nature, that did not focus exclusively on PDCs but also assessed canines displaced in the middle of the alveolar process and were, thus, excluded from the present review (Alessandri Bonetti et al., 2010; 2011). Another reason for the dissimilarity could be the younger dental developmental age in the participants. Differences in the initial canine position, as well as the different observation times, could have further influenced the results. Double extraction may favorably affect the position of the first premolar as well, thus improving local conditions for natural or induced alignment of the canine and allowing the beginning of treatment at an earlier stage, if necessary (Alessandri Bonetti et al., 2010; 2011).

6.2. Strengths and limitations

The strengths of the present review include the methodology that followed well-established guidelines and the fact that it focused exclusively on randomized controlled trials. In addition, an attempt was made to summarize the quality of available evidence, and thus provide an insight into the strength of the relevant recommendations based on the GRADE approach (Guyatt et al., 2011). Moreover, the search strategy employed was all inclusive, covering electronic, manual, and gray literature material up to March 2021, and comprehensive, including every available randomized controlled trial, irrespective of language, date, and status of publication. Every effort to decrease bias in the methodology employed was made. Screening, verification of eligibility, abstraction of information, assessment of risk of bias, and of the quality of evidence were performed in duplicate, and any disagreement was resolved by discussion until a final consensus was achieved. Finally, the random effects model was employed during exploratory quantitative data synthesis to incorporate any observed heterogeneity (Higgins et al., 2019). In the context of the present review, heterogeneity can arise from diversity in terms of the characteristics of population groups, settings, and follow-up (e.g., ethnic origin, dental and skeletal age, differences in the employed diagnostic criteria and definition of successful eruption and assessment).

The limitations of the present review arise mainly from the characteristics of the retrieved information. As already mentioned, the located studies were limited, and two of them came from the same research group, rendering quantitative assessments indicative and exploratory until additional research becomes available. Nevertheless, alternative summaries can be less transparent and potentially less valid (Valentine et al., 2010), and even information from two studies can be synthesized as long as pooling is meaningful (Ryan et al., 2015). Another limitation may arise from the inclusion of individuals with bilateral PDCs in the analyzed material, as in the included studies, relevant statistical adjustments were not employed or considered. A meta-analysis of such material ideally requires the entire data set (Smaïl-Faugeron et al., 2014). However, this kind of elaboration was not feasible. Naoumova et al. showed no difference in the successful outcome correlation between unilateral or bilateral cases, enabling their analysis as independent observations.

According to McSherry and Richardson (1999) in children less than 10 years old, the maxillary canines normally appear to be palatally positioned in radiographs. As in some of the included studies, the participants were as young as 8 years of age, and the initial diagnosis was based on OPG, an overestimation of the possibility for palatal impaction or an incorrect diagnosis regarding positioning can be considered. This means that part of the canines diagnosed as palatally displaced and considered at high risk of impaction may have erupted normally, as the path of eruption may improve during further growth, development and maturation of the dentition (Peck, 2011). Spontaneous eruption and changes in the radiographic position of the erupting teeth might be also related to space conditions in the dental arch (Hadler-Olsen, 2019), however, this parameter was not thoroughly assessed (Hadler-Olsen, 2020). Panoramic radiographs can be considered good enough for assessing the canine position when the need for 3D information is not crucial for treatment planning (Björksved et al., 2019), but only CBCT can provide precise information on the localization of the impacted tooth and the possibility of root resorption (Oenning, 2018; Sosars et al., 2020).

Another limitation is that the patients included in the studies reviewed came from a single ethnic background, which affects the generalizability of the final result and may not be relevant to all ethnic groups. Furthermore, due to insufficient information, it was not possible to conduct analyses for small study effects, publication bias, or subgroup analyses for specific characteristics. Finally, the small number of individuals analyzed resulted in subsequent problems regarding the precision of the effect estimates. Thus, to a degree, the exact magnitude of the benefit from the studied interceptive practices still remains undetermined. However, the importance of interception cannot be underestimated, as it results in reduced prevalence of impacted canines in geographical regions that adopt such interventions systematically within their health system (Lövgren et al., 2019).

Recommendations for future research

Since canine impaction is a relatively common phenomenon, and its management potentially complex and challenging, the need for well-designed RCTs on interceptive management with better standardization and appropriate reporting based on the research design could be useful. It would also be beneficial to have future RCTs examining different groups from ethnic backgrounds other than Caucasian, to find if any differences exist. Moreover, to fully understand the effect of these strategies, further investigation of the possible predictors of success, inclusion in the analyses of patient-reported outcomes (such as quality of life and analyses of any possible adverse effects) should be carried out.

7. CONCLUSIONS

Based on the results of this systematic review and meta-analysis, the extraction of the deciduous canine might improve the position of palatally displaced canines. Further studies at low risk of bias and with sufficient sample sizes are needed in order to enrich the available evidence, increase the precision of the observed effect estimates and unequivocally guide clinical decisions.

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9. APPENDICES

Appendix 1. Eligibility criteria.

Domain	Inclusion criteria	Exclusion criteria
Participants	▪ Individuals in the mixed dentition, of any gender and ethnicity, presenting with unilateral or bilateral palatally displaced permanent canines verified radiographically.	▪ Subjects with craniofacial anomalies or syndromes of the head and neck region.
Interventions	▪ Extraction of a primary maxillary canine or canines or other primary teeth. ▪ Various interceptive orthodontic procedures (such as, but not limited to rapid maxillary expansion, transpalatal arch, headgear, etc.) combined with or without extraction.	
Comparisons	▪ No intervention. ▪ Extraction of primary canines only. ▪ Comparison between alternative or adjunctive interventions. ▪ Delayed treatment as for example in cases where initially a patient was randomized to the non-extraction group but at a later observation because of lack of improvement, or even worsening of the canine position, the primary tooth is extracted for ethical reasons.	
Outcomes	▪ Positional changes of the permanent maxillary canine over time as assessed in OPG or CBCT (mesial inclination, i.e. alpha angle, etc.; vertical position, i.e. distance D from the dental arch, distance from the palatal plane, etc.; canine cusp tip to midline position, i.e. sectors, distance in mm, etc.). Where needed, numerical data were transformed in the desired formats and tested statistically using MedCalc (©2016 MedCalc, Belgium) and QuickCalcs (©2016 GraphPad Software, Inc. USA) and Standard Deviations were estimated following Wan et al., (2014) and Ramirez and Cox (2012). Previous studies have shown that there is no difference in the correlation between unilateral or bilateral cases enabling their analysis as independent observations (Naoumaova et al., 2015).	
Study design	▪ Randomized clinical trials with at least 12 months of observation period after the intervention.	▪ Animal studies. ▪ Non-comparative studies (case reports and case series). ▪ Systematic reviews and meta-analyses.

Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014 Dec 19;14:135.
Ramirez A, Cox C. Improving on the Range Rule of Thumb," Rose-Hulman Undergraduate Mathematics Journal 2012; 13 (2): Article 1.

Appendix 2. Strategy for database search (up to March 25th, 2021).

Database	Search strategy	Hits
PubMed http://www.ncbi.nlm.nih.gov	(((randomized controlled trial) OR (controlled clinical trial) OR randomized[tiab] OR placebo[tiab] OR (drug therapy) OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[mh] NOT humans[mh])) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*) Filters activated: Human	**497**
Cochrane Central Register of Controlled Trials http://onlinelibrary.wiley.com	(orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*) in Record Title OR (orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*) in Abstract - (Word variations have been searched)	**51**
Cochrane Database of Systematic Reviews http://onlinelibrary.wiley.com	(orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*) in Record Title OR (orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*) in Abstract - (Word variations have been searched)	**2**
Scopus https://www.scopus.com	TITLE-ABS((orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*))	**1136**
Web of Science™ Core Collection http://apps.webofknowledge.com	TOPIC: ((orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*)) Timespan: All years. Search language=Auto	**1167**
Arab World Research Source http://0-web.a.ebscohost.com.amclb.iii.com	TI ((orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*)) OR AB ((orthodon*) AND (canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*))	**2**
ClinicalTrials.gov http://clinicaltrials.gov	(orthodontic OR orthodontics) AND (canine OR canines OR cuspid OR cuspids) AND (impacted OR impaction OR unerupted OR displaced OR ectopic OR malpositioned OR malposition)	**5**
ProQuest Dissertations and Theses Global https://search.proquest.com	ti((canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*)) OR ab((canine* OR cuspid*) AND (impact* OR unerupt* OR displace* OR ectop* OR malpos*)) Filters activated: Full text; Applied filters: dentistry	**32**

Appendix 3. Excluded records with reasons for exclusion.

Record	Reason for exclusion
Naoumova J. Interceptive Treatment Of Palatally Displaced Canines. Swed Dent J Suppl. 2014;(234):7-118.	Dissertation based on which a paper was later published
Hadler-Olsen S. Ectopic and normal maxillary canine eruption: maxillary incisor root resorption and interceptive treatment. Philosophiae Doctor Dissertation. University of Tromsø, Norway, 2019.	Dissertation based on which a paper was later published
Baccetti T, Mucedero M, Leonardi M, Cozza P. Interceptive treatment of palatal impaction of maxillary canines with rapid maxillary expansion: a randomized clinical trial. Am J Orthod Dentofacial Orthop. 2009 Nov;136(5):657-61.	No follow-up data
Baccetti T, Sigler LM, McNamara JA Jr. An RCT on treatment of palatally displaced canines with RME and/or a transpalatal arch. Eur J Orthod. 2011 Dec;33(6):601-7. doi: 10.1093/ejo/cjq139. Epub 2010 Nov 8.	No follow-up data
Naoumova J, Kjellberg H. The use of panoramic radiographs to decide when interceptive extraction is beneficial in children with palatally displaced canines based on a randomized clinical trial. Eur J Orthod. 2018 Nov 30;40(6):565-574.	No follow-up data
Armi P, Cozza P, Baccetti T. Effect of RME and headgear treatment on the eruption of palatally displaced canines: a randomized clinical study. Angle Orthod. 2011 May;81(3):370-4.	No outcomes of interest
Naoumova J, Kürol J, Kjellberg H. Extraction of the deciduous canine as an interceptive treatment in children with palatally displaced canines - part II: possible predictors of success and cut-off points for a spontaneous eruption. Eur J Orthod. 2015 Apr;37(2):219-29.	No outcomes of interest
Alessandri Bonetti G, Incerti Parenti S, Zanarini M, Marini I. Double vs single primary teeth extraction approach as prevention of permanent maxillary canines ectopic eruption. Pediatr Dent. 2010 Sep-Oct;32(5):407-12.	Did not focus on palatally displaced canines
Alessandri Bonetti G, Zanarini M, Incerti Parenti S, Marini I, Gatto MR. Preventive treatment of ectopically erupting maxillary permanent canines by extraction of deciduous canines and first molars: A randomized clinical trial. Am J Orthod Dentofacial Orthop. 2011 Mar;139(3):316-23.	Did not focus on palatally displaced canines
Assessment of Extraction of Primary Canines in Treating Mesioangular Displaced Permanent Canines. ClinicalTrials.gov Identifier: NCT0368452	Study protocol [authors contacted but no response]
Interceptive Study of Ectopic Eruption of Permanent Maxillary Canine Teeth. ClinicalTrials.gov Identifier: NCT02675036	Study protocol of a published paper.