The impact of premature extraction of primary teeth on the subsequent need for orthodontic treatment

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The candidate confirms that the work submitted is her own and that appropriate credit has been given where reference has been made to the work of others.

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DEDICATION

I dedicate this work to my mother and my late father for their love and encouragement.

GLOBAL ABSTRACT

Background: Premature Extraction of Primary Teeth (PEPT) is a common finding in any paediatric population. However, there are no systematic reviews or studies to date providing a reliable evidence base regarding PEPT and orthodontic need.

Aims: To conduct a systematic review to systematically evaluate the effect of PEPT on malocclusion and to conduct a study in Bradford and Airedale district to explore this association.

Materials and Methods: A thorough search strategy was developed and used to locate studies assessing the effect of PEPT on malocclusion and space loss. A methodological assessment was also carried out for included studies to assess risk of bias.

A regional oral epidemiological survey of 12-year-old children in Bradford and Airedale was carried out in 2008/2009. As part of this oral health needs assessment, information on orthodontic need was also collected. A study group was formed of the children who had their orthodontic need assessed in the oral epidemiological survey and had their dental records available through the Salaried Dental Service (SDS). A multilevel logistic regression model was developed to explore the factors associated with orthodontic need.

Results: Twenty-five studies were appraised for the systematic review. There was only one study assessing malocclusion following PEPT that fulfilled the predefined inclusion criteria which concluded that PEPT led to an increased incidence of malocclusion.

Out of 366 children who were surveyed in the oral epidemiological survey from Bradford and Airedale, 116 had accessed SDS. Out of those, 107 children met the inclusion criteria. An increased total number of PEPT was positively associated with orthodontic need (odds ratio: 1.18, CI – 1.01 to 1.37).

Conclusions: There was some evidence to suggest that malocclusion and thus orthodontic need was increased by the previous history of PEPT. The only predictor exhibiting significance was the total number of primary teeth lost.

ABSTRACT 1 (FOR CHAPTER 1)

Background: There are no systematic reviews to date investigating the effect of PEPT on malocclusion in the permanent dentition. A systematic review to establish the relationship between PEPT and malocclusion would help in treatment planning paediatric dental patients.

Aims: The primary aim of this systematic review was to consider evidence regarding malocclusion and orthodontic need associated with PEPT. The secondary aim was to examine the effect of PEPT and loss of space in primary and mixed dentitions.

Materials and Methods: Electronic database and reference list searching were conducted according to the predefined protocol. The studies reporting PEPT with a comparison group who did not suffer PEPT were included in the systematic review. Split-mouth design was also included where PEPT quadrant was compared to the quadrant without PEPT providing an intra-arch comparison. A methodological assessment was carried out for each of the included studies.

Results: There were 491 studies identified from electronic databases and 23 from reference list screening following search strategy. Following filtering process, 25 studies were appraised for the systematic review. Out of these, 17 studies were included in the systematic review, one study (published in two parts) reported on malocclusion and 15 studies reported on space dimensions. PEPT led to malocclusion and space loss.

Conclusions: None of the studies that fulfilled the inclusion criteria of the systematic review reported on orthodontic need associated with PEPT. One study included in the review reported that malocclusion was associated with PEPT. Most of the studies reporting space dimensions used a split-mouth design and with an inadequate follow-up period to assess the subsequent impact on malocclusion.

ABSTRACT 2 (FOR CHAPTER 2)

Background: PEPT is common in paediatric population. Clinical guidelines urge dentists to restore primary teeth. There are no robust studies to date assessing PEPT and orthodontic need in the United Kingdom.

Aims: The primary aim of this study was to determine whether there was a difference in orthodontic need based on previous history of PEPT. The secondary aims were to establish whether ethnicity and gender had any effect on orthodontic need. Also, if orthodontic need was influenced by the timing of extraction of primary teeth, type of primary tooth, position of these teeth in dental arches or total number of teeth lost.

Materials and Methods: As part of the national oral epidemiological survey of 12-year old-children, a representative sample was selected randomly from Bradford and Airedale. Information collected from the survey included individual demographics, dental health status and orthodontic need. Following ethical consideration, this information was linked with data held by the local SDS. SDS has been the only provider of dental extractions under general anaesthesia in the district. Retrospective dental information was collected about PEPT for children who were treated in the SDS. A multilevel logistic regression model was developed to explore the factors associated with orthodontic need.

Results: Three hundred and sixty-six children were surveyed in Bradford and Airedale of which 116 had accessed SDS historically. These children who were seen in SDS formed the study group. In comparison, children seen in SDS were significantly different to children who had not accessed the service. These children were from ethnic minorities, were more deprived and had high caries rate ($p<0.001$). For the 107 children who met the inclusion criteria and seen by the SDS, an increased total number of PEPT was positively associated with orthodontic need (odds ratio: 1.18, CI – 1.01 to 1.37).

Conclusions: There was a significant difference in ethnicity, deprivation and dental caries status of children who accessed SDS as compared to children who did not. The total number of PEPT showed a positive association with increased orthodontic need.

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Glossary

AAPD	American Academy of Pediatric Dentistry
AC	Aesthetic Component
BASCD	British Association for the Study of Community Dentistry
BSPD	British Society of Paediatric Dentistry
CONSORT	Consolidated Standards of Reporting Trials
CS	Conscious sedation
DAI	Dental Aesthetic Index
DHC	Dental Health Component
dmft	decayed, missing, filled teeth in primary dentition
DMFT	decayed, missing, filled teeth in permanent dentition
GA	General Anaesthesia
GDP	General Dental Practitioner
ICON	Index of Complexity, Outcome and Need
IMD	Index of Multiple Deprivation
IOTN	Index of Orthodontic Treatment Need
LA	Local Anaesthesia
MeSH	Medical Subject Headings
NHS	National Health Service
NHS-DEP	NHS Dental Epidemiology Programme
NWPHO	North West Public Health Observatory
PEPT	Premature Extraction of Primary Teeth
RCS	Royal College of Surgeons
RCT	Randomised Controlled Trial
SDS	Salaried Dental Service
SIGN	Scottish Intercollegiate Guidelines Network
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TDO	The Dental Observatory

CHAPTER 1

1.1 INTRODUCTION

The long-term impact of Premature Extraction of Primary Teeth (PEPT) has received limited attention in published literature. Clinical guidelines urge clinicians to restore primary teeth where possible and advise that this will maintain the space required for the permanent dentition to erupt into thereby reducing a potential cause of crowding and malocclusion in the permanent dentition. Prospective and retrospective cohort and cross sectional studies have reported that space loss occurs following extraction of the primary molars. There are a few studies that report the effect of this space loss on the development of subsequent malocclusion and need for orthodontic treatment. There is no published research in the United Kingdom looking at PEPT and its effect in orthodontic need in the permanent dentition.

While reviewing the literature on the subject it became obvious that there was a number of studies reporting outcomes in this field. However there was a lack of exhaustive literature review or a systematic review which attempted to summerise the outcomes. It was decided therefore to carry out an initial general review of the literature followed by a systematic review. The literature review and systematic review of the literature are presented in this chapter.

1.2 REVIEW OF THE LITERATURE

1.2.1 Introduction

There is an apparent paucity of well-designed studies providing clear evidence linking PEPT in primary dentition and its orthodontic consequences in the permanent dentition. PEPT is the most common biological cause for space loss and malocclusion in permanent dentition. This is because dental caries involving the primary dentition is common in deprived and disadvantaged populations. Worldwide, 60-90% of school age children have dental caries (World Health Organization, April 2012).

1.2.2 Causes of PEPT

Dental caries affecting primary teeth is the most significant factor leading to PEPT. Other factors that may lead to premature loss of primary teeth include congenital or developmental disorders, premature exfoliation of primary teeth particularly of primary canines as a result of eruption of permanent canines, ectopic eruption of permanent teeth especially of first permanent molars, dental trauma and orthodontic extractions either as interceptive treatment to alleviate or prevent malocclusion (Willet, 1933, Durward, 2000, Rock, 2002). In addition to these, periapical pathology of primary teeth and pathology such as tumours may cause disorders of eruption (Ngan et al., 1999).

In epidemiological surveys, PEPT is reported by the 'm' (missing) component of $d_3$mft. The most recent national survey of 5-year-old children reported a mean of missing teeth as 0.12 for England while mean $d_3$mft was 1.11. There was variability according to region, for example for the district of Bradford and Airedale, mean of missing teeth was 0.40 where mean $d_3$mft was 2.42 (NHS Dental Epidemiology Programme for England, Oct 2009).

1.2.2.1 Dental caries in primary dentition

National epidemiological surveys of children's dental health have been undertaken since 1985 and these were coordinated by UK Department of Health and British Association for the Study of Community Dentistry (BASCD). Over the recent years, NHS Dental Epidemiology Programme (NHS-DEP) for England have produced protocols with timetables for oral epidemiological surveys at regional and national level since its establishment in 2007 and BASCD has an important advisory role (The Dental Observatory, June 2010). Organisations involved in NHS-DEP are BASCD, The Dental Observatory (TDO) and the North West Public Health Observatory (NWPHO). Regional and national dental health data is important to target preventive programmes and plan dental services to meet national and regional needs (The Dental Observatory, June 2010).

The most recent oral epidemiological survey (2007/2008) reported on the dental health of five year old children across England. The index used in the survey was $d_3$mft (obviously decayed into dentine, missing due to decay and filled primary teeth per child). In England, the average $d_3$mft per child was 1.11. It must be noted that $d_3$mft takes into account obvious dental decay into dentine, which is identifiable on visual examination and is used in oral epidemiological surveys. There were more children who were free from obvious dentinal decay (69.1%) as compared to those with dentinal decay (30.9%). However, the average $d_3$mft of children who had obvious dentinal caries was 3.45 presenting a skewed distribution of caries (NHS Dental Epidemiology Programme for England, Oct 2009). These results suggested that there has been an improvement in dental health of this age group of children as compared to previous published survey of 2005/2006 where 39.4% of the children examined had obvious dentinal caries (Pitts et al., 2007, NHS Dental Epidemiology Programme for England, Oct 2009). However, this comparison has to be interpreted with caution as the consent processes were different in these two surveys (White et al., 2007, Dyer et al., 2008).

1.2.2.2 Consequences of dental caries

Dental caries is associated with a number of complications, with pain being the most frequently reported consequence in a questionnaire based study (Nuttall et al., 2006). There are significant morbidities which may be related to caries including the risk of acute dental care and hospitalisation (Majewski et al., 1988). Dental infection may lead to systemic complications and the risk is increased especially in medically compromised children (Fayle et al., 2001, Kandiah et al., 2010).

Other detrimental effects of dental caries are difficulties with oral function, pain, infection, sleep disturbance, behavioural disturbance, poor self-confidence, poor aesthetics and disruption of school attendance (Fayle et al., 2001, Nuttall et al., 2006, Kandiah et al., 2010). Dental caries has also been linked to inadequate growth and poorer quality of life. This compared with the effect of treating caries which demonstrated a remarkable improvement to the quality of life of pre-school children (Sheiham, 2006). When caries remains untreated in young children, it carries a high rate of morbidity and also children with severe caries weighing significantly less than age-matched controls (Acs et al., 1999).

A policy document on management of caries in the primary dentition by the British Society of Paediatric Dentistry (BSPD) state that a combination management strategy including prevention and conservation is required for managing dental caries in the primary dentition (Fayle et al., 2001, Kandiah et al., 2010). This policy document states that extraction is the most basic way of managing dental caries for unrestorable teeth. A recently published guideline on prevention and management of dental caries in children described various management strategies. These included complete caries removal, partial caries removal, no caries removal and extraction or review with view to extraction if pain or sepsis develops (Scottish Dental Clinical Effectiveness Programme, April 2010). This guideline makes it very clear that sepsis should not be left untreated and active caries in primary teeth should not be left unmanaged. Scottish Health Board's Dental Epidemiological Programme observed that dental sepsis was closely associated with socio-economic deprivation and the level of oral sepsis was higher in cases of untreated dental caries (Pine et al., 2006).

The British Society of Paediatric Dentistry (BSPD) suggests that if there is active oral disease, then adequate treatment is necessary to avoid any of the detrimental consequences of dental disease (Fayle et al., 2001, Kandiah et al., 2010). The American Academy of Pediatric Dentistry (AAPD) states clearly in their guideline that objectives of intervention in developing dentition of a child is to improve occlusion and hold leeway space in early mixed dentition stage (American Academy on Pediatric Dentistry Clinical Affairs Committee-Developing Dentition Subcommittee, 2008-2009).

1.2.2.3 Management options

Dental conservation and extraction can be carried out under Local Anaesthesia (LA), Conscious Sedation (CS) or General Anaesthesia (GA). Behaviour management with LA is the main method of delivering pain-free dental treatment to children (Hosey, 2002), although may not be appropriate for all children. Many children who are unable to cope for dental treatment under LA should be considered for treatment under CS or GA (National Institute for Health and Clinical Excellence, 2010). When a tooth is diagnosed with sepsis or infection, then the only definitive treatment option is extraction of the offending tooth.

Service provision for CS is limited with these techniques practised in hospital or primary care setting such as Salaried Dental Services (SDS) where this care is frequently led by community based specialists or consultants. Many anxious children who are unable to cope for dental treatment or pre-cooperative children who lack coping skills or understanding to be able to cope for dental treatment (Chadwick, 2002) have dental treatment carried out under GA. Apart from behavioural factors, there are clinical indications for provision of GA which are outlined and discussed in recent national guidelines (Davies et al., 2008, Association of Paediatric Anaesthetists of Great Britain and Ireland, 2011).

Between 1997-2006, over half of hospital admissions in England for dental conditions were due to dental caries and the peak age for dental extractions of carious teeth was in 5-year-old children (Moles and Ashley, 2009). A recent review of paediatric dental GA services in Yorkshire and the Humber region concluded that there was a wide variation on provision of dental GA and differing availability of restorative dental care under GA (Ní Chaollaí et al., 2010). Less than half of the GA lists provided restorative care and frequently restorative care was only available for children with special needs or significant medical conditions. This resulted in extractions under GA as the option available to most children (Ní Chaollaí et al., 2010). Therefore dental extractions under GA even where teeth are restorable is the predominant treatment option for children unable to tolerate dental treatment under LA.

1.2.3 Prevalence of PEPT

Prevalence of PEPT varies in a paediatric population depending upon a number of factors like the presence of fluoridated water, socio-economic status of the population, level of caries and also treatment philosophy of the treating clinician. PEPT due to dental caries is a common finding in paediatric populations and has been reported in the range of 20-65% in published literature (Hoffding and Kisling, 1978a, Pedersen et al., 1978, Northway and Wainright, 1980, Melsen and Terp, 1982). Schachter (1943) reported that the incidence of PEPT increased with age, from 16% in 5 year olds as compared to 62% on 8 year old children (Schachter, 1943). A more recent study reported that extractions due to caries peaked in 5 year old children while non-caries related extraction was most common in 13 year old children (Moles and Ashley, 2009).

1.2.4 Definition of PEPT

There are many different definitions for Premature Extraction/ loss of Primary Teeth (PEPT) according to published literature. These include missing primary tooth on examination when the permanent successor could not be palpated (Bjork, 1964, Ronnerman, 1977, Pedersen et al., 1978), loss of primary canines and first primary molars earlier or while the children were in first grade; and the loss of primary second molars earlier or while the child was in the second grade (Hoffding and Kisling, 1978a) missing primary tooth for at least 6 months prior to contralateral tooth in the same arch (Kronfeld, 1953) or a missing primary tooth on two successive examinations approximately a year apart (Northway et al., 1984).

A definition of PEPT is difficult as eruption patterns of permanent teeth can deviate for either genetic or environmental reasons. An appropriate definition should take dental age of the child into account. This is because chronological age may not necessarily predict child's various stages of dental development. However, for the purpose of the review and systematic review, PEPT was defined as any primary tooth that was extracted prior to the natural exfoliation of the tooth. This definition was chosen as extraction of primary teeth was the main cause of premature loss of primary teeth.

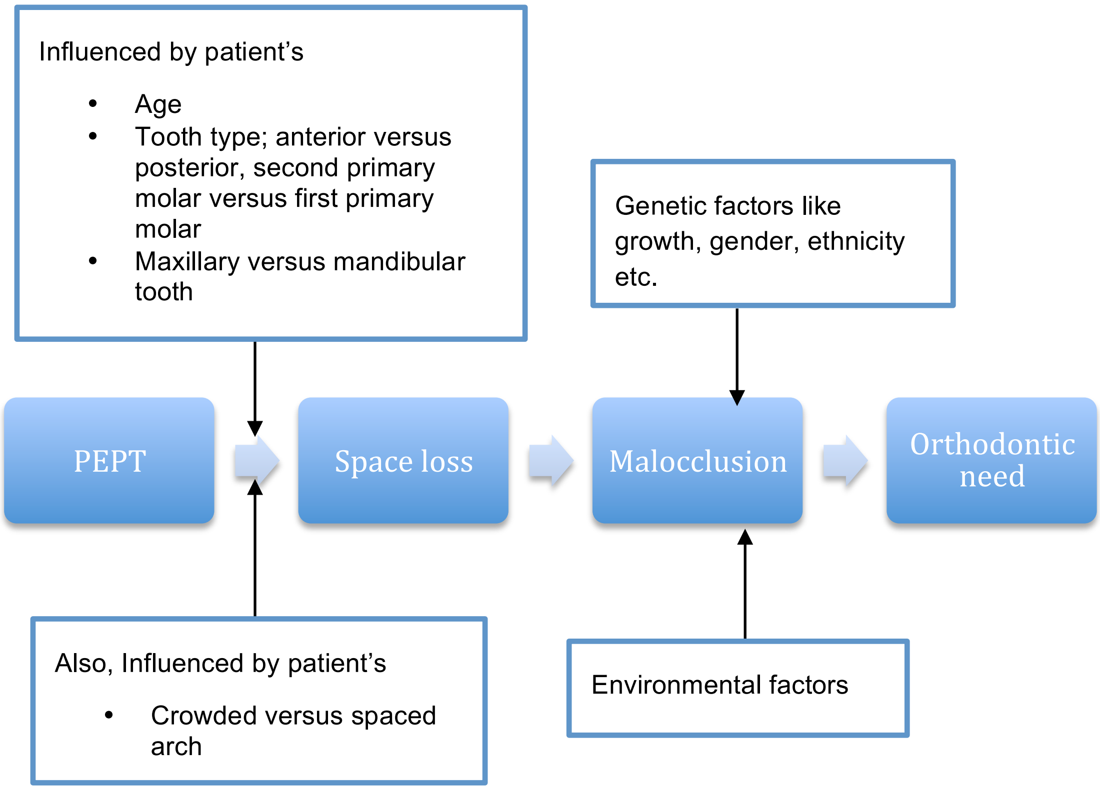
1.2.5 Effect of PEPT on space loss and subsequent development of malocclusion

PEPT may lead to space loss in the developing dentition and this resultant space discrepancy may lead to malocclusion in the permanent dentition. The aetiology of malocclusion is complex with involvement of both inherited genetic and environmental factors. Malocclusion arises from a complex interplay of both of these factors (Mitchell, 2007). PEPT is an environmental factor that has potential to cause or exacerbate malocclusion and this may lead to increase in orthodontic need.

A complex interplay of these factors associated with PEPT and malocclusion is illustrated in Figure 1.1. A twin study of 202 subjects concluded that PEPT did not always lead to malocclusion and environmental factors were not significant in all cases

(Lundstrum, 1955). According to Lundstrum (1955) crowding or spacing within a dental arch was subject to genetic and environmental variation with profound influence of the former (Lundstrum, 1955). According to Brandhorst (1932) premature loss of teeth is a controllable aetiological factor leading to malocclusion. It has been reported that 20% cases of malocclusion were contributed by PEPT (Brandhorst, 1932).

Figure 1.1 Flowchart illustrating the effect of premature extraction of primary tooth (PEPT) leading to malocclusion.



1.2.5.1 Assessment of space loss

Space loss in a dental arch could be assessed by the use of arch dimensions like arch perimeter, arch width, arch length, space occupied by first and second primary molars (D and E space), extraction space and crowding or spacing in the arch. These are described in the following section.

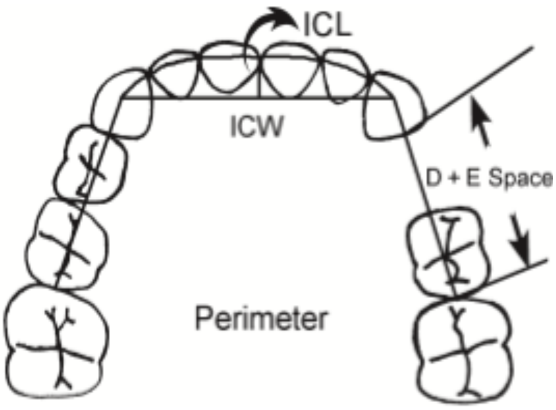
Arch perimeter

Arch perimeter is determined by measuring from the mesial midpoint of the permanent first molar (or the distal midpoint of the primary second molar if the permanent molar was missing) through the cusp tip of the canine and the incisal edges of the incisors to the opposite mesial midpoint of the permanent first molar (or the distal midpoint of the primary second molar if the permanent molar was missing). This definition was used by Lin *et al* (2011) in a recent publication (see Figure 1.2). Measurement can be undertaken by taking individual measurements of two incisor segments (right incisor segment and left incisor segment) and two buccal segments (right buccal segment and left buccal segment) (Magnusson, 1979) or it can be measured by the aid of a brass wire (Nance, 1947, Lin and Chang, 1998, Lin et al., 2011).

Segments of arch perimeter (incisor and posterior segments) were reported in some studies (Clinch and Healy, 1959, Ronnerman and Thilander, 1977). One of the studies used six segments rather than four segments (Linder-Aronson, 1960, Leighton, 1981). Measurement of arch perimeter ignores malpositioned or missing teeth and spacing so that the measurement represents an ideal arch form. Arch perimeter is also known are arch circumference. 'Arch length' is also used as a synonym for arch perimeter. Hemi-perimeter of the dental arch was also used for assessment of space by split-mouth study design (de Boer, 1982, Macena et al., 2011). Both of these studies reporting on arch hemi-perimeter used relevant segments of the arch (incisor segment and buccal segment).

Arch perimeter or hemi-perimeter would reduce as a result of space loss. But assessment of arch perimeter and hemi-perimeter should consider development of the dental arch as part of normal growth and development.

Figure 1.2 Arch perimeter.



Source: Lin *et al* (2011).

ICL- Intercanine length; ICW- Intercanine width, D and E space- space occupied by first and second primary molars.

Arch width

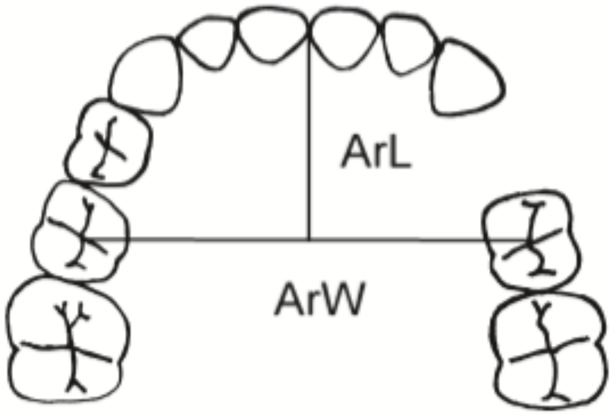
Arch width is the distance between the central fossae on the occlusal surfaces of the two contralateral primary second molars (Lin et al., 2011). Figure 1.3 demonstrates arch length as 'ArW'. One of the studies also reported various intermolar widths in the same arch; between first primary molars, first permanent molars and second permanent molars and also inter-alveolar width (Sayin and Turkkahraman, 2006).

Arch width may allow assessment of drifting pattern of teeth eg. when first permanent molars drift mesially, then arch width would reduce.

Arch length

Arch length is the perpendicular distance from the contact point of the central incisors to the arch width (Lin et al., 2011). Arch length is frequently referred to as arch depth. Figure 1.3 demonstrates arch length as 'ArL'. Various arch length measurements were used in one study where arch length measurements were taken at canine region, primary first molar region, primary second molar region and permanent first molar regions to quantify drifting patterns of teeth (Rao and Sarkar, 1999).

Figure 1.3 Arch width (ArW) and arch length (ArL).



Source: Lin *et al* (2011).

D and E space

D and E space is the distance between the mesial midpoint of the permanent first molar (or the distal midpoint of the primary second molar if the permanent molar was missing) and the distal midpoint of the primary canine (Northway and Wainright, 1980). D and E space is demonstrated in Figure 1.2. Since the definition of D and E space by Northway and Wainright (1980), further split-mouth studies reported on this measurement (Lin and Chang, 1998, Park et al., 2009, Lin et al., 2011).

Other arch measurements

Other arch measurements like intercanine width and intercanine length were also reported in some papers. Figure 1.2 also demonstrates intercanine width 'ICW' and intercanine length at 'ICL' described by Lin *et al* (2011). Other studies reported on space deficiencies or crowding for space assessments (Ronnerman, 1965, Ronnerman, 1977, Kau et al., 2004, Sayin and Turkkahraman, 2006). Some studies reported on the extraction space (Padma Kumari and Retnakumari, 2006, Macena et al., 2011).

Stability of incisive papilla is utilised greatly in prosthodontics when replacement of teeth are planned. A study showed that the average distance from posterior end of the incisive papilla to the labial surfaces of central incisors was 12-13 mm (Ehrlich and Gazit, 1975). Thus incisive papilla can be considered as a landmark within a dental arch as a neurovascular bundle is closely related to it and is independent on the alveolar bone. Alveolar bone could be either lost or remodelled following dental extractions. Likewise, palatal rugae have been shown to be a stable landmark to assess dental casts in a study of 94 adult patients over a period of 15 months (Almeida et al., 1995). Soft tissue landmarks such as incisive papilla and palatal rugae are of particular importance when studying occlusal effects in developing dentitions when hard tissues are changing due to growth and development. Use of these landmarks were utilised by some studies (Linder-Aronson, 1960, Northway et al., 1984, Park et al., 2009). In these studies, median raphe was used for orientation frame (Linder-Aronson, 1960), various points in the palatal rugae to study directional changes (Northway et al., 1984) and superimposition of palatal rugae matching various registration points to quantify angulation and inclination changes (Park et al., 2009). Unfortunately, lower dental arch does not have such stable landmarks although by occlusion of a lower arch with an upper arch it could be indirectly related to palatal rugae (Northway et al., 1984).

1.2.5.2 Effect of PEPT on space loss

There are a number of publications looking at the effect of space loss following PEPT. A cross-sectional survey of 100 children with a previous history of premature loss of first or second primary molars has been reported (Breakspear 1951) while most of the other studies were longitudinal cohorts with the number of children included in the study ranging from 19 to 107 (Seipel, 1949, Clinch and Healy, 1959, Linder-Aronson, 1960, Seward, 1965, Kisling and Hoffding, 1979, Northway et al., 1984).

Space loss following PEPT has been studied either by clinical measurement or by the use of dental casts. A biometric study on dental casts was performed on 41 children who were 14 or 15 years old (Linder-Aronson, 1960). The resulting space loss was quantified where unilateral extraction had taken place. PEPT history was gathered retrospectively and found that there was arch perimeter loss of 0.74 +/- 0.3 mm on the extraction side as opposed to the control side. This measurement was statistically significant with p value of < 0.01 (Linder-Aronson, 1960). However, clinical significance of such small measurement and small sample size were limitations of this study that were recognised by the author. A recent study looking at space loss after loss of first primary molar have used computerised software to scan dental casts to study spatial changes with increased precision (Park et al., 2009) and conclusion was in agreement with Linder-Aronson (1960).

A comprehensive longitudinal study of 107 children from a growth sample from the age of six years were observed for the effects of premature loss of primary molars (Northway et al., 1984). These children were followed up for an average of approximately six years. Premature loss of primary molars occurred in 66% of the cases and these children were assessed yearly for dimension of space loss, direction of space loss, influence of age on the rate of space loss, regaining of the lost space with emergence of secondary teeth and finally the effect on molar relationship. The effect on arch length in maxilla and mandible was significant when first as well as second primary molars were lost. The space lost was mainly due to the forward movement of permanent molars while canine migration was only significant at particular age of 9 years in mandible and 8 to 11 years in maxilla. Relatively more space was lost in the first year following extraction with the rate of space loss age related in maxilla but not in mandible (Northway et al., 1984). None of the groups in this study showed consistent shift for space regaining and it was shown that the loss of second primary molars had the most detrimental effect on molar relationship. This was in agreement with other studies (Breakspear, 1961, Ronnerman, 1977).

It is generally agreed that space loss related to premature loss of second primary molars is more significant in a developing dentition as compared to first primary molars thus the second primary molar is regarded as the ‘key’ tooth in the primary dentition (Brauer, 1941, Breakspear, 1951, Clinch and Healy, 1959, Breakspear, 1961, Ronnerman, 1977, Kisling and Hoffding, 1979, Rock, 2002). Space loss associated with loss of primary first molars is controversial. Seipel (1949) and Ronnerman and Thailander (1977) believed that premature loss of first primary molars led to clinically insignificant loss of space and this space was regained as the dentition developed to mixed and eventually to full permanent dentition.

Northway (2000) carried out a longitudinal study and performed spatial analysis of study casts to evaluate space loss of primary first molars. Although the sample size was very small in this longitudinal study with only 13 cases, it concluded that space was regained in the late mixed dentition but directional changes in dental arches after loss of primary first molars led to mesial displacement of permanent canines and positioned it labially in the arch (Northway, 2000). Northway described this phenomenon as 'blocked out' position. This was in agreement with another study (Kronfeld, 1953). Out of 13 cases only two cases failed to develop a 'blocked out' canine. The title of the paper 'The not-so-harmless maxillary first molar extraction' sums up the author's conclusions (Northway, 2000).

In a recent systematic review on the effect of extraction of first primary molars (Tunison et al., 2008), 79 studies were analysed out of which only three studies fulfilled their inclusion criteria. The authors concluded that premature loss of primary first molars led to space loss of a magnitude that was clinically insignificant. Space loss of 1.5 mm per side in the mandible and 1mm in the maxilla in most cases was thought to be clinically insignificant although these measurements were statistically significant (Tunison et al., 2008). As this measurement was clinically insignificant, the authors questioned routine use of space maintainers to maintain space of the first primary molars. Out of the three studies included in this review, two studies investigated space loss after premature loss of primary mandibular first molars (Lin and Chang, 1998, Padma Kumari and Retnakumari, 2006) and the third study reported space loss after premature loss of a primary maxillary first molar (Lin et al., 2007). Since the third study reporting space dimensions at 6 months, participants from the same study were followed up for 12 months (Lin et al., 2011). This study reported that space loss was significant on the extraction side compared to the control side but there was no significant change in arch length. This led to a conclusion that space loss following extraction of upper primary molars was due to distal migration of primary canines (Lin et al., 2011).

Age at the time of PEPT has been shown to be an important factor with more space loss associated with younger children (Northway and Wainright, 1980). Thus premature loss of primary molars prior to the eruption of the first permanent molars has been reported with more space loss as compared to following eruption of first permanent molars (Clinch and Healy, 1959, Richardson, 1965). There is varying opinion with regard to space loss following extractions of two adjacent primary molars (first and second primary molars) in comparison to second primary molars only. Some authors reported that the combined space loss in the same quadrant was less than space loss following extraction of second primary molars (Breakspear, 1951, Clinch and Healy, 1959) while one study reported no difference (Seward 1965). However, Northway and colleague (Northway et al., 1984) reported that the combined space loss following extraction of adjacent primary molars differed in the maxilla and mandible. Combined space loss was more in the maxillary arch but not in the mandibular arch. More space loss occurred following loss of primary molars in the maxillary arch as compared to the mandibular arch (Seward, 1965). Reporting on a longitudinal sample of 12 extraction sites following PEPT on 25 children, Seward (1965) found that extraction space was closed in all cases apart from one in maxillary arch. Crowded dental arches showed more space loss following PEPT as compared to spaced arches (Lundstrum, 1955, Richardson, 1965).

The effect of space regaining while eruption of permanent successors (to compensate for initial loss following PEPT) in the permanent dentition was demonstrated in a longitudinal study where a sample of 46 children was followed up 4-5 years later (Magnusson, 1979). There was space loss of at least 2.5 mm on the side of PEPT in the younger age group with full primary dentitions and part of the space lost was regained during dental development when the child reached the late mixed dentition (Magnusson, 1979). Seipel (1949) reported on 50 unilateral PEPT cases examined for 10 years and found that space loss at the side of PEPT was 1.9 ± 0.3 mm thus questioning the need to provide space maintainers in all cases of PEPT (Seipel, 1949). However, both of these studies had small sample sizes to draw any meaningful conclusions.

A review paper discussing incidence and nature of space closure following PEPT described differing opinions of researchers by saying ‘there are almost as many contrasting opinions and conclusions as there are papers’ (Owen, 1971). The Faculty of Dental Surgery, Royal College of Surgeons (RCS) published a guidance which stated that important factors when considering space loss which were the degree of crowding, type of tooth lost and age of the child (Rock, 2002). Early loss of a primary incisor has been said to have little effect while early loss of primary canines or molars is more detrimental leading to space loss in developing dentitions. This RCS guidance pointed out that there was a lack of well-designed prospective studies and the recommendations were based on best available evidence (Rock, 2002).

The studies that investigated space dimensions within a dental arch following PEPT have demonstrated that PEPT led to space loss in the affected arch. The split-mouth studies also demonstrated that space loss occurred in the affected quadrant.

1.2.5.3 Assessment of malocclusion

An index for orthodontic treatment need identifies and prioritises patients who are in need of orthodontic treatment. Any index should be valid and have high reliability. There are a number of indices available to assess orthodontic treatment need namely Index of Orthodontic Treatment Need (IOTN) (Brook and Shaw, 1989), Dental Aesthetic Index (DAI) (Cons et al., 1989) and Index of Complexity, Outcome and Need (ICON) (Daniels and Richmond, 2000). IOTN is used to assess and prioritise the need for orthodontic treatment of children in the UK. This provides an objective, repeatable and reliable method to assess malocclusion to find out who can benefit the most from treatment of malocclusion (British Orthodontic Society). Specialist orthodontic practices and orthodontic departments in hospital settings use this standardised tool to identify individuals who are most likely to benefit from orthodontic treatment. It has been used increasingly in the United Kingdom and it helps to prioritise orthodontic treatment to individuals with greatest treatment need where resources are limited (Brook and Shaw, 1989).

1.2.5.3.1 Index of Orthodontic Treatment Need (IOTN)

IOTN was developed to incorporate two components, the Dental Health Component (DHC) and the Aesthetic Component (AC). The DHC assesses orthodontic treatment priority from functional and dental health points of view and hence measures features of malocclusion. The AC assesses levels of dental attractiveness which relates to orthodontic treatment justification on socio-psychological basis. The DHC of IOTN consists of 5 grades that record occlusal traits with grade 1 representing almost perfection to grade 5 representing severe dental health problems indicating ‘great need’ for orthodontic problem. The AC rates dental attractiveness on a scale of 1 to 10 showing different levels of dental attractiveness based on colour photographs (Brook and Shaw, 1989). The DHC alone is widely used in clinical settings (Mitchell, 2007).

NHS authorities use both components of IOTN to define treatment need and to commission orthodontic services for children under 18 years of age. It is widely accepted that the DHC of 4 and 5 without considering the AC indicates ‘great need’ for orthodontic treatment. Some individuals with the DHC of 3 associated with a high AC of 6 (sometimes referred to as IOTN 3.6) or above may also benefit from orthodontic treatment (British Orthodontic Society, 2009). Thus, children with a DHC of 4 and above or with IOTN 3.6 (DHC of 3 and AC 6 or greater) are eligible for provision of orthodontic treatment under the National Health Service (NHS). The DHC of IOTN recorded for children at the age of 11 years has been shown to be reliable until the age of 19 years (Cooper et al., 2000). IOTN has also shown to be reliable with high Kappa scores of over 0.8 (Beglin et al., 2001).

IOTN defines orthodontic treatment need in an objective method from a dentist’s view. There is less emphasis on the perception of the child and their parents or the impact of malocclusion. Thus, a discrepancy was reported between a clinician’s objective treatment need and the perceived need (O'Brien et al., 2006, Hamdan, 2004). This variability between clinical objective need and perceived need by patients or parents led some authors to suggest combining IOTN with subjective measures like Quality of Life or Child Perception Questionnaire to identify orthodontic need (Tsakos, 2008, de Oilveira et al., 2008).

1.2.5.3.2 Index of Orthodontic Treatment Need (IOTN) in epidemiological surveys

IOTN has another use in oral health surveys to record the prevalence of orthodontic treatment need in a population. This is because the IOTN can be measured in a structured way. Modification of the IOTN known as the modified IOTN has been suggested for use in epidemiological surveys (Burden et al., 2001). The modified IOTN assessments are carried out by trained oral survey examiners. The DHC of the modified IOTN were reduced to a two grade scale by simplification of the original DHC; grades 1, 2 and 3 was classed as no definite need for orthodontic treatment (DHC of the modified IOTN=0) and grades 4 and 5 as great need for orthodontic treatment (DHC of the modified IOTN=1). In order to record the worst malocclusion trait, a hierarchical method was used which is referred by an acronym ‘MOCDO’.

- Missing teeth (includes hypodontia and ectopic teeth)
- Overjet (includes increased overjet and reverse overjets)
- Crossbite
- Displacement of contact points (crowding)
- Overbite (includes increased overbite and open bite)

The AC of the modified IOTN was also reduced to a two grade scale; with grouping of the original AC grades of 1 to 7 grouped as no definite need for orthodontic treatment (AC of the modified IOTN=0) and AC grades of 8 and above as definite need for orthodontic treatment (AC of the modified IOTN=1). The modified IOTN was shown to have good or excellent intra-examiner agreement (mean Kappa=0.74). Simplification of the original IOTN to the modified IOTN has been described to overcome training and increase reliability of BASCD examiners who are non-specialists (Burden et al., 2001).

1.2.5.4 Effect of PEPT on malocclusion

It has been reported that PEPT can increase orthodontic need by 20 - 28% (Brandhorst, 1932, Willet, 1933) but this figure could be as high as 65% (Lyons, 1924). Children who had suffered PEPT exhibited increased orthodontic need by 3.6 times compared to the group of children without PEPT (Miyamoto et al., 1976). Premature loss of primary canine also resulted in increased incidence of anterior crowding (Miyamoto et al., 1976). A randomised controlled trial (RCT) concluded that lower incisor crowding was reduced following extraction lower primary canines, however the arch perimeter decreased leading to less space available for lower permanent canines to erupt in correct occlusal alignment (Kau et al., 2004).

Malocclusion following PEPT was studied in a cross-sectional study of 723 Danish children out of which 45% had experienced PEPT (Pedersen et al., 1978). Various features of malocclusion were compared to the group of children with a history of PEPT to the group without history of PEPT. It was concluded that PEPT resulted in increased features of malocclusion in sagittal, vertical and transverse planes. These features were more marked if PEPT occurred in the maxilla when compared to the mandible. Bilateral or unilateral distal occlusion (Angle's molar relationship Class II), overbite, midline discrepancy and crossbite were the features of malocclusion which were associated with PEPT. Orthodontic need of these patients were assessed by the authors clinically and concluded that PEPT led to an increase in orthodontic need and thus stressed the importance of maintaining all primary teeth up to their natural exfoliation time (Pedersen et al., 1978). The authors mentioned that intra-examiner and inter-examiner reliability were checked in the first 30 cases and they were consistent but failed to quantify the agreement. Other common malocclusion traits following PEPT were labial placement of upper canines, impaction of second premolars and mesial migration of permanent molars which were consistent with other published studies (Kisling and Hoffding, 1979, Northway et al., 1984, Northway, 2000).

Another cross-sectional study of 915 Italian children reported on malocclusion following premature loss of permanent and primary teeth (Melsen and Terp, 1982). PEPT occurred in 204 out of 915 children. Malocclusion was significantly lower in the non-extraction group as compared to the extraction groups. Thus, it was concluded that premature extraction of either permanent or primary teeth led to an increase in orthodontic need (Melsen and Terp, 1982). This study did not report on intra-examiner or inter-examiner reliability for malocclusion traits reported in the study.

The RCS guidance previously described stated that 'tooth is the ideal space maintainer and every effort should be made to retain primary molars until the proper time for their natural loss' (Rock, 2002). Thus, the most efficient method of preventing space loss or eventual malocclusion and thus orthodontic need is to maintain all primary teeth throughout the transition from primary to full permanent dentition.

The studies that investigated malocclusion following PEPT have demonstrated that PEPT led to increase in features of malocclusion. However none of the studies that reported malocclusion used orthodontic indices such as IOTN, DAI or ICON.

1.2.6 Space Maintainers

Broadly, space maintenance is a means of preventing space loss and thereby malocclusion of the permanent teeth following PEPT or following loss of permanent teeth due to trauma. There are fixed and removable types of space maintainers. Removable ones are easier to fabricate but compliance could be poor. Fixed ones overcome compliance issue but constant reviews are necessary. A number of studies reported on survival of space maintainers and high failure rates in the range of 24 - 63% were reported (Qudeimat and Fayle, 1998, Tulunoglu et al., 2005, Moore and Kennedy, 2006, Fathian et al., 2007, Sasa et al., 2009). A six year follow-up study reported a low failure rate of 12.7% (Tulunoglu et al., 2005). However, the same study experienced the highest loss of follow up of 52% in comparison to other studies. The most common reason for failure in all these studies was cement failure and solder breakage. The methodologies were inconsistent in these studies to make them comparable. Studies were either based at dental hospitals (Qudeimat and Fayle, 1998, Tulunoglu et al., 2005, Sasa et al., 2009) or at private practice (Moore and Kennedy, 2006, Fathian et al., 2007).

Space maintainers are recommended following thorough risk assessment of expected occlusal disturbance against plaque accumulation and increased risk of developing caries. Although popular and frequently used in America and some European countries, space maintainers are not used routinely in the United Kingdom. The main reason for this is because children who require space maintainers are at high risk of developing caries and their caries risk would be increased further following use of oral appliances like space maintainers. Another reason is high failure rates of space maintainers as discussed previously.

1.2.7 Orthodontic need of 12-year-old children

The most recent oral epidemiological survey (2008/2009) of 12 year old children reported on the oral health of this cohort. It was reported that 31.6% of 89,442 children examined in England had great need for orthodontic treatment according to the modified IOTN (either DHC 4, 5 or AC 8, 9, 10) (NHS Dental Epidemiology Programme for England, 2011). The worst malocclusion trait based on a hierarchical method was used referred by an acronym ‘MOCDO’ described in section 1.2.5.3.2 previously. Thus information on all categories of malocclusion were not available.

Perceived need for orthodontic treatment was reported on 35.4% of the examined children and 19.3% were identified as having both orthodontic need and demand (NHS Dental Epidemiology Programme for England, 2011).

1.2.8 Conclusions of the literature review

There was a clinical consensus among clinicians that PEPT may lead to an increase in features of malocclusion and consequently orthodontic need in the permanent dentition. However, the evidence to support this assumption was less apparent in published literature (Pedersen et al., 1978, Melsen and Terp, 1982). Clinical guidelines provided by professional bodies like the British Society of Paediatric Dentistry and the American Academy on Pediatric Dentistry urge clinicians to restore primary teeth where possible (Fayle et al., 2001, American Academy on Pediatric Dentistry Clinical Affairs Committee-Developing Dentition Subcommittee, 2008-2009). There is a large volume of literature and guidelines looking at space maintenance in primary and mixed dentition (Dugoni et al., 1992, Brothwell, 1997, Ngan et al., 1999).

From this literature review the following conclusions were drawn:

- There was a lack of standardised, valid and reproducible methods to quantify and report space loss.
- There was a lack of reporting of standardised measures of malocclusion such as IOTN.
- There was a general suggestion that PEPT led to space loss which in turn led to malocclusion and thus orthodontic need. But, these results were from a multitude of study designs with poor reporting of results and outcome.
- An apparent paucity of well designed studies providing clear evidence linking PEPT in the primary dentition and its orthodontic consequences in the permanent dentition warrant a systematic review on the topic to assess the quality of evidence available and ensure all literature is identified and assessed. Results from this systematic review would help to inform treatment planning intervention for dental caries and inform resources needed to treat dental caries in the paediatric population.

1.3 AIMS OF THE SYSTEMATIC REVIEW

1.3.1 Primary aim of the systematic review

- To establish if orthodontic need is associated with PEPT.

1.3.2 Objectives of the Systematic Review

- To examine the effect of PEPT and loss of space in the primary and mixed dentition.
- To explore the effect of space loss in the primary or mixed dentition, subsequent malocclusion and orthodontic need in the permanent dentition.

1.3.2 Null hypotheses

- There is no difference in malocclusion and orthodontic need among children who suffer PEPT compared to children who do not suffer PEPT.
- There is no difference in space dimensions in dental arches following PEPT when compared to dental arches where PEPT has not taken place. There is no difference in space dimensions in the quadrant where PEPT has taken place compared to the quadrant where PEPT has not taken place (intra-arch comparison).

1.4 MATERIALS AND METHODS

1.4.1 Criteria for considering studies

A protocol for this systematic review was registered with the Centre for Reviews and Dissemination, which is part of the National Institute for Health Research and is a department of the University of York. This protocol is available online (see Appendix I, Nabina Bhujel, Monty Duggal, Peter Day. Premature extraction of primary teeth and subsequent malocclusion and orthodontic need: a systematic review. PROSPERO

2013:CRD42013004200 Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013004200).

The inclusion and exclusion criteria used for this review were as follows:

1.4.1.1 Types of studies

Study design algorithm available from SIGN (Scottish Intercollegiate Guidelines Network) available from http://www.sign.ac.uk was used to assess the type of study (see Appendix II).

- Controlled trials, cohort studies and case control studies that assessed the effects of premature extraction/loss of primary teeth were included in the review
- All studies that had a comparison group to the PEPT group were considered
- Split-mouth study design comparing unilateral loss of primary teeth compared to the intact quadrant as a control was also included in the review and analysed separately.

1.4.1.2 Types of participants

Studies with participants who suffered PEPT in the primary or mixed dentition were included in the systematic review. All participants with age groups in primary and mixed dentitions were considered. Participants reported in terms of dental age rather than chronological age would be desirable.

For assessment of malocclusion, the age group of the children would have to be in the full permanent dentition. Thus, ideally the study would have children followed from the time of PEPT until the eruption of their full permanent dentitions at approximately 12 years.

For the assessment of space, any age group of participants in the primary or mixed dentition were included.

1.4.1.3 Intervention

Intervention group was PEPT group where premature extraction or loss of a primary tooth or teeth occurred prior to natural exfoliation. The comparison group was children who did not suffer PEPT. Such a control group would allow reasonable comparison to be made and conclusions drawn upon as malocclusion is a complex interplay of intra-arch and inter-arch irregularities. For split-mouth study design with intra-arch comparison, PEPT in a quadrant was compared to the contra-lateral control quadrant without PEPT.

1.4.1.4 Types of outcome measures

1.4.1.4.1 Orthodontic outcomes

Orthodontic consequences can be measured using various outcomes.

- Malocclusion based on Angle's Class I, Class II and Class III malocclusion with additional features like overbite and overjet (Hoffding and Kisling, 1978a, Hoffding and Kisling, 1978b, Pedersen et al., 1978).
- Orthodontic need (Pedersen et al., 1978, Melsen and Terp, 1982).
- Complexity of orthodontic treatment in the future (duration of orthodontic treatment or need for further extractions as part of orthodontic treatment (Pedersen et al., 1978, Melsen and Terp, 1982).
- Crowding, mal-alignment, rotation of teeth, ectopic eruption and jaw displacements.
- Clinically the most relevant way of assessing orthodontic need would be the use of a designated index like the IOTN (Brook and Shaw, 1989). IOTN was developed in the 1980s and is currently widely used in the NHS to prioritise and target orthodontic care optimally to children who would benefit the most by having orthodontic treatment (British Orthodontic Society, 2009).

1.4.1.4.2 Space outcomes

Various outcomes were used to investigate space loss. These included arch perimeter, hemi-perimeter, arch length, arch width, incisor inclination and incisor position. Another frequently reported outcome was the D and E space defined by Northway (1984) as the distance between the mesial midpoint of the first permanent molar (or distal midpoint of the second primary molar) and the distal midpoint of the primary canine. Northway (1984) reported that D and E space was a segment of the arch that was easily defined and monitored limiting the number of factors that could influence space dimension. Soft tissue features such as the incisive papilla and palatal rugae were also frequently used as they provide stable landmarks for measurements (Linder-Aronson, 1960, Northway et al., 1984, Park et al., 2009).

1.4.2 Exclusion criteria

- Cross-sectional surveys were excluded as it was difficult to ascertain the influence of PEPT. This was because temporal relationship between PEPT and development of space loss and malocclusion was important and this relationship would be missed when assessing the effects of PEPT at the same time.
- Studies including premature extraction of permanent tooth/ teeth.
- Studies where orthodontic outcome in the permanent dentition or space dimension in the primary and mixed dentition were not recorded.
- Studies lacking a control group of children or control quadrant without PEPT.

1.4.3 Search strategy for identification of studies

A comprehensive search strategy was constructed taking into account population, interventions, comparators, outcome and study design frequently referred in research literature as PICOS (Population, Interventions, Comparators, Outcome and Study design). This was suggested by Centre for Reviews and Dissemination (Centre for Reviews and Dissemination, Jan 2009). To capture as many potential studies as possible a structured electronic search, reference list screening and search for unpublished studies was carried out.

1.4.3.1 Electronic search strategy

A search was carried out for relevant studies with OVID bibliographical databases using a structured search. Search strategy used included subject headings and keyword search to capture the concept of malocclusion and orthodontics related to PEPT. Electronic databases searched were MEDLINE (from 1st Jan 1946 to week 3 of March 2013), EMBASE (EMBASE classic and EMBASE from 1st Jan 1947 to 3rd April 2013), PubMed (1st Jan 1996 to week 3 of April 2013) and Cochrane Central Register of Controlled Trials (CENTRAL). Detailed search strategy used for MEDLINE and EMBASE are listed as Appendices (Appendix III and Appendix IV) respectively.

Search terms using keywords in title and abstract:

i) Child; young person; adolescent

ii) Tooth loss; tooth extraction; teeth extraction; premature extraction; premature loss; exodontia

iv) Deciduous tooth; deciduous teeth; deciduous dentition; primary tooth; primary teeth; primary dentition; baby tooth; baby teeth; mixed dentition

v) Malocclusion; Index of Orthodontic Treatment Need, orthodontic outcome; orthodontic need; orthodontic consequences; orthodontic adj permanent; orthodontic adj secondary; space loss; dental crowding; dental occlusion; diastema; malocclusion Angle class I; malocclusion Angle class II; malocclusion Angle class III; open bite.

vi) Secondary dentition; secondary teeth; permanent dentition; permanent teeth; adult teeth

Medical subject headings (MesH) for MEDLINE and Pubmed (from 1st Jan 1946 for MEDLINE, from 1st Jan 1996 for Pubmed)

i) Adolescent; child; child, preschool

ii) Tooth loss; tooth extraction

iii) Dentition mixed; dentition, primary; tooth deciduous

iv) Malocclusion (exploded which included following sub-headings: dental occlusion; diastema; malocclusion Angle class I; malocclusion Angle class II; malocclusion Angle class III, open bite); dentition permanent, Index of Orthodontic Treatment Need

Elsevier Life Thesaurus (Emtree) for EMBASE (from 1st Jan 1947)

i) Adolescent; child; preschool, child

ii) Tooth extraction

iii) Deciduous tooth

iv) Malocclusion; secondary dentition

1.4.3.2 Other searches

Screening of reference lists of potential studies were also carried out to yield potentially relevant studies. Unpublished literature was searched electronically on ClinicalTrials.gov (www.clinicaltrials.gov) and the National Research Register (www.controlled-trials.com). Language of publications was restricted to English. Hand search strategy was not carried out for this systematic review.

1.4.4 Study selection process

All studies identified by the search strategy described above that appeared to fulfil the inclusion criteria were scanned based on their title and abstracts. This allowed exclusion of studies that were not relevant to the review question. The entire article was obtained and assessed for inclusion when studies did not have an abstract but title suggested it could be of relevance and also when an abstract provided insufficient information to make a decision about inclusion.

1.5 Assessment of methodological quality of selected studies

Data extraction form (Appendix V) was designed based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement endorsed by the World Health Organization (von Elm et al., 2007). STROBE was the most suitable guideline as most of the studies were observational rather than controlled trials. For each of the studies included in the review the following data were recorded:

- The year of article publication.
- Type of the study.
- Sample size and demographics of the participants.
- Detailed description of intervention, control group and outcomes used.
- Duration of the study.

The data extraction form was tested for consistency and all above information was collected for each study.

1.5.1 Strategy for data synthesis

A narrative synthesis was provided from included studies structured around assessment and quantification of orthodontic need and space loss. Included studies were assessed for study quality, study setting and outcomes of the PEPT, and subsequently compared to those in the control group. Subgroup analyses were carried out where relevant and valid data were available for comparison of PEPT and the control group. It was suspected that meta-analysis was unlikely due to heterogeneity of the studies in design and outcome measures reported.

1.5.2 Risk of bias assessment

Studies included in the review were assessed for risk of bias based on the following specific six criteria. These criteria were drawn from recommendations by the STROBE and the Cochrane Collaboration (von Elm et al., 2007, Higgins and Green, 2011) and modified according to the topic of the systematic review.

- **Definition of inclusion/ exclusion criteria**

Unmet: not defined.

Met: well defined.

- **Definition of outcome**

Unmet: not defined.

Met: well defined.

- **Intervention and control group comparability**

Unmet: large potential for confounding or not discussed.

Met: good comparability of groups or confounding adjusted for.

- **Follow-up of participants**

Inadequate: when less than 80% of patients who entered the trial were included in the final analysis.

Adequate: when at least 80% of patients who entered the trial were included in the final analysis.

- **Examiner reliability**

Inadequate: Inter and intra-examiner reliability not reported.

Adequate: Inter and intra-examiner reliability reported and with acceptable agreement.

- **Blinding on assessment of outcome**

Unmet: not reported.

Met: well defined.

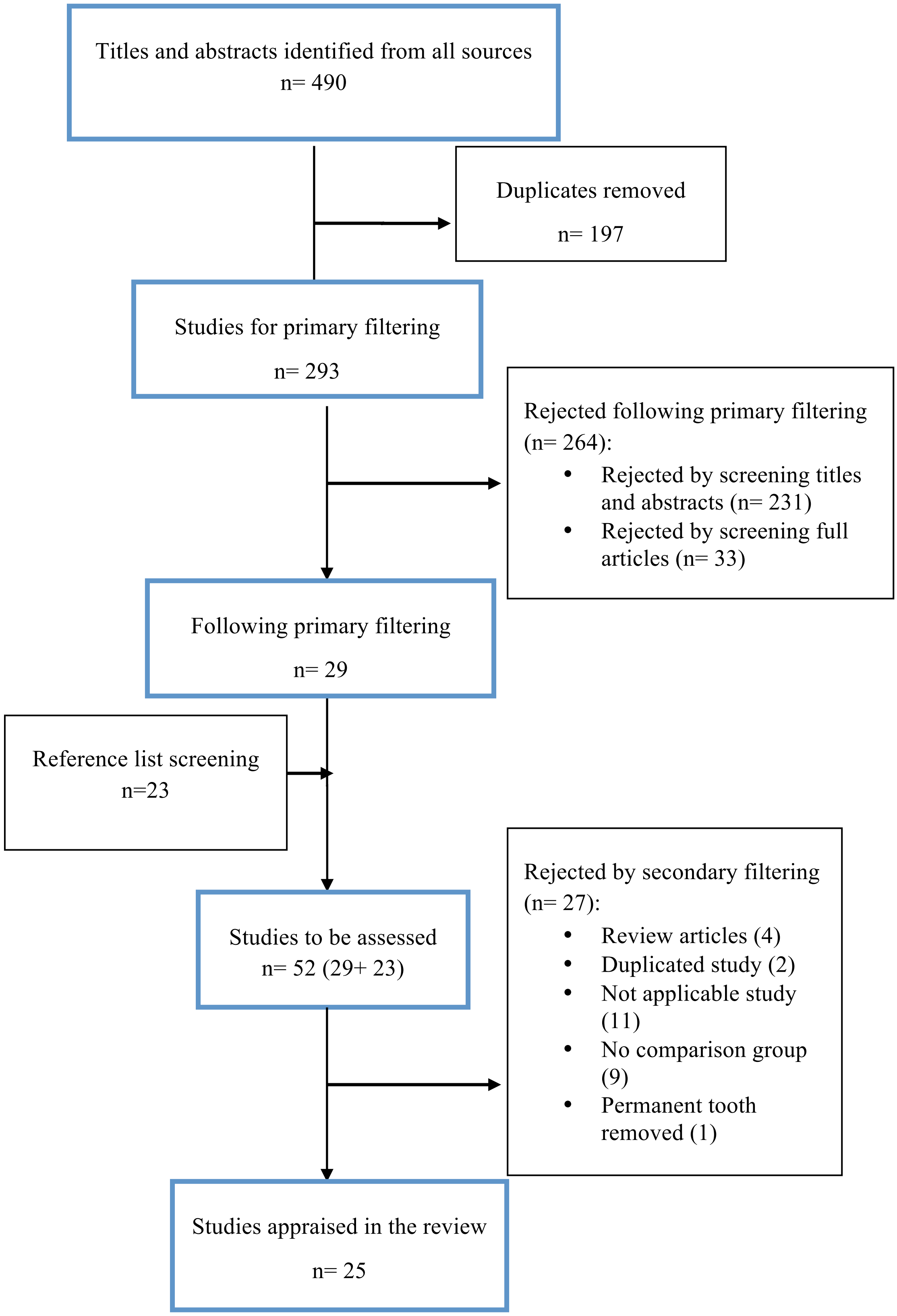
A study was judged to have a low risk of bias when at least five of the above criteria were met; moderate risk of bias if three or four of the criteria were met and high risk of bias if none or up to two of the criteria were met. These criteria were included in the data extraction form described previously with an overall validity score given to each of the studies as high, moderate or low risk of bias.

1.6 SEARCH RESULTS

Searches from all sources identified 490 studies. After removing duplicates, there were 293 studies to be assessed. A primary filtering process rejected 231 studies on screening of titles and abstracts. A further 33 studies were rejected following screening of full articles where abstracts were not available or when the abstracts did not provide sufficient information to include or exclude the study. Reference list screening of the remaining 29 studies revealed 23 potentially relevant studies (Appendix VI). At this stage of the study selection process, no attempts were made to identify studies lacking a control group or the type of study. Then, a secondary filtering process was carried out and 27 further studies were excluded with 25 remaining to be assessed. Out of 27 excluded studies there were 11 studies which were not related to the topic of PEPT, four were review articles, two were duplicated studies with more than one publication related to the same sample, one study looked at premature extraction of permanent teeth and nine studies lacked a comparison group (see Figure 1.2).

There were two studies identified as unpublished studies on the subject. Both were Master's degree thesis, one awarded by University of Montreal (1977) and one by University of Toronto (1949). The former one was also published as a research article (Northway et al., 1984), thus treated as a duplicate publication with more information added from the thesis. The latter one was requested via interlibrary loan from the British Library. It has been confirmed that the British Library does not hold a copy and a copy directly from University of Toronto, Canada is still to arrive.

Figure 1.4 Flowchart of the study selection process.



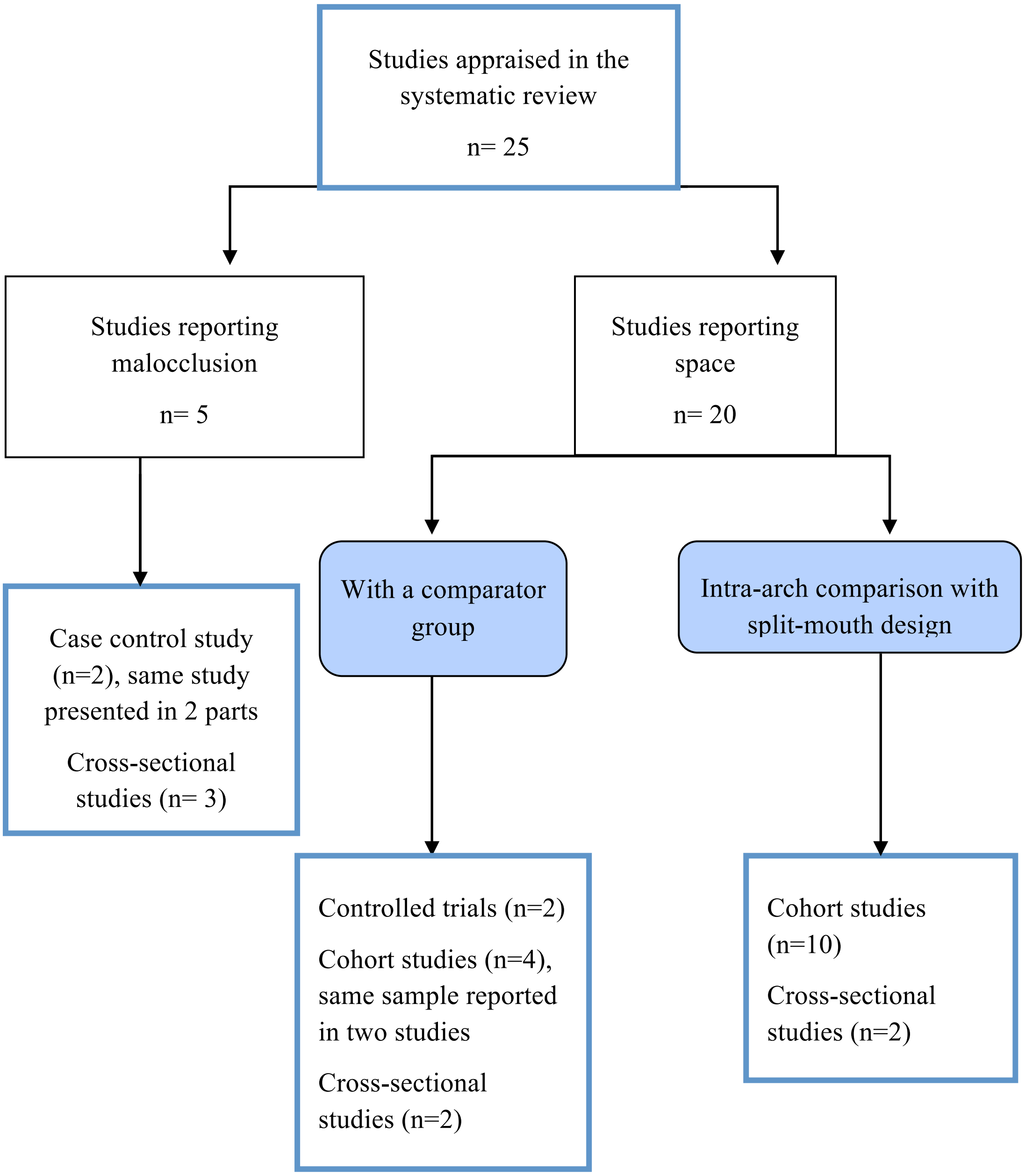
1.7 DESCRIPTION OF SELECTED STUDIES

Full text reports of all selected studies (n=25) were examined (see Figure 1.3). Data were extracted from the remaining 25 studies using the standardised data extraction form. There were five studies reporting on malocclusion following PEPT out of which three were cross-sectional studies and thus were excluded from the review according to the exclusion criteria stated in the protocol (Miyamoto et al., 1976, Pedersen et al., 1978, Melsen and Terp, 1982). Data extraction sheet used for these studies are included in Appendix VII. The remaining two studies were the same study reported in two parts and was a case control study (Hoffding and Kisling, 1978a, Hoffding and Kisling, 1978b). This was the only study included in the review to assess malocclusion following PEPT where comparison was carried out with children who did not have PEPT.

Eight studies assessed space loss following PEPT. Data extraction sheet used for these studies are included in Appendix VIII. Two of the studies were cross-sectional (Rao and Sarkar, 1999, Ronnerman and Thilander, 1978) and were excluded from the review, thus six remaining studies were included out of which two were controlled trials (Sayin and Turkkahraman, 2006, Kau et al., 2004) and four were of cohort design (Clinch and Healy, 1959, Ronnerman, 1965, Ronnerman, 1977, Leighton, 1981). Two studies (Ronnerman, 1965, Ronnerman, 1977) were based on the same sample, thus reported as one study in this systematic review.

The remaining 12 studies were of split-mouth design assessing PEPT in a quadrant and comparison was made to the quadrant where there were no premature extractions. This allowed intra-arch comparison. Two of these studies were cross-sectional (Rosenzwig and Klein, 1960, Magnusson, 1979) and were excluded from the review. Data extraction sheet used for these studies are included in Appendix VIII.

Figure 1.5 Flowchart of the studies appraised in the systematic review.



1.7.1 Studies reporting on malocclusion

The only study reporting on malocclusion that fulfilled the inclusion criteria for the review was a study by Hoffding and Kisling (1978), which was a case control study of 550 children, presented in two parts. This study was based at two Danish municipalities of Denmark, Jutland and Zealand. The aim of this study was to evaluate the effects of PEPT on occlusion and space conditions in the permanent dentition.

Study participants

There were 550 children out of whom there were 327 children with history of PEPT and 223 without history of PEPT. Children with a history of premature extractions of permanent teeth and or orthodontic extractions were excluded from the study, thus the PEPT group had a final number of 231. Although it was reported that age at the time of survey was 13 to 14 years, mean age of the participants was not reported. Ethnicity of the participants was also not stated but can be assumed to be mostly Caucasians.

Intervention

Children with previous history of PEPT formed the intervention group. Out of 231 children in PEPT group, maxillary arch was involved in 32 children, mandibular arch in 97 children and both arches in 102 children. The outcome was compared to children with no history of PEPT.

Outcomes reported

Any feature of malocclusion was reported as the primary outcome. This information was collected from epidemiological surveys and features of malocclusion used in this study were maxillary overjet, sagittal molar relationship and space conditions in incisor and posterior segments. Maxillary overjet was defined as the distance from the most prominent point on the incisal edges of the maxillary central incisors to the most prominent point on the labial surfaces of the lower incisors. Molar occlusion was registered on both sides judged by the relationship of the mesial contact points of the maxillary and mandibular first permanent molars. Half or more than half of the cusp width was recorded as deviation from normal. While assessing space conditions, crowding was registered if there was a space deficiency of 2 mm or more within an arch.

When any sign of malocclusion described above was considered, frequency of malocclusion in cases of PEPT was 90% compared to 80% where there was no history of PEPT. This difference was statistically significant. When features of malocclusion were assessed individually, PEPT was not significantly associated to maxillary overjet and distal molar occlusion (Angle's molar classification Class II). However PEPT was significantly associated with mesial molar occlusion (Angle's molar classification Class III). Frequency of crowding was also statistically higher in PEPT group with 49% in comparison to 29% in the control arch.

Methodological assessment

The overall risk of bias was moderate in this study. Four out of six of our predefined risk assessment criteria were met.

- Definition of inclusion/ exclusion criteria: Inclusion and exclusion criteria were well defined in the study.
- Definition of outcome: Outcome reported in the study was well defined.
- Intervention and control group comparability: There was good comparability between PEPT group and control group apart from premature extractions.
- Follow-up of participants: As it was a case control study and the dental records of PEPT were taken retrospectively. All children fulfilling inclusion criteria were included in the study and retrospective information was collected for approximately seven years.
- Examiner reliability: Examiner reliability for features of malocclusion was not reported in the study.
- Blinding on assessment of outcome: Blinding was not reported in this study.

1.7.2 Studies reporting on space with a comparator group

There were six studies fulfilling inclusion criteria for this group of studies. However two published studies reported on the same data (Ronnerman, 1965, Ronnerman, 1977), thus reported as one study in this systematic review. There was one RCT (Kau et al., 2004) and one controlled trial (Sayin and Turkkahraman, 2006) and both of these studies were investigating the effects of premature extraction of both lower primary canines. Remaining two studies used a cohort design (Clinch and Healy, 1959, Leighton, 1981).

Study participants

Study ID	**Characteristics of studies participants**
(Clinch and Healy, 1959)	59 children were followed up from the age of 3-4 years to 13-14 years. Male to female ratio and ethnicity of the study participants were not reported.
(Kau et al., 2004)	97 children between the ages of 8-9 years were recruited and followed up for a minimum of one year. Male to female ratio was not reported. Ethnicity of these children was Caucasian.
(Leighton, 1981)	36 children were included. Various measurements were collected at ages 3-4 years, 8-9 years, 14-15 years and 17-25 years. Further details about age of the children were not reported. Male to female ratio was 18:18. Ethnicity was not reported.
(Ronnerman, 1965, Ronnerman, 1977)	187 children with mean age of 12.9 years were studied. Male to female ratio was 108:79 (Ronnerman, 1965) and 105: 81 (Ronnerman, 1977). It was not clear why this ratio was different although there was an acknowledgement that the same data was used for both studies. Ethnicity was not reported.
(Sayin and Turkkahraman, 2006)	32 children with mean age of 8.91 years were recruited and followed-up for a minimum of one year. Male to female ratio was 16:16. Ethnicity was not reported.

Intervention

Study ID	**Intervention**
(Clinch and Healy, 1959)	29 out of 59 children had a history of PEPT (primary first and/or primary second molar). This group was compared to remaining children (n=30) who did not suffer PEPT.
(Kau et al, 2004)	A RCT of 97 children out of which 55 children had premature extraction of both lower primary canines following randomisation. This group was compared to remaining children (n=42) who did not have premature extraction of lower primary canines.
(Leighton, 1981)	18 out of 36 children had history of PEPT (lower primary molars). This group was compared to remaining children (n=18) who did not suffer premature extractions.
(Ronnerman, 1965 and Ronnerman, 1977)	161 children out of 187 had history of PEPT (primary molars). This group was compared to remaining children (n=26) who did not suffer premature extractions.
(Sayin and Turkkahraman, 2006)	A clinical trial of 32 children out of which 16 had premature extraction of both lower primary canines. This group was compared to remaining children (n=16) who did not have premature extraction of lower primary canines.

Outcomes reported

Study ID	**Outcomes reported**
(Clinch and Healy, 1959)	Arch dimensions like arch perimeter and arch length were not reported. Space loss in the maxillary and mandibular arches was reported. Early extraction cases when PEPT was at the age of 3-4 years in upper premolar-molar segment lost an average of 6.18 mm when compared to late loss (after the age of 3-4 years) of 3.52 mm. The control group lost 2.72 mm space. Corresponding results for mandibular arch were 3.93 mm, 3.99 mm and 3.1 mm respectively. Space was measured from dental casts.
(Kau et al, 2004)	Arch perimeter reduced more in the extraction group, 2.95 mm compared to the control 1.51 mm. Inter-molar distance showed insignificant change in both groups. Crowding index was reduced in both intervention and control group. There was significant reduction of crowding of lower incisors in intervention group with premature extractions of lower primary canines (6.03 mm) compared to the control group (1.27 mm).
(Leighton, 1981)	Arch perimeter had significant changes in the intervention group, -5.07 mm compared to the control -3.26 mm. The intervention group showed reduction in space, -3.13 mm compared to the control -0.34 mm. Space was measured from dental casts.

Outcomes reported (continued)

(Ronnerman, 1965 and Ronnerman, 1977)	Arch dimensions like arch perimeter and arch length were not reported. Loss of one primary molar in a quadrant when tooth lost before 7.5 years resulted in significantly less relative space (more space loss) when compared no control group (percentage not known, only p value given for various age groups). Relative spacing was insignificant when tooth was lost after 7.5 years. The incidence of crowding was more in the intervention group in maxillary arch, 24% compared to the control group 13%. Corresponding results for mandibular quadrants were 27% and 8% respectively. Second primary molar loss led to more crowding than first primary molar loss.
(Sayin and Turkkahraman, 2006)	There was no difference in arch length, intermolar width, interalveolar width and molar position. Lower incisors were significantly more retruded in the intervention group with premature extraction of lower primary canines.

Methodological assessment

Table 1.1 Summary of the risk of bias assessment of five space studies included in the review.

Quality assessment	**Clinch & Healy, 1959**	**Kau et al, 2004**	**Leighton, 1891**	**Ronnerman, 1965 and Ronnerman, 1977**	**Sayin & Turkkahraman, 2006**
Definition of inclusion/ exclusion criteria	Met: well defined	Met: well defined	Met: well defined	Unmet: not defined well	Met: well defined
Definition of outcome	Unmet: not defined	Met: well defined	Unmet: not defined	Met: well defined	Unmet: not defined
Intervention and control group comparability	Met: good comparability	Met: good comparability	Met: good comparability	Met: good comparability	Met: good comparability
Follow-up of participants	Adequate: cohort study followed for 11 years	Inadequate: per protocol analysis	Adequate: cohort study followed for 13 years	Adequate: cohort study followed for 4 years	Adequate: 100% participants retained
Examiner reliability	Inadequate: not reported	Adequate: single examiner, pilot with 30 study casts	Inadequate: measured twice but agreement score not reported	Inadequate: two examiners measured but agreement score not reported	Adequate: single examiner, reliability co-efficient 0.964
Blinding on assessment of outcome	Unmet: not reported	Met: examiner blinded	Unmet: not reported	Unmet: not reported	Unmet: not reported
Global validity	**Moderate risk of bias**	**Low risk of bias**	**Moderate risk of bias**	**Moderate risk of bias**	**Low risk of bias**

Low risk of bias- at least five of the criteria met; **Moderate risk of bias**- three or four of the criteria met; **High risk of bias**- none to two of the criteria met.

1.7.3 Split-mouth studies

There were 12 split-mouth studies reporting on space considerations following PEPT. Out of these two were cross-sectional studies (Rosenzwig and Klein, 1960, Magnusson, 1979) and thus excluded as per review protocol. Therefore, 10 studies reported below were included in the systematic review.

Study participants

Study ID	**Characteristics of study participants**
(de Boer, 1982)	446 five-year-old children were followed till 9-10 years. Male to female ratio and ethnicity of the study participants were not reported.
(Lin and Chang, 1998)	21 children with mean age of 6 years 11 months (range 5.1 years-7.2 years) were recruited for the study. Follow-up time was 8 months. Male to female ratio was 12:9. Ethnicity of the participants was not reported.
(Lin et al., 2011)	13 children with mean age of 6 years (± 0.74) were recruited for the study. Follow-up time was 12 months. Male to female ratio was 5:8. Ethnicity of the participants was not reported.
(Linder-Aronson, 1960)	41 children with age of 14-15 years were selected and retrospective PEPT data was presented. Male to female ratio was 22:19. Ethnicity of the participants was not reported.
(Macena et al., 2011)	55 children of ages 8 years or 9 years were recruited. Follow up time was 10 months. Male to female ratio was 17:16. Ethnicity of the participants was not reported.
(Northway et al., 1984)	107 children were followed for approximately 6 years. This sample was taken from a growth sample of 260 males and 295 females, male to female ratio of 107 children was not reported. All children were of French-Canadian origin.

Study participants (continued)

(Padma Kumari and Retnakumari, 2006)	30 were included in this study, age of the children was reported as 6 years to 9 years. Follow-up time was 8 months. Male to female ratio and ethnicity were not reported.
(Park et al., 2009)	13 children with the mean age at initial exam of 7 years 11 months were included in the study. Follow-up time was between 8 months to 23 months (mean 12 months). Male to female ratio was 8:5. Ethnicity of the participants was not reported.
(Ronnerman and Thilander, 1977)	65 children were included in the study who had serial dental casts at ages 9 years, 11 years and 13 years. Male to female ratio and ethnicity were not reported.
(Venkaiah et al., 1974)	30 children with the mean age of 8 years to 11 years were included in the study. Follow-up time was 5 months. Male to female ratio and ethnicity were not reported.

Intervention

Study ID	**Intervention**
(de Boer M, 1982)	Part I of the study assessed 21 maxillary and 27 mandibular arches with unilateral molar loss (first or second primary molar). Part II of the study assessed 156 maxillary quadrants and 68 mandibular quadrants. Control group was the sound quadrant.
(Lin and Chang, 1998)	21 children with unilateral loss of mandibular first primary molar were assessed.
(Lin et al, 2011)	13 children with unilateral loss of maxillary first primary molar were assessed.
(Linder-Aronson, 1960)	41 children with unilateral loss of primary canine, first primary molar and/or second primary molar were assessed.
(Macena et al, 2011)	55 children with unilateral loss of first and/ or second primary molar were assessed.
(Northway et al, 1984)	71 children with premature extractions of primary molar/s was assessed and compared to the contralateral sound quadrant.
(Padma Kumari & Retnakumari, 2006)	30 children with unilateral loss of mandibular molar were assessed.
(Park et al, 2009)	13 children with unilateral loss maxillary first primary molar were assessed.
(Ronnerman and Thilander, 1977)	27 cases of unilateral loss of first primary molar and 38 cases of unilateral loss of second primary molar were assessed.
(Venkaiah, 1974)	30 cases of unilateral extraction of first primary molars were assessed.

Outcomes reported

Study ID	**Outcomes reported**
(de Boer M, 1982)	Arch perimeter was not reported. Arch length and arch width were not reported. Lateral segment space (space between lateral incisor to first permanent molar) was reported. Extraction of second primary molar at the age of 5-6 years led to space loss; 8 mm in maxillary arch and 6.5 mm in mandibular arch.
(Lin and Chang, 1998)	There was insignificant difference in arch perimeter. There were insignificant differences in arch length and arch width. D and E space in the extraction side was significantly shorter after 8 months (16.84±1.86 mm) than the control side (17.83±1.3 mm) and less than initial measurement (18.06±1.81 mm).
(Lin et al, 2011)	Arch perimeter was significantly greater at 12 months after tooth extraction. There were insignificant difference in arch length and arch width measurement at initial and 12 months later. D and E space was insignificantly different in extraction side compared to the control at initial examination, but significantly reduced on extraction side than control 15.84 mm vs 16.92 mm in 12 months time.
(Linder-Aronson, 1960)	Hemi-perimeter on extraction side compared to control side was not significantly different. Arch length and arch width were not reported. D and E space was not reported.
(Macena et al, 2011)	Arch hemi-perimeter was significantly reduced in cases of extraction of lower second primary molars. There were insignificant changes in cases of other molars. Arch length was significantly reduced in cases of upper second primary molars. There were insignificant changes in cases of other molars. Arch width was not reported. D and E space was not reported. However, extraction space reported, significant reduction after loss of second primary molars.

(Northway et al, 1984)	Arch perimeter was not reported. Arch length and arch width were not reported. D and E space was reported. For maxillary arch, average yearly D and E space loss were 0.3 mm, 0.7 mm and 0.9 mm for first primary molar loss, second primary molar loss and both primary molar loss respectively. Corresponding values for mandibular arch were 0.5 mm, 0.9 mm and 0.7 mm respectively.
(Padma Kumari and Retnakumari, 2006)	Arch perimeter was not statistically significant between extraction and the control side at 2, 4, 6 and 8 months. Arch length and arch width measurements were not statistically significant in extraction and the control sides at 2, 4, 6 and 8 months. D and E space was not reported. However, extraction space was reported, lower first primary molar extraction side showed significant reduction at 2, 4, 6 and 8 months, values were 7.72±0.56 mm, 7.03±0.56 mm, 6.62± 0.56 mm and 6.64± 0.44 mm respectively.
(Park et al, 2009)	Arch perimeter was significantly increased at final examination as compared to the initial examination. Arch length and arch width were significantly increased at final examination compared to the initial examination. D and E space was not significantly different on the extraction side compared to the control.
(Ronnerman and Thilander, 1977)	Arch perimeter was significantly reduced in extraction side compared to the control. Arch length and arch width were not reported. D and E space or extraction space were not reported.
(Venkaiah, 1974)	Arch perimeter was not reported. Arch length and arch width were not reported. D and E space was not reported. Extraction space was reported, difference in extraction space closure between the extraction and non-extraction side was not statistically significant, although both sides showed tendency for space closure.

Methodological assessment

Table 1.2 Summary of the risk of bias assessment of split-mouth studies included in the review.

Quality assessment	**de Boer M, 1982**	**Lin and Chang, 1998**	**Lin et al, 2011**	**Linder-Aronson, 1960**	**Macena et al, 2011**
Definition of inclusion/ exclusion criteria	Met: well defined	Met: well defined	Met: well defined	Met: well defined	Met: well defined
Definition of outcome	Unmet: not defined	Met: well defined	Met: well defined	Met: well defined	Met: well defined
Intervention and control group comparability	Met: good comparability	Met: good comparability	Met: good comparability	Met: good comparability	Met: good comparability
Follow-up of participants	Inadequate: not reported	Adequate: 100% participants retained	Adequate: 100% participants retained	Inadequate: retrospective cohort study	Adequate: 87% followed up
Examiner reliability	Inadequate: not reported	Adequate: single examiner, 2 measurements and accuracy of 0.1mm	Adequate: Kappa scores over 0.9	Adequate: measurement error calculated, measured twice	Inadequate: single examiner but score or error not reported
Blinding on assessment of outcome	Unmet: not reported	Unmet: not reported	Unmet: not reported	Unmet: not reported	Unmet: not reported
Global validity	**High risk of bias**	**Low risk of bias**	**Low risk of bias**	**Moderate risk of bias**	**Moderate risk of bias**

Low risk of bias- at least five of the criteria met; **Moderate risk of bias**- three or four of the criteria met; **High risk of bias**- none to two of the criteria met.

Methodological assessment (continued)

Table 1.3 Summary of the risk of bias assessment of split-mouth studies included in the review.

Quality assessment	**Northway et al, 1984**	**Padma Kumari & Retnakumari, 2006**	**Park et al, 2009**	**Ronnerman & Thilander, 1977**	**Venkaiah, 1974**
Definition of inclusion/ exclusion criteria	Met: well defined	Met: well defined	Met: well defined	Met: well defined	Unmet: not well defined
Definition of outcome	Met: well defined	Met: well defined	Met: well defined	Met: well defined	Met: well defined
Intervention and control group comparability	Met: good comparability	Met: good comparability	Met: good comparability	Met: good comparability	Met: good comparability
Follow-up of participants	Adequate: participants with study casts for 4 consecutive years were included	Inadequate: 75% participants retained	Adequate: 85% participants retained	Inadequate: not reported	Adequate: 100% participants retained
Examiner reliability	Adequate: 225 paired recordings showed SD of 0.26mm	Inadequate: not reported	Inadequate: single examiner, agreement score not reported	Inadequate: not reported	Inadequate: not reported
Blinding on assessment of outcome	Unmet: not reported	Unmet: not reported	Unmet: not reported	Unmet: not reported	Unmet: not reported
Global validity	**Low risk of bias**	**Moderate risk of bias**	**Moderate risk of bias**	**Moderate risk of bias**	**Moderate risk of bias**

Low risk of bias- at least five of the criteria met; **Moderate risk of bias**- three or four of the criteria met; **High risk of bias**- none to two of the criteria met.

1.8 DISCUSSION

This systematic review was undertaken for the purpose of evaluating scientific evidence concerning malocclusion and space changes following PEPT.

1.8.1 Methodology of the systematic review

1.8.1.1 The review process

The search criteria was developed by the Principle Investigator (Nabina Bhujel) following consultation with two supervisors experienced in systematic reviews (Dr Peter Day and Prof Monty Duggal). Electronic searching, reference list searching and grey literature search was carried out by the Principal Investigator following the prior published protocol. For screening process, one reviewer (Nabina Bhujel) read titles and abstracts or full length articles and excluded unrelated studies. For 25 studies appraised in the systematic review (included and excluded studies), two data reviewers (Nabina Bhujel and Prof Monty Duggal) performed data extraction. Both the reviewers also assessed the validity of included studies and agreed on the overall validity of the studies. The systematic review protocol was followed strictly during study selection and the review process to prevent protocol deviation.

1.8.1.2 Language restriction

Language of publication considered in this review was restricted to English although this may have led to a language bias. There were many studies identified in this review that were carried out in Europe and thus may have been reported in other European languages. Restriction to English language only was chosen for ease of appraisal to avoid the need for language translation and interpretation. However, a recently published review concluded that there was no evidence of a systematic bias by the use of language restrictions in systematic reviews (Morrison et al., 2012). Further research in this field would be useful to determine the impact of language restriction to English.

1.8.1.3 Indexing of publications

Most of the studies included in any systematic review were sourced from electronic sources like MEDLINE and EMBASE. Indexing for these electronic databases have evolved and more subject headings are being introduced. For example, IOTN is now a Medical Subject Heading (MeSH) in MEDLINE since 2012, which was previously indexed under MeSH ‘dental health surveys’ and ‘malocclusion’ from 1975 to 2011.

This review may have missed important studies prior to the development of MEDLINE (prior to 1946) and EMBASE (prior to 1947). Thus reference list searching and use of another electronic resource, PUBMED were also utilised. Free terms search using ‘premature loss of primary teeth’ in PUBMED identified four more studies that were not included in either MEDLINE or EMBASE. This could be because PUBMED also holds citations previous to 1966 that have not been updated with current MeSH headings (US National Library of Medicine, 2013). Reference list searching identified a further 23 potentially relevant studies. A systematic review looking at dental arch space changes following premature loss of first primary molars also highlighted that using electronic resources only were insufficient as many of the studies were published prior to 1966 (Tunison et al., 2008).

1.8.1.4 Methodological assessment

There is no gold standard for methodological assessment of studies. The Cochrane Collaboration recommends the use of risk of bias table and there is a set criteria for risk of bias assessment. These are assessments for sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting and other issues (Higgins and Green, 2011). A risk of bias table was generated for included studies in this systematic review, as most studies were not controlled trials, a set of criteria was used that reflected most of the studies which were observational. This was modified from STROBE and the Cochrane Collaboration (von Elm et al., 2007, Higgins and Green, 2011).

1.8.2 Assessment of the studies

1.8.2.1 Reporting criteria

Consolidated Standards of Reporting Trials (CONSORT) Statement was initially developed in 1996 and recently updated and many health journals support reporting as per CONSORT to report RCTs (Moher et al., 2010). CONSORT Statement is a checklist of 25 items. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement was developed in 2007 for the reporting of observational research (von Elm et al., 2007). The STROBE statement is a checklist of 22 items, 18 of these items are common to all observational designs while four are specific for cohort, case-control, or cross-sectional studies (von Elm et al., 2007). These CONSORT and STROBE checklists relate to the title, abstract, introduction, methods, results and discussion sections of articles. None of the studies included in this review were adequately reported when compared to CONSORT or STROBE statements. Many of the studies were carried out prior to the development of these guidelines. It must be borne in mind that many of the studies appraised in this systematic review were published prior to the 21st century when reporting of scientific research was not as rigorous.

Significant information was not reported in almost all studies identified and appraised in this review. Examples of these are hypothesis statement, selection criteria, sample size calculation, information if operating clinicians, researchers or participants were blinded and relevant scores for their agreement. None of the studies included a flow diagram to show the number of participants at each stage of the study, thus this information was difficult to extract from these studies. CONSORT and STROBE statements both support use of flow diagrams.

1.8.2.2 Types of studies

Twenty-five studies were appraised for this review, out of which seven studies were cross-sectional studies. Cross-sectional studies were excluded from this review, as there is no temporal relationship of exposure to outcome. Time of exposure is particularly important for the subject of this systematic review as there is a defined period for PEPT depending on dental age of the patient. For example, for a child who was examined at the age of 10 years cannot be assessed for premature loss of primary incisors (incisors are expected to exfoliate by this age) and this would result in a high risk of bias. Cross-sectional studies are important in health research and are valued for hypothesis generation. In most cases when a hypothesis is derived on the basis of cross-sectional studies, further analytical studies with either case control or cohort design are required to examine the temporal nature of intervention and outcome.

Ideal study design looking at the effects of PEPT would be a RCT with follow-up of children until at least they are in the full permanent dentition. The only RCT included in this review was looking at the effects of premature extraction of lower primary canines (Kau et al., 2004). This study followed participants for a minimum of only one year. Unfortunately a year is inadequate to study the effects of PEPT in the permanent dentition. The most appropriate follow-up period was in the study by Clinch and Healy (1959) reporting the effects of PEPT from approximately the age of 3- 4 years until 13-14 years. It should be borne in mind that the risk of attrition bias is increased with long follow-up times. Attrition bias has potential to affect both internal and external validity of a study. Internal validity could be affected if the associations between variables are affected or if there is differential dropout between the different arms of the study. External validity could be affected when the results from a study could not be generalisable to the original study population. The cost associated in conducting a study with long term follow-up should also be considered.

Space studies with a comparator group (a control group without PEPT) were appropriate to study the overall effect of space loss as compared to split-mouth studies. This is because the overall effect of space or malocclusion has to take into account intra-arch effects. For example, the effect of a loss of primary canine may result in centre-line shift and this cannot be accounted for by examining split-mouth studies. Some split-mouth studies reported on features of malocclusion (Ronnerman and Thilander, 1977, Northway et al., 1984). Although split mouth maximised these concerns by using stable reference points within an arch such as palatal rugae (Northway et al., 1984). However for the reason discussed above, split-mouth design were not used to report any features of malocclusion in this systematic review. However, split-mouth design was useful to compare the extraction quadrant to the non-extraction quadrant to assess space loss in the short to medium term.

1.8.2.3 Participants

Demographics

The number participants included in this review ranged from 13 children (Padma Kumari and Retnakumari, 2006, Lin et al., 2011) to 550 children (Hoffding and Kisling, 1978a). None of the studies reported outcome based on the gender of participants. Ethnicity of participants in most of the included studies was also not reported. One comprehensive cohort study by Northway (1984) explained that the number of children included were limited, thus results were not analysed according to participant's gender. The same study also reported ethnicity of participants which was well defined, ethnicity was French Canadian origin where three out of four grandparents were of that origin (Northway et al., 1984).

Appropriate power calculations should be performed to determine the ideal sample size required to assure that a study is valid. None of the studies included in the review reported on sample size calculation. It may be difficult to achieve required sample size from one centre, thus planning a multi-centre trial may be beneficial to increase sample size. There was one multi-centre trial involving three centres in three different countries (Kau et al., 2004), but the study failed to report on sample size.

Features of malocclusion depend on ethnicity, race and sex (El-Mangoury and Mostafa, 1990, Proffit et al., 2007a). For example, Class II malocclusion was more prevalent among Europeans when compared to Oriental populations and Class III malocclusion was more prevalent among African and Oriental populations (Proffit et al., 2007a). Class III malocclusion was three times more prevalent among males as compared to females in a population of 18 to 25 year old Egyptians (El-Mangoury and Mostafa, 1990). Thus reporting of patient's demographic features are important to detect if a population group is homogenous in terms of race and ethnicity and also to assess for external validity of the study.

Follow-up period

Follow-up of the participants is very important to study the effect of PEPT on malocclusion. From this systematic review, it was evident that most of the studies did not have adequate follow-up periods. The only study reporting on malocclusion included in this systematic review had a follow-up period of approximately seven years. This was a case control study where information of PEPT was collected retrospectively by reviewing dental records (Hoffding and Kisling, 1978a).

Space studies had follow-up ranging from one year (Sayin and Turkkahraman, 2006) approximately 10 years or more (Clinch and Healy, 1959, Leighton, 1981). Most of the split-mouth studies were followed for a short period of time from five months to a year. Value of such inadequate follow-up periods would have to be viewed with caution in clinical practice.

1.8.2.4 Intervention

The intervention group of a study should be clearly defined. Ideally, the intervention and the control group should be distinguishable on the exposure of interest (in the topic of this systematic review it is PEPT) and indistinguishable in other aspects. All the included studies reported on intervention group as the PEPT group. Any study without a comparison group was excluded from the systematic review, as the estimation of effect was unlikely to be accurate without a comparison or control group. This is because dental arch measurements are not static and change systematically during periods of growth and development in children. However split-mouth studies where the extraction side or quadrant was compared to the non-extraction side were included. These studies were included to study space considerations. It was recognised that these studies would have limited value to study the effects of PEPT on malocclusion as intra-arch relationship such as midline shift and ectopic eruption are also features of malocclusion.

Another important consideration is that the control group has to be free from interproximal caries that could also result in space loss (Northway and Wainright, 1980). Thus careful consideration is needed to make sure that the control group is the most appropriate comparison as space loss due to caries may have occurred well before PEPT. Only one study reported outcome based on sound teeth (including minor caries and restored teeth), carious teeth and extracted teeth (Northway et al., 1984). Other studies considered in this systematic review failed to report on caries status of the control group.

1.8.2.4 Outcome

With all study designs appraised in this systematic review, it was noted that direct comparison of the studies was difficult as various outcomes were reported. Outcome measures used in a study should be valid and have an objective measurement. It should also be clearly defined before data collection stage of the study. When more than one outcome was reported, it should be clear as to which outcome was the primary outcome. None of the studies appraised reporting more than one outcome measure fulfilled this criterion. During the process of this systematic review, it was clear that outcome measures of malocclusion were valid and objective eg. IOTN. But, this was not the case for studies reporting on space dimensions.

Space

All space studies with a comparator group included in this systematic review reported on crowding in the experimental group (Clinch and Healy, 1959, Ronnerman, 1977, Leighton, 1981, Kau et al., 2004). Split-mouth design studies mainly reported on D and E space comparing the extraction side to the contralateral control side. Although some of these studies reported on arch perimeter, this was for intra-arch comparison (Lin and Chang, 1998, Padma Kumari and Retnakumari, 2006, Park et al., 2009, Lin et al., 2011). There was one split-mouth study reporting on hemi-perimeter to compare the extraction side to the control side (Macena et al., 2011).

Northway and Wainright (1984) reported that D and E space could be easily defined and monitored. However, other factors like 'Leeway space of Nance' (Nance, 1947) could not be taken into account when reporting D and E space. The Leeway space is defined as the difference in combined width of the primary canine, first primary molar and second primary molar to combined width of their permanent successors (Proffit et al., 2007b). In mandibular arch, Leeway space is about 2.5 mm on each side and in the maxillary arch it is approximately 1.5 mm on each side (Proffit et al., 2007b). Similarly primate spaces are normal in the primary dentition and are present mesial to the maxillary canines and distal to the mandibular canines (Baume, 1950). Thus, measuring D and E space in mandibular arch does not take account of the primate spaces.

It was evident that various parameters used to report space loss made comparison of the studies was difficult. It also remains unknown whether quantification of space using measurements like arch perimeter, arch length are valid while undergoing normal dental development specially during the mixed dentition phase (Moorrees and Chadha, 1965). However these measurements provide details of the entire dental arch rather than an individual component of the dental arch.

Malocclusion

There was only one study included in this systematic review looking at the effects of PEPT on malocclusion. There were two cross-sectional studies that reported on the effect of PEPT on orthodontic need, complexity of orthodontic need and whether children who suffered PEPT were likely to have orthodontic extractions in the future (Pedersen et al., 1978, Melsen and Terp, 1982). The outcomes used in these studies would have been valuable in determining the orthodontic need. For reasons described previously cross-sectional studies were not included in this systematic review. Clinically, the most relevant and appropriate method of reporting orthodontic need would be to use the IOTN index. This allows drawing clinically important conclusions based on a set of outcomes that is well recognised and used widely. However, IOTN was only developed in 1989 and all the studies reporting on malocclusion were prior to this date. Further, it would be useful to record the details on the criteria used to classify and record malocclusion.

1.8.2.5 Blinding

A study should be carried out with plans for appropriate blinding. Apart from one study where the examiner was blinded towards the intervention or the control group (Kau et al., 2004) while other studies failed to report on this criterion. Allocation concealment, double blinded RCT is the gold standard. Certain clinical situations may be either impossible or not easy to plan for a double blinded study (Day and Altman, 2000). Considering the topic of the systematic review, it would not be possible to blind the PEPT group of patients with the control group. Similarly, it may not be possible to blind investigators unless the investigator is the not the clinician carrying out any treatment and be involved with any patient while they are receiving clinical care. It has been shown that the effect estimates could be overestimated when blinding was not incorporated within a RCT (Schulz et al., 1995). Although double blinding is impossible to assess effects of PEPT, attempts should be made to utilise trained and calibrated examiners who are not investigators and ideally unaware of the intervention status (in this case previous history of PEPT) of the participants. Although this is not possible in studies with split-mouth design, attempts should be made to report agreement scores and take repeated measurements to minimise bias.

1.8.3 Clinical significance

A review by Tunison et al (2008) concluded that there was statistically significant space loss following premature extraction of upper first primary molars. However it was argued that statistical significance may not result in clinical significance. It was found that space loss was 1mm per arch side for maxilla and 1.5 mm per arch side for mandible and these measurements were unlikely to be of significance in most clinical scenarios (Tunison et al., 2008).

Another important aspect when assessing space loss is that space loss may have occurred due to other factors apart from PEPT. Lack of consideration of normal dental arch changes may lead to overestimation of the effect of PEPT on space. It is well known that space available for lower incisors after eruption of these teeth is negative for a few years. Thus a small amount of lower incisor crowding during this stage of dental development was considered normal (Moorrees and Chadha, 1965). This is due to the difference in mesiodistal dimension of primary to permanent incisors and is termed incisor liability. Some studies reported that arch perimeter was increased following PEPT (Park et al., 2009, Lin et al., 2011). This suggested that normal dental development did continue and it should not be misinterpreted as the effect of PEPT. It is important to take normal growth and development patterns into account.

When considering factors like drifting patterns of teeth, terminal plane of the primary molars should also be considered. Flush terminal plane relationship of primary molars is considered the normal relationship and this relationship guides the eruption of first permanent molars. For example, if maxillary primary molars have drifted mesially due to loss of first primary molar, then the terminal plane relationship could be altered (Ngan et al., 1999). Similarly, availability or unavailability of primate space could also complicate terminal plane relationship (Ngan et al., 1999).

Occlusal factors like crowding and lack of space, drifting patterns of various teeth and intercuspation of first permanent molars could potentially affect resultant space loss (Hoffding and Kisling, 1978a, Hoffding and Kisling, 1978b). First permanent molars were more mesially placed on the side of extraction when comparison was made to the contra-lateral side (Linder-Aronson, 1960). Children with crowding had shorter and narrower arches irrespective of PEPT, thus crowding could be an important predisposing factor leading to space loss (Ronnerman and Thilander, 1977). Space loss was significant on extraction side compared to the control but this significance was not retained until the age of 13 years. This was in agreement with Magnusson (1979) who reported that space lost during initial stages of dental development was recovered during later stages of dental development.

The measurement of space dimensions only in an arch is unlikely to predict future malocclusion and thus orthodontic need. Thus a study reporting on orthodontic need should have an index such as IOTN as the primary outcome of that study.

1.8.4 Future research directions

- Ideally a RCT or a prospective cohort study with long follow-up period of about 10 years from the time of PEPT until the presence of full permanent dentition is required to establish the effect of PEPT on malocclusion. Another option would be a long term cohort study possibly an additional arm of a large prospective cohort study. Some authors have used similar methodology. A study by Northway and Wainwright (1984) used a cohort based on a growth sample. A study by Clinch and Healy (1959) used a cohort of children born at the same maternity hospital.

- Outcome of a study should be clearly defined. Ideally any outcome measure should be valid and widely used eg. IOTN to assess malocclusion. For assessment of space dimensions arch perimeter, arch length and arch width would be appropriate. If more than one outcome is reported, then primary outcome needs to be specified at the protocol stage. Examiner reliability should be reported for all outcome measures reported.

- In the methodology, intervention or exposure group should be well defined from the control group with clear inclusion and exclusion criteria. Intervention group would be children with PEPT and control group without PEPT. These children should be followed-up from the time of PEPT to the full permanent dentition.

1.9 Recommendations and conclusions

The studies assessing the consequences on developing dentition following PEPT were mostly either cross-sectional or cohort studies where sample sizes were small. There are no randomised controlled studies looking at the effects of PEPT on malocclusion and subsequently on orthodontic need resulting from PEPT.

SIGN guidelines available from http://www.sign.ac.uk (Appendix X) were used for evidence statements and grades of recommendations. The following recommendations are drawn from the basis of this systematic review.

- PEPT increases the frequency of features of malocclusion (all features of malocclusion included) (Evidence level 2+, Recommendation grade C).
- PEPT increases the frequency of crowding (Evidence level 2+, Recommendation grade C).
- PEPT leads to reduced space in affected segment of the arch (Evidence level 2+, Recommendation grade C).
- PEPT of lower primary canines bilaterally leads to reduced arch perimeter (Evidence level 1+, Recommendation grade B).

The following recommendations are drawn from the general review of the literature.

- PEPT increases orthodontic need (Evidence level 2-, Recommendation grade D).
- PEPT increases the complexity of orthodontic treatment as judged by increased length of orthodontic treatment over 12 months (Evidence level 2-, Recommendation grade D).
- PEPT increases likelihood of orthodontic extractions of permanent teeth (Evidence level 2-, Recommendation grade D).

CHAPTER 2

2.1 INTRODUCTION

Premature extraction of primary teeth (PEPT) is common in paediatric population. The systematic review in the previous chapter demonstrated limited evidence available to quantify the long term effects of PEPT. There is no publication to date in the UK looking at the effect of PEPT and malocclusion in the permanent dentition. Thus such a study would add to literature (especially if utilising a rigorous methodology) and would aid in treatment planning paediatric dental patients.

This research was presented at the 11th European Academy of Peadiatric Dentistry Congress at Strasbourg (2012) in the young researcher award as an oral presentation. The abstract submitted to the conference is attached as Appendix XI. Further, a version of this study will be submitted for publication and is attached as Appendix XII.

2.1.2 Caries experience in Bradford and Airedale

In the district of Bradford and Airedale, West Yorkshire there are inequalities in oral health of 5-year-old children. West Yorkshire has $d_3$mft of 2.42 which is more than twice the national average of England at 1.11(NHS Dental Epidemiology Programme for England, Oct 2009). Large variation in caries experience also exists within the district of Bradford and Airedale with the inner city experiencing much higher levels of caries as compared to other regions (Bradford and Airedale Teaching Primary Care Trust, 2007). A report of a survey from Bradford and Airedale showed that the severity of dental caries in Asian children was almost twice more when compared to their White peers with $d_3$mft of 3.52 and 1.89 respectively (Bradford and Airedale Teaching Primary Care Trust, 2006). Table 2.1 illustrates the population and sample of 5-year-old children in England, Yorkshire and the Humber and Bradford and Airedale and their dental caries experience based on clinical examination in oral epidemiological surveys.

Table 2.1 Dental care indicator d_3mft in England, Yorkshire and the Humber and Bradford and Airedale.

Region	5-year-old population	Drawn sample	Examined	Mean d_3mft	Mean d_3mft (% d_3mft>0)
England	558,566	209,152	139,727	1.11	3.45
Yorkshire and the Humber	55,808	13,882	8,916	1.51	3.73
Bradford and Airedale	7,050	1,427	750	2.42	4.42

Source: NHS Dental Epidemiology Programme for England Oct 2009.

2.1.3 Orthodontic need of 12-year-old children in Bradford and Airedale

National oral epidemiological survey carried out in 2008/2009 showed that in the district of Bradford and Airedale, there were 6,730 children aged 12 years attending mainstream education. In Bradford and Airedale, orthodontic need of 12-year-old children was higher than that of England at 41% (see Table 2.2). It was further reported that demand for orthodontic treatment (defined by children who thought their teeth needed straightening and were prepared to wear braces) was 36% and children who were in need of orthodontic treatment and were prepared to wear braces was 24%. Both of these values were higher than that of England at 35% and 19% respectively.

Table 2.2 Orthodontic status in England, Yorkshire and the Humber and Bradford and Airedale.

Region	12-year-old population	Drawn sample	Examined	Orthodontic Need	Orthodontic Demand	Orthodontic Need and Demand	Children wearing brace
England	608,460	120,642	89,442	28,269 (31.6%)	31,681 (35.4%)	17,238 (19.3%)	7,105 (7.9%)
Yorkshire and the Humber	63,037	8,801	6,234	2,156 (34.6%)	2,042 (32.8%)	1,195 (19.2%)	363 (5.8%)
Bradford and Airedale	6,730	851	586*	241 (41.1%)	213 (36.3%)	141 (24.1%)	26 (4.4%)

Source: (NHS Dental Epidemiology Programme for England, 2011)

Need = Not wearing appliance and AC >8 OR not wearing appliance and DHC of definite orthodontic need (DHC of Modified IOTN=1).
Demand = Not wearing appliance and think teeth need straightening and prepared to wear a brace.
Need and Demand = Not wearing appliance and AC >8 and DHC of definite orthodontic need (DHC of Modified IOTN=1) and they think teeth need straightening and prepared to wear braces.

Note: * 586 children were examined in Bradford and Airedale district according to the published national protocol. However only 366 children were examined on school based surveys in Bradford and Airedale. This discrepancy has been explained by the addition of extra children to the original 366 once home postcodes for each child were checked. School postcodes were used for examination of 366 children while national data made use of home postcodes of 586 children. The same reason shows a discrepancy of the sample size of the oral epidemiological survey as well (See Appendix XIII and Appendix XIV).

2.1.3 Role of Salaried Dental Service (SDS)

Salaried Dental Service (SDS), Bradford District Care Trust provides dental care for children in the district of Bradford and Airedale, many with high and complex dental treatment need. SDS is a primary care service where there is provision of consultant led specialist services in Paediatric Dentistry and specialist led services in Special Care Dentistry. SDS takes referral from local General Dental Practitioners (GDPs) and other primary and secondary healthcare providers (general practitioners, medical and surgical specialists, health visitors, school nurses and social care).

SDS has 10 clinics and provides dental services mainly under LA. There are also facilities for dental treatment under inhalation sedation. Another important role of SDS is to provide dental treatment under GA. It is the only provider of GA services for dental treatment in the district of Bradford and Airedale. Regular paediatric GA lists are operated from Bradford Royal Infirmary and Airedale General Hospital mostly as day cases. GA services have been provided by SDS for this district for over 20 years.

Currently within SDS, there is very limited capacity for restorative care of carious primary teeth under GA for fit and healthy children. Children who are medically compromised or identified as having special needs have access to comprehensive care under GA which includes provision of restorative care. This means that many restorable carious primary teeth are extracted in fit and healthy children when they are unable to tolerate treatment under LA with or without CS.

In Bradford and Airedale, there is an increased prevalence of dental caries. For many of the children with extensive dental caries, they are referred by their GDP to the SDS. These young children frequently undergo extraction of all their carious primary teeth under GA. NHS Business Service Authority primary care data for 2010 for Bradford and Airedale showed that two thirds of all primary teeth extracted were carried out within SDS.

2.2 AIMS OF THIS STUDY

This study aimed to investigate if PEPT led to an increased need for orthodontic treatment based on the modified IOTN in a paediatric population in the district of Bradford and Airedale. For this study PEPT was defined as any primary tooth that was extracted prior to its natural exfoliation by a clinician over a course of dental treatment either under LA or GA.

The primary aim was to determine whether orthodontic need was increased in children who had a positive history of PEPT.

The secondary aims were:

1. To establish if orthodontic need was influenced by gender and ethnicity.
2. To establish if orthodontic need was influenced by the timing of extraction of primary teeth, position of the tooth in dental arch, the tooth type and the total number of primary teeth lost prematurely.
3. To explore and compare individual characteristics of children who were seen in SDS to children who were not seen in SDS.

2.2.1 NULL HYPOTHESIS

The null hypotheses were as follows:

1. There is no difference in the orthodontic need based on modified IOTN among children who had a history of PEPT when compared to children who did not.

2. There is no difference in the orthodontic need based on gender and ethnicity.

3. Orthodontic need was uninfluenced by the timing of premature extraction of primary teeth, position of the tooth in dental arch, the tooth type and the total number of teeth lost by premature extraction.

4. There is no difference in individual characteristics of patients seen in SDS compared to those who were not seen in SDS.

2.3 MATERIALS AND METHODS

2.3.1 Introduction

This was a case control study of 12-year-old children based in Bradford and Airedale. This study considered orthodontic need based on the modified IOTN on children and explored whether comparisons could be made to previous history of PEPT. The study population was drawn from oral epidemiological surveys of 12-year-old children attending mainstream education. NHS Dental Epidemiology Programme coordinated this national oral epidemiological survey. The survey was carried out in the academic year 2008/2009.

2.3.2 Ethical considerations

Bradford Research Ethics committee was written to for advice about the data set and intentions to use the data for purposes of this study. It was made clear that patient identifiable information would be used only to link patients from the oral epidemiological survey of 12-year-old children and dental records held by SDS. This study was approved as a service evaluation by the Bradford Research Ethics Committee (see Appendix XIII). Thus full ethical approval was not required from the National Research Ethics Service (NRES).

The Principal Investigator (Nabina Bhujel) ensured that this study was conducted in full accordance of the ethical principles, the laws and regulations of the UK. Annonymisation was conducted by the Principal Investigator whereby patient identifiable data was only used to match patient demographics from 12-year-old epidemiological survey and dental records held by Bradford and Airedale SDS. Once individual records were linked all personal identifiable information was removed from the database and a unique reference number assigned to each child was used thereafter.

2.3.3 Data set

In the district of Bradford and Airedale there were 5,588 12-year-old children attending mainstream education. A representative sample of 600 children was randomly selected following the national protocol of NHS Dental Epidemiology Programme (NHS Dental Epidemiology Programme for England, Sep 2008). From this sample, the need for positive consent from parents or guardians who had parental responsibility and children themselves and also attendance at school on the day of the survey, led to 366 (61%) children being examined. Each child was also involved and was asked if they had any questions before they were willing to participate in the survey. Thus examinations were only carried out on children who met the following criteria regarding consent (NHS Dental Epidemiology Programme for England, Sep 2008):

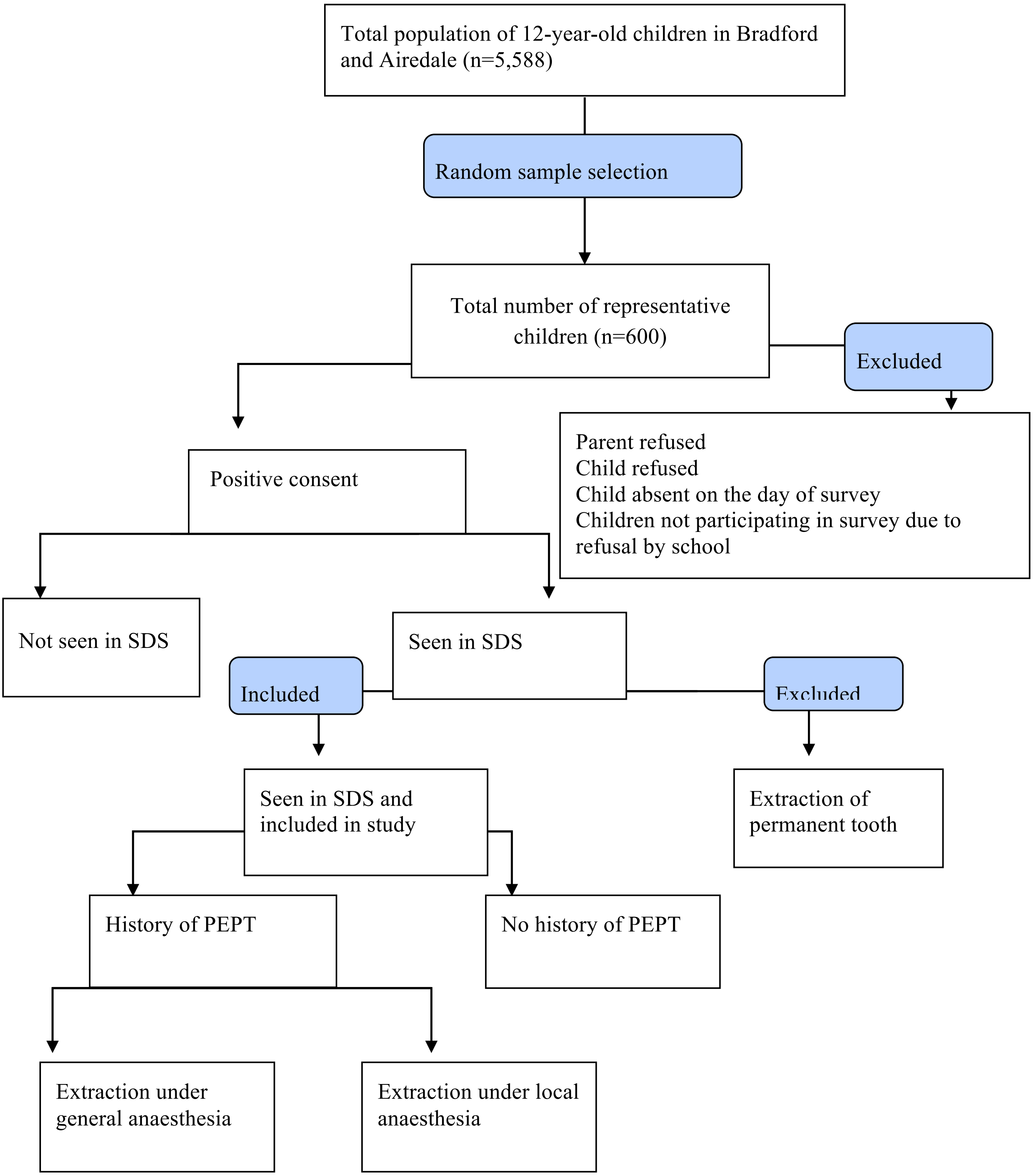
1. whose parents or guardian with parental responsibility had not refused permission and
2. who had received an explanation of the nature and purpose of the survey using the standard script and
3. who had been given an opportunity to ask questions and
4. who had given expressed or implied consent by their words or actions.

Survey information obtained on 366 children was linked to dental records held by SDS with respect to each child.

For each of 366 children identified from the survey, their name and date of birth was matched against dental records held by SDS. Firstly it was noted if any of the children in the survey had been seen in SDS previously. Electronic notes (provided by Kodak R4®, PracticeWorks, Carestream Health Inc) were examined first to identify if any these children had attended SDS in the past since 2003. Since around 2003, SDS held electronic dental records of patients using the service and previous to this hand written records were used. Then archiving databases held by SDS were checked against patient's name and date of birth. Patient's record cards were archived in SDS if a patient was not undergoing an active course of treatment and had not been seen in the last three years. If the name and date of birth from the survey matched with the SDS records either from electronic records or from archived records, then the child would be classed as seen in SDS.

Where a positive link was identified using name and date of birth, further data was collected from the SDS records about their past history of PEPT. If the child's age and date of birth did not match, then the child was considered as not having accessed SDS in the past for their dental care. There were two children who had matching date of birth and home address but names were recorded with first name as second and vice versa in the survey as compared to SDS records. These two children were included as seen in SDS as their recorded date of birth and address was the same in the survey and SDS records. For sampling framework of children included in the study see Figure 2.1.

Figure 2.1 Flowchart of the potential number of 12-year-old children in Bradford and Airedale who would be available for inclusion in this study.



SDS- Salaried Dental Service; PEPT- Premature Extraction of Primary Tooth.

Patient identifiable information of subjects was only used to match patient demographics from the 12-year-old dental epidemiological survey to SDS dental records. Following the matching process and to assure anonymity of the children involved, each child was given a unique identification number. A proforma was developed which captured individual demographics of children, survey information and whether they accessed SDS or not. If they had accessed SDS in their past and had suffered PEPT, then this information was also collected using a proforma (see Appendix XVI). Data collection proforma was piloted on 15 children to include children who accessed SDS but had no treatment in SDS (five children), accessed SDS and had treatment under GA (five children) and accessed SDS and had treatment under LA (five children). After the pilot, date of examination of the survey was added to the data collection proforma. This allowed calculation of age at the time of PEPT which was one of the predictor variables included in the study. Information collected from the survey and from Bradford SDS is detailed in Table 2.3. A database was created on SPSS (version 18) to transfer data from data collection proforma. SPSS (version 18) was also utilised for statistical reporting and analyses.

Table 2.3 Information collected from 12-year-old dental epidemiological survey and from retrospective dental notes in Bradford and Airedale Salaried Dental service (SDS).

Information from the 12-year-old dental epidemiological survey	Information from dental notes in Bradford Salaried Dental Service (SDS)
Name Date of Birth Gender Ethnicity Home postcode Date of dental survey DMFT Dental health component of the modified Index of Orthodontic Treatment Need Aesthetic component of the Index of Orthodontic Treatment Need	Seen or not seen in SDS If seen in SDS: * Whether history of premature extraction of primary tooth or not *Whether extractions were done under general anaesthesia or local anaesthesia *Date of extraction/s *No of tooth/teeth extracted *Tooth notation/s for extracted tooth/teeth

2.3.4 Statistical analysis

There were numerous meetings with a co-supervisor (Ms Theresa Munyombwe) to discuss about database and appropriate statistics to be used. Categorical data in the study were summarised using frequencies and proportions. Continuous variables were summarised using means and standard deviation if normally distributed. Medians and inter-quartile ranges were used in case of skewed data. These analyses were computed using SPSS version 18. Significance level chosen for this study was at $p < 0.05$. All continuous variables used in the study were checked for normality using a histogram and the Shapiro-Wilk test. This test is based on the null hypothesis that the data is normally distributed. Thus for the Shapiro-Wilk test, if the p value was less than 0.05, then the data could not be modelled by a normal distribution.

Data was initially analysed at child level to compare the groups of children who were either seen or not seen in SDS. The Pearson's Chi-Square statistics (χ^2) allowed comparison of these two groups in terms of gender, ethnicity, DHC and AC of the modified IOTN. For continuous variables, age at the time of survey, DMFT of children and overall Index of Multiple Deprivation (IMD) (2007) the data was examined for normality using histogram and Shapiro-Wilk test. The results departed from normality thereby necessitating the need for non-parametric statistics, the independent sample Mann-Whitney U test.

PEPT was compared for children having their treatment under GA and LA. Age at the time of extraction and the number of extractions were not normally distributed and independent sample Mann-Whitney U test allowed comparison of the groups in these two aspects. Pearson's Chi-Square statistics (χ^2) allowed comparison of proportion of teeth with respect to whether they were maxillary or mandibular teeth and the tooth type. The tooth type was divided into three subgroups: anterior, first primary molar and second primary molar.

2.3.4.1 Multilevel modelling

Multilevel modelling was employed for 107 children who were seen in SDS in their past. A specific statistical software, MLwiN (v2.1) was used to fit multilevel model. MLwiN was developed by the Centre for Multilevel Modelling, University of Bristol. It uses maximum likelihood estimation and Markov Chain Monte Carlo (MCMC). The outcome variable chosen for the study was the DHC of the modified IOTN, which had a binary outcome (either 'need' or 'no need'). The number of teeth lost by PEPT in the same child was not independent and it is well known that ignoring such a hierarchical structure would lead to underestimation of standard errors of regression coefficients (Rabash et al., 2009). Multilevel modelling accounted for clustering of data and in this study, teeth were nested within a child. We therefore chose to account for the clustering within a person by using a multilevel modelling approach.

Model building started with the recognition that the data showed two level hierarchy. The higher level was set at the child level and the lower level at the tooth level (see Table 2.4). This hierarchical nature of the data accounted for multiple extractions at the same time point in a child or multiple extractions in the same child over multiple visits eg. different time points.

Table 2.4 Demonstration of hierarchy used for model building in the data.

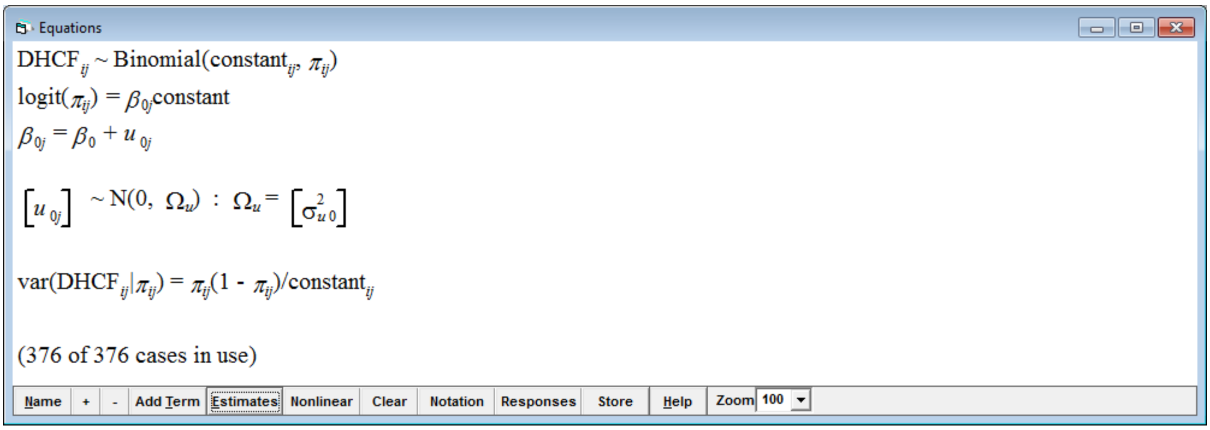
Level 2	Child Level
Level 1	Tooth level (tooth type)

Logistic regression with a two level random intercept model was used to describe outcome variable with predictors. Thus, logistic regression by the use of logit function was employed to model the variables. The logit function is also known as the link function because it connects or links the values of predictor variables to the probability of occurrence defined by the dependent variable. The predictor variables selected were based on clinical knowledge and these included gender, ethnicity, age at the time of PEPT, specific tooth type and the total number of teeth extracted as a result of PEPT. The tooth type was divided into anterior, first primary molar and second primary molar.

Highly correlated predictor variables were excluded from the model, thus a reduced model with important predictors was chosen. A two-level random intercept model was fitted to allow the intercept β_o to vary among patients. The null model for random intercept is displayed below (see Figure 2.2). To avoid colinearity problems and model not converging, highly correlated predictor variables were excluded from the model. For example Spearman's correlation coefficient (ρ) was conducted to three predictor variables, tooth type (anterior, first primary molar and second primary molar), second primary molars compared to other teeth and maxillary or mandibular teeth. It was found that second primary molars compared to other teeth were highly correlated to maxillary or mandibular teeth with Spearman's correlation coefficient of 0.93. Thus the variables comparing second primary molars and other teeth were excluded from the model as clinically information about maxillary and mandibular teeth was thought to be more valuable. Random intercept model used on 376 lower level cases (tooth level) nested on 107 higher level cases (child level). Figure 2.3 demonstrates the use of 376 tooth level cases for model building.

Figure 2.2 Model building based on the Null Model with the Dental Health Component (DHC) of the Index of Orthodontic Treatment Need.

Figure 2.3 A two-level random intercept model was fitted to allow the intercept β_o to vary among patients with 376 lower level (tooth level) cases.



2.3.5 Selection criteria

2.3.5.1 Inclusion criteria

All 12-year-old children who participated in the oral epidemiological survey conducted by NHS Dental Epidemiology Programme in 2008/2009 and had orthodontic need recorded by use of the modified IOTN in Bradford and Airedale district were included in the study.

2.3.5.2 Exclusion criteria

Any child with a history of premature extraction of permanent tooth/teeth was excluded from the study.

2.3.5 Storage and handling of participants' identifiable data

All data collected for the research was stored in a locked filing cabinet at the Teaching Office at Westbourne Green Dental Department, which is one of the clinics of Bradford and Airedale SDS, Bradford District Care Trust. This area was restricted and inaccessible to the public for data protection. Access to the data was restricted to the Principal Investigator (Nabina Bhujel) and the supervising consultant (Dr Peter Day). Both hold contracts with the SDS and are governed by SDS information governance policy.

The annoymisation of data in accordance to ethical principals was conducted as described in section 2.3.2. All subjects were only known by their unique identification number. Electronic version of the database was carried in an encrypted memory stick by the primary investigator in line with SDS information governance policy. All personal identifiable and research data will be stored for a maximum of one year following completion of the research. Following this time these will be destroyed as per confidential waste.

2.4 RESULTS

The following section represents the results of the study. The order of the description of results is the same as described in the Materials and Method section (section 2.2).

2.4.1 Survey sample from 12-year-old oral epidemiological survey

Of the 600 representative sample, 366 children participated in the 12-year-old oral epidemiological survey conducted by NHS Dental Epidemiological Programme in Bradford and Airedale district in 2008/2009. All surveyed children were examined following positive consent from parent/ guardian having parental responsibility for the child. Parents of 37 children refused to participate, 60 children refused to participate, 99 children were absent and one school with 38 children refused to participate and these children were excluded from the survey.

2.4.2 Data linkage to Salaried Dental Service (SDS) records

Data linkage to SDS dental records was carried out by the use of individual demographics. It was found that 116 children (31.6%) had accessed SDS during their childhood prior to the date of the epidemiological survey. The demographics of 366 children surveyed were divided into two groups, as 'seen in SDS' and 'not seen in SDS' and they are reported in Table 2.5. There was insignificant differences in terms of gender, the DHC and the AC of the modified IOTN with $p > 0.05$. A significant difference ($p \leq 0.01$) was found for age at examination of the survey. Highly significant differences were found in terms of ethnicity, DMFT and the overall IMD (2007) between children who were seen in SDS and not seen in SDS with $p \leq 0.001$. A higher proportion of children seen in SDS came from a 'non-white' ethnicity, were younger at the time of examination of the survey, from a more deprived background (higher IMD 2007) and had higher levels of dental caries (higher DMFT).

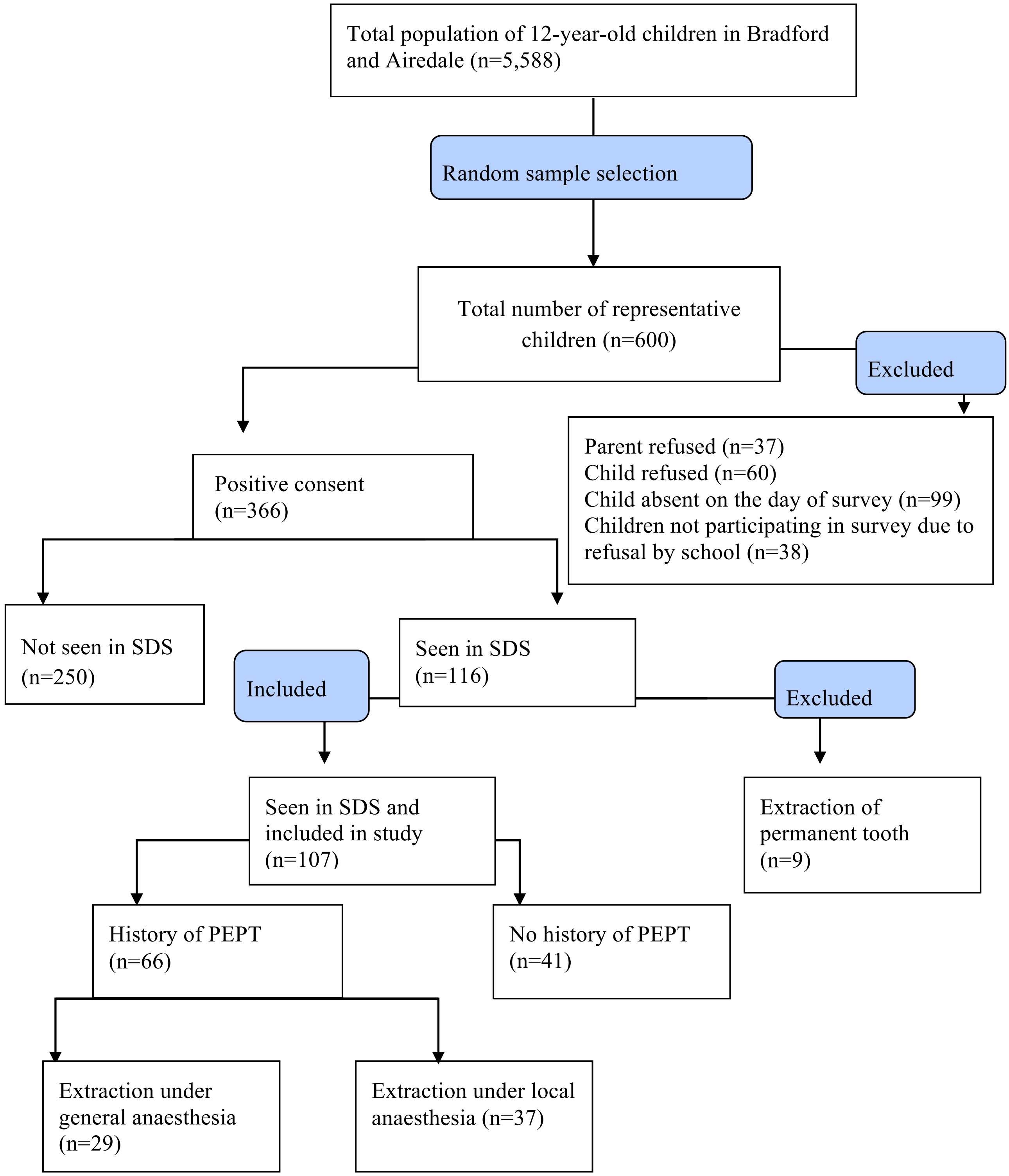
Table 2.5 Description of patient groups 'seen in SDS' and 'not seen in SDS' by gender, ethnicity, the Dental Health Component and the Aesthetic Component of the modified Index of Orthodontic Treatment Need, age at examination of the survey, DMFT and overall Index of Multiple Deprivation score.

	Children seen in Salaried Dental Service (n=116)	**Children not seen in Salaried Dental Service (n=250)**	***p* value**
Gender n (%)	Male, n=65 (60.7%) Female, n=42 (39.3%)	Male, n=145 (58%) Female, n=105 (42%)	0.62
Ethnicity n (%)	White, n=23 (21.5%) Non-white, n=84 (78.5%)	White, n=160 (64%) Non-white, n=90 (36%)	0.001**
Dental Health Component n (%)	No need, n=46 (43%) Need, n=61 (57%)	No need, n=122 (48.8%) Need, n=128 (51.2%)	0.31
Aesthetic Component n (%)	No need, n=88 (82.2%) Need, n=19 (17.8%)	No need, n=217 (86.8%) Need, n=33 (13.2%)	0.26
Age at the time of survey in months Median (IQR)	148 (146-152)	150 (147-153)	0.01*
DMFT Median (IQR)	2 (0-3)	1 (0-2)	0.001**
Overall Index of Multiple Deprivation Median (IQR)	49.25 (36.06-60.95)	27.86 (17.84-48.03)	0.001*

* $p \leq 0.01$; ** $p \leq 0.001$.

From the sample of 600 12-year-old children attending mainstream education in Bradford and Airedale, 250 children were not seen in SDS in the past while 116 had accessed SDS for dental services in the past. Figure 2.4 illustrates the number of children included and excluded in the survey and the study. This figure also illustrates the number of children who were seen in SDS and had a positive history of previous PEPT.

Figure 2.4 Flowchart of the number of the 12-year-old children in Bradford and Airedale who were available for inclusion in this study of the orthodontic implications of premature extraction of primary teeth.



SDS- Salaried Dental Service; PEPT- premature extraction of primary tooth.

2.4.3 Study sample

One hundred sixteen children were seen in SDS, nine children (7.8%) had extraction/s of permanent tooth/ teeth and thus were excluded from the study according to our exclusion criteria. Sixty-six children (56.9%) had a history of PEPT and the remaining 41 children did not have a positive history of PEPT. Out of 66 children seen in SDS and had a history of PEPT, 29 children had dental extractions under GA and the remainder, 37 children had their extractions under LA. Descriptive summaries of child level data for 'need' and 'no need' for orthodontics for 107 children seen in SDS and 66 children who were seen in SDS and had a positive history of PEPT are shown in Tables 2.6 and 2.7.

Table 2.6 Descriptive statistics of patient groups according to orthodontic 'need' and 'no need' for children seen in Salaried Dental Service (n=107).

	Children with orthodontic 'need' (n=61)	Children with orthodontic 'no need' (n=46)
Gender n (%)	Male, n=35 (57.4%) Female, n=26 (42.6%)	Male, n=30 (65.2%) Female, n=16 (34.8%)
Ethnicity n (%)	White, n=15 (24.6%) Non-white, n=46 (75.4%)	White, n=8 (17.4%) Non-white, n=38 (82.6%)
DMFT Median (IQR)	2 (0-3)	1.5 (0-3)
Overall Index of Multiple Deprivation Median (IQR)	48.02 (25.37-61.94)	51.57 (40.92-60.05)
History of PEPT Yes/no	Yes, n= 37 (60.7%) No, n=24 (39.3%)	Yes, n=29 (63%) No, n=17 (37%)

Table 2.7 Descriptive statistics of patient groups according to orthodontic 'need' and 'no need' for children seen in Salaried Dental Service and had experienced premature extraction of primary teeth (PEPT) (n=66).

	Children with orthodontic 'need' (n=38)	Children with orthodontic 'no need' (n=28)
Number of teeth lost by PEPT Median (IQR)	6.5 (2-9)	4 (1-6)
Teeth lost under Local Anaesthesia v. General Anaesthesia	Local Anaesthesia, n=19 (50%) General Anaesthesia, n=19 (50%)	Local Anaesthesia, n= 18 (35.7%) General Anaesthesia, n=10 (64.3%)
Maxillary v. mandibular tooth	Maxillary tooth, n=117 (53.9%) Mandibular tooth, n=100 (46.1%)	Maxillary tooth, n=58 (48.7%) Mandibular tooth, n=61 (51.3%)
Age at the time of PEPT in months Median (IQR)	79 (67-92)	80 (72-94)
Tooth type lost by PEPT	Anterior, n=49 (22.6%) First primary molar, n=84 (38.7%) Second primary molar, n=84 (38.7%)	Anterior, n=16 (13.4%) First primary molar, n=57 (47.9%) Second primary molar, n=46 (38.7%)

Sixty-six children had a history of premature extraction of primary teeth with 29 children having had extractions under GA and the remainder, 37 children, had their extractions under LA. Extraction modalities, GA was compared to LA by the use of independent sample Mann-Whitney U test to compare the groups in terms of age at the time of PEPT and the number of teeth lost by PEPT. Age at the time of PEPT and the number of teeth lost by PEPT were significantly different in these two groups (p value=0.001). Children who were treated under GA were significantly younger and had suffered more premature extractions. However, there was no difference in terms of which tooth was removed under GA and LA. The Pearson's Chi-Square statistics (χ^2) showed insignificant differences in terms of which arch (maxillary or mandibular) teeth they were extracted from and which specific tooth was lost by PEPT. This is illustrated in Table 2.8.

Table 2.8 Tooth level analysis of premature extractions of primary tooth (PEPT) carried out in Salaried Dental Service (SDS) under General Anaesthesia and Local Anaesthesia on 29 and 37 children respectively.

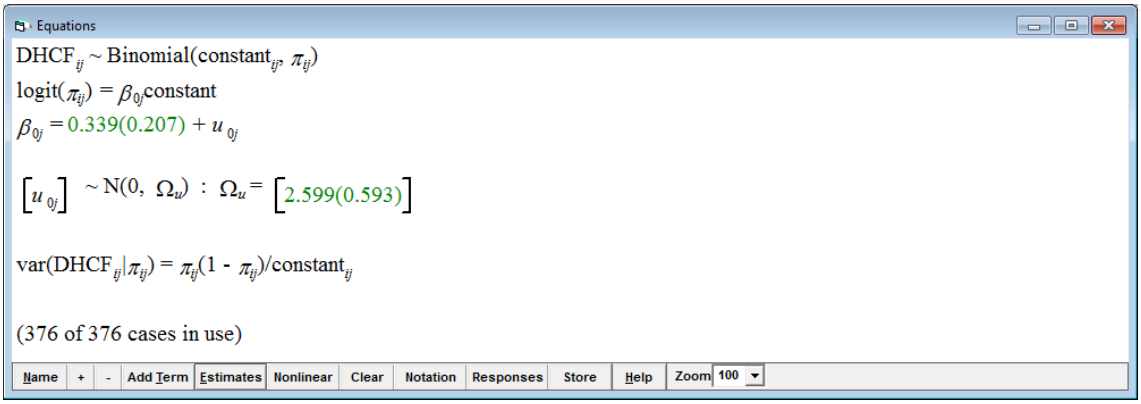
	PEPT under General Anaesthesia (GA)	PEPT under Local Anaesthesia (LA)	*p* value
Age at extraction in months, median (IQR)	75 (66-81)	89 (79.5-103)	0.001**
Number of extractions of teeth Median (IQR)	n=239 8 (7-12)	n=97 2 (1-4)	0.001**
Maxillary or mandibular tooth	Maxillary tooth (n=130, 54.4%) Mandibular tooth (n=109, 45.6%)	Maxillary tooth (n=45, 46.4%) Mandibular tooth (n=52, 53.6%)	0.18
Tooth type	Anterior tooth (n=48, 20.1%) First primary molar (n=97, 40.6%) Second primary molar (n=94, 39.3%)	Anterior tooth (n=17, 17.5%) First primary molar (n=44, 45.4%) Second primary molar (n=36, 37.1%)	0.71

** p<0.001.

2.4.4 Multilevel modelling equation

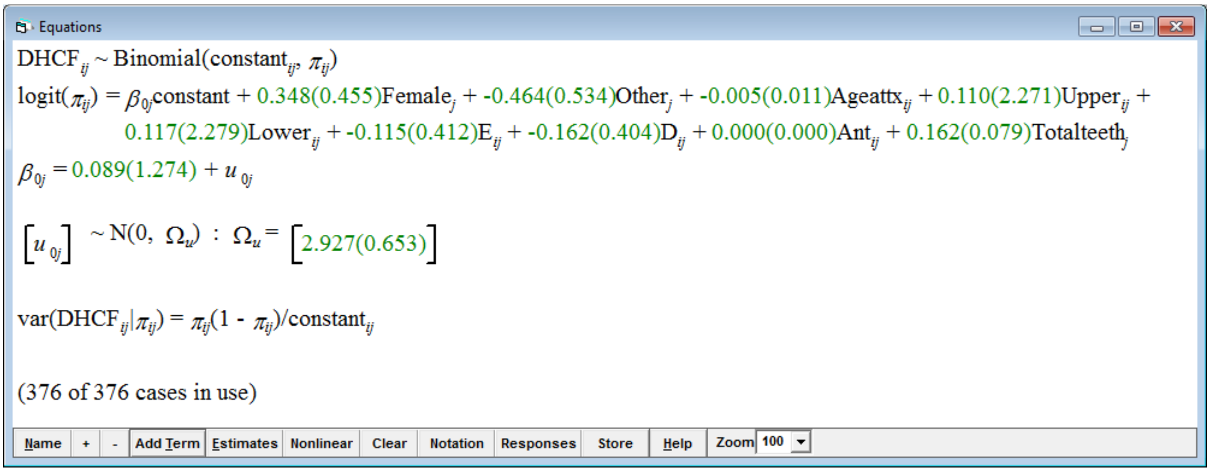
One hundred seven children were seen in the SDS, thus there were 376 cases at lower level (tooth level) among 107 cases at higher level (child level) out of which 41 children did not have history of PEPT. The adjusted results from the multilevel logistic model indicated that, there was significant patient variation (p=0.001) and thus necessitating need for multilevel modelling. Figure 2.5 illustrates the null model with fixed and random effects.

Figure 2.5 Null Model showing estimates for fixed and random part of the model.



The final fitted model displayed an intercept for child level (j) as 0.089 + μ_{oj} where the variation of μ_{oj} was estimated at 2.927 (SE= 0.653). Wald test demonstrated significant variation among individuals as 0.653x 1.96 was higher than 2.927. However, it assumes that the variation parameters were normally distributed (see Figure 2.6).

Figure 2.6 Random intercept model with predictor variables, gender; ethnicity; age at the time of PEPT; whether tooth lost was from maxillary or mandibular arch; the specific tooth type and the total number of teeth lost by PEPT.



The only significant predictor of the chosen outcome variable, the DHC of the IOTN was the total number of teeth as a result of PEPT. Table 2.9 demonstrates all predictor variables included in the final model, their intercept, 95% confidence interval of the odds ratio and the effect size if relevant. Increase in total number of teeth as a result of PEPT led to a significant increase in orthodontic need (odds ratio: 1.18 with 95% confidence interval 1.01-1.37). There was an 18% increase in orthodontic need in the permanent dentition for every primary tooth lost as a result of PEPT. However, this effect was small. Other predictors included in the model such as gender, ethnicity, age at the time of extraction, whether it was a maxillary tooth or mandibular tooth, the specific tooth type were not significantly associated with orthodontic need. Tooth type grouped teeth lost by PEPT into second primary molar, first primary molar and anterior tooth.

Table 2.9 Multilevel random intercept model for 336 teeth lost by PEPT in 66 children to investigate predictor variables to influence orthodontic need in 107 children seen in SDS. The coefficient estimates of variables, their standard error (), odds ratio, 95% confidence interval of the odds ratio () and size of effect are given for the model.

	Variables		Null Model	Random Intercept model with covariates	Odds ratio (95% CI)	Size of effect
Fixed effect			0.35(0.21)	0.09(1.27)		
Child level	Gender (ref Male)	Female v. Male		0.35(0.45)	1.42(0.58 to 3.45)	
	Ethnicity (ref White)	Others v.White		-0.46(0.53)	0.63(0.22 to 1.79)	
	Total teeth lost by PEPT			0.16(0.08)	1.18(1.01 to 1.37)*	18%
Tooth level	Age at PEPT			-0.01(0.01)	.96(0.12 to 8.59)	
	Tooth type (Maxillary or mandibular tooth)	Maxillary v. no extraction		0.11(2.27)	1.12(0.01 to 95.68)	
		Mandibular v. no extraction		0.12(2.28)	1.12(0.01 to 97.89)	
	Tooth type (second primary molar, first primary molar or anterior tooth)	Second primary molar v. no extraction		-0.12(0.41)	.89(0.4 to 1.2)	
		First primary molar v. no extraction		-0.16(0.40)	0.85(0.39 to 1.88)	
		Anterior tooth v. no extraction		0.0(0.0)	1(1 to 1)	
Random effect			2.6(0.59)	2.93(0.66)		

PEPT- Premature Extraction of Primary Teeth; SDS- Salaried Dental Service; * p< 0.05.

2.5 DISCUSSION

2.5.1 Introduction and Principal finding

This study aimed to determine whether there was an increase in orthodontic need in children who had a positive history of PEPT. This dataset is essentially a combination of two different datasets from an oral epidemiological survey and SDS records. As identified in chapter one no previous research had specifically investigated the association of orthodontic need to PEPT. The findings of this study confirmed that PEPT was associated with an increased need for orthodontic treatment in the permanent dentition. The results have confirmed clinical experience of clinicians involved in treating paediatric dental patients. This finding would support current guidelines in Paediatric Dentistry (Fayle et al., 2001, American Academy on Pediatric Dentistry Clinical Affairs Committee-Developing Dentition Subcommittee, 2008-2009, Kandiah et al., 2010) to restore as many primary teeth as were appropriate and feasible.

2.5.2 Strengths of this study

2.5.2.1 Sample selection for the survey

The sampling framework for the national oral epidemiological surveys are well established and follow a specific protocol with well defined inclusion and exclusion criteria (NHS Dental Epidemiology Programme for England, Sep 2008). Survey results are felt to be externally valid and generalisable to population level in the region. Thus, from the use of the survey as a basis of the study sample, it can be assumed that results obtained from this study could be generalisable to the population of Bradford and Airedale.

2.5.2.2 Collection of survey information

Oral epidemiological survey examination was performed according to a specific protocol and the examiners were calibrated accordingly and followed strict diagnostic criteria (Pine et al., 1997, Nugent and Pitts, 1997, Pitts et al., 1997). Dental caries was reported by DMFT but only caries that were clinically seen into dentine were recorded as carious. With regards to orthodontic need, the modified IOTN was used. Specialist orthodontists in specialist practices or hospital settings assess orthodontic need using the full range of the IOTN. This allows clinical assessment of orthodontic need and assesses eligibility of orthodontic treatment under NHS, which safeguards equity to access orthodontic treatment. The DHC and the AC were taken into account for this. For the purpose of oral epidemiological surveys the modified IOTN index was used. This was appropriate as experienced dentists who are non-specialists conduct the oral epidemiological surveys. The modified IOTN has shown high validity with a Cohen's κ score of 0.74 and the average sensitivity and specificity scores were 0.90 and 0.84 respectively (Burden et al., 2001). These scores demonstrate that the modified IOTN is a reliable index to be used by non-specialists.

2.5.2.3 Study setting

Bradford and Airedale district offered a unique population base to study PEPT for various reasons. This region has a greater level of dental caries in the primary dentition with a mean $d_3$mft of 2.42 compared to the national average of 1.11 (NHS Dental Epidemiology Programme for England, Oct 2009). Thus it could be expected that PEPT was more common in this group of patients and this had been demonstrated by three times more missing teeth as compared to the UK national average (NHS Dental Epidemiology Programme for England, Oct 2009).

Another factor that made Bradford and Airedale attractive for study setting was that SDS had been the only provider of dental treatment under GA in the district for the last 20 years. Consequently, if a child had undergone extractions under GA then this was likely to be identified by reviewing their SDS dental record as long as they had accessed SDS services. Furthermore, the 12-year-old survey results for 2008/2009 revealed high orthodontic need in the local population of Bradford and Airedale with a 10% greater prevalence, 41.1% compared to UK national average of 31.6% (NHS Dental

Epidemiology Programme for England, 2011). Approximately two thirds of the extractions for children under the age of 10 years were carried out in SDS.

2.5.2.4 Inclusion and exclusion criterion

There was a clearly documented inclusion and exclusion criterion in this study. All children included in the study had orthodontic need recorded by the use of modified IOTN and had accessed SDS in the past.

The exclusion criteria was that any child who had premature extraction of any permanent tooth. Only a relatively small proportion of children (n=9, 7.8%) were excluded from the study. If included, this would have been a confounding variable that would have affected orthodontic need by having extraction/s of permanent tooth/teeth regardless of history or PEPT. Previous publications reported that extraction of lower first permanent molars led to intra-arch, inter-arch and skeletal problems (Abu Aihaija et al., 2000, Normando and Cavacami, 2010). A retrospective study found that half of the cases of extraction of first permanent molars developed favourable occlusion without orthodontic intervention (Jalevik and Moller, 2007).

2.5.3 Limitations of this study

2.5.3.1 Survey information

Examiners for oral epidemiological surveys were trained to collect information for the survey which included assessment of dental decay and orthodontic need. Survey examiners were trained and calibrated for assessment of dental caries. However, for orthodontic need, they were trained but not calibrated (Yorkshire and Humber Public Health Observatory, November 2012). Thus internal and external validity of orthodontic need assessment could be questioned. This was the first national 12-year-old survey which reported on orthodontic need and demand, thus comparison to previous surveys could not be accessed.

2.5.3.1 Consent for the survey

This was the first survey where positive consent from parents' was required for survey examination of children. This was not a requirement in previously carried out epidemiological surveys of children. Thus, there was potential for response bias in the sample. The overall response rate for England was 66.6% for 5 year old children who were surveyed while previously the response rate of at least 75% was achieved (NHS Dental Epidemiology Programme for England, Oct 2009).

For Bradford and Airedale 12-year-old survey, the response rate was 61%, which was comparable to the England data. NHS Dental Epidemiology Programme is exploring ways to improve response rates, thus in turn attempting to make surveys representative of the population (NHS Dental Epidemiology Programme for England, Oct 2009). There were some discussions whether these two methods of gaining consent compromises the validity of conclusions drawn from surveys and whether children with caries were more likely to opt out of the survey (White et al., 2007, Dyer et al., 2008, Monaghan et al., 2011).

2.5.3.2 Orthodontic need assessment

Orthodontic need was assessed by the use of the modified IOTN. The modified IOTN reported orthodontic need based on the DHC and the AC similar to the IOTN but the modified IOTN was simplified as and had only two outcomes, either need or no need. Under NHS, orthodontic treatment is available for children with the DHC of the IOTN of either 4 or 5 which is defined as increased need for orthodontic treatment. This is the same for assessment of orthodontic need under the modified IOTN. However, under NHS orthodontic treatment is also available for borderline cases where the DHC is 3 with the AC of more than 6 (on a scale of 1 to 10). The modified IOTN reported as orthodontic need when AC was more than 7. Thus, clinically relevant threshold of the IOTN 3.6 (the DHC of 3 with the AC of 6) could not be used in this present study. Such information would have been valuable to ascertain who would qualify for orthodontic treatment under NHS.

2.5.3.3 Sample selection for the study

This study showed that children who accessed SDS were from 'non-white' ethnic background, had higher levels of dental decay (higher DMFT) and were socially deprived (higher IMD). This was in agreement with other studies. Different caries experience based on ethnicity has been well recognised at a regional level (Prendergast et al., 1997, Bradford and Airedale Teaching Primary Care Trust, 2006). Regression analysis in a previously reported study showed a significant relationship between ethnicity and caries experience even after controlling for material deprivation. Asian children showed an increase in caries experience as demonstrated by increased dmft as compared to White children and Afro-Caribbean children (Prendergast et al., 1997). Thus it has to be said that the conclusion from this research can only be restricted to the group of patients who accessed SDS who had higher levels of dental caries and were more deprived and not generalisable to the population of Bradford and Airedale.

There was a significant difference in age at the time of examination of the survey on comparison of the groups as to whether they had accessed SDS in the past or not. But, on analysis it was noted that the difference in median was two months, which can be described as clinically insignificant. Moreover, the survey data was taken from a 12-year-old survey where all sampled children were aged 12 years.

2.5.3.4 Retrospective study

Although orthodontic need was assessed as part of the oral epidemiological survey, the study data was also based on SDS dental records. As SDS information collected for each child was based on retrospective information, there were a number of biases introduced in the study. The study relied on accuracy of dental records written by the operating clinician that formed part of patient's dental records. The study also relied on such information being available when requested especially if the dental records were archived. Names of the study children were checked on SDS databases of archived notes. It is the policy of SDS to archive dental records if a course of treatment has been inactive for three years. Computerised electronic records started in SDS only since early 2003. When considering 12-year-old children who were surveyed (date of birth

1996/1997), if only electronic dental records were looked at a large portion of the children who were included in the study group could have been missed.

If any name included in the survey matched SDS dental records either electronically or from archiving databases, then it confirmed that the child was seen in SDS. If their name was held in archiving databases held by SDS, then paper notes were retrieved from archiving. Of the paper notes recovered, it was impossible to be absolutely sure that there were no additional episodes of extractions carried out within or outside SDS.

It was assumed that subjects who were seen in SDS were seen exclusively in SDS and did not access dental care outside of SDS. But this was unlikely to be true for all subjects and the same child could have accessed services from GDP and SDS. As SDS is a primary care setting with secondary specialist care facilities, GDP might have extracted some teeth and referred for more extractions, either under LA, CS or GA. Unless further information was to be collected for each child from Dental Services, NHS Business Services Authority (previously Dental Practice Board), it would not be possible to say which child had undergone extractions in SDS as well as with GDP. Moreover some children could have accessed urgent services from a local hospital under care of maxillofacial unit and had undergone extractions.

2.5.3.5 Relatively small study

When considering the history of PEPT among children seen in SDS (n=107), it must be noted that 66 children had a positive history of PEPT. This study had a relatively small sample size and the results had to be interpreted cautiously. Due to the limited sample size, it was not possible to divide PEPT based on different tooth types (eg primary canine, first primary molar or second primary molar) and perform subgroup analysis with this information.

It was not possible to carry out a power calculation as SDS records were collected retrospectively. However this study gives a valuable lead to future research looking at PEPT and orthodontic need.

2.5.4 Statistical analysis

It was recognised that within the sample of this study children had undergone multiple extractions either at the same time point or at different time points. It was also known that teeth removed from the same child were not independent from each other. This was a result of nesting of teeth within an individual. The statistical methodology used in the study was appropriate as it accounted for clustering of the data within individuals. The multilevel modelling approach accounted for the dependence of multiple data from the same child. Ignoring this dependence would result in an underestimation of standard errors and increased false positives for subgroup analysis (Rabash et al., 2009).

Predictor variables used were based on clinical knowledge. However, the predictors included in the model unfortunately did not explain much about individual variation. Important predictors of the outcome such as time lag between PEPT and eruption of permanent teeth and also orthodontic parameters at the time of extraction such as skeletal base, centrelines, molar relationship and crowding were unavailable. As these predictors were unavailable, they were excluded from the model.

This study was an exploratory study with no priori hypothesis. Therefore there was no priori sample size calculation for subgroup analysis and this could have led to important predictors not reaching statistical significance due to lack of power. However we followed Peduzzi's recommendation of 10 events per predictor during model building (Peduzzi et al., 1996).

2.5.5 Clinical implications

The findings of this study confirmed clinical experience and clinical guidelines that PEPT was associated with an increased need for orthodontic treatment in the permanent dentition. The only predictor to show a significant positive association with orthodontic need was the total number of primary teeth extracted. Restoring primary teeth can be achieved using techniques and materials with a proven track record of longevity.

Sometimes the use inhalation sedation and LA and the provision of comprehensive dental care under GA is necessary. In certain cases where conventional treatments are not feasible other methods such as the placement of preformed metal crowns using the Hall Technique could be considered (Innes et al., 2011). Each of these procedures will take precious clinical time from trained clinicians. They also incur costs in terms of time of parents or guardians and children themselves as well as financial costs to healthcare providers like NHS. These factors should be offset against potential costs associated with orthodontic treatment for children in the future.

Prevention of orthodontic need and malocclusion is likely to have greater universal benefits to a population due to inequitable access to orthodontic care from children with a more deprived background despite their similar or greater impacts to their quality of life (Mandall et al., 2000, Morris and Landes, 2006, Drugan et al., 2007, Locker, 2007). This difference in uptake for orthodontic treatment could be as a result of regularity of dental visits, access to general dental services within a population and orthodontic treatment cost although there are specified pre-defined criteria for assessing orthodontic treatment under NHS. Masood *et al* (2013) found that malocclusion had a significantly negative impact on oral health related quality of life in young people .The DHC of IOTN scores of participants were highly correlated to oral health related quality of life. Participants with higher IOTN scores reported greater psychological discomfort and functional limitation (Masood et al., 2013).

Analysis of the number of teeth extracted under local or general anaesthesia confirmed clinical experience that treatment under GA was more frequently prescribed for younger children with significant dental disease in multiple quadrants. The number of teeth extracted under GA was higher than previously reported for exodontia under GA (Holt et al., 1999, Albadri et al., 2006). The odds ratio calculated from the multilevel model, extrapolated an 18% increase in subsequent need for orthodontic treatment for every primary tooth extracted. Thus limiting the number of premature extractions of primary teeth would be beneficial and would appear to reduce subsequent orthodontic need in the permanent dentition. Clinicians involved in providing dental care for children with caries should aim to limit the number of extractions of primary teeth where practicable and feasible.

2.5.6 Future Research directions

On the basis of this study it appears that PEPT leads to an increase in orthodontic need. Current literature provides insufficient orthodontic effects of PEPT. Therefore further research is needed to provide stronger evidence on the orthodontic effects of PEPT. As discussed in chapter one, the ideal study design to explore the impact of PEPT and subsequent orthodontic need would be a RCT with follow-up until completion of the full permanent dentition or a long-term prospective cohort study following children from primary dentition to full permanent dentition. Long follow-up periods of approximately 10 years make these methodologies difficult with increased chance of attrition bias in the study. For example, a follow-up cohort study of children receiving dental care under GA showed less than 10% attending clinical appointment at three months following treatment (Jamjoom et al., 2001). Innovative methodologies to maintain the cohort would be needed to ensure results are valid and generalisable to the study population.

A larger sample size would be useful to observe interactions between many of the predictor variables used in this study. A future study with a larger sample size with adequate power would be beneficial and may contribute to identifying further significant relationships that may have been lost due to a type II error in this study. From the proportion of maxillary and mandibular teeth lost by PEPT on children with orthodontic need (refer to Table 2.7) sample size would be 637 maxillary teeth and 637 mandibular teeth. This figure assumes a significance level of 0.05 and power of 80%. However consideration must be given for participant withdrawal and loss to follow-up.

2.6 CONCLUSIONS

This study is the first in the United Kingdom to assess the impact of extractions in the primary dentition and its effect on orthodontic need in the permanent dentition. The results of this study have given a very important insight in this topic. It can be concluded that:

1. Children seen in SDS were significantly different in terms of the level of dental caries, deprivation and ethnicity. These children had higher levels of dental caries, were more deprived and were more likely to be from ethnic minorities.
2. Gender and ethnicity of the children who suffered PEPT was not significantly associated with increased orthodontic need.
3. The timing of extraction of primary teeth, the position of the teeth in dental arch (maxillary or mandibular) and the tooth type (anterior, first primary molar, second primary molar) were not significantly associated with increased orthodontic need.
4. The total number of teeth lost as a result of premature extraction was significantly associated with increased orthodontic need.
5. Each prematurely extracted primary tooth led to an 18% increase in orthodontic need in the permanent dentition.
6. This is a novel study linking much needed clarification on the important issue of PEPT and orthodontic need in a paediatric population.

2.7 REFERENCES

ABU AIHAIJA, E. S., MCSHENY, P. F. & RICHARDSON, A. 2000. A cephalometric study of the effect of extraction of lower first permanent molars. *J Clin Pediatr Dent,* 24**,** 195-8.

ACS, G., SHULMAN, R. & NG, M. W. 1999. The effect of dental rehabilitation on the body weight of children with early childhood caries. *Pediatr Dent,* 21**,** 109-13.

ALBADRI, S., LEE, S., LEE, G., LLEWELYN, R., BLINKHORN, A. & MACKIE, I. 2006. The use of general anaesthesia for the extraction of children's teeth. Results from two UK dental hospitals. *Eur Arch Paediatr Dent,* 7**,** 110-5.

ALMEIDA, M. A., PHILLIPS, C., KULA, K. & TULLOCH, C. 1995. Stability of the palatal rugae as landmarks for analysis of dental casts. *Angle Orthod,* 65**,** 43-8.

AMERICAN ACADEMY ON PEDIATRIC DENTISTRY CLINICAL AFFAIRS COMMITTEE-DEVELOPING DENTITION SUBCOMMITTEE 2008-2009. Guideline on management of the developing dentition and occlusion in pediatric dentistry. *Pediatr Dent,* 30 (7 Suppl)**,** 184-195.

ASSOCIATION OF PAEDIATRIC ANAESTHETISTS OF GREAT BRITAIN AND IRELAND. 2011. *Guidelines for the mangement of children referred for dental extractions under general anaesthesia* [Online]. Association of Paediatric Anaesthetists of Great Britain and Ireland, 21 Portalnd Place, London W1B 1PY: Association of Paediatric Anaesthetists of Great Britain and Ireland, 21 Portalnd Place, London W1B 1PY. Available: http://www.rcoa.ac.uk/document-store/guidelines-the-management-of-children-referred-dental-extractions-under-general.

BAUME, L. J. 1950. Physiological tooth migration and its significance for the development of occlusion. I. The biogenetic course of the deciduous dentition. *J Dent Res,* 29**,** 123-32.

BEGLIN, F. M., FIRESTONE, A. R., VIG, K. W., BECK, F. M., KUTHY, R. A. & WADE, D. 2001. A comparison of the reliability and validity of 3 occlusal indexes of orthodontic treatment need. *Am J Orthod Dentofacial Orthop,* 120**,** 240-6.

BJORK, A. 1964. A method for epidemiological registration of malocclusion. *Acta Odontol Scand,* 22**,** 27-44.

BRADFORD AND AIREDALE TEACHING PRIMARY CARE TRUST 2006. The oral health of 5 year old children living in Bradford and Airedale tPCT. Bradford and Airedale Teaching Primary Care Trust.

BRADFORD AND AIREDALE TEACHING PRIMARY CARE TRUST 2007. Choosing Better Oral Health. Bradford and Airedale Oral Health Strategy and Action Plan (2007- 2010).

BRANDHORST, O. 1932. Promoting normal development by maintaining the function of the deciduous teeth. *Am Dent A J,* 19**,** 1196-1203.

BRAUER, J. 1941. A report of 113 early or premature extractions of primary molars and the incidence of closure of space. *Journal of Dentistry for Children,* 8**,** 222-224.

BREAKSPEAR, E. K. 1951. Sequelae of early loss of deciduous molars. *Dent Rec (London),* 71**,** 127-34.

BREAKSPEAR, E. K. 1961. Further observations on early loss of decicuous molars. *Dent. Pract. Dent. Rec. ,* 11**,** 233-52.

BRITISH ORTHODONTIC SOCIETY. *What is IOTN?* [Online]. British Orthodontic Society. Available: http://www.bos.org.uk/orthodonticsandyou/orthodonticsandthenhs/whatisiotn [Accessed 16/12/2010.

BRITISH ORTHODONTIC SOCIETY 2009. The Justification for Orthodontic Treatment. *British Orthodontic Society, 12 Bridewell Place London EC4V 6AP.* British Orthodontic Society, 12 Bridewell Place London EC4V 6AP.

BROOK, P. H. & SHAW, W. C. 1989. The development of an index of orthodontic treatment priority. *Eur J Orthod,* 11**,** 309-20.

BROTHWELL, D. J. 1997. Guidelines on the use of space maintainers following premature loss of primary teeth. *J Can Dent Assoc,* 63**,** 753, 757-60, 764-6.

BURDEN, D. J., PINE, C. M. & BURNSIDE, G. 2001. Modified IOTN: an orthodontic treatment need index for use in oral health surveys. *Community Dent Oral Epidemiol,* 29**,** 220-5.

CENTRE FOR REVIEWS AND DISSEMINATION Jan 2009. *Systematic Reviews, CRD's guidance for undertaking reviews in health care,* York, CRD, University of York.

CHADWICK, B. 2002. Non-pharmacological behaviour management. Royal college of surgeons of England.

CLINCH, L. M. & HEALY, M. J. R. 1959. A longitudinal study of the results of premature extraction of deciduous teeth between 3-4 and 13-14 years of age. *Dent Practit,* 9**,** 109-127.

CONS, N. C., JENNY, J., KOHOUT, F. J., SONGPAISAN, Y. & JOTIKASTIRA, D. 1989. Utility of the dental aesthetic index in industrialized and developing countries. *J Public Health Dent,* 49**,** 163-6.

COOPER, S., MANDALL, N. A., DIBIASE, D. & SHAW, W. C. 2000. The reliability of the Index of Orthodontic Treatment Need over time. *J Orthod,* 27**,** 47-53.

DANIELS, C. & RICHMOND, S. 2000. The development of the index of complexity, outcome and need (ICON). *J Orthod,* 27**,** 149-62.

DAVIES, C., HARRISON, M. & ROBERTS, G. 2008. *Guidelines for the use of General Anaesthesia in Paediatric Dentistry* [Online]. Royal College of Surgeons of England. Available: http://www.rcseng.ac.uk/fds/publications-clinical-guidelines/clinical_guidelines/documents/Guideline for the use of GA in Paediatric Dentistry May 2008 Final.pdf.

DAY, S. J. & ALTMAN, D. G. 2000. Statistics notes: blinding in clinical trials and other studies. *BMJ,* 321**,** 504.

DE BOER, M. 1982. Early loss of primary molars. *Nederlands Tijdschrift voor Tandheelkunde,* 89**,** 8-28.

DE OILVEIRA, C. M., SHEIHAM, A., TSAKOS, G. & O'BRIEN, K. D. 2008. Oral health-related quality of life and the IOTN index as predictors of children's perceived needs and acceptance for orthodontic treatment. *Br Dent J. ,* 12**,** 1-5.

DRUGAN, C. S., HAMILTON, S., NAQVI, H. & BOYLES, J. R. 2007. Inequality in uptake of orthodontic services. *Br Dent J,* 202**,** E15; discussion 326-7.

DUGONI, S. A., CHEE, S. O. & HARNICK, D. J. 1992. Mixed-dentition treatment. *American Journal of Orthodontics & Dentofacial Orthopedics,* 101**,** 501-8.

DURWARD, C. S. 2000. Space maintenance in the primary and mixed dentition. *Annals of the Royal Australasian College of Dental Surgeons,* 15**,** 203-5.

DYER, T. A., MARSHMAN, Z., MERRICK, D., WYBORN, C. & GODSON, J. H. 2008. School-based epidemiological surveys and the impact of positive consent requirements. *Br Dent J,* 205**,** 589-92.

EHRLICH, J. & GAZIT, E. 1975. Relationship of the maxillary central incisors and canines to the incisive papilla. *J Oral Rehabil,* 2**,** 309-12.

EL-MANGOURY, N. H. & MOSTAFA, Y. A. 1990. Epidemiologic panorama of dental occlusion. *Angle Orthod,* 60**,** 207-14.

FATHIAN, M., KENNEDY, D. B. & NOURI, M. R. 2007. Laboratory-made space maintainers: a 7-year retrospective study from private pediatric dental practice. *Pediatr Dent,* 29**,** 500-6.

FAYLE, S. A., WELBURY, R. R. & ROBERTS, J. F. 2001. British Society of Paediatric Dentistry: a policy document on management of caries in the primary dentition. *Int J Paediatr Dent,* 11**,** 153-157.

HAMDAN, A. M. 2004. The relationship between patient, parent and clinician perceived need and normative orthodontic treatment need. *Eur J Orthod,* 26**,** 265-71.

HIGGINS, J. P. T. & GREEN, S. 2011. *Cochrane Handbook for Systematic Reviews of Interventions*, The Cochrane Collaboration.

HOFFDING, J. & KISLING, E. 1978a. Premature loss of primary teeth: part I, its overall effect on occlusion and space in the permanent dentition. *Journal of Dentistry for Children,* 45**,** 279-83.

HOFFDING, J. & KISLING, E. 1978b. Premature loss of primary teeth: part II, the specific effects on occlusion and space in the permanent dentition. *Journal of Dentistry for Children,* 45**,** 284-7.

HOLT, R. D., AL LAMKI, S., BEDI, R., DOWEY, J. A. & GILTHORPE, M. 1999. Provision of dental general anaesthesia for extractions in child patients at two centres. *Br Dent J,* 187**,** 498-501.

HOSEY, M. T. 2002. UK National Clinical Guidelines in Paediatric Dentistry. Managing anxious children: the use of conscious sedation in paediatric dentistry. *Int J Paediatr Dent,* 12**,** 359-72.

INNES, N. P., EVANS, D. J. & STIRRUPS, D. R. 2011. Sealing caries in primary molars: randomized control trial, 5-year results. *J Dent Res,* 90**,** 1405-10.

JALEVIK, B. & MOLLER, M. 2007. Evaluation of spontaneous space closure and development of permanent dentition after extraction of hypomineralized permanent first molars. *Int J Paediatr Dent,* 17**,** 328-35.

JAMJOOM, M. M., AL-MALIK, M. I., HOLT, R. D. & EL-NASSRY, A. 2001. Dental treatment under general anaesthesia at a hospital in Jeddah, Saudi Arabia. *Int J Paediatr Dent,* 11**,** 110-6.

KANDIAH, T., JOHNSON, J. & FAYLE, S. A. 2010. British Society of Paediatric Dentistry: a policy document on management of caries in the primary dentition. *Int J Paediatr Dent,* 20 Suppl 1**,** 5.

KAU, C. H., DURNING, P., RICHMOND, S., MIOTTI, F. A. & HARZER, W. 2004. Extractions as a form of interception in the developing dentition: a randomized controlled trial. *Journal of Orthodontics,* 31**,** 107-14.

KISLING, E. & HOFFDING, J. 1979. Premature loss of primary teeth: Part V, treatment planning with due respect to the significance of drifting patterns. *Journal of Dentistry for Children,* 46**,** 300-6.

KRONFELD, S. M. 1953. The effects of premature loss of primary teeth and sequence of eruption of permanent teeth on malocclusion. *Journal of Dentistry for Children,* 31**,** 302-313.

LEIGHTON, B. C. 1981. Longitudinal study of features which might influence space loss after early extraction of lower deciduous molars. *Proceedings of the Finnish Dental Society,* 77**,** 95-103.

LIN, Y. T. & CHANG, L. C. 1998. Space changes after premature loss of the mandibular primary first molar: a longitudinal study. *J Clin Pediatr Dent,* 22**,** 311-6.

LIN, Y. T., LIN, W. H. & LIN, Y. T. 2007. Immediate and six-month space changes after premature loss of a primary maxillary first molar. *J Am Dent Assoc,* 138**,** 362-8.

LIN, Y. T., LIN, W. H. & LIN, Y. T. J. 2011. Twelve-month space changes after premature loss of a primary maxillary first molar. *Int J Paediatr Dent,* 21**,** 161-6.

LINDER-ARONSON, S. 1960. The effect of premature loss of deciduous teeth. A Biometric study in 14 and 15 year olds. *Acta Odontologica Scandinavica,* 18**,** 101-122.

LOCKER, D. 2007. Disparities in oral health-related quality of life in a population of Canadian children. *Community Dent Oral Epidemiol,* 35**,** 348-56.

LUNDSTRUM, A. 1955. The significance of early loss of deciduous teeth in the etiology of malocclusion. *American Journal of Orthodontics & Dentofacial Orthopedics,* 41**,** 819-826.

LYONS, D. 1924. The importance of the early recongnition of dental disorders in children. *Dent Cosmos,* 66**,** 535-538.

MACENA, M. C., TORNISIELLO KATZ, C. R., HEIMER, M. V., DE OLIVEIRA E SILVA, J. F. & COSTA, L. B. 2011. Space changes after premature loss of deciduous molars among Brazilian children. *Am J Orthod Dentofacial Orthop,* 140**,** 771-8.

MAGNUSSON, T. E. 1979. The effect of premature loss of deciduous teeth on the spacing of the permanent dentition. *European Journal of Orthodontics,* 1**,** 243-9.

MAJEWSKI, R., SYNDER, C. W. & BERNAT, J. E. 1988. Dental emergencies presenting to a children’s hospital. *Journal of Dentistry for Children,* 55**,** 339-342.

MANDALL, N. A., MCCORD, J. F., BLINKHORN, A. S., WORTHINGTON, H. V. & O'BRIEN, K. D. 2000. Perceived aesthetic impact of malocclusion and oral self-perceptions in 14-15-year-old Asian and Caucasian children in greater Manchester. *Eur J Orthod,* 22**,** 175-83.

MASOOD, Y., MASOOD, M., ZAINUL, N. N., ARABY, N. B., HUSSAIN, S. F. & NEWTON, T. 2013. Impact of malocclusion on oral health related quality of life in young people. *Health Qual Life Outcomes,* 11**,** 25.

MELSEN, B. & TERP, S. 1982. The influence of extractions caries causa on the developmet of malocclusion and need for orthodontic treatment. *Swed Dent J Supplement,* 15**,** 163-169.

MITCHELL, L. 2007. *The aetiology and classification of malocclusion,* New York: Oxford University Press, Oxford University Press Inc.

MIYAMOTO, W., CHUNG, C. S. & YEE, P. K. 1976. Effect of premature loss of deciduous canines and molars on malocclusion of the permanent dentition. *Journal of Dental Research,* 55**,** 584-90.

MOHER, D., HOPEWELL, S., SCHULZ, K. F., MONTORI, V., GOTZSCHE, P. C., DEVEREAUX, P. J., ELBOURNE, D., EGGER, M. & ALTMAN, D. G. 2010. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ,* 340**,** c869.

MOLES, D. R. & ASHLEY, P. 2009. Hospital admissions for dental care in children: England 1997-2006. *Br Dent J,* 206**,** E14; discussion 378-9.

MONAGHAN, N. P., JONES, S. J. & MORGAN, M. Z. 2011. Do parents of children with caries choose to opt out of positive consent dental surveys in Wales? *Br Dent J,* 210**,** E1.

MOORE, T. R. & KENNEDY, D. B. 2006. Bilateral space maintainers: a 7-year retrospective study from private practice. *Pediatr Dent,* 28**,** 499-505.

MOORREES, C. F. & CHADHA, J. M. 1965. Available Space for the Incisors during Dental Development--a Growth Study Based on Physiologic Age. *Angle Orthod,* 35**,** 12-22.

MORRIS, E. & LANDES, D. 2006. The equity of access to orthodontic dental care for children in the North East of England. *Public Health,* 120**,** 359-63.

MORRISON, A., J., P., HUSEREAU, D., MOULTON, K., CLARK, M., FIANDER, M., MIERZWINSKI-URBAN, M., CLIFFORD, T., HUTTON, B. & RABB, D. 2012. The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. *Int J Technol Assess Health Care,* 28**,** 138-44.

NANCE, H. N. 1947. The limitations of orthodontic treatment; mixed dentition diagnosis and treatment. *Am J Orthod,* 33**,** 177-223.

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE 2010. Sedation in children and young people. National Institute for Heath and Clinical Excellence, MidCity Place, 71 High Holborn, London, WC1V 6NA: National Institute for Heath and Clinical Excellence.

NGAN, P., ALKIRE, R. G. & FIELDS, H., JR. 1999. Management of space problems in the primary and mixed dentitions. *Journal of the American Dental Association,* 130**,** 1330-9.

NHS DENTAL EPIDEMIOLOGY PROGRAMME FOR ENGLAND. 2011. *Primary Care Trust and Strategic Health Authority Orthodontic Results Tables and Summary (Revised 27.04.2011)* [Online]. Available: http://www.nwph.net/dentalhealth/survey-results-12.aspx [Accessed 10/08/2011.

NHS DENTAL EPIDEMIOLOGY PROGRAMME FOR ENGLAND. Oct 2009. *Oral Health Surveys of 5 year old children 2007/2008* [Online]. Available: http://www.nwph.net/dentalhealth/reports/NHS_DEP_for_England_OH_Survey_5yr_2007-08_Report.pdf.

NHS DENTAL EPIDEMIOLOGY PROGRAMME FOR ENGLAND Sep 2008. Oral Health Survey of 12 year old Children in England, 2008/2009, National Protocol.

NÍ CHAOLLAÍ, A., ROBERTSON, S., DYER, T., BALMER, R. & FAYLE, S. 2010. An evaluation of paediatric dental general anaesthesia in Yorkshire and the Humber. *Br Dent J,* 209**,** 1-6.

NORMANDO, D. & CAVACAMI, C. 2010. The influence of bilateral lower first permanent molar loss on dentofacial morphology- a cehalometric study. *Dental Press J Orthdo,* 15 100-6.

NORTHWAY, W. M. 2000. The not-so-harmless maxillary primary first molar extraction.[Erratum appears in J Am Dent Assoc 2001 Feb;132(2):154]. *Journal of the American Dental Association,* 131**,** 1711-20.

NORTHWAY, W. M., WAINRIGHT, R. L. & DEMIRJIAN, A. 1984. Effects of premature loss of deciduous molars. *Angle Orthodontist,* 54**,** 295-329.

NORTHWAY, W. M. & WAINRIGHT, R. W. 1980. D E space--a realistic measure of changes in arch morphology: space loss due to unattended caries. *J Dent Res,* 59**,** 1577-80.

NUGENT, Z. J. & PITTS, N. B. 1997. Patterns of change and results overview 1985/6-1995/6 from the British Association for the Study of Community Dentistry (BASCD) coordinated National Health Service surveys of caries prevalence. *Community Dent Health,* 14 Suppl 1**,** 30-54.

NUTTALL, N. M., STEELE, J. G., EVANS, D., CHADWICK, B., MORRIS, A. J. & HILL, K. 2006. The reported impact of oral condition on children in the United Kingdom, 2003. *Br Dent J,* 200**,** 551-5.

O'BRIEN, K., WRIGHT, J. L., CONBOY, F., MACFARLANE, T. & MANDALL, N. 2006. The child perception questionnaire is valid for malocclusions in the United Kingdom. *Am J Orthod Dentofacial Orthop,* 129**,** 536-40.

OWEN, D. G. 1971. The incidence and nature of space closure following the premature extraction of deciduous teeth: a literature study. *Am J Orthod,* 59**,** 37-49.

PADMA KUMARI, B. & RETNAKUMARI, N. 2006. Loss of space and changes in the dental arch after premature loss of the lower primary molar: a longitudinal study. *Journal of the Indian Society of Pedodontics & Preventive Dentistry,* 24**,** 90-6.

PARK, K., JUNG, D.-W. & KIM, J.-Y. 2009. Three-dimensional space changes after premature loss of a maxillary primary first molar. *International Journal of Paediatric Dentistry,* 19**,** 383-9.

PEDERSEN, J., STENSGAARD, K. & MELSEN, B. 1978. Prevalence of malocclusion in relation to premature loss of primary teeth. *Community Dentistry & Oral Epidemiology,* 6**,** 204-9.

PEDUZZI, P., CONCATO, J., KEMPER, E., HOLFORD, T. R. & FEINSTEIN, A. R. 1996. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol,* 49**,** 1373-9.

PINE, C. M., HARRIS, R. V., BURNSIDE, G. & MERRETT, M. C. 2006. An investigation of the relationship between untreated decayed teeth and dental sepsis in 5-year-old children. *Br Dent J,* 200**,** 45-7; discussion 29.

PINE, C. M., PITTS, N. B. & NUGENT, Z. J. 1997. British Association for the Study of Community Dentistry (BASCD) guidance on the statistical aspects of training and calibration of examiners for surveys of child dental health. A BASCD coordinated dental epidemiology programme quality standard. *Community Dent Health,* 14 Suppl 1**,** 18-29.

PITTS, N. B., BOYLES, J., NUGENT, Z. J., THOMAS, N. & PINE, C. M. 2007. The dental caries experience of 5-year-old children in Great Britain (2005/6). Surveys co-ordinated by the British Association for the study of community dentistry. *Community Dent Health,* 24**,** 59-63.

PITTS, N. B., EVANS, D. J. & PINE, C. M. 1997. British Association for the Study of Community Dentistry (BASCD) diagnostic criteria for caries prevalence surveys-1996/97. *Community Dent Health,* 14 Suppl 1**,** 6-9.

PRENDERGAST, M. J., BEAL, J. F. & WILLIAMS, S. A. 1997. The relationship between deprivation, ethnicity and dental health in 5-year-old children in Leeds, UK. *Community Dent Health,* 14**,** 18-21.

PROFFIT, W. R., FIELDS, H. W. & SARVER, D. M. 2007a. Early stages of development. *Contemporary Orthodontics.* 4th ed.: St. Louis, Missouri, Mosby.

PROFFIT, W. R., FIELDS, H. W. & SARVER, D. M. 2007b. Malocclusion and dentofacial deformity in contemporary society. *Contemporary Orthodontics.* 4th ed.: St. Louis, Missouri, Mosby.

QUDEIMAT, M. A. & FAYLE, S. A. 1998. The longevity of space maintainers: a retrospective study. *Pediatr Dent,* 20**,** 267-72.

RABASH, J., STEELE, F., BROWNE, W. & GOLDSTEIN, H. 2009. A user's guide to MLwiN. Centre for multilevel modelling, University of Bristol.

RAO, A. K. & SARKAR, S. 1999. Changes in the arch length following premature loss of deciduous molars. *J Indian Soc Pedod Prev Dent,* 17**,** 29-32.

RICHARDSON, M. E. 1965. The relationship between the relative amount of space present in the deciduous dental arch and the rate and degree of space closure subsequent to the extraction of a deciduous molar. *Dent Pract Dent Rec,* 16**,** 111-8.

ROCK, W. P. 2002. UK National Clinical Guidelines in Paediatric Dentistry. Extraction of primary teeth -- balance and compensation. *International Journal of Paediatric Dentistry,* 12**,** 151-3.

RONNERMAN, A. 1965. Early extraction of deciduous molars and canines--its incidence and influence on spacing. *Rep Congr Eur Orthod Soc,* 41**,** 153-68.

RONNERMAN, A. 1977. The effect of early loss of primary molars on tooth eruption and space conditions. A longitudinal study. *Acta Odontol Scand,* 35**,** 229-39.

RONNERMAN, A. & THILANDER, B. 1977. A longitudinal study on the effect of unilateral extraction of primary molars. *Scand J Dent Res,* 85**,** 362-72.

RONNERMAN, A. & THILANDER, B. 1978. Facial and dental arch morphology in children with and without early loss of deciduous molars. *American Journal of Orthodontics,* 73**,** 47-58.

ROSENZWIG, K. A. & KLEIN, H. 1960. Loss of space by extraction of primary molars. *J Dent Child,* 17**,** 275-276.

SASA, I. S., HASAN, A. A. & QUDEIMAT, M. A. 2009. Longevity of band and loop space maintainers using glass ionomer cement: a prospective study. *Eur Arch Paediatr Dent,* 10**,** 6-10.

SAYIN, M. O. & TURKKAHRAMAN, H. 2006. Effects of lower primary canine extraction on the mandibular dentition. *Angle Orthodontist,* 76**,** 31-5.

SCHACHTER, H. 1943. The incidence and effect of premature extraction of deciduous teeth. *Br Dental J,* 75**,** 57-61.

SCHULZ, K. F., CHALMERS, I., HAYES, R. J. & ALTMAN, D. G. 1995. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA,* 273**,** 408-12.

SCOTTISH DENTAL CLINICAL EFFECTIVENESS PROGRAMME April 2010. Prevention and mangement of dental caries in children. Dundee Dental Education Centre, Frankland Building, Small's Wynd, Dundee DD1 4HN.

SEIPEL, C. M. 1949. Prevention of malocclusion. *Dent Rec (London),* 69**,** 224-32.

SEWARD, F. S. 1965. Natural Closure of Deciduous Molar Extraction Spaces. *Angle Orthod,* 35**,** 85-94.

SHEIHAM, A. 2006. Dental caries affects body weight, growth and quality of life in pre-school children. *Br Dent J,* 201**,** 625-626.

THE DENTAL OBSERVATORY June 2010. NHS Dental Epidemiology Programme for England. The Dental Observatory.

TSAKOS, G. 2008. Combining normative and psychosocial perceptions for assessing orthodontic treatment needs. *J Dent Educ,* 72**,** 876-85.

TULUNOGLU, O., ULUSU, T. & GENC, Y. 2005. An evaluation of survival of space maintainers: a six-year follow-up study. *J Contemp Dent Pract,* 6**,** 74-84.

TUNISON, W., FLORES-MIR, C., ELBADRAWY, H., NASSAR, U. & EL-BIALY, T. 2008. Dental arch space changes following premature loss of primary first molars: a systematic review. *Pediatric Dentistry,* 30**,** 297-302.

US NATIONAL LIBRARY OF MEDICINE. 2013. http://www.nlm.nih.gov/pubs/factsheets/dif_med_pub.html [Online].

VENKAIAH, V., PRASAD, A. R. & RAJENDRAN, V. C. 1974. A study of the space closure following premature extraction of primary first molar. *J Indian Dent Assoc,* 46**,** 305-11.

VON ELM, E., ALTMAN, D. G., EGGER, M., POCOCK, S. J., GOTZSCHE, P. C. & VANDENBROUCKE, J. P. 2007. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Bull World Health Organ,* 85**,** 867-72.

WHITE, D. A., MORRIS, A. J., HILL, K. B. & BRADNOCK, G. 2007. Consent and school-based surveys. *Br Dent J,* 202**,** 715-7.

WILLET, R. 1933. Premature loss of deciduous teeth. *Angle Orthod,* 3**,** 106-111.

WORLD HEALTH ORGANIZATION. April 2012. *Oral health; WHO Fact sheet no 308* [Online]. Available: http://www.who.int/mediacentre/factsheets/fs318/en/.

YORKSHIRE AND HUMBER PUBLIC HEALTH OBSERVATORY November 2012. Orthdontic assessment of 12-year-olds in Yorkshire and the Humber, 2008/09.

List of Appendices

Appendix I. Systematic review protocol used for registration with international prospective register of systematic reviews (PROSPERO).

Premature extraction of primary teeth and subsequent malocclusion and orthodontic need: a systematic review

Review question(s)

- To establish if orthodontic need increases following premature extraction of primary teeth

Secondary aim

- To examine the effect of premature extraction of primary teeth and loss of space in the primary and mixed dentition
- To explore the effect of space loss in the primary or mixed dentition and the subsequent malocclusion and orthodontic 'need' in the permanent dentition

Null hypothesis

- Orthodontic need remains unchanged following premature extraction of primary teeth

Search strategy

Databases to be searched are MEDLINE via OVID, EMBASE via OVID, PubMed and the Cochrane Library. The language of publication is restricted to English. Any study published before the date of the search will be included. The searches will be re-run just before final analyses and further studies included if appropriate.

Unpublished literature will be electronically searched on ClinicalTrials.gov (www.clinicaltrials.gov) and the National Research Register (www.controlled-trials.com). References of included studies and 'near misses' will be checked to identify other publications. Authors will be contacted to clarify the findings of their study where necessary.

Search terms using keywords in title and abstract:

i) Child; young person; adolescent

ii) Tooth loss; tooth extraction; teeth extraction; premature extraction; premature loss; exodontia

iv) Deciduous tooth; deciduous teeth; deciduous dentition; primary tooth; primary teeth; primary dentition; baby tooth; baby teeth; mixed dentition

v) Malocclusion; Index of Orthodontic Treatment Need, orthodontic outcome; orthodontic need; orthodontic consequences; orthodontic adj permanent; orthodontic adj secondary; space loss; dental crowding; dental occlusion; diastema; malocclusion Angle class I; Malocclusion Angle class II; malocclusion Angle class III; open bite.

vi) Secondary dentition; secondary teeth; permanent dentition; permanent teeth; adult teeth

Medical subject headings (MesH) for MEDLINE and Pubmed (from 1st Jan 1946 for MEDLINE, from 1st Jan 1996 for Pubmed)

i) Adolescent; child; child, preschool

ii) Tooth loss; tooth extraction

iii) Dentition mixed; dentition, primary; tooth deciduous

iv) Malocclusion (explode which includes following sub-headings: dental occlusion; diastema; malocclusion Angle class I; Malocclusion Angle class II; malocclusion Angle class III, open bite); dentition permanent, Index of Orthodontic Treatment Need

Elsevier Life Thesaurus (Emtree) for EMBASE (from 1st Jan 1947-)

i) Adolescent; child; preschool, child

ii) Tooth extraction

iii) Deciduous tooth

iv) Malocclusion; secondary dentition

Types of study to be included

- RCT
- Prospective and retrospective cohort studies
- Case control studies

Condition or domain being studied

Dental caries involving the primary dentition is common in deprived and disadvantaged population. Worldwide 60-90% of school age children have dental caries (WHO fact sheet no 318, April 2012). In United Kingdom, caries level in 5 year old children is low (national average $d_3$mft 1.1). Approximately 70% of 5 year old children are caries free, however the average $d_3$mft for children with caries was 3.45 (Oral Health Survey of 5 year old Children 2007/2008, October 2009, NHS Dental Epidemiology Programme for England). Premature extraction of primary tooth is common treatment for dental caries across many countries.

At present there is clinical consensus that premature extraction of primary teeth leads to increase in malocclusion and consequent orthodontic need in the permanent dentition but the evidence to support this assumption is less apparent in the published literature. Therefore a literature review to establish the strength of this association is important to help treatment planning when dentists are presented with young children with dental caries.

Participants/ population

Studies with children in the primary or mixed dentition who had undergone premature extraction of their primary tooth or teeth and are then followed up to establish the effect on their resulting malocclusion and thus orthodontic need. We plan to include studies looking at premature extraction of primary teeth and subsequent space loss in the primary and mixed dentition. Split-mouth study design with premature unilateral extraction will be included.

Exclusion criteria:

- Studies including premature extraction of permanent tooth/ teeth.
- Studies where orthodontic outcome in the permanent dentition or space loss in the primary and mixed dentition is not recorded.

Intervention(s), exposure(s)

Premature extraction of a primary tooth or teeth (e.g. prior to the time they would naturally fall out).

Comparator/ control

Children who did not suffer premature extraction of primary tooth/teeth.

Outcome

Primary outcome:

Any orthodontic outcome recorded (eg. orthodontic need, orthodontic irregularities or malocclusion)

Secondary outcome:

Space loss in the primary/ mixed or permanent dentition.

Data extraction (selection and coding)

Each title and abstract from studies will be assessed based on the inclusion criteria after which the full text for the study will be reviewed. For those studies which meet or appear to meet the inclusion criteria, the full text of the study will be reviewed. Title and full text assessment will be carried out by two reviewers (NB and PD) independently.

Data extraction will be carried out using customized data extraction proforma for included studies in the review by two reviewers (NB and PD) independently. Following information will be included:

i) Study identification using first author's name and year of publication.

ii) Study design.

iii) Participants in the study including sample size and number of cases and control.

iv) Duration of follow-up following premature extraction of primary tooth.

v) Orthodontic outcome or malocclusion in permanent dentition.

vi) Space loss in primary and/ or mixed dentition.

Strategy for data synthesis

A narrative synthesis will be provided from included studies structured around assessment and quantification of orthodontic need. Included studies will be assessed for study quality, study setting and details of the premature extraction of primary teeth and those in the control group.

Risk of bias (quality) assessment

All included studies will be assessed for risk of bias. This will be done independently by two reviewers (NB and PD) and disagreements will be resolved by discussion or passed to the third reviewer (MD).

Analysis of subgroups or subsets

- Gender differences.
- Differences in timing of primary tooth or teeth extractions.
- Extraction of maxillary tooth/teeth v. mandibular tooth/teeth.
- Extraction of anterior tooth/teeth v. posterior tooth/teeth.
- Extraction of secondary primary molars v. first primary molars.
- Extraction under local anaesthesia v. extraction under general anaesthesia.
- Split mouth design with unilateral extractions on one side of the arch only.

Dissemination plans

The review team will present the findings of this review in a peer reviewed dental journal and at appropriate paediatric dentistry conferences.

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Dec 2013

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Conflicts of interest

None known

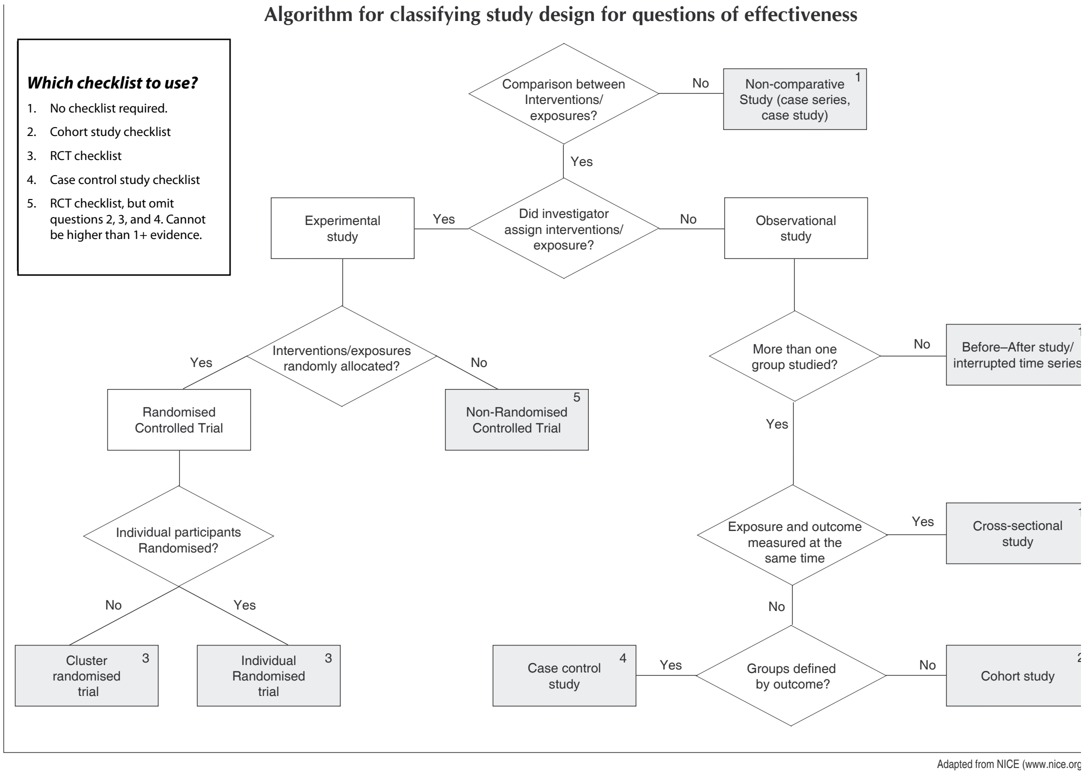
Language

English

Country

UK

Appendix II. SIGN algorithm for classifying study design for questions of effectiveness.



Appendix III. Search strategy used and results from MEDLINE.

MEDLINE search 03/04/2013

#	Searches	Results	Search Type
1	Adolescent/	1516292	Advanced
2	Child/	1293662	Advanced
3	Child, Preschool/	712955	Advanced
4	1 or 2 or 3	2280479	Advanced
5	child.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1580730	Advanced
6	young person.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	525	Advanced
7	adolescent.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1524988	Advanced
8	5 or 6 or 7	2378515	Advanced
9	4 or 8	2378515	Advanced
10	Tooth Loss/	2507	Advanced
11	Tooth Extraction/	14917	Advanced
12	10 or 11	17244	Advanced
13	tooth loss.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	3670	Advanced
14	tooth extraction.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	15615	Advanced
15	teeth extraction.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	646	Advanced
16	premature extraction.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	29	Advanced
17	premature loss.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	434	Advanced
18	exodontia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	238	Advanced
19	13 or 14 or 15 or 16 or 17 or 18	19382	Advanced
20	12 or 19	19382	Advanced
21	Dentition, Mixed/	1680	Advanced
22	Dentition, Primary/	1112	Advanced
23	Tooth, Deciduous/	8754	Advanced
24	21 or 22 or 23	10946	Advanced
25	deciduous tooth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	401	Advanced
26	deciduous teeth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1897	Advanced
27	deciduous dentition.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique	667	Advanced

	identifier]		
28	primary tooth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	395	Advanced
29	primary teeth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	2055	Advanced
30	primary dentition.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1202	Advanced
31	baby tooth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	4	Advanced
32	baby teeth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	36	Advanced
33	mixed dentition.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1284	Advanced
34	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	6981	Advanced
35	24 or 34	12721	Advanced
36	exp Malocclusion/	28272	Advanced
37	Dentition, Permanent/	1013	Advanced
38	"Index of Orthodontic Treatment Need"/	36	Advanced
39	36 or 37 or 38	29179	Advanced
40	malocclusion.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	26384	Advanced
41	orthodontic outcome.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	11	Advanced
42	orthodontic need.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	25	Advanced
43	orthodontic consequences.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	9	Advanced
44	(orthodontic adj permanent).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	0	Advanced
45	(orthodontic adj secondary).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1	Advanced
46	space loss.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	147	Advanced
47	dental crowding.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	120	Advanced
48	dental occlusion.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	13823	Advanced
49	diastema.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary	1302	Advanced

	concept, rare disease supplementary concept, unique identifier]		
50	malocclusion Angle Class I.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1022	Advanced
51	malocclusion Angle Class II.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	4261	Advanced
52	malocclusion Angle Class III.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	2298	Advanced
53	open bite.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1899	Advanced
54	40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53	38876	Advanced
55	secondary dentition.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	61	Advanced
56	secondary teeth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	23	Advanced
57	permanent dentition.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1702	Advanced
58	permanent teeth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	3839	Advanced
59	adult teeth.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	74	Advanced
60	55 or 56 or 57 or 58 or 59	5415	Advanced
61	39 or 54 or 60	44020	Advanced
62	9 and 20 and 35 and 61	357	Advanced
63	limit 62 to english language	264	Advanced

Appendix IV. Search strategy used and results from EMBASE.

EMBASE search 03/04/2013

#	Searches	Results	Search Type
1	adolescent/	1236227	Advanced
2	child/	1366777	Advanced
3	preschool child/	495747	Advanced
4	1 or 2 or 3	2225039	Advanced
5	child.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1858848	Advanced
6	young person.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	978	Advanced
7	adolescent.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1260380	Advanced
8	5 or 6 or 7	2470323	Advanced
9	4 or 8	2470323	Advanced
10	tooth extraction/	17398	Advanced
11	tooth loss.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	2344	Advanced
12	tooth extraction.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	18050	Advanced
13	teeth extraction.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	220	Advanced
14	premature extraction.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	33	Advanced
15	premature loss.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	570	Advanced
16	exodontia.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	241	Advanced
17	10 or 11 or 12 or 13 or 14 or 15 or 16	20809	Advanced
18	deciduous tooth/	9483	Advanced
19	deciduous tooth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	9583	Advanced
20	deciduous teeth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	2448	Advanced
21	deciduous dentition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	853	Advanced
22	primary tooth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	437	Advanced
23	primary teeth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	2248	Advanced
24	primary dentition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1326	Advanced
25	baby tooth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	3	Advanced
26	baby teeth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer,	35	Advanced

	device trade name, keyword]		
27	mixed dentition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1366	Advanced
28	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27	12902	Advanced
29	malocclusion/	25581	Advanced
30	secondary dentition/	43	Advanced
31	29 or 30	25621	Advanced
32	malocclusion.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	26510	Advanced
33	orthodontic outcome.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	12	Advanced
34	orthodontic need.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	26	Advanced
35	orthodontic consequences.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	10	Advanced
36	(orthodontic adj permanent).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	0	Advanced
37	(orthodontic adj secondary).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1	Advanced
38	space loss.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	172	Advanced
39	dental crowding.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	143	Advanced
40	dental occlusion.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	761	Advanced
41	diastema.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1362	Advanced
42	malocclusion Angle Class I.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1	Advanced
43	malocclusion Angle Class II.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	5	Advanced
44	malocclusion Angle Class III.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	2	Advanced
45	open bite.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1742	Advanced
46	32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45	28452	Advanced
47	secondary dentition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	111	Advanced
48	secondary teeth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	37	Advanced
49	permanent dentition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	1993	Advanced
50	permanent teeth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	4636	Advanced
51	adult teeth.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer,	95	Advanced

	device trade name, keyword]		
52	47 or 48 or 49 or 50 or 51	6498	Advanced
53	31 or 46 or 52	34282	Advanced
54	9 and 17 and 28 and 53	313	Advanced
55	limit 54 to english language	222	Advanced

Appendix V. Data extraction sheet used in the systematic review.

Data extraction form (Study ID)

Citation:		
Aim/ Objectives		
Methods		
Study design:		
Setting:		
Intervention:		
Definition of premature extraction/ loss:		
Participants Experimental: n=	Age:	Sex:
Control: n=		
Total: n=		
Inclusion/ Exclusion:		
Dropouts:		
Ethnicity:		
Follow up time:		
Dental age consideration: Yes ☐ No ☐ If yes, further notes		
Unit of analysis/ quantitative variables:		
Statistical methods:		
Outcome		
Primary outcome:		
Secondary outcome:		
Gender differences:		
Difference in timing of extraction/loss:		
Max. vs. Man. teeth:		
Ant vs. Post. teeth:		
D vs. E:		
Treatment under LA vs GA:		
Data source:		
Methods to reduce bias:		

Results		
Internal validity		
Definition of inclusion and exclusion:		
Definition of outcome:		
Treatment and control group comparability:		
Follow up of participants:		
Examiner reliability:		
Blinding:		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☐
Further notes:		
Limitations		
Notes and comments		
Conflict of interest		
Ethical approval		

Appendix VI. List of reference list screening of potentially relevant studies.

Screening of the reference list of following articles revealed potential studies for the review

RONNERMAN, A. & THILANDER, B. 1978. Facial and dental arch morphology in children with and without early loss of deciduous molars. *American Journal of Orthodontics,* 73**,** 47-58.

1. CLINCH, L. M. & HEALY, M. J. R. 1959. A longitudinal study of the results of premature extraction of deciduous teeth between 3–4 and 13–14 years of age. *D. Practitioner* 9**,** 109-126.
2. LINDER-ARONSON, S. 1960. The effect of premature loss of deciduous teeth. A Biometric study in 14 and 15 year olds. *Acta Odontologica Scandinavica,* 18**,** 101-122.
3. LUNDSTRUM, A. 1955. The significance of early loss of deciduous teeth in the etiology of malocclusion. *American Journal of Orthodontics & Dentofacial Orthopedics,* 41**,** 819-826.
4. RICHARDSON, M. E. 1965. The relationship between the relative amount of space present in the deciduous dental arch and the rate and degree of space closure subsequent to the extraction of a deciduous molar. *Dent Pract Dent Rec,* 16**,** 111-8.
5. RONNERMAN, A. 1965. Early extraction of deciduous molars and canines--its incidence and influence on spacing. *Rep Congr Eur Orthod Soc,* 41**,** 153-68.
6. RONNERMAN, A. 1977. The effect of early loss of primary molars on tooth eruption and space conditions. A longitudinal study. *Acta Odontol Scand,* 35**,** 229-39.
7. RONNERMAN, A. & THILANDER, B. 1977. A longitudinal study on the effect of unilateral extraction of primary molars. *Scand J Dent Res,* 85**,** 362-72.

PARK, K., JUNG, D.-W. & KIM, J.-Y. 2009. Three-dimensional space changes after premature loss of a maxillary primary first molar. *International Journal of Paediatric Dentistry,* 19**,** 383-9.

8. LIN, Y. T., LIN, W. H. & LIN, Y. T. 2007. Immediate and six-month space changes after premature loss of a primary maxillary first molar. *J Am Dent Assoc,* 138**,** 362-8.
9. NORTHWAY, W. M. & WAINRIGHT, R. W. 1980. D E space--a realistic measure of changes in arch morphology: space loss due to unattended caries. *J Dent Res,* 59**,** 1577-80.

LEIGHTON, B. C. 1981. Longitudinal study of features which might influence space loss after early extraction of lower deciduous molars. *Proceedings of the Finnish Dental Society,* 77**,** 95-103.

10. BREAKSPEAR, E. K. 1961. Further observations on early loss of decicuous molars. *Dent. Pract. Dent. Rec. ,* 11**,** 233-52.
11. POSEN, A. L. 1965. The Effect of Premature Loss of Deciduous Molars on Premolar Eruption. *Angle Orthod,* 35**,** 249-52.

12. UNGAR, A. L. 1938. Incidence and effect of premature loss of deciduous teeth. *Am J Orthodont & Oral Surg,* 24**,** 613-621.

MIYAMOTO, W., CHUNG, C. S. & YEE, P. K. 1976. Effect of premature loss of deciduous canines and molars on malocclusion of the permanent dentition. *Journal of Dental Research,* 55**,** 584-90.

13. CARR, L. M. 1963. The effect of extraction of deciduous molars on the eruption of bicuspid teeth. . *Australian Dental Journal,* 8**,** 130-136.
14. OWEN, D. G. 1971. The incidence and nature of space closure following the premature extraction of deciduous teeth: a literature study. *Am J Orthod,* 59**,** 37-49.
15. ROSENZWIG, K. A. & KLEIN, H. 1960. Loss of space by extraction of primary molars. *J Dent Child,* 17**,** 275-276.

NORTHWAY, W. M., WAINRIGHT, R. L. & DEMIRJIAN, A. 1984. Effects of premature loss of deciduous molars. *Angle Orthodontist,* 54**,** 295-329.

16. BREAKSPEAR, E. K. 1951. Sequelae of early loss of deciduous molars. *Dent Rec (London),* 71**,** 127-34.
17. KRAKOIAK, F. J. 1966. Growth potential of mandible as a factor in mesial movement of the permanent first molar. . *J Dent Child,* 33**,** 331-336.
18. KRONFELD, S. M. 1953. The effects of premature loss of primary teeth and sequence of eruption of permanent teeth on malocclusion. *Journal of Dentistry for Children,* 31**,** 302-313.
19. SEIPEL, C. M. 1949. Prevention of malocclusion. *Dent Rec (London),* 69**,** 224-32.

PADMA KUMARI, B. & RETNAKUMARI, N. 2006. Loss of space and changes in the dental arch after premature loss of the lower primary molar: a longitudinal study. *Journal of the Indian Society of Pedodontics & Preventive Dentistry,* 24**,** 90-6.

20. JOHNSEN, D. C. 1980. Space observation following loss of the mandibular first primary molars in mixed dentition. *ASDC J Dent Child,* 47**,** 24-7.
21. LIN, Y. T. & CHANG, L. C. 1998. Space changes after premature loss of the mandibular primary first molar: a longitudinal study. *J Clin Pediatr Dent,* 22**,** 311-6.

KISLING, E. & HOFFDING, J. 1979. Premature loss of primary teeth: part III, drifting patterns for different types of teeth after loss of adjoining teeth. *Journal of Dentistry for Children,* 46**,** 34-8.

22. KISLING, E. & HOFFDING, J. 1979. Premature loss of primary teeth: part IV, a clinical control of Sannerud's space maintainer, type I. *ASDC J Dent Child,* 46**,** 109-13.

SEWARD, F. S. 1965. Natural Closure of Deciduous Molar Extraction Spaces. *Angle Orthod,* 35**,** 85-94.

23. BRAUER, J. E. 1941. A report of 113 early or premature extractions of primary molars and the incidence of closure of space. *J Dent Child,* 8**,** 222-224.

Appendix VII. Data extraction sheets for malocclusion studies.

Data extraction form (Hoffding & Kisling, 1978)

Citation:		
Hoffding J, Kisling E. Premature loss of primary teeth: part I, its overall effect on occlusion and space in the permanent dentition. *Journal of Dentistry for Children* 1978;**45**(4):279-83. Hoffding J, Kisling E. Premature loss of primary teeth: part II, the specific effects on occlusion and space in the permanent dentition. *Journal of Dentistry for Children* 1978;**45**(4):284-7.		
Aim/ Objectives	To evaluate effects on occlusion and space in permanent dentition following premature extraction/loss of primary teeth	
Methods		
Study design: Case-control study		
Setting: 2 Danish municipalities, Jutland and Zealand		
Intervention: Premature extraction of primary teeth compared to no extraction		
Definition of premature extraction/ loss: Loss of primary canines and first primary molars before or while child was in the first grade and the loss of primary second molars before or while the child was in the second grade.		
Participants Experimental: n=550 children (327 with premature extraction, 223 without), after exclusion 231 children 26 Cs, 370 Ds, 368 Es	Age: 13-14 yrs (7th grade) Mean etc not stated	Sex: Not stated
Control: n= 182 without premature extraction		
Total: n=413		
Inclusion/ Exclusion: Permanent teeth extractions and orthodontic extractions (n=137), thus final number 231 with premature extraction and 182 without		
Dropouts: Not reported		
Ethnicity: Not reported		
Follow up time: 7 years but premature extraction data collected retrospectively		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Child		
Statistical methods: Frequencies tested by Fisher's test, p value 0.001		
Outcome		
Primary outcome: Any sign of malocclusion		
Secondary outcome: Overjet, distal molar occlusion, mesial molar occlusion, crowding, deep bite, rotation, midline deviation		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not recorded		
Max. vs. Man. teeth: Ratio 270: 494 but no comparison between groups reported		
Ant vs. Post. teeth: Ratio 26Cs, 370 Ds, 368 Es but no comparison between groups reported		
D vs. E: ratio 370:368 but no comparison between groups reported		
Treatment under LA vs GA: Not reported		
Data source: Epidemiological registrations by Danish Public Health Services and retrospective review of dental records		

Methods to reduce bias: Excluded inadequate dental records, permanent tooth extraction and those who had already started orthodontic treatment		
Results		
Any sign of malocclusion was significantly higher in the groups with premature loss compared to without premature loss p<0.01, frequency 90% vs 80%		
Maxillary overjet and Class II malocclusion not significantly different in the two groups (premature extraction and non-extraction group)		
Class III malocclusion significantly higher in premature extraction group, p<0.01		
Crowding in at least one segment (arch divided into 3 segments) significantly higher in premature extraction group, p<0.001, frequency 49% vs 29%		
Deep bite, rotation of teeth and midline deviation not significantly different in the two groups		
Premature extraction in the mandibular arch did not lead a to significant increase in overjet in this subgroup		
Class II malocclusion and crowding significantly higher in subgroup where upper Es were lost (without loss of teeth in opposing quadrant), p<0.01		
Maxillary overjet grades (I and II) ie the complexity of maxillary overjet was not different when premature loss in mandible		
Internal validity		
Definition of inclusion and exclusion: Yes		
Definition of outcome: Yes Maxillary OJ: grade I ≥ 6mm but less than 9mm, grade II ≥ 9mm Mesial and distal occlusion: grade I deviation ≥ half cusp width, grade II ≥ full cusp width Crowding > 2mm in one of the 3 segments in one arch		
Treatment and control group comparability: Yes		
Follow up of participants: N/A, retrospective analysis		
Examiner reliability: Calibration and intra and inter examiner reproducibility not reported		
Blinding: Not reported		
Global validity		
High risk of bias:	Low risk:	Moderate: ☑
Further notes: To same ethnic population but this is not reported		
Limitations		
Epidemiological survey utilised for dentolaveolar malocclusion is not clear		
Which features of malocclusion were used were not available		
Premature extraction of primary teeth based on retrospective review of dental notes		
Dental age was not reported		
Measurement of spacing or crowding not discussed in detail		
Notes and comments		
Grading of overjet, mesial and distal malocclusion into Grade I and II		
Crowding of 2mm or more was used which may not be clinically significant		
Epidemiological survey were carried out when children were in full permanent dentition		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Melsen & Terp, 1982)

<table>
<tr><td colspan="3">Citation:</td></tr>
<tr><td colspan="3">Melsen, B. & Terp, S. 1982. The influence of extractions caries cause on the development of malocclusion and need for orthodontic treatment. Swedish Dental Journal - Supplement, 15, 163-9.</td></tr>
<tr><td>Aim/ Objectives</td><td colspan="2">To analyse frequency of malocclusion and the need for orthodontic treatment as a result of loss of primary and permanent teeth</td></tr>
<tr><td colspan="3">Methods</td></tr>
<tr><td colspan="3">Study design: Cross sectional study</td></tr>
<tr><td colspan="3">Setting: Suburbs in Northern Italy, examined in summer camps or at school</td></tr>
<tr><td colspan="3">Intervention: Primary extractions, FPM extractions (possibly primary teeth as well), permanent extractions compared to no extraction group</td></tr>
<tr><td colspan="3">Definition of premature extraction/ loss: Not defined but implied if tooth not present at the time of examination, then considered to have undergone premature extraction</td></tr>
<tr><td>Participants
Experimental: n=204 with premature extraction or defective primary teeth (a subgroup of overall study)</td><td>Age: dental age, see below</td><td>Sex: M: F= 121: 83 (PEPT group)</td></tr>
<tr><td>Control: n= 473, no extraction</td><td></td><td></td></tr>
<tr><td>Total: n= 915 with other groups</td><td></td><td></td></tr>
<tr><td colspan="3">Inclusion/ Exclusion: Children of North Italian origin attending community school, previous orthodontic treatment wearing appliance were excluded (925-10)</td></tr>
<tr><td colspan="3">Dropouts: Not stated</td></tr>
<tr><td colspan="3">Ethnicity: Caucasian (North Italian origin)</td></tr>
<tr><td colspan="3">Follow up time: N/A, cross- sectional survey</td></tr>
<tr><td colspan="3">Dental age consideration: Yes ☑ No ☐
If yes, further notes
Stages of dental maturity, stage 1= incisors erupting, stage 2= incisors erupted, stage 3= canines and/ or premolars erupting, stage 4= above fully erupted</td></tr>
<tr><td colspan="3">Unit of analysis/ quantitative variables: Child and possibly tooth</td></tr>
<tr><td colspan="3">Statistical methods: No statistical method applied, only descriptive statistics used</td></tr>
<tr><td colspan="3">Outcome</td></tr>
<tr><td colspan="3">Primary outcome: Orthodontic need
Need divided into need for treatment, further extraction and major treatment (major treatment >12 mths)</td></tr>
<tr><td colspan="3">Secondary outcome: Occlusal anomalies (sagittal, vertical, transversal) and alignment anomaly</td></tr>
<tr><td colspan="3">Gender differences: Ratio for premature loss M:F= 121:83, no difference in malocclusion between genders found from an earlier study, thus no further analysis in results</td></tr>
<tr><td colspan="3">Difference in timing of extraction/ loss: No</td></tr>
<tr><td colspan="3">Max. vs. Man. teeth: Not reported</td></tr>
<tr><td colspan="3">Ant vs. Post. teeth: Not reported</td></tr>
<tr><td colspan="3">D vs. E: Not reported</td></tr>
<tr><td colspan="3">Treatment under LA vs GA: Not reported</td></tr>
<tr><td colspan="3">Data source: Clinical examination</td></tr>
</table>

Methods to reduce bias: Exclusion applied
Results
Orthodontic need was increased by premature extractions of primary teeth 60% PEPT vs 42%
With respect to overall malocclusion, PEPT 70% vs 63% Sagittal anomalies, PEPT 61% vs 72% Vertical, PEPT 27% vs 54% Transverse, PEPT 34% vs 49%
Need for further extractions, PEPT 20% vs 7%
Need for major tx, PEPT 56% vs 40%
Frequency of children without malocclusion was lower in any of the extraction groups, paper reports saying 'significantly' lower but no p value or detail of statistical test is not given
Alignment anomaly, PEPT 27% vs 31%
Paper compared outcome with PEPT, FPM extraction, other permanent extraction and no extraction group
Internal validity
Definition of inclusion and exclusion: Defined inclusion and exclusion criteria
Definition of outcome: No
Treatment and control group comparability: Groups with and without premature extraction are comparable, homogenous genetic background
Follow up of participants: N/A, cross sectional study
Examiner reliability: Not reported, previously tested objective method used
Blinding: Not reported
Global validity
High risk of bias: ☑ | Low risk: ☐ | Moderate: ☐
Further notes: Dental stage 4 includes with canines and premolars fully erupted, thus PEPT cannot be assessed accurately
Limitations
Attempted to get a homogenous ethnic group so that internal (genetic) factors are minimised
Measurement method and reliability not discussed
Dental age taken into consideration but may have missed children who had PEPT previously
Outcome measures are not clearly defined and reported
Notes and comments
No statistical test mentioned although results are described saying 'significantly', no p value
Numbers on table not adding up to the total number reported, the subgroups are possibly not mutually exclusive, thus difficult to extract PEOT group information
Conflict of interest
Not reported
Ethical approval
Not reported

Data extraction form (Miyamoto et al, 1976)

Citation:		
Miyamoto, W., Chung, C. S. & Yee, P. K. 1976. Effect of premature loss of deciduous canines and molars on malocclusion of the permanent dentition. *Journal of Dental Research,* 55**,** 584-90.		
Aim/ Objectives	To determine the effect of premature loss of the deciduous canines, first and second molars on malalignment and crowding in permanent dentition	
Methods		
Study design: Cross sectional with retrospective information		
Setting: Hawaii- born schoolchildren		
Intervention: PEPT compared with children without PEPT		
Definition of premature extraction/ loss: Not defined		
Participants Experimental: n= Not reported Divided into age groups and result for same patient is repeated a number of times	Age: 11 yrs or older, most 15-17 yrs	Sex: M: F= Not reported
Control: n= Not reported		
Total: n= 960		
Inclusion/ Exclusion: Children who missed a year or more of dental treatment and age more than 6 yrs at first exam and less than 8 yrs at final exam		
Dropouts: Not stated		
Ethnicity: Indigient Honolulu		
Follow up time: At least 5 years, note stated clearly		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Tooth lost		
Statistical methods: Chi squared tests to compare proportions. Regression to compare ages of children who received orthodontic treatment		
Outcome		
Primary outcome: Minor and major mal-alignment Minor- Teeth rotated by 45 degrees or displaced up to 2mm from ideal alignment, major- anything beyond above		
Secondary outcome: Crowding (mm) of incisors, canines and premolars		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: Not reported		
Ant vs. Post. teeth: Not reported		
D vs. E: Not reported		
Treatment under LA vs GA: Not reported		
Data source: Epidemiological survey information linked with retrospective dental records		
Methods to reduce bias: Exclusions applied Proportions of which teeth lost not clear		

Results		
Major mal- alignment in PEPT group divided into D and E group (For Ds, frequency 51%, for Es frequency of 48% for one or two teeth lost) C extraction does not lead to significant major mal-alignment		
Crowding not related to loss of Ds and Es but related to loss of Cs Mean crowding for loss of Cs are reported, no loss 1.75mm, 1 C lost 2.56 and 2 Cs 5mm		
Children having orthodontic treatment increased by PEPT		
Internal validity		
Definition of inclusion and exclusion: Not defined		
Definition of outcome: No		
Treatment and control group comparability: Possibly		
Follow up of participants: N/A, cross sectional study		
Examiner reliability: Not reported		
Blinding: Not reported		
High risk of bias: ☑	Low risk: ☐	Moderate: ☐
Further notes: Same child measured repeatedly at different ages		
Limitations		
Mainly relied on retrospective dental notes		
The age groups are not mutually exclusive as the same children were measured and reported multiple times, these results would not be independent of each other		
Non-significant values are not reported, only significant findings were discussed		
Notes and comments		
Inconsistent results with regards to Cs, may be crowding leads to premature loss of Cs rather than the reverse!		
No clear result explaining the number of Cs, Ds And Es lost		
Children who had orthodontic treatment may not be the ones who had orthodontic need		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Pederson et al, 1978)

Citation:		
Pederson, J., Stensgaard, K. & Melsen, B. 1978. Prevalence of malocclusion in relation to premature loss of primary teeth. *Community Dentistry & Oral Epidemiology,* 6**,** 204-9.		
Aim/ Objectives	To compare the frequencies of sagittal, vertical and transverse occlusal anomalies in children with and without premature loss of primary teeth	
Methods		
Study design: Cross sectional		
Setting: Silkeborg, Denmark		
Intervention: Children with premature loss compared to children without loss		
Definition of premature extraction/ loss: Yes, if tooth was missing when permanent successor could not be palpated		
Participants Experimental: n= 359	Age: 9-11 yrs	Sex: M:F= 366:357
Control: n= 364 (without loss)		
Total: n= 723		
Inclusion/ Exclusion: Not reported		
Dropouts: N/A, cross sectional study		
Ethnicity: Not reported		
Follow up time: N/A, cross sectional study		
Dental age consideration: Yes ☑ No ☐ If yes, further notes Children divided in dental stages, stage 1-4, permanent tooth palpated		
Unit of analysis/ quantitative variables: Child		
Statistical methods: T tests and fisher's exact test		
Outcome		
Primary outcome: Malocclusion features (Sagital: bilateral distal occlusion, unilateral distal occlusion, mesial occlusion, maxillary overjet; vertical: deep bite, anterior open bite; transverse: midline deviation, cross bite) Grade I and II		
Secondary outcome: Orthodontic need, extraction or permanent teeth required and major appliance therapy		
Gender differences: Not stated		
Difference in timing of extraction/loss: Not taken into account		
Max. vs. Man. teeth: ratio 281: 629, significant distal occlusion when extraction in maxilla		
Ant vs. Post. teeth: 99 Cs, 391 Ds, 420 Ds		
D vs. E: Ratio 391: 420 but not reported for outcome		
Treatment under LA vs GA: Not recorded		
Data source: Examination of children		
Methods to reduce bias: Defined PEPT, children divided into dental stages to take into account of the dental age Intra and inter examiner agreement on 30 cases		
Results		

Need for tx, PEPT 73% vs 58%, p value <0.001
Need for further extractions, PEPT 32% vs 12%, p value <0.001
Major appliance therapy, PEPT 35% vs 23%
Malocclusion eg distal molar occlusion, deep bite, midline displacement, cross bite increased in PEPT group, p values , 0.001, 0.05, 0.01, 0.01 respectively. However maxillary OJ and open bite not different in the two groups
Need for tx increased when extraction in maxilla, 88% vs 63%, p value 0.001
Internal validity
Definition of inclusion and exclusion: No
Definition of outcome: Yes, referred to previously used method for epidemiological surveys
Treatment and control group comparability: Risk of selection bias
Follow up of participants: N/A, cross sectional survey
Examiner reliability: 2 examiners checked 30 cases for intra and inter examiner reliability
Blinding: No
Global validity
High risk of bias: ☑ Low risk: ☐ Moderate: ☐
Further notes:
Limitations
Exposure (PEPT) and malocclusion features assessed at the same time, missed children in dental stage 4 who had premature extractions
Kappa scores not reported for intra and inter examiner reliability
Majority of children had extractions of 1 or 2 teeth, would have been useful to know if number of extractions were significant for orthodontic need/ malocclusion
Limited generalizability due to high risk of bias
Notes and comments
Used epidemiological method for recording malocclusion which appears thorough
Dental stage 3 and 4 could not be assessed for PEPT as they would have got canines and premolars either partially erupted or fully erupted, if retrospective dental notes were available, this would have been useful
Conflict of interest
Not reported
Ethical approval
Not reported

Appendix VIII. Data extraction sheets for space studies.

Data extraction form (Clinch & Healy, 1959)

Citation:		
Clinch LM, Healy MJR. A longitudinal study of the results of premature extraction of deciduous teeth between 3–4 and 13–14 years of age. *D Practitioner* 1959;**9**:109-26.		
Aim/ Objectives	To study occlusion as a result of premature extraction of primary teeth between 3-4 and 13-14 years (over 11 year period)	
Methods		
Study design: Cohort (? prospective) study		
Setting: Children born in the same maternity hospital (hospital not specified)		
Intervention: PEPT group compared to no PEPT		
Definition of premature extraction/ loss: Not defined		
Participants Experimental: n=29/59	Age: 3-4 yrs followed to 13-14 yrs	Sex: Not stated
Control: n= 11/59 selected randomly		
Total: n= 106, 59 at final observation		
Inclusion/ Exclusion: permanent tooth extraction		
Dropouts: 47		
Ethnicity: Not reported		
Follow up time: 11 years		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Child, dental arch divided into 4 sections, dental cast measurement		
Statistical methods: Mean and SD, correlation but each case behaved individually, thus not able to apply tests		
Outcome		
Primary outcome: Dental arch spacing (in mm)		
Secondary outcome: None		
Gender differences: Not reported		
Difference in timing of extraction/loss: Yes, compared early PEPT and late PEPT		
Max. vs. Man. teeth: Not reported		
Ant vs. Post. teeth: Not reported		
D vs. E: Not reported		
Treatment under LA vs GA: Not reported		
Data source: Dental cast measurement		
Methods to reduce bias: Measurement error stated, same children followed		

Results		
Early extraction cases (3-4 yrs) before eruption of 6s, more space loss but upper arch more space loss than lower eg in upper premolar- molar segment, early loss 6.18 mm vs late loss 3.52 mm vs control 2.72 Lower premolar- molar segment, early loss 3.93 vs late 3.99 vs 3.1		
10/29 (34%) no crowding, thus 66% had crowding lower anteriors		
Positive correlation of crowding and extraction space loss		
Internal validity		
Definition of inclusion and exclusion: Yes		
Definition of outcome: No		
Treatment and control group comparability: Yes, cohort followed over time		
Follow up of participants: Yes, 11 yrs		
Examiner reliability: Measuring error was assessed, SD for single tooth was ±0.19		
Blinding: Not reported		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes: Ethnicity not reported		
Limitations		
Dental age not taken into account		
Measurement error and examiner validity not discussed		
Extremely heterogeneous data		
‘Early loss’ and ‘other’ group definition not clear		
Notes and comments		
Correlation calculated between space loss (differential spacing between first and final cast) and available space/ crowding, significant correlation, this means crowded arches behave differently to normal arches		
Data considered for statistical test but not carried out due to heterogeneity		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Kau et al, 2004)

Citation:		
Kau CH, Durning P, Richmond S, Miotti FA, Harzer W. Extractions as a form of interception in the developing dentition: a randomized controlled trial. *Journal of orthodontics* 2004;**31**(2):107-14.		
Aim/ Objectives	To determine if extractions of lower primary canines are an effective procedure to relieve crowding of the lower labial segment	
Methods		
Study design: RCT		
Setting: Multicentre; dental clinics in South Wales, Italy and Germany		
Intervention: Orthodontic extraction of lower primary canines compared to no extraction		
Definition of premature extraction/ loss: Not defined but experimental group is the extraction group		
Participants Experimental: n= 55 children who underwent lower canines extraction	Age: between 8-9 yrs	Sex: Not reported
Control: n= 42, no extraction		
Total: n= 97		
Inclusion/ Exclusion: Inclusion criteria clearly stated		
Dropouts: Extraction group 2; non extraction group 12		
Ethnicity: Caucasian		
Follow up time: 1-2 yrs, minimum 1 yr		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Child		
Statistical methods: Mann- Whitney test		
Outcome		
Primary outcome: Lower incisor crowding according to Little's Index		
Secondary outcome: Arch length, intermolar width, overbite, overjet, lower clinical crown heights (in mm) and lower incisor tooth inclination		
Gender differences: Not reported		
Difference in timing of extraction/loss: N/A		
Max. vs. Man. teeth: N/A		
Ant vs. Post. teeth: N/A		
D vs. E: N/A		
Treatment under LA vs GA: Not reported		
Data source: Outcome measures taken from dental casts		
Methods to reduce bias: Randomisation, comparability of extraction and control group		

Results		
Significant change in Little's Index between baseline and follow up Crowding reduced in both groups but significant reduction in the extraction group (6.03 mm in extraction group vs 1.27 mm, $p < 0.05$)		
Arch length reduced more in extraction group (2.95 mm vs 1.51mm, $p < 0.05$)		
Inter-molar distance showed non-significant change in both groups ($p > 0.05$)		
No significant difference in overbite (p=0.06), No significant difference in overjet change (p=0.06)		
Clinical crown heights significantly greater in extraction group ($p < 0.05$), Incisor inclination showed non-significant change in both groups ($p > 0.05$)		
Internal validity		
Definition of inclusion and exclusion: Defined inclusion criteria well		
Definition of outcome: Yes (used Little's Index)		
Treatment and control group comparability: Both groups had Little's irregularity index of 6mm or more		
Follow up of participants: Minimum 1 year, per protocol analysis		
Examiner reliability: Single examiner, pilot with 30 dental casts (author and gold standard), no agreement value given		
Blinding: Examiner blinded to which treatment was received while examining dental casts		
Global validity		
High risk of bias: ☐	Low risk: ☑	Moderate: ☐
Further notes:		
Limitations		
Dental age was not discussed		
Not based on intention to treat analysis		
Minimum follow up of one year is not conclusive to measure anterior crowding and arch dimensions		
Notes and comments		
Well-designed multicenter study but assessment of malocclusion and crowding could not be assessed in 1-2 years, long term follow up is required		
Measurement method and reliability discussed well		
Outcome measures are clearly reported		
Conflict of interest		
Not reported		
Ethical approval		
Reports approved by relevant ethical committees but not stated which committees were involved		

Data extraction form (Leighton, 1891)

<table>
<tr><td colspan="3">Citation:</td></tr>
<tr><td colspan="3">Leighton BC. Longitudinal study of features which might influence space loss after early extraction of lower deciduous molars. Proceedings of the Finnish Dental Society 1981;77(1-3):95-103.</td></tr>
<tr><td>Aim/ Objectives</td><td colspan="2">To examine if space loss is more severe in children who had PEPT earlier and if it is related to pre-existing crowding in lower arches</td></tr>
<tr><td colspan="3">Methods</td></tr>
<tr><td colspan="3">Study design: Cohort (? prospective) study</td></tr>
<tr><td colspan="3">Setting: Not reported</td></tr>
<tr><td colspan="3">Intervention: PEPT group compared to no PEPT group</td></tr>
<tr><td colspan="3">Definition of premature extraction/ loss: Not defined</td></tr>
<tr><td>Participants
Experimental: n= 18
Measurements at 3-4 yrs, 8-9 yrs, 14-15 yrs, 17-25 yrs</td><td>Age: See participants, no mean stated</td><td>Sex: exp group M: F= 11:7; control 7: 11</td></tr>
<tr><td>Control: n= 18</td><td></td><td></td></tr>
<tr><td>Total: n= 36</td><td></td><td></td></tr>
<tr><td colspan="3">Inclusion/ Exclusion: Cohort group followed for at least 13 yrs</td></tr>
<tr><td colspan="3">Dropouts: Not reported</td></tr>
<tr><td colspan="3">Ethnicity: Not reported</td></tr>
<tr><td colspan="3">Follow up time: Minimum 13 yrs</td></tr>
<tr><td colspan="3">Dental age consideration: Yes ☐ No ☑
If yes, further notes</td></tr>
<tr><td colspan="3">Unit of analysis/ quantitative variables: child</td></tr>
<tr><td colspan="3">Statistical methods: Student’s t-test</td></tr>
<tr><td colspan="3">Outcome</td></tr>
<tr><td colspan="3">Primary outcome: Arch perimeter (six sections) and spacing/ crowding of lower arch</td></tr>
<tr><td colspan="3">Secondary outcome: None</td></tr>
<tr><td colspan="3">Gender differences: Crowding/ spacing M: F= 4.02 mm: 2.87 (not significant)</td></tr>
<tr><td colspan="3">Difference in timing of extraction/loss: Amount of crowding/ spacing weakly correlated to age at extraction (co-eff 0.08)</td></tr>
<tr><td colspan="3">Max. vs. Man. teeth: N/A, only studied lower arches</td></tr>
<tr><td colspan="3">Ant vs. Post. teeth: Not reported</td></tr>
<tr><td colspan="3">D vs. E: Not reported</td></tr>
<tr><td colspan="3">Treatment under LA vs GA: Not reported</td></tr>
<tr><td colspan="3">Data source: ? casts recorded at hospital, reported</td></tr>
<tr><td colspan="3">Methods to reduce bias: Extraction group and non-extraction group same number of participants
No blinding, agreement not reported</td></tr>
<tr><td colspan="3">Results</td></tr>
</table>

Change in arch periphery PEPT group, -5.07 vs no PEPT, -3.26 (p value significant, t- value -1.99)		
Crowding/ spacing PEPT, -3.13 vs no PEPT, -0.34		
Crowding/ spacing at 14-15 yrs highly correlated to crowding/ spacing at 3-4 yrs (coeff 1.25) and change in crowding/ spacing between 3-4 yrs and 8-9 yrs (0.98), poorly correlated to age of extraction and type of tooth and the number of tooth extracted		
Crowding/ spacing of the lower arch in primary dentition more important than age of extraction, no of teeth lost		
Internal validity		
Definition of inclusion and exclusion: Yes		
Definition of outcome: No definition		
Treatment and control group comparability: Yes		
Follow up of participants: Min 13 yrs		
Examiner reliability: Measured twice and mean of these recordings taken		
Blinding: Not reported		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes: How measurement was carried out not described in detail		
Limitations		
5 cases had extraction of permanent teeth but only after 14-15 yrs at least in the lower arch, this may have implications about crowding and spacing		
No blinding mentioned, not known how many examiners were involved		
Notes and comments		
Differing proportion of M:F in PEPT and other group but tests done between M:F which revealed differing arch sizes and teeth size		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Rao & Sarkar, 1999)

Citation:		
Rao AK, Sarkar S. Changes in the arch length following premature loss of deciduous molars. *J Indian Soc Pedod Prev Dent* 1999;**17**(1):29-32.		
Aim/ Objectives	To determine the amount of reduction in the arch length due to the premature loss of deciduous molars in the mixed dentition	
Methods		
Study design: Cross-sectional survey		
Setting: Outpatient Department of Paedodontics and Preventive Dentistry, Dr R Ahmed Dental College, Calcutta, India		
Intervention: Unilateral loss of primary molars (D or E or both)		
Definition of premature extraction/ loss: No		
Participants Experimental: n= 29 with unilateral loss of primary molar	Age: 6-10 yrs	Sex: Not reported
Control: n= 53 without premature loss		
Total: n= 82		
Inclusion/ Exclusion: 82 divided into 2 groups, unilateral loss group and control group		
Dropouts: N/A, cross sectional study		
Ethnicity: Not reported		
Follow up time: N/A, cross sectional study		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Arch lengths at extraction and control cases		
Statistical methods: Student t- test to compare arch length with and without premature loss of primary molars		
Outcome		
Primary outcome: Arch lengths at different regions (canine, primary first molar, primary second molar and permanent first molar)		
Secondary outcome: None		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: See results		
Ant vs. Post. teeth: Not reported		
D vs. E: See results		
Treatment under LA vs GA: Not reported		
Data source: Dental casts measurements using Karkhaus callipers		
Methods to reduce bias: Exposure and control group, unilateral loss only considered with all other quadrants intact		
Results		

Extraction group has significantly reduced arch length (at permanent first molar region) when compared to non extraction group in maxilla and mandible apart from the case of lower Ds, all other cases p value at least <0.05		
Arch length (at primary canine level) was increased in all cases but significant increase was in the cases of upper D and E loss, upper D loss and lower D and E loss		
Arch length reduction (at permanent first molar region) was more in maxilla than mandible		
Internal validity		
Definition of inclusion and exclusion: PEPT group (unilateral loss of D or E or both, period of absence of tooth following premature loss between 6 mths- 1 yr, remaining dentition healthy), control group (no extensive caries or malformations, no history of orthodontic treatment or space maintenance)		
Definition of outcome: Yes		
Treatment and control group comparability: Yes		
Follow up of participants: N/A		
Examiner reliability: Single examiner carried out all measurement, agreement not discussed		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☑	Low risk: ☐	Moderate: ☐
Further notes: No temporal relationship as cross sectional study, thus high risk of bias		
Limitations		
Cross sectional study and history of primary molar extractions were not clear		
Arch length measured at various points but other arch dimensions like arch width and perimeter not used		
Notes and comments		
Only arch length measured, other parameters not measured and discussed		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Ronnerman, 1965)

Citation:		
Ronnerman, A. 1965. Early extraction of deciduous molars and canines--its incidence and influence on spacing. *Rep Congr Eur Orthod Soc,* 41**,** 153-68.		
Aim/ Objectives	To examine the effect on spacing following loss of primary molars and canines	
Methods		
Study design: Cohort (? prospective) study		
Setting: Not reported		
Intervention: PEPT group compared to no PEPT		
Definition of premature extraction/ loss: No but graded for loss of teeth at different ages		
Participants Experimental: n= 161	Age: Mean 12.9 yrs, group I= extraction before 7.5 yrs, group II= extraction of D between 7.5-9 yrs; Es and Cs between 7.5- 10yrs, group III= Ds after 9yrs, Ds and Cs after 10 yrs	Sex: M: F= 108: 79
Control: n= 26		
Total: n= 211		
Inclusion/ Exclusion: 6 had hypodontia, thus excluded		
Dropouts: 24 (187 at final examination from 211)		
Ethnicity: Not stated but states fairly representative of inner Stockholm		
Follow up time: 4 yrs (ages of 9, 11 and 13 yrs)		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Quadrant		
Statistical methods: Only descriptives used		
Outcome		
Primary outcome: Space deficiency defined Group I= deficiency up to 0.5mm, group II= 06- 3.5 mm, group III=>3.5 mm		
Secondary outcome: N/A		
Gender differences: Not reported		
Difference in timing of extraction/loss: Upper arch, both molars missing group I 67% crowding vs group II 26% vs group III 9%		
Max. vs. Man. teeth: Max PEPT (molars only) vs no PEPT group crowding (0.6 mm and above) in 24% vs 13%; in lower quadrants, molar PEPT 27% vs 8%		
Ant vs. Post. teeth: Not recorded (only Cs, Ds and Es looked at)		
D vs. E: Upper quadrants D loss group had crowding 15%, E loss 26%, both loss 35% compared to no PEPT 8% Lower quadrants D loss group had crowding 5%, E loss 16%, both loss 32% compared to no PEPT 4%		
Treatment under LA vs GA: Not reported		
Data source: School surveys and record cards of the patients		
Methods to reduce bias: 2 examiners to assess study casts, defined groups based on clinical significance		
Results		

In upper quadrants, PEPT (molars only) vs no PEPT group crowding (0.6 mm and above) present in 24% vs 13% In lower quadrants, molar PEPT 27% vs 8%		
Upper quadrants D loss group had crowding 15%, E loss 26%, both loss 35% compared to no PEPT 8% Lower quadrants D loss group had crowding 5%, E loss 16%, both loss 32% compared to no PEPT 4%		
Upper arch, both molars missing group I 67% crowding vs group II 26% vs group III 9% Lower arch, both molars missing group I 95% crowding vs group II 84% vs group III 68%		
No differences between right and left side, but no statistical test applied		
Internal validity		
Definition of inclusion and exclusion: Not clearly stated apart from hypodontia patients excluded		
Definition of outcome: Yes, clear		
Treatment and control group comparability: Yes (but other factors eg SES)		
Follow up of participants: 4yrs		
Examiner reliability: Examined by two examiners but no score for agreement intra and inter- operatively		
Blinding: Not applied		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes:		
Limitations		
Only spacing discussed, arch perimeter not discussed		
Space assessment initially by naked eye, if deficiency suspected then used calipers		
Divided into quadrants, so changes to centerlines, arch perimeter not included		
Notes and comments		
Use of arch perimeter not included		
Spacing/ crowding graded, age group and PEPT also graded		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Ronnerman, 1977)

NB: Referred to Ronnerman (1965), same data used

<table>
<tr><td colspan="3">Citation:</td></tr>
<tr><td colspan="3">Ronnerman, A. 1977. The effect of early loss of primary molars on tooth eruption and space conditions. A longitudinal study. Acta Odontol Scand, 35, 229-39.</td></tr>
<tr><td>Aim/ Objectives</td><td colspan="2">To examine the effect of early loss of primary molars on arch space and also eruption of incisors</td></tr>
<tr><td colspan="3">Methods</td></tr>
<tr><td colspan="3">Study design: Cohort (? prospective) study</td></tr>
<tr><td colspan="3">Setting: Dental clinics where patient accessed dental care, study casts made at age 9, 11 and 13 yrs</td></tr>
<tr><td colspan="3">Intervention: PEPT group compared to no PEPT group</td></tr>
<tr><td colspan="3">Definition of premature extraction/ loss: No but age group graded for loss of teeth at different ages</td></tr>
<tr><td>Participants
Experimental: n= 140 with PEPT</td><td>Age:
Mean not known, study casts at age 9, 11 and 13 yrs</td><td>Sex: M:F=
105: 81</td></tr>
<tr><td>Control: n= 46</td><td></td><td></td></tr>
<tr><td>Total: n= 186</td><td></td><td></td></tr>
<tr><td colspan="3">Inclusion/ Exclusion: Not stated, says previously stated (Ronnerman, 1965)</td></tr>
<tr><td colspan="3">Dropouts: Not reported</td></tr>
<tr><td colspan="3">Ethnicity: Not reported</td></tr>
<tr><td colspan="3">Follow up time: 4 yrs (9 to 13 yrs)</td></tr>
<tr><td colspan="3">Dental age consideration: Yes ☐ No ☑
If yes, further notes</td></tr>
<tr><td colspan="3">Unit of analysis/ quantitative variables: Crowding/ spacing recorded in segments</td></tr>
<tr><td colspan="3">Statistical methods: Fischer’s test for effect of PEPT, t- test for clinical crown height</td></tr>
<tr><td colspan="3">Outcome</td></tr>
<tr><td colspan="3">Primary outcome: Space deficiency defined
Group I= deficiency up to 0.5mm, group II= 06- 3.5 mm, group III=>3.5 mm</td></tr>
<tr><td colspan="3">Secondary outcome: Eruption stage of incisors</td></tr>
<tr><td colspan="3">Gender differences: Non PEPT group incisor crowding upper jaw M: F= 18% vs 15%, lower jaw 8% vs 15%</td></tr>
<tr><td colspan="3">Difference in timing of extraction/loss: Not stated, previously stated (Ronnerman, 1965)</td></tr>
<tr><td colspan="3">Max. vs. Man. teeth: Not reported</td></tr>
<tr><td colspan="3">Ant vs. Post. teeth: Not reported</td></tr>
<tr><td colspan="3">D vs. E: Not reported</td></tr>
<tr><td colspan="3">Treatment under LA vs GA: Not reported</td></tr>
<tr><td colspan="3">Data source: Not reported in this article, previously stated (Ronnerman, 1965)</td></tr>
<tr><td colspan="3">Methods to reduce bias: Crowding/ spacing defined, age groups separated</td></tr>
<tr><td colspan="3">Results</td></tr>
</table>

Loss of one primary molar in a quadrant when tooth lost before 7.5 yrs resulted in significantly less relative space when compared no PEPT group, only p value given for various age groups, numbers not given Relative spacing not significant for tooth lost after 7.5 yrs		
Pattern of eruption of premolar is different in PEPT group vs no PEPT group		
The clinical crown length of upper central and lateral incisors are also affected by PEPT		
The study also looked in detail crowding/ spacing or arches without PEPT		
Internal validity		
Definition of inclusion and exclusion: Not reported		
Definition of outcome: Yes, crowding/ spacing clearly defined		
Treatment and control group comparability: Yes		
Follow up of participants: 4 yrs		
Examiner reliability: Not reported, intra and inter examiner agreement not discussed		
Blinding: Not reported		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes:		
Limitations		
Data source not discussed well		
Assessment of crowding/ spacing not discussed ie how study casts were measured etc		
Notes and comments		
Many variables being used and multiple testing used, the section looking at early loss of a primary molar, result presented only in terms of p value and significance level. It is not clear which statistical test was applied		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Ronnerman & Thilander, 1978)

Citation:		
Ronnerman, A. & Thailander, B. 1978. Facial and dental arch morphology in children with and without early loss of deciduous molars. *American Journal of Orthodontics,* 73**,** 47-58.		
Aim/ Objectives	To investigate whether there is relationship between space conditions in dental arches and facial morphology in persons in children with and without early loss of primary molars	
Methods		
Study design: Cross sectional study		
Setting: Not reported		
Intervention: Premature loss group compared to children without premature loss of primary molars		
Definition of premature extraction/ loss: No		
Participants Experimental: n= 47	Age: mean age 15yrs 8 mths	Sex: M:F= 19:28 (exp group) 28:29 (control group)
Control: n= 57		
Total: n= 124 (20 excluded, thus final no 104)		
Inclusion/ Exclusion: 20, hypodontia, supernumerary, ortho tx or unacceptable quality cephalogram		
Dropouts: N/A, cross sectional study		
Ethnicity: Not reported		
Follow up time: N/A, cross sectional study		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Child		
Statistical methods: Fisher's test used to compare groups		
Outcome		
Primary outcome: 1. Reference points and lines in ceph 2. Arch lengths, intercanine width, space, palatal vault height		
Secondary outcome: None		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: Not reported		
Ant vs. Post. teeth: Not reported		
D vs. E: Not reported		
Treatment under LA vs GA: Not reported		
Data source: Cephalograms and study casts		
Methods to reduce bias: Measurement error reported		
Results		

For cephalometrics, only distance subspinale to ptergomaxillare was significantly different in the two groups, reduced in PEPT group ($p < 0.05$)		
For dental arch, children with premature loss had significantly shorter arch length and less relative space in both arches, also reduced arch width in maxilla		
Subgroup analysis when children divided into 2 groups, extraction or no extraction (with crowding and no crowding) showed many significant differences in both craniofacial and dental arch morphology		
Premature extractions has no general influence on space conditions		
Children with crowding have shorter and narrower jaws irrespective of premature loss		
Internal validity		
Definition of inclusion and exclusion: Not clear		
Definition of outcome: No specific main outcome (as above) Many variables recorded and tested		
Treatment and control group comparability: Possibly but not clear if homogenous population assessed or not eg. ethnicity		
Follow up of participants: N/A, cross sectional study		
Examiner reliability: Not reported		
Blinding: Not reported		
Global validity		
High risk of bias: ☑	Low risk: ☐	Moderate: ☐
Further notes: No temporal relationship of outcome with risk factor		
Limitations		
Subspinale mainly used for soft tissue measurement only. Other variables like growth pattern not taken into account.		
Which teeth taken out were not taken into account		
Notes and comments		
Many variables recorded and tests applied		
There is no main outcome variable, thus results are very confusing		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Sayin & Turkkahraman, 2006)

Citation:		
Sayin MO, Turkkahraman H. Effects of lower primary canine extraction on the mandibular dentition. *Angle Orthodontist* 2006;**76**(1):31-5.		
Aim/ Objectives	To investigate the effects of early mandibular primary canine extractions on permanent incisor and first molar positions, dental and alveolar arch width and arch length	
Methods		
Study design: Controlled trial		
Setting: Not reported		
Intervention: Lower C extraction group compared to non extraction		
Definition of premature extraction/ loss: N/A, lower Cs extracted in tx group		
Participants Experimental: n= 16 with lower Cs extracted	Age: Mean 8.94 tx group, 8.88 control	Sex: M: F= 5:11 in tx group 11:5 in control
Control: n= 16		
Total: n= 32		
Inclusion/ Exclusion: Clearly defined Inclusion: Class I skeletal, mixed dentition, no hypodontia, no premature loss of any tooth, minimal loss of tooth dimension by caries or attrition, no ortho tx Exclusion: ortho tx		
Dropouts: None		
Ethnicity: Not stated		
Follow up time: Mean of 1.1 yr teatment group, 1 yr control group		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Child/ variables crowding and arch parameters/ cephalometric reference points		
Statistical methods: Descriptives, intragroup comparison with paired t-test, intergroup comparison with independent samples t-test		
Outcome		
Primary outcome: Crowding, arch length, intermolar width I (between mesiolingual cusp tips of lower Ds), intermolar width II (between mesiobuccal cusp tips of lower Es), permanent intermolar width (between mesiobuccal cusp tips of lower 6s), interalveolar width (distance between mucogingival junctions below the buccal grooves of the right and left 6s); various lines and angles in ceph		
Secondary outcome: N/A		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: N/A		
Ant vs. Post. teeth: N/A		
D vs. E: N/A		
Treatment under LA vs GA: Not reported		
Data source: Dental cast measurement using caliper to nearest 0.01mm One examiner performed all measurements		
Methods to reduce bias: Matching with respect to chronological age and observation period. Crowding significantly different in the two groups		

Results		
Intergroup comparison revealed that lower incisors were retruded more in treatment group compared to control as revealed by incisor position and incisor inclination, $p < 0.05$ over the observation period of about a year		
No differences in the two groups in arch length, intermolar and interalveolar widths and molar position		
Internal validity		
Definition of inclusion and exclusion: Clearly stated		
Definition of outcome: Not clear		
Treatment and control group comparability: Matched for observation period, sex and age but crowding different in two groups		
Follow up of participants: 100% retained		
Examiner reliability: Measured by one examiner, reliability co-eff 0.964 or higher		
Blinding: Not reported		
Global validity		
High risk of bias: ☐	Low risk: ☑	Moderate: ☐
Further notes:		
Limitations		
Extraction and non extraction groups are not comparable, extraction group had crowding >1.6mm, control group less than 1.6 mm		
Observation period of about a year is not enough to make judgement about occlusion in long term		
Just 16 patients may provide enough power to the study, no mention of power calculation		
Ethnicity of the patients not discussed which may influence their occlusion. However, age and sex was matched		
Notes and comments		
All important measurements were taken into consideration for arch dimensions and cephalometric analysis		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Appendix IX. Data extraction sheets for split-mouth studies.

Data extraction form (de Boer, 1982)

Citation:		
de Boer M. Early loss of primary molars. *Nederlands tijdschrift voor tandheelkunde* 1982;**89**(Suppl 21):8-28.		
Aim/ Objectives	Part I- To investigate spatial loss found at the age of 9 to 10 yrs in cases where previous loss of primary molar has occurred. Part II- To investigate space conditions at the age of 16 to 17 in the lateral segments in cases of one or both primary molars lost.	
Methods		
Study design: Retrospective cohort study		
Setting: Not clear, based in municipality of Meppel, Netherlands		
Intervention: PEPT quadrant vs sound quadrant without PEPT or proximal defects		
Definition of premature extraction/ loss: 'early extraction is meant an extraction either prior to the start of the study (before the age of 5-6 yrs) or prior to one of the subsequent dental inspections- the interval between two successive dental inspections being approximately half a year.'		
Participants Experimental: n=446 children, see below: Part I- 21 upper arches with unilateral molar loss; 27 lower arches with unilateral molar loss Part II- 156 upper quadrants and 68 lower quadrants	Age: Mean not reported, aged 5 yrs	Sex: Not reported
Control: n= sound quadrants		
Total: n= see above		
Inclusion/ Exclusion: Unilateral cases where only one molar lost and this was compared to the unaffected quadrant		
Dropouts: Not reported		
Ethnicity: Not reported		
Follow up time: Part I- till 9-10 yrs, Part II- from age 5/6 yrs to 16-17 yrs		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Arches		
Statistical methods: No statistical tests applied, only descriptive reported		
Outcome		
Primary outcome: Difference in space between extraction and sound quadrant Crowding and spacing in quadrants		
Secondary outcome: None		
Gender differences: Not reported		
Difference in timing of extraction/loss:		
Max. vs. Man. teeth: Reported, see results		
Ant vs. Post. teeth: Not reported		
D vs. E: Reported, see results		
Treatment under LA vs GA: Not reported		
Data source: Serial study models of children		
Methods to reduce bias: Not reported		

Same arch as control group, longitudinal study
Results
Part I- Extraction of E at the age of 5-6 yrs can lead to a marked loss of space in the lateral segment, 8mm in upper arch vs 6.5mm in lower arch
Part II- Very early loss (prior to 7.5 -8.5 yrs), early loss (after 7.5 yrs- 8.5yrs), no loss in lower arches, percentages of crowding are 59%, 39% and 34% respectively at age 16 yrs. In upper arches percentages of crowding are 69%, 64% and 48% respectively. In upper arch, no loss vs D vs E vs both in terms of crowding are 34% vs 25% vs 50% vs 62%. In lower arch, no loss vs D vs E vs both in terms of crowding are 48% vs 70% vs 50% vs 76%. Percentage of crowding higher in cases where there was crowding in primary dentition, 26% more in upper arch as compared to arches with spacing, corresponding figure for lower arch is 30%.
Internal validity
Definition of inclusion and exclusion: PEPT quadrant vs sound quadrant
Definition of outcome: Not clear
Treatment and control group comparability: Yes, same arch
Follow up of participants: From 5-6 yrs til 9-10 yrs for spatial measurement, 16 yrs for crowding/ spacing, dropouts not reported
Examiner reliability: Not reported
Blinding: Not reported
Global validity
High risk of bias: ☑ | Low risk: ☐ | Moderate:☐
Further notes:
Limitations
Space and crowding cannot be taken just from quadrant
Overall assessment was not possible as it is unilateral study
Subgroup analysis ended up with small sample sizes
Notes and comments
Early loss and very early loss defined by taking into account chronological age but this should really take into account of the eruption times on individual teeth
How measurement was carried out was not discussed and calibration of measurement
Definition of crowding and spacing not clear
Conflict of interest
Not reported
Ethical approval
Not reported

Data extraction form (Lin & Chang, 1998)

Citation:		
Lin YT, Chang LC. Space changes after premature loss of the mandibular primary first molar: a longitudinal study. *J Clin Pediatr Dent* 1998;**22**(4):311-6.		
Aim/ Objectives	To evaluate the space changes after premature loss of the primary mandibular first molar	
Methods		
Study design: Prospective cohort study		
Setting: Children's Dental Clinic of Chang Gung Memorial Hospital, Kaohsiung Medical Centre, Taiwan		
Intervention: PEPT of mandibular primary molar		
Definition of premature extraction/ loss: N/A, experimental quadrant had an extraction of a mandibular primary molar		
Participants Experimental: n=21 quadrants with unilateral loss of mandibular first primary molar	Age: Mean 6yrs 11 mths (5.1 yrs- 7.2 yrs)	Sex: M:F= 12: 9
Control: n= 21 quadrants without loss of mandibular molar		
Total: n= 21		
Inclusion/ Exclusion: Clearly defined, 6s about to erupt, co-operative for impression taking, unilateral loss of lower D but intact opposite arch. Exclusions were hypodontia and if space maintainers were planned to be used		
Dropouts: None		
Ethnicity: Not stated		
Follow up time: Approx 8 mths		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: D and E space, defined as the distance between the mesial midpoint of the first permanent molar and distal midpoint of primary cuspid		
Statistical methods: D and E space measured, initial D and E space as control, paired t test for longitudinal cast measurement and student t- test for difference in experiment and control		
Outcome		
Primary outcome: D and E space		
Secondary outcome: Arch length, arch width and arch perimeter		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: Not reported		
Ant vs. Post. teeth: N/A		
D vs. E: N/A		
Treatment under LA vs GA: Not reported		
Data source: Investigation of study casts		
Methods to reduce bias: Single examiner took all measurements, 2 measurements were taken with accuracy of 0.1mm		
Results		

D and E space change in the extraction side was significantly shorter after 8 mths (16.84± 1.86mm) than the control side (17.83± 1.3mm) and less than initial measurement (18.06± 1.81mm), $p < 0.001$		
There were no significant differences in arch width, arch length and arch perimeter after 8 months following extraction		
Thus, extraction space closed by drifting of teeth on either side of extraction space ie. C moving distally and E moving mesially but more by C moving distally as arch length has remained unchanged but possibly related to eruption of incisors which needed more space		
Internal validity		
Definition of inclusion and exclusion: Yes, see above		
Definition of outcome: Yes, see above		
Treatment and control group comparability: Yes, unilateral extraction compared to no extraction		
Follow up of participants: 100%, all 21 followed up to 8 mths		
Examiner reliability: One examiner did all measurement but no intra-examiner agreement reported		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☐	Low risk: ☑	Moderate: ☐
Further notes:		
Limitations		
Split mouth design which may be a cause of bias		
Follow up of 8 months may not be adequate to study the effects of space loss		
Notes and comments		
Challenged use of space maintainers looking at overall arch dimensions		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Lin & Lin, 2011)

Citation:		
Lin YT, Lin WH. Twelve-month space changes after premature loss of a primary maxillary first molar. *Int J Paediatr Dent* 2011;**21**(3):161-6.		
Aim/ Objectives	The aim of this study was to investigate dental arch space problems arising as a result of premature loss of a primary maxillary first molar.	
Methods		
Study design: Prospective cohort study		
Setting: Children's Dental Clinic of the Chang Gung Memorial Hospital-Kaohsiung Medical Centre, Taiwan		
Intervention: Unilateral extraction vs control with no extraction		
Definition of premature extraction/ loss: Yes; 'the absence of a permanent tooth after extraction of the primary molar'		
Participants Experimental: n= 13 children with unilateral loss of upper D	Age: Mean 6.0 yrs (±0.74)	Sex: M:F= 5:8
Control: n= 13, contralateral unaffected side		
Total: n= 19		
Inclusion/ Exclusion: 6		
Dropouts: None		
Ethnicity: Not reported		
Follow up time: 12 months		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Arch parameters, see below		
Statistical methods: Reliability co-efficients to compare consistency and reliability of examiners, both intra and interexaminer >0.900, Paired and unpaired t test for D and E space, p value < 0.05		
Outcome		
Primary outcome: D and E space (the distance between the mesial midpoint of the permanent first molar and the distal midpoint of the primary canine)		
Secondary outcome: Arch width (the distance between the central fossae on the occlusal surfaces of the two primary second molars); arch length (the perpendicular distance from the contact point of the central incisors to the arch width); intercanine width (the distance between cusp tips of the two primary canines); intercanine length (the perpendicular distance from the contact point of the central incisors to the intercanine width); arch perimeter (the arc measured from the mesial midpoint of the permanent first molar through cusp tip of the canine and incisal edges of the incisors to the opposite mesial midpoint of the permanent first molar, measured with the aid of brass wire)		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: N/A		
Ant vs. Post. teeth: N/A		
D vs. E: N/A		
Treatment under LA vs GA: Not reported		

Data source: Serial dental casts		
Methods to reduce bias: Examiner reliability, comparison to intact control side, exclusion of cases who had extensive caries and loss to follow		
Results		
D and E space not different in extraction side compared to control at initial examination, but significantly smaller on extraction side than control 15.84 mm vs 16.92 mm, p= 0.01 in 12 mths time		
Intercanine width, intercanine length and arch perimeter significantly greater in 12 mths after tooth extraction, about 1mm space gained for each parameter		
There was no significant difference in arch width and arch length in measurement at initial and 12 mths later		
Thus extraction space loss is mainly by distal migration of Cs		
Internal validity		
Definition of inclusion and exclusion: Clearly stated, inclusion: no major craniofacial disease, 6s about to erupt or just erupted, co-operative for impressions, unilateral loss of upper D with intact contralateral side, parents did not want space maintenance		
Definition of outcome: Yes		
Treatment and control group comparability: Yes, unilateral study		
Follow up of participants: All 13 cases were followed to 12 mths		
Examiner reliability: Intra and inter-examiner reliability reported for all measurements, all >0.9		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☐	Low risk: ☑	Moderate: ☐
Further notes:		
Limitations		
Unilateral study, thus potential risk of bias		
Follow up only until 12 mths		
Only 13 cases, thus small sample size		
Notes and comments		
Study challenges uses of space maintainers as most of the space lost was due to distal migration of Cs with arch length unchanged but small sample size of only 13 children with unilateral loss of upper Ds and intact contralateral side		
This was a follow on study with study results published for 6 months were it was reported that D and E space was lost but arch dimensions were not consistent with this study		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Linder-Aronson, 1960)

Citation:		
Linder-Aronson S. The effect of premature loss of deciduous teeth. A Biometric study in 14 and 15 year olds. *Acta Odontologica Scandinavica* 1960;**18**(2):101-22.		
Aim/ Objectives	To investigate: the extent of premature loss of deciduous teeth causing crowding to permanent dentition, the extent of displacement of midline in upper jaw, the extent of mesial migration of upper 6s, extent of mesio-lingual rotation of upper 6s	
Methods		
Study design: Retrospective cohort study		
Setting: Public Dental Care Centre, Froson, Sweden		
Intervention: Unilateral loss of primary teeth (C, D, E)		
Definition of premature extraction/ loss: Not defined		
Participants Experimental: n= 41	Age: 14-15 yr olds and dental notes retrospectively	Sex: M:F= 22: 19
Control: n= 41		
Total: n=41 children		
Inclusion/ Exclusion: Only unilateral loss was selected, other pattern of extractions were excluded		
Dropouts: Only unilateral loss selected		
Ethnicity: Not reported		
Follow up time: Not reported		
Dental age consideration: Yes ☐ No ☑ If yes, further notes (but, divided into very early loss, early loss and late loss depending on chronological age)		
Unit of analysis/ quantitative variables: Hemi- arch parameters		
Statistical methods: t test		
Outcome		
Primary outcome: Crowding or spacing calculated from arch perimeter and tooth widths for that quadrant		
Secondary outcome: None		
Gender differences: Ratio as above but not reported for outcome		
Difference in timing of extraction/loss:		
Max. vs. Man. teeth: 25 vs 16 cases, Max. teeth crowding in extraction side in 10 cases vs 9 cases in control side, Man. Teeth crowding extraction side 6 vs 5 in control side		
Ant vs. Post. teeth: N/A		
D vs. E: Various combinations of PEPT, not separated for outcome		
Treatment under LA vs GA:		
Data source: Study models made from alginate impressions and measurement transferred onto paper in stereograph		
Methods to reduce bias: Dental arch divided into 6 sections, anatomical landmark midline raphae taken into account for midline measurements		
Results		

Dental arch (hemi-perimeter) on extraction side compared to control side was not significantly different		
Arch measurement (hemi-perimeter) significantly less when very early loss has taken place (loss before 7 yrs old), but this group only consisted of 7 children out of 41		
No significant relation between premature loss and midline displacement in the upper jaw in 25 cases, mean value is 0.06± 0.19mm when 0.00 is the control value that suggest no midline shift		
6s on the side of extraction is more mesially placed than the control side with mean value of 1.01± 0.28mm, p< 0.01		
No difference in mesio- lingual rotation of 6s between premature loss and control side		
Internal validity		
Definition of inclusion and exclusion: Yes		
Definition of outcome: Yes		
Treatment and control group comparability: Yes		
Follow up of participants: 14-15 yrs old, dental records looked retrospectively, dropouts not reported		
Examiner reliability: Measurement error calculated, measurements done twice but examiner calibration or agreement not reported		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes:		
Limitations		
Relied on dental notes that were recorded annually, risk of selection bias		
Noted midline measurement in 25 upper arch was difficult due to indistinct median raphae		
Notes and comments		
Incisive papilla not used for midline measurements		
Occlusion specially sagittal relationship might have been affected by the extraction side		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Macena et al, 2011)

Citation:		
Macena MC, Tornisiello Katz CR, Heimer MV, de Oliveira e Silva JF, Costa LB. Space changes after premature loss of deciduous molars among Brazilian children. *Am J Orthod Dentofacial Orthop* 2011;**140**(6):771-8.		
Aim/ Objectives	To assess dimensional changes in the dental arches after premature loss of first and second deciduous molars in Brazilian schoolchildren.	
Methods		
Study design: Prospective cohort study (unilateral)		
Setting: Camaragibe, Pernambuco, Brazil		
Intervention: PEPT quadrant compared to control quadrant		
Definition of premature extraction/ loss: N/A Experimental quadrant had extraction and other quadrant not		
Participants Experimental: n=55 hemi- arch	Age: 8-9 yrs	Sex: M:F= 31% M, 69% F
Control: n= 55 hemi- arch		
Total: n=87		
Inclusion/ Exclusion: 24 excluded, thus reduced to 63		
Dropouts: 8, thus at final number 55		
Ethnicity: Not reported		
Follow up time: 3, 6 and 10 months		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: Hemi- arch		
Statistical methods: ANOVA, paired t test and student t- test, p value 0.05		
Outcome		
Primary outcome: Dental space at extraction site		
Secondary outcome: Dental arch length, hemi- perimeter of the dental arch		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: Ratio 21:25		
Ant vs. Post. teeth: N/A		
D vs. E: Ratio 20:35, significant space loss in case of Es only in both arches		
Treatment under LA vs GA: Not reported		
Data source: Dental cast measurements		
Methods to reduce bias: Split mouth design, one examiner measuring casts		
Results		

Most frequently extracted tooth was lower Es, 22/55 subjects, Significant extraction space reduction after loss of Es, P< 0.001 when measurements were taken before extraction, at 3 mths, 6 mths and 10 mths		
Most of the space loss in cases of Es occurred in the first 3 months, upper Es regained some space but this was not the case for lower Es, initial and 10 mths extraction space reduced significantly in both cases, p< 0.01		
Arch length showed significant change consistently only in cases of upper Es ie. reduction in arch length, p< 0.05		
Arch hemi-perimeter was reduced in case of extraction of lower Es only, p< 0.001		
Internal validity		
Definition of inclusion and exclusion: Yes; inclusion criteria are unilateral extraction indicated for one primary molar either to maxillary or mandibular arch, all 4 incisors erupted or in process of eruption, first permanent molars and in occlusion, premolars not erupted, primary canine in the quadrant of extraction. Exlusions were development syndromes or abnormalities, loss of other primary teeth, hypondontia, open bite, cross bite, current or past orthodontic treatment.		
Definition of outcome: Yes, clearly defined		
Treatment and control group comparability: Yes same arch		
Follow up of participants: Measurements at 3, 6 and 10 mths with 87% participants retained		
Examiner reliability: Dental casts measured by same examiner		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☐	Low risk: ☑	Moderate: ☐
Further notes:		
Limitations		
Follow up of only 10 months may not be enough for clinical cases where teeth are lost for much longer period than this		
Possibility of midline discrepancy not taken into account		
Hemi-perimeter may not be an appropriate measurement as loss only on unilateral side may be compensated by the other side in the same arch		
Notes and comments		
Only unilateral loss included in the study, thus bias introduced by extraction of other teeth was reduced, but split mouth study may have introduced other types of bias, mainly selection bias		
Occlusal instability may have resulted if lost teeth from the other arch to the one being studied as this was not explained in exclusion criteria		
Conflict of interest		
Not reported		
Ethical approval		
Research committee of the Pernambuco State University		

Data extraction form (Magnusson, 1979)

Citation:		
Magnusson TE. The effect of premature loss of deciduous teeth on the spacing of the permanent dentition. *European Journal of Orthodontics* 1979;**1**(4):243-9.		
Aim/ Objectives	To investigate the prevalence of premature loss of deciduous canines and or molars and its effect on the space in the dental arches	
Methods		
Study design: Cross sectional survey		
Setting: Subjects were school children from Reykjvik, Iceland, setting not made clear		
Intervention: Unilateral loss of primary teeth		
Definition of premature extraction/ loss: Yes, according to Bjork, 'the succeeding permanent tooth shall not have penetrated the mucous membrane nor palpable immediately beneath it'		
Participants Experimental: n= 46 unilateral loss	Age: Not reported	Sex: M:F= 27:19
Control: n= 46 control 'side' of the arch		
Total: n= 55		
Inclusion/ Exclusion: 5/55 excluded due to hypodontia and loss of 6s		
Dropouts: 4/55, thus final number 46		
Ethnicity: Not reported		
Follow up time: N/A, cross sectional survey		
Dental age consideration: Yes ☑ No ☐ If yes, further notes: divided into dental stages DS2, DS3 and DS4		
Unit of analysis/ quantitative variables:		
Statistical methods: t- test		
Outcome		
Primary outcome: Arch perimeter divided into incisor and canine-premolar segment		
Secondary outcome:		
Gender differences: M:F ratio 27:19		
Difference in timing of extraction/loss:		
Max. vs. Man. teeth: 8 vs 38 cases		
Ant vs. Post. teeth:		
D vs. E:		
Treatment under LA vs GA: Not reported		
Data source: Measurements in dental casts, accuracy of 0.1mm		
Methods to reduce bias: Single examiner, all measurements were carried out twice and by same author, error less than 5%		
Results		

There was no significant difference in incisor segments and canine- premolar segments in premature loss and control side in maxillary arches		
In mandibular arches, the mean difference in canine- premolar segment was significantly different in DS 2 but shows progressive reduction in DS 2 to DS 4, the values were -3.7, -1.5 and -0.8 mm respectively		
In mandibular arches, the mean difference in incisor segment was not significantly different		
Internal validity		
Definition of inclusion and exclusion: Yes		
Definition of outcome: Yes		
Treatment and control group comparability: Yes as unilateral loss compared to control group		
Follow up of participants: 46/55		
Examiner reliability: Single examiner		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☑	Low risk: ☐	Moderate: ☐
Further notes: No temporal relationship as cross- sectional survey		
Limitations		
Analytical cross- sectional study, as subjects are not followed up, difficult to reach conclusion about causation		
There were only 8 cases of maxillary unilateral extractions, thus sample size very limited to generalise for other maxillary arches		
Notes and comments		
Concluded that space lost in initial stages were recovered in latter stages throughout development		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Northway et al, 1984), also based on Thesis

<table>
<tr><td colspan="3">Citation:</td></tr>
<tr><td colspan="3">Northway WM, Wainright RL, Demirjian A. Effects of premature loss of deciduous molars. Angle Orthodontist 1984;54(4):295-329.</td></tr>
<tr><td>Aim/ Objectives</td><td colspan="2">To compare mean spatial changes in the dental arch subsequent to premature loss of deciduous molars with the changes that occur in undisturbed arches</td></tr>
<tr><td colspan="3">Methods</td></tr>
<tr><td colspan="3">Study design: Cohort study</td></tr>
<tr><td colspan="3">Setting: Based on Montreal growth sample data, starting at the age of 6yrs</td></tr>
<tr><td colspan="3">Intervention: D & E space compared to intact quadrants (cariesfree, restored and mild- caries)</td></tr>
<tr><td colspan="3">Definition of premature extraction/ loss: ‘A tooth absent at two consecutive annual recordings’</td></tr>
<tr><td>Participants
Experimental: n= 71/107 children</td><td>Age: Cohort started at age 6yrs</td><td>Sex: Taken from a growth sample of 260 males and 295 females, sex not reported for 107 children included in the study</td></tr>
<tr><td>Control: n= other quadrants not affected by PEPT or severe caries (control group was a combination of cariesfree, restored and mild caries groups pooled)</td><td></td><td></td></tr>
<tr><td>Total: n= 107 children</td><td></td><td></td></tr>
<tr><td colspan="3">Inclusion/ Exclusion: Excluded 18/107 children due to severe caries</td></tr>
<tr><td colspan="3">Dropouts: All children had at least 4 yearly study models</td></tr>
<tr><td colspan="3">Ethnicity: French Canadian children (3/4 grandparents of French Canadian origin)</td></tr>
<tr><td colspan="3">Follow up time: Mean 5.9 yrs</td></tr>
<tr><td colspan="3">Dental age consideration: Yes ☐ No ☑
If yes, further notes</td></tr>
<tr><td colspan="3">Unit of analysis/ quantitative variables: D & E space</td></tr>
<tr><td colspan="3">Statistical methods: ANOVA among the different groups at each age</td></tr>
<tr><td colspan="3">Outcome</td></tr>
<tr><td colspan="3">Primary outcome: D & E space (the distance between the mesial midpoint of the first permanent molar and the distal midpoint of the cuspid) in reference to the palatal rugae</td></tr>
<tr><td colspan="3">Secondary outcome: Palatal anatomical landmarks and Flush terminal plane to assess malocclusion</td></tr>
<tr><td colspan="3">Gender differences: Pooled results only (discussed that differences was not possible to analyse due to small sample size)</td></tr>
<tr><td colspan="3">Difference in timing of extraction/loss: See results</td></tr>
<tr><td colspan="3">Max. vs. Man. teeth: Average space loss in maxilla D loss, 0.3mm; E loss, 0.7mm; D and E loss 0.9mm, same figures for mandible 0.5mm, 0.9mm and 0.7mm</td></tr>
<tr><td colspan="3">Ant vs. Post. teeth: N/A, only molars included</td></tr>
<tr><td colspan="3">D vs. E: See above</td></tr>
</table>

<table>
<tr><td colspan="3">Treatment under LA vs GA: Not reported</td></tr>
<tr><td colspan="3">Data source: Digitised dental casts with 0.2mm</td></tr>
<tr><td colspan="3">Methods to reduce bias: Used digitized casts with 02mm precision with 348 registration points, these reference points used by previous researchers; unilateral study design with severe caries excluded</td></tr>
<tr><td colspan="3">Results</td></tr>
<tr><td colspan="3">Upper arch, average yearly D and E space loss was 0.3mm, 0.7mm and 0.9mm for D loss, E loss and D and E loss groups respectively. Greatest divergence was D and E loss group with control group at 4.3mm
Lower arch, average yearly D and E space loss was 0.5mm, 0.9mm and 0.7mm for D loss, E loss and D and E loss groups respectively. Greatest divergence was E loss group with control group at 3.7mm</td></tr>
<tr><td colspan="3">Cuspid migration was in the range of 1-1.5mm and molar migration in the range of 2-3mm with exception of D loss group in both arches where cuspid displacement was mesial rather than distal</td></tr>
<tr><td colspan="3">Rate of space loss in the first year was significantly more than in successive years. Extraction in younger children caused more space loss than older children (D and E space loss compared between 6, 7 ,8 yr olds to 9, 10, 11 yr olds) in maxilla but not in mandible. Extraction in maxilla at age 6, 7 and older group led to space loss of 4.1mm, 2.1mm and less than 1.5 mm respectively. Extractions in mandible at all ages led to average loss from 2.6mm- 3.2mm</td></tr>
<tr><td colspan="3">There was no significant shift to provide space for permanent teeth in the maxilla mandible apart from lower D and E loss group</td></tr>
<tr><td colspan="3">In upper arch, E loss and D and E loss led to disto-occlusion
In lower arch, E loss and D and E loss led to mesio-occlusion</td></tr>
<tr><td colspan="3">Internal validity</td></tr>
<tr><td colspan="3">Definition of inclusion and exclusion: Yes</td></tr>
<tr><td colspan="3">Definition of outcome: Yes</td></tr>
<tr><td colspan="3">Treatment and control group comparability: Yes</td></tr>
<tr><td colspan="3">Follow up of participants: Average of 5.9 years</td></tr>
<tr><td colspan="3">Examiner reliability: Reproducibility among 225 paired recordings showed SD of 0.26mm</td></tr>
<tr><td colspan="3">Blinding: Not reported</td></tr>
<tr><td colspan="3">Global validity</td></tr>
<tr><td>High risk of bias: ☐</td><td>Low risk: ☑</td><td>Moderate: ☐</td></tr>
<tr><td colspan="3">Further notes:</td></tr>
<tr><td colspan="3">Limitations</td></tr>
<tr><td colspan="3">As D and E space reported for each quadrant for all groups, it could not be taken into account intra and inter arch relationship</td></tr>
<tr><td colspan="3">It was not discussed the criteria for severe caries, reported as seen on study cast but this could have been a source of bias</td></tr>
<tr><td colspan="3">Notes and comments</td></tr>
<tr><td colspan="3">D & E space that provides a section of the arch that is easily defined</td></tr>
<tr><td colspan="3">Conflict of interest</td></tr>
<tr><td colspan="3">Not stated</td></tr>
<tr><td colspan="3">Ethical approval</td></tr>
<tr><td colspan="3">Not stated</td></tr>
</table>

Data extraction form (Padma Kumari & Retnakumari, 2006)

Citation:		
Padma Kumari B, Retnakumari N. Loss of space and changes in the dental arch after premature loss of the lower primary molar: a longitudinal study. *Journal of the Indian Society of Pedodontics & Preventive Dentistry* 2006;**24**(2):90-6.		
Aim/ Objectives	To evaluate the space changes in the extracted side, to determine the changes in dental arch width, to observe changes in the dental arch width, to evaluate the changes in the dental arch perimeter.	
Methods		
Study design: Prospective cohort study		
Setting: Department of Paedodontics, Thiruananthapuram, India		
Intervention: Premature loss compared to control quadrant		
Definition of premature extraction/ loss: Yes, 'unerupted permanent predecessor for at least 2 years after extraction of deciduous first molar'		
Participants Experimental: n= 30 unilateral loss	Age: 6-9 yrs	Sex: Not reported
Control: n= 30 control sides		
Total: n= 40		
Inclusion/ Exclusion: See below		
Dropouts: 10/40, thus final number 30		
Ethnicity: Not reported		
Follow up time: 8 mths (monitored from before extraction over 2, 4, 6 and 8 mths)		
Dental age consideration: Yes ☐ No ☑ If yes, further notes:		
Unit of analysis/ quantitative variables: Premature loss quadrant		
Statistical methods: Paired t- test		
Outcome		
Primary outcome: Extraction space measured as the distance between lower C and E		
Secondary outcome: Arch width, arch length and arch perimeter		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: N/A		
Ant vs. Post. teeth: N/A		
D vs. E: N/A		
Treatment under LA vs GA: Not reported		
Data source: Repeated dental casts		
Methods to reduce bias: Restriction to a type of tooth only chosen to reduce selection bias,		
Results		

Lower D 'space' in extracted side showed significant reduction at 2, 4, 6 and 8 mths, values were 7.72± 0.56, 7.03± 0.56, 6.62± 0.56 and 6.64± 0.44 respectively, most space lost in the first 4 mths		
Arch length measurements were not statistically significant in extraction and control sides at 2, 4, 6 and 8 mths		
Arch width measurements were not statistically significant in extraction and control sides at 2, 4, 6 and 8 mths		
Arch perimeter measurements were not statistically significant in extraction and control sides at 2, 4, 6 and 8 mths		
Internal validity		
Definition of inclusion and exclusion: Inclusion critetia were 6s erupted, only unilateral loss with intact anteriors, anteroposterior and lateral arch relationships were acceptable and parents willing to not space maintenance		
Definition of outcome: Yes		
Treatment and control group comparability: Yes, split mouth style		
Follow up of participants: 30/40		
Examiner reliability: Not reported		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes:		
Limitations		
Limited sample size of 30, unilateral design		
M: F ratio and ethnicity not reported		
Follow up to 8 mths only		
Notes and comments		
Longitudinal study but only followed up for 8 months which may or may not be relevant in the long term		
Concluded that space lost was mainly due to distal migration of Cs rather than mesial migration of Es as arch length, arch width and arch perimeter remained not significantly different		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Park et al, 2009)

Citation:		
Park K, Jung D-W, Kim J-Y. Three-dimensional space changes after premature loss of a maxillary primary first molar. *International Journal of Paediatric Dentistry* 2009;**19**(6):383-9.		
Aim/ Objectives	To examine spatial changes subsequent to premature loss of a maxillary primary first molar after the eruption of the first permanent molars, also to investigate the amount of tooth movement in primary canines, primary second molars and permanent first molars adjacent to the extraction site	
Methods		
Study design: Prospective cohort study		
Setting: Department of Pediatric Dentistry at Samsung Medical Center, Seoul, South Korea		
Intervention: Unilateral loss of upper D compared to control side		
Definition of premature extraction/ loss: Yes, 'premature extraction of a maxillary primary first molar at least 12 mths ahead of the expected eruption of the permanent successors'		
Participants Experimental: n= 13 unilateral loss	Age: At initial exam mean=7 yrs 11 mths, mean at final exam= 8 yrs 11 mths	Sex: M:F= 8:5
Control: n= 13		
Total: n= 13 (split mouth style)		
Inclusion/ Exclusion: 2/13 excluded (lost upper D from the control side)		
Dropouts: None		
Ethnicity: Not reported		
Follow up time: Mean 12 mths (8-23 mths)		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables: D & E space at extraction and control side		
Statistical methods: Paired t- test between initial and final measurements, Student t- test to compare between extraction side to control, directional differences in angulation and inclination between the extraction and the control sides were compared by 2 way ANOVA		
Outcome		
Primary outcome: D and E space defined as the distance between the mesial midpoint of the first permanent molar and distal midpoint of the primary canine		
Secondary outcome: Angulation and inclination changes of Cs and Es		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: N/A		
Ant vs. Post. teeth: N/A		
D vs. E: N/A		
Treatment under LA vs GA: Not reported		
Data source: Computer- interfaced laser scanner of dental casts		
Methods to reduce bias: 3-D laser scanner with ±20um precision		

Results		
The mean D and E space before extraction was not significantly different in extraction and control side (16.47 mm vs 16.09 mm)		
The mean D and E space after extraction was not significantly different in extraction and control side (15.9 mm vs 15.78 mm)		
There was no significant difference in the amount of space loss on extraction side compared to control, p=0.33		
For Cs, Es and 6s, there were no significant differences in the amount of inclination and angulation changes between the extraction and the control sides		
Arch width, arch length and perimeter significantly increased at the final examination compared to the initial examination, p< 0.05		
Internal validity		
Definition of inclusion and exclusion: Inclusion criteria (premature extraction of a maxillary primary first molar at least 12 mths ahead of the expected eruption of the permanent successors, unilateral extraction with intact contralateral side, maxillary permanent incisors and 6s have erupted, maxillary primary canines and second molars were present and Class I molar relationships on both sides		
Definition of outcome: Yes		
Treatment and control group comparability: Yes		
Follow up of participants: Mean 12 mths (8- 23 mths), 2/13 dropouts		
Examiner reliability: One examiner carried out all measurements, no reliability score given		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes:		
Limitations		
Only 11 cases for final analysis, thus small sample size		
Accuracy of the 3-d scanner not discussed		
Notes and comments		
The cases included all cases where 6s have already erupted, thus this does not answer cases where Ds are lost before eruption of 6s		
Conflict of interest		
Not reported		
Ethical approval		
By the Institutional Review Board of Samsung Medical Center		

Data extraction form (Ronnerman & Thilander, 1977)

<table>
<tr><td colspan="3">Citation:</td></tr>
<tr><td colspan="3">Ronnerman A, Thilander B. A longitudinal study on the effect of unilateral extraction of primary molars. Scand J Dent Res 1977;85(5):362-72.</td></tr>
<tr><td>Aim/ Objectives</td><td colspan="2">To establish the consequences of early extraction of the first or second primary molar with respect to space conditions, need for orthodontic treatment and the time of tooth eruption</td></tr>
<tr><td colspan="3">Methods</td></tr>
<tr><td colspan="3">Study design: Cohort study (retrospective)</td></tr>
<tr><td colspan="3">Setting: Department of Orthodontics, University of Gothenburg, Sweden</td></tr>
<tr><td colspan="3">Intervention: Premature extraction of Ds or Es</td></tr>
<tr><td colspan="3">Definition of premature extraction/ loss: Yes, ‘the subsequent permanent tooth was covered with bone at the first examination at the age of 10 yrs’</td></tr>
<tr><td>Participants
Experimental: n=
Group 1: 27 cases of unilateral loss of Ds (taken from Ronnerman, 1965)
Group 2: 38 cases of unilateral loss of Es</td><td>Age:
Serial dental casts at ages 9,11 and 13 for group I and ages 10 and 12 for group II</td><td>Sex: Not reported</td></tr>
<tr><td>Control: n= Quadrant without premature loss</td><td></td><td></td></tr>
<tr><td>Total: n= 65</td><td></td><td></td></tr>
<tr><td colspan="3">Inclusion/ Exclusion:</td></tr>
<tr><td colspan="3">Dropouts:</td></tr>
<tr><td colspan="3">Ethnicity: Not reported</td></tr>
<tr><td colspan="3">Follow up time: 2-4 years</td></tr>
<tr><td colspan="3">Dental age consideration: Yes ☐ No ☐
If yes, further notes</td></tr>
<tr><td colspan="3">Unit of analysis/ quantitative variables:</td></tr>
<tr><td colspan="3">Statistical methods: For comparison within groups, paired t- test and for comparison between 2 groups, fisher’s non- parametric test</td></tr>
<tr><td colspan="3">Outcome</td></tr>
<tr><td colspan="3">Primary outcome: Incisor and canine- premolar segment in dental arch</td></tr>
<tr><td colspan="3">Secondary outcome: Orthodontic need</td></tr>
<tr><td colspan="3">Gender differences: Not reported</td></tr>
<tr><td colspan="3">Difference in timing of extraction/loss: Not reported</td></tr>
<tr><td colspan="3">Max. vs. Man. teeth: See results</td></tr>
<tr><td colspan="3">Ant vs. Post. teeth: N/A, only D and E loss included</td></tr>
<tr><td colspan="3">D vs. E: See results</td></tr>
<tr><td colspan="3">Treatment under LA vs GA: Not reported</td></tr>
<tr><td colspan="3">Data source: Measurements of casts, slide calipers with precision 0.1mm, for orthodontic treatment indication: dental radiographs, case history cards and study casts</td></tr>
<tr><td colspan="3">Methods to reduce bias: Unilateral loss cases selected</td></tr>
<tr><td colspan="3">Results</td></tr>
</table>

For group with unilateral loss of upper Ds, lateral segment and arch perimeter (incisor segment and lateral segment) was significantly less in extraction side at 8.9 yrs compared to control, $p < 0.05$. However, in later at the age of 13 yrs, there was no significant difference in extraction and control sides		
For group with unilateral loss of lower Ds, lateral segment and arch perimeter (incisor segment and lateral segment) was significantly less in extraction side at 9 yrs and 11 yrs compared to control, $p < 0.01$		
For group with unilateral loss of upper and lower Es, lateral segment was significantly less in extraction side at 10 yrs and 12 yrs compared to control, $p < 0.01$		
Need for orthodontic treatment in D loss group was 11/27 cases		
Orthodontic treatment in E loss group was carried out in 26/38 cases		
Internal validity		
Definition of inclusion and exclusion: Unilateral loss compared to control side		
Definition of outcome: Yes for arch measurement		
Treatment and control group comparability: Yes		
Follow up of participants: All cases had serial casts, dropouts not reported		
Examiner reliability: Not reported		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☐	Low risk: ☐	Moderate: ☑
Further notes: Examiner reliability not reported, orthodontic need not defined		
Limitations		
Orthodontic need was discussed but no comparison made to the quadrant where premature loss had occurred or children without premature loss		
It is not clear how orthodontic need was defined and how this group was identified		
Subgroups analysis shows limited sample size		
Notes and comments		
Upper D cases= 13, lower D cases= 14, upper E cases= 14, lower E cases= 24		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Rosenzwig & Klein, 1960)

Citation:		
Rosenzwig KA, Klein H. Loss of space by extraction of primary molars. *J Dent Child* 1960;**17**:275-76.		
Aim/ Objectives	To assess possible damage resulting from neglect of primary teeth	
Methods		
Study design: Cross sectional survey		
Setting: Children from a subrub of Jerusalem treated at school dental clinic		
Intervention: Premature loss compared to control side		
Definition of premature extraction/ loss: No		
Participants Experimental: n= 61 unilateral loss Upper D= 13, lower Ds= 19, upper Es= 12 and lower Es= 17	Age: 9- 11 yrs	Sex: Ratio not reported
Control: n= Side where there was no premature loss		
Total: n= 166 children		
Inclusion/ Exclusion: 61 arches consisting one premature loss of primary molar		
Dropouts: N/A, cross sectional survey		
Ethnicity: Not reported		
Follow up time: N/A, cross sectional survey		
Dental age consideration: Yes ☐ No ☑ If yes, further notes		
Unit of analysis/ quantitative variables:		
Statistical methods: No statistical test, only mean and standard deviation recorded		
Outcome		
Primary outcome: Average space (between the embrasures of adjacent teeth)		
Secondary outcome: None		
Gender differences: Not reported		
Difference in timing of extraction/loss: Not reported		
Max. vs. Man. teeth: Ratio 25 vs 36		
Ant vs. Post. teeth: N/A		
D vs. E: Ratio 32 vs 29		
Treatment under LA vs GA: Not reported		
Data source: Clinical measurement		
Methods to reduce bias: Unilateral design of the study		
Results		

Premature loss of primary molars resulted in loss of space compared to control side		
Space loss occurred in maxillary and mandibular arches		
Difference in extraction and control side for upper D, lower D, upper E and lower E were 1.3, 1.7, 3 and 2 mm respectively		
Internal validity		
Definition of inclusion and exclusion: Unilateral loss of primary molar, cases with succedaneous eruption of premolars were excluded		
Definition of outcome: Yes		
Treatment and control group comparability: Yes		
Follow up of participants: N/A, cross sectional study		
Examiner reliability: Not reported		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☑	Low risk: ☐	Moderate: ☐
Further notes:		
Limitations		
Cross sectional study and record to premature loss not linked and thus details about premature loss not known		
Clinical measurement taken, examiner reliability, agreement not discussed		
No serial measurements, thus it is not known if space regained		
Notes and comments		
Noted that it reports 'significant' difference but no statistical test was undertaken		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Data extraction form (Venkaiah, 1974)

<table>
<tr><td colspan="3">Citation:</td></tr>
<tr><td colspan="3">Venkaiah V, Prasad AR, Rajendran VC. A study of the space closure following premature extraction of primary first molar. J Indian Dent Assoc 1974;46(8):305-11.</td></tr>
<tr><td>Aim/ Objectives</td><td colspan="2">To investigate consequences of premature loss of primary teeth</td></tr>
<tr><td colspan="3">Methods</td></tr>
<tr><td colspan="3">Study design: Prospective cohort study</td></tr>
<tr><td colspan="3">Setting: Department of Orthodontics, Dental College, Banglore</td></tr>
<tr><td colspan="3">Intervention: Premature loss of upper or lower D compared to on extraction side</td></tr>
<tr><td colspan="3">Definition of premature extraction/ loss: No</td></tr>
<tr><td>Participants
Experimental: n= 30 cases of unilateral extraction of Ds</td><td>Age:
8-11 yrs</td><td>Sex: Not reported</td></tr>
<tr><td>Control: n= 30 non extraction sides</td><td></td><td></td></tr>
<tr><td>Total: n= 30, see above</td><td></td><td></td></tr>
<tr><td colspan="3">Inclusion/ Exclusion: 30 cases included</td></tr>
<tr><td colspan="3">Dropouts: None</td></tr>
<tr><td colspan="3">Ethnicity: Not reported</td></tr>
<tr><td colspan="3">Follow up time: 5 mths</td></tr>
<tr><td colspan="3">Dental age consideration: Yes ☐ No ☑
If yes, further notes</td></tr>
<tr><td colspan="3">Unit of analysis/ quantitative variables: Reference points for extraction and non extraction sides</td></tr>
<tr><td colspan="3">Statistical methods: t-test to compared extraction to non extraction side</td></tr>
<tr><td colspan="3">Outcome</td></tr>
<tr><td colspan="3">Primary outcome: Antero- posterior position of 6s; space close after extractions</td></tr>
<tr><td colspan="3">Secondary outcome: None</td></tr>
<tr><td colspan="3">Gender differences: Not reported</td></tr>
<tr><td colspan="3">Difference in timing of extraction/loss: Not reported</td></tr>
<tr><td colspan="3">Max. vs. Man. teeth: Mesial migration of 6s compared for maxillary and mandibular teeth was not statistically significant</td></tr>
<tr><td colspan="3">Ant vs. Post. teeth: N/A</td></tr>
<tr><td colspan="3">D vs. E: N/A</td></tr>
<tr><td colspan="3">Treatment under LA vs GA: Not reported</td></tr>
<tr><td colspan="3">Data source: Measurements on study models using vernier callipers</td></tr>
<tr><td colspan="3">Methods to reduce bias:
Unilateral study, reference points used was clearly defined</td></tr>
<tr><td colspan="3">Results</td></tr>
</table>

Difference in mesial migration of 6s between extraction and non extraction side was not statistically significant, although both sides showed mesial migration, mean value of mesial migration was 0.40 mm for both sides		
Difference in extraction space closure between extraction and non extraction side was not statistically significant, although both sides showed tendency for space closure		
There was no statistical difference in position of 6s and extraction space in terms of maxillary and mandibular arches		
Internal validity		
Definition of inclusion and exclusion: Inclusions (anterior crowding, natural exfoliation of Cs), exclusions not stated		
Definition of outcome: Yes, arch lengths at various points: A point (between central incisors) to D point (mesio- lingual line angle at cervical margin of 6) B point (incisal edge on distal surface of lateral incisor) to D point (central pit of E)		
Treatment and control group comparability: Yes, as split mouth style		
Follow up of participants: 5 mths follow up with 100% participants		
Examiner reliability: Not reported		
Blinding: Not reported although double blindness not possible		
Global validity		
High risk of bias: ☑	Low risk: ☐	Moderate: ☐
Further notes: Follow up period very short to provide meaningful clinical implication		
Limitations		
Anterior crowding was stated as inclusion but this was not defined		
Follow up of only 5 mths is not adequate in clinical scenarios		
Measurement error not reported		
Notes and comments		
Reference points used has not been demonstrated as stable landmarks by other researchers, thus validity of the measurements could be questioned		
Age group was divided into groups (group I: 8-9 yrs, group II: 9-10 yrs, group III: 10-11 yrs)		
Conflict of interest		
Not reported		
Ethical approval		
Not reported		

Appendix X. SIGN evidence statements and grades of recommendations.

ANNEX B: KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATIONS

A At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good practice points

✔ Recommended best practice based on the clinical experience of the guideline development group

Appendix XI. Abstract submitted for oral presentation at the 11th European Academy of Peadiatric Dentistry Congress at Strasbourg (2012).

Nabina Bhujel[1,2], Monty Duggal[2], Theresa Munyombwe[2], Jenny Godson[3], Peter Day[1,2]

[1]Salaried Dental Service, Bradford District Care Trust

[2]Leeds Dental Institute
[3]NHS Bradford and Airedale

Background: Premature extraction of primary teeth (PEOT) is common. There is little evidence that the space loss resulting from PEOT increases the need for orthodontic treatment in the permanent dentition in the UK.

Aims: The primary aim was to investigate if PEOT leads to increase in need for orthodontic treatment based on Index of Orthodontic Treatment Need (IOTN).

Materials and Methods: As part of the national oral epidemiological survey of 12 years olds, information was collected from a representative sample of Bradford children. Data included demographics, dental health status and orthodontic need. Following ethical approval, this information was matched with data held by the local Salaried Dental Service (SDS) who are the only provider of dental extractions under general anaesthetic in the area. Information collected included: PEOT, age at time of extractions, number of extracted teeth, which teeth were extracted and how extractions were carried out. Due to the data structure, multi-level modeling was undertaken to correlate orthodontic need with these factors.

Results: From the 366 children surveyed, 112 children had accessed SDS services. PEOT occurred in 71 children. Significantly more children from ethnic minorities, poor socioeconomic status and high caries rates accessed SDS. The total number of teeth extracted showed significant positive association to orthodontic need.

Conclusions: In this retrospective study, the number of primary teeth extracted was significantly associated with an increased subsequent need for orthodontic treatment.

Appendix XII. Research article submitted for publication to Journal of Dentistry.

The impact of premature extraction of primary teeth on the subsequent 'need' for orthodontic treatment

Nabina Bhujel[1,2]

Monty Duggal[2]

Theresa Munyombwe[3]

Jenny Godson[2,4]

Peter Day[1,2 *]

[1]Salaried Dental Service, Bradford District Care Trust

[2]Leeds Dental Institute, University of Leeds

[3]Centre for Epidemiology and Biostatistics, LIGHT, University of Leeds, United Kingdom

[4]Directorate of Health and Wellbeing, Public Health England

[*]Corresponding author, email: p.f.day@leeds.ac.uk, tel: 01133436139

Abstract (250 words) ***currently 235 words***

Objectives: The primary aim of this study was to investigate if premature extraction of primary teeth was associated with the 'need' for orthodontic treatment in the permanent dentition.

Methods: As part of NHS Dental Epidemiology Programme a sample of 366, twelve year old children from Bradford and Airedale were examined. The dental survey collected data on patient demographics, dental health status and orthodontic 'need'. Demographic details from the survey were linked with local Salaried Dental Service (SDS) clinical records to identify if they had accessed this service. Retrospective dental information was collected about premature extraction of primary teeth for children who were treated in the SDS. A multilevel logistic regression model was used to explore the factors associated with orthodontic 'need'.

Results: From the 366 children who were surveyed in Bradford, 116 children had accessed the local SDS historically. These children formed the study group. Significantly more children from ethnic minorities, low socioeconomic backgrounds and high caries rate ($p<0.001$) were seen in the SDS compared to remainder of the children seen in the dental survey. For the 107 children who accessed SDS and met the inclusion criteria, an increased total number of premature extraction of primary teeth was positively associated with orthodontic 'need' (odds ratio: 1.18, CI – 1.01 to 1.37).

Conclusions: In the study group, orthodontic 'need' in the permanent dentition was significantly associated to the number of primary teeth extracted in their early childhood.

Clinical significance: (max 50 words- currently 35 words)

This small study supports clinical guidelines urging clinicians to effectively restore primary teeth where possible. Clinicians should try to minimise the number of primary teeth extracted to reduce the orthodontic 'need' in the permanent dentition.

Keywords (up to 6): Tooth extraction, primary tooth, malocclusion, orthodontic need, premature

Introduction

The long-term impact of premature extraction of primary teeth has received limited attention in the research literature. Clinical guidelines provided by professional bodies[1, 2] urge clinicians to restore primary teeth where possible, and advise that this will maintain the space required for the permanent dentition to erupt into thereby reducing a potential cause of crowding and malocclusion in the permanent dentition. Prospective and retrospective cohorts and cross sectional studies, have reported that space loss occurs following extraction of the primary molars.[3-7] There are, however, fewer studies that demonstrate the effect of this space loss on the development of subsequent malocclusion and 'need' for orthodontic treatment.[8, 9]

Approximately every four years the NHS Dental Epidemiology Programme undertakes a dental survey of 12 year old children who attend mainstream secondary school in England. This national survey uses a robust sampling framework with aim of collecting information from a representative sample of 12 year old children.[10] As part of the 2008/2009 sample, an orthodontic 'need' assessment was reported for the first time. The dental survey used a modified version of the Index of Orthodontic Treatment Need designed for epidemiological studies and is based on Dental Heath Component and Aesthetic Component.[10, 11] The dental and orthodontic examinations were carried out by trained dentists.[10]

In Yorkshire and the Humber, UK, there is a high prevalence of dental caries in young children. In Bradford and Airedale, over half of five year old children have obvious dental caries into dentine and for this group at least four teeth are involved.[12] For many of the children with extensive dental caries in Bradford, they are referred by their General Dental Practitioners to the Salaried Dental Service (SDS). These young children will frequently undergo extraction of all their carious primary teeth under general anaesthesia. The SDS is the only local provider for dental treatment under general anaesthesia but also provides a full range of paediatric dental services including dental treatment under local anaesthesia and inhalation sedation. NHS Business Service Authority primary care data for 2010 in Bradford, showed two thirds of all primary teeth extracted were carried out within SDS.

The primary aim of this study was to investigate if Premature Extraction of Primary Tooth (PEPT) was associated with an increase in the orthodontic 'need'. Secondary aim of this study was to compare individual characteristics of children seen within SDS. For this study PEPT was defined as any primary tooth extracted prior to natural exfoliation by a clinician over a course of dental treatment either under local anaesthesia or general anaesthesia.

Materials and Methods

Data set

Following discussions with Bradford Research Ethics Committee, the data linkage between the 12 year old dental survey for Bradford and Airedale and SDS dental records was classified as a service evaluation. The dental survey was carried out in the academic year 2008/2009. In Bradford and Airedale district there were 5,588 children aged 12 years old attending mainstream education. A representative sample of 600 children was randomly selected. From this sample, the need for attendance at school on the day of the survey and positive consent from parents and children themselves, led to 366 children being examined. The sampling framework is detailed in figure 1.

For each of 366 children, their name, date of birth and address were matched against dental records held by SDS. Paper dental records from archiving and electronic records (provided by Kodak R4® by Practiceworks) were examined to identify if any of these children had attended SDS in the past. Where a positive link was identified, further data was collected from the SDS records about PEPT. If the child's name and date of birth did not match, then the child was considered to not have accessed dental care in SDS. Patient identifiable information of subjects was only used to match patient demographics from 12 year old dental health survey to SDS dental records. Following the matching process and to assure anonymity of the children involved, each subject was given a unique identification number. Using a proforma, data was collected from the dental survey and SDS dental records and the information collected is detailed in table 1.

All 12 year old children who participated in epidemiological survey conducted by NHS Dental Epidemiology Programme in 2008/ 2009 in Bradford and Airedale district were eligible for this study. These children had orthodontic 'need' assessment recorded using the modified Index of Orthodontic Treatment Need. Children who had premature extraction of permanent tooth/teeth were excluded from the study sample.

Statistical analysis

All data was entered onto an SPSS spreadsheet (Statistical Package for the Social Science) version 21.0 (SPSS Inc, Chicago, U.S.A.). Quantitative data were summarised using means and standard deviation if normally distributed and medians and inter quartile range if skewed. Data was examined for normality using the Shapiro-Wilks test. Categorical data was summarised using frequencies and proportions. The Pearson's Chi- Square statistics (χ^2) was used to compare the two groups (children seen in SDS and those not seen in SDS) in terms of gender, ethnicity, dental health component and aesthetic component of the Index of Orthodontic Treatment Need. The Mann-Whitney U test was used to compare age at the time of extraction, DMFT and overall Index of Multiple Deprivation in the two groups since the data was not normally distributed. A significance level of $p <0.05$ was used.

For children with history of PEPT, further evaluation was undertaken between how these extractions were carried out, namely a comparison between general anaesthesia and local anaesthesia. The Pearson's Chi-Square statistics (χ^2) was used to compare the gender, ethnicity, tooth type (maxillary or mandibular teeth or first primary molar or second primary molar) distributions and whether extractions were carried out under local anaesthesia or general anaesthesia. The Mann-Whitney U test was used to compare the total number of teeth lost by PEPT and age at extraction since the data was not normally distributed.

Multilevel modelling

For the 107 children who were seen in SDS, a multilevel model was developed using MLwiN (v2.1) software, to identify factors associated with orthodontic 'need'. A multilevel logistic regression model was used to identify factors associated with orthodontic 'need' in children seen within SDS. The outcome variable for the model was the dental health component of Index of Orthodontic Treatment Need ('need' or 'no need').

The predictor variables selected were based on clinical knowledge and these included gender, ethnicity, age at the time of PEPT, specific tooth type and the total number of teeth extracted as a result of PEPT. Associations between the various predictive factors and orthodontic 'need' were quantified by odds ratios, 95% confidence intervals and p values.

Results

Children characteristics

From the 366 children examined in the survey, 116 (31.6%) children had accessed SDS during their childhood prior to the dental health survey and are shown in figure 1. The demographics of 366 children surveyed were divided into two groups, as 'seen in SDS' and 'not seen in SDS' and they are reported in table 2. Children seen in the SDS were significantly more likely to come from a 'non- white' ethnicity, to be younger at the time of the dental health survey examination, to come from a more deprived background (increased overall Index of Multiple Deprivation score) and to have a higher level of dental caries.

One hundred sixteen children were seen in SDS, nine children (7.8%) had extraction/s of a permanent tooth or teeth and thus were excluded from the study. Therefore the study group comprised of 107 children. Sixty six children (56.9%) had a history of PEPT with 29 children had extractions under general anaesthesia and the remainder, 37 children had extractions under local anaesthesia. Forty one children (35.3%) were seen in SDS but had no history of PEPT. Descriptive summaries of child level data for 'need' and 'no need' for orthodontic for 107 children seen in SDS are shown in table 3.

When comparing the groups who had treatment under general anaesthesia and local anaesthesia, age at the time of extraction was significantly different between these two groups ($p<0.001$) with a median age of 75 months (IQR 66-81) for general anaesthetic compared to 89 months (IQR 79.5-103) for local anaesthetic. The number of primary teeth extracted was also significant ($p<0.001$), with a median of eight teeth (IQR 7-12) for general anaesthetic compared to two teeth for local anaesthetic (IQR 1-4). Therefore children who were treated under general anaesthesia were younger and had a greater number of premature extractions. There were insignificant differences in the specific tooth types or from which arch the extractions were carried out.

Multilevel modelling

There were 376 primary teeth extracted (teeth were set at the lower level) from 107 children (children were set at the higher level) of which 41 children did not have history of PEPT. The multilevel logistic model indicated that, there was significant variation at a patient level ($p=0.001$). From the variables investigated the only significant independent predictors of orthodontic 'need' was the total number of PEPT (table 4). Increased total number of teeth extracted as a result of PEPT led to a significant increase in orthodontic 'need' (odds ratio of 1.18 (CI-1.01-1.37). The odds ratio shows an 18% increase in orthodontic 'need' in permanent dentition for every primary tooth lost as a result of PEPT. Other predictors such as gender, ethnicity, age at the time of extraction, whether it was maxillary tooth or mandibular tooth, the specific tooth type were not significantly associated with orthodontic 'need'.

Discussion

Principal finding

The findings in the population studied showed that PEPT was associated with an increased 'need' for orthodontic treatment in the permanent dentition.

Strength and weakness

Bradford and Airedale offered an unique setting to study PEPT as a result of high prevalence of risk factors for dental caries. This district has an increased level of dental caries in primary dentition at the age of five years with mean $d_3$mft of 2.42 compared to the national average of 1.11.[12] Many of these young children were treated by extractions as shown by the two fold increase in prevalence of missing teeth as compared to the national average of 12 %.[12] Furthermore, over the last 20 years the only provider of dental treatment under general anaesthesia in the district has been the SDS. Consequently if a child had undergone extractions under general anaesthesia then this was likely to be identified by reviewing their SDS clinical records. In Bradford and Airedale approximately a third of 12 year old children were estimated as having orthodontic 'need' which is comparable to other regions despite the higher levels of disease and increased proportion treated by extraction.

Children with premature extraction of first permanent molars were excluded from this study as this is a confounding variable. Extraction of lower first permanent molars is associated with intra-arch, inter-arch and skeletal problems and consequently these permanent extractions may be associated with orthodontic need.[13, 14] A retrospective study found half of the cases of extraction of first permanent molars developed favourable occlusion without orthodontic intervention.[15]

This was the first national dental survey were orthodontic 'need' was reported. The methodology used to assess orthodontic 'need' was a modified version of the Index of Orthodontic Treatment Need. This had a simple binary outcome with children recorded as 'need' or 'no need'.[11] The full dental health component of the Index of Orthodontic Treatment Need composes a scale of one to five.[16] The modified version recorded children with scores four and five in the category of 'need' for orthodontic treatment.[11] Similarly, for the aesthetic component a simple binary outcome was recorded as 'need' or 'no need'.[11] The full aesthetic component ranges from one to ten.[16] For the modified version only scores eight to ten were recorded as 'need'. Children in the dental survey were classified as 'need' or 'no need' in both the dental health and aesthetic categories. For 107 children seen in SDS, 57% children were classified as needing orthodontics based on the dental health component and 17.7% based on the aesthetic component. All children who were classed as having orthodontic 'need' using aesthetic component were also included as having 'need' according to the dental health component. This modified criteria for orthodontic 'need' is more stringent than the current NHS orthodontic eligibility criteria which is set at children meeting a dental health component of three if they have an aesthetic component of six or above.[17] Thus, the dental survey methodology would have missed a small number of these borderline cases.

The modified dental health and aesthetic components of the Index of Orthodontic Treatment Need have previously been validated for use in epidemiological surveys.[11] For Bradford and Airedale dental survey, two examiners undertook the dental survey. They were trained in the modified Index of Orthodontic Treatment Need. However calibration was not undertaken as part of this training and therefore internal and external validity of the orthodontic assessment could be questioned. Furthermore the Index of Orthodontic Treatment Need does not describe the likely complexity of orthodontic treatment. This would have been a valuable information as it would have allowed comparison with the Pedersen et al. study.[9] This study[9] showed that PEPT led to an increase in a number of individual malocclusion features, such as class II malocclusion, deep bite, midline displacement and cross bite as well being associated with increased complexity of orthodontic treatment with extraction of permanent tooth more likely in order to correct these malocclusion features.

The 2008/2009 twelve year old dental survey was the first national survey to introduce positive consent.[10] This was not a requirement in previously conducted surveys of 12 year old children. Response rate for national dental surveys are lower since introduction of positive consent.[18] The representative nature of the sample was evaluated, with a national average of 24% of selected children not participating. This was caused by absenteeism from school on the day of the survey as well as parent and child opting out of the survey.[18] Although this survey was evaluated for its representative nature and found to be generalisable to the wider childhood population, surveys using positive consent in other age groups have led to concerns with children who have increased levels of dental caries were more likely to opt out.[19, 20]

In this small study, only 66 children out of 107 children were identified as experiencing PEPT in the SDS. This study relied on retrospective collection of information from dental records which limits what information was available. For example details were only available for teeth extracted by the SDS. Therefore some children seen by the SDS may also have had further teeth extracted in general dental practice. It is also unknown how many children who were not seen in the SDS had extractions of their carious teeth at their own dentist. A prospective cohort of 739 young children seen in General Dental Service showed 10% of children with caries had a primary molar extracted over a 3 year time period.[21] Finally a few children will have had teeth extracted by Oral and Maxillofacial colleagues as a result of an acute hospital admission associated with a facial swelling.

Previous literature[3, 5, 8, 22, 23] has shown that space loss following PEPT was more marked in a number of clinical situations such as maxillary compared to mandibular extractions, posterior teeth extractions compared to anterior teeth or when a second primary molar was extracted as compared to a first primary molar. This research did not show a significant difference in orthodontic 'need' with respect to these clinical situations. This is likely to be related to the limited size of the sample in this study. However, the results from this study will help for future estimations of sample size to investigate orthodontic 'need' following extractions of different primary teeth.

Results looking at child level descriptive led to conclusion that children seen in SDS were more likely to be 'non-white', were younger, had higher levels of dental disease (higher DMFT index) and more socially deprived (higher IMD score). Differing levels of dental caries based on ethnicity has been recognised at regional level in previous publications demonstrating significant relationship in regression analysis. Asian children showed increased caries experience as compared to White and Afro-Caribbean children and this difference was maintained even when controlled for material deprivation.[24, 25] Median age difference of children seen and not seen in SDS was two months at the time of dental survey examination; although statistically significant, it is unlikely to have had a clinical significance.

Statistical analysis

The statistical methodology used in this study was appropriate as it accounted for the clustering of the data within individuals. The multilevel modelling approach accounted for the dependence of multiple data from the same child. Ignoring this dependence will result in underestimation of standard errors and increased false positives for subgroup analysis.[26]

Predictor variables used were based on clinical knowledge. However the predictors included in the model did not explain much individual variation. Important predictors of the outcome such as time lag between extraction of primary tooth and eruption of permanent tooth and orthodontic parameters at the time of extraction such as skeletal base, centrelines, molar relationship and crowding were unavailable. This study was exploratory with no priori hypothesis therefore there was no priori sample size calculation for subgroup analysis. This could have led to important predictors not reaching statistical significance due to lack of power. However we followed Peduzzi's recommendation of 10 events per predictor during model building.[27]

Implications for future

The findings of this study confirm clinical experience and clinical guidelines by finding that PEPT was associated with an increased 'need' for orthodontic treatment in the permanent dentition. The only predictor to show a significant positive association with orthodontic 'need' was the number of primary teeth extracted. This finding would support current guidelines in Paediatric Dentistry[1, 2] to restore primary teeth were appropriate and feasible. Restoring primary teeth can be achieved in a number of ways including the use of 'Hall crowns' which have been shown to be easier for young children to tolerate [28], conventional restorative approach using materials with proven track records of longevity, the use inhalation sedation and local anaesthesia and the provision of comprehensive dental care under general anaesthesia. Each of these procedures will take clinical time and therefore incur costs in terms of time for parent, child and dental team as well as financial costs to health care funders. These should be offset against costs associated with orthodontic treatment. Prevention of orthodontic 'need' and malocclusion is likely to have great universal benefits to the population as a result of the inequitable access to orthodontic care from children with a more deprived background despite their similar or greater impacts to their quality of life.[29-32]

Ideal study design to explore the impact of PEPT and subsequent orthodontic 'need' would be a randomised control trial with follow up until full permanent dentition or a long term prospective cohort study following children from primary dentition to full permanent dentition. Long term follow up periods of approximately ten years makes these methodologies difficult. For example follow up cohort studies of children receiving dental care under general anaesthesia showed less than 10% attending clinical appointment at three months following treatment.[33] Innovative methodologies to maintain the cohort would be needed to ensure valid and generalisable results are achieved.

Analysis of the number of teeth extracted under local or general anaesthetic confirms clinical advice that treatment under general anaesthetic is more frequently prescribed for younger children with significant dental disease in multiple quadrants. The number of teeth extracted under general anaesthetic was higher than previously reported for exodontia under general anaesthesia.[34, 35] The odds ratio calculated from the multilevel model, extrapolate an 18% increase in subsequent 'need' for orthodontic treatment for every primary tooth extracted. Thus limiting the number of premature extractions of primary teeth would be beneficial and would appear to reduce subsequent orthodontic 'need' in the permanent dentition.

Conclusion

This study is the first in the United Kingdom to assess the impact of extractions in primary dentition on development of malocclusion in the permanent dentition. Multilevel modelling identified that in this high caries group of children the total number of teeth lost as a result of premature extraction was significantly associated with increased orthodontic 'need'. Each primary tooth extracted prematurely led to an 18% increase in orthodontic 'need' in permanent dentition. Clinicians involved in providing dental care for children with caries should aim were practicable and feasible to limit the number of extractions of primary teeth. This study also highlighted that children seen in SDS are significantly different in terms of level of dental caries, deprivation and ethnicity.

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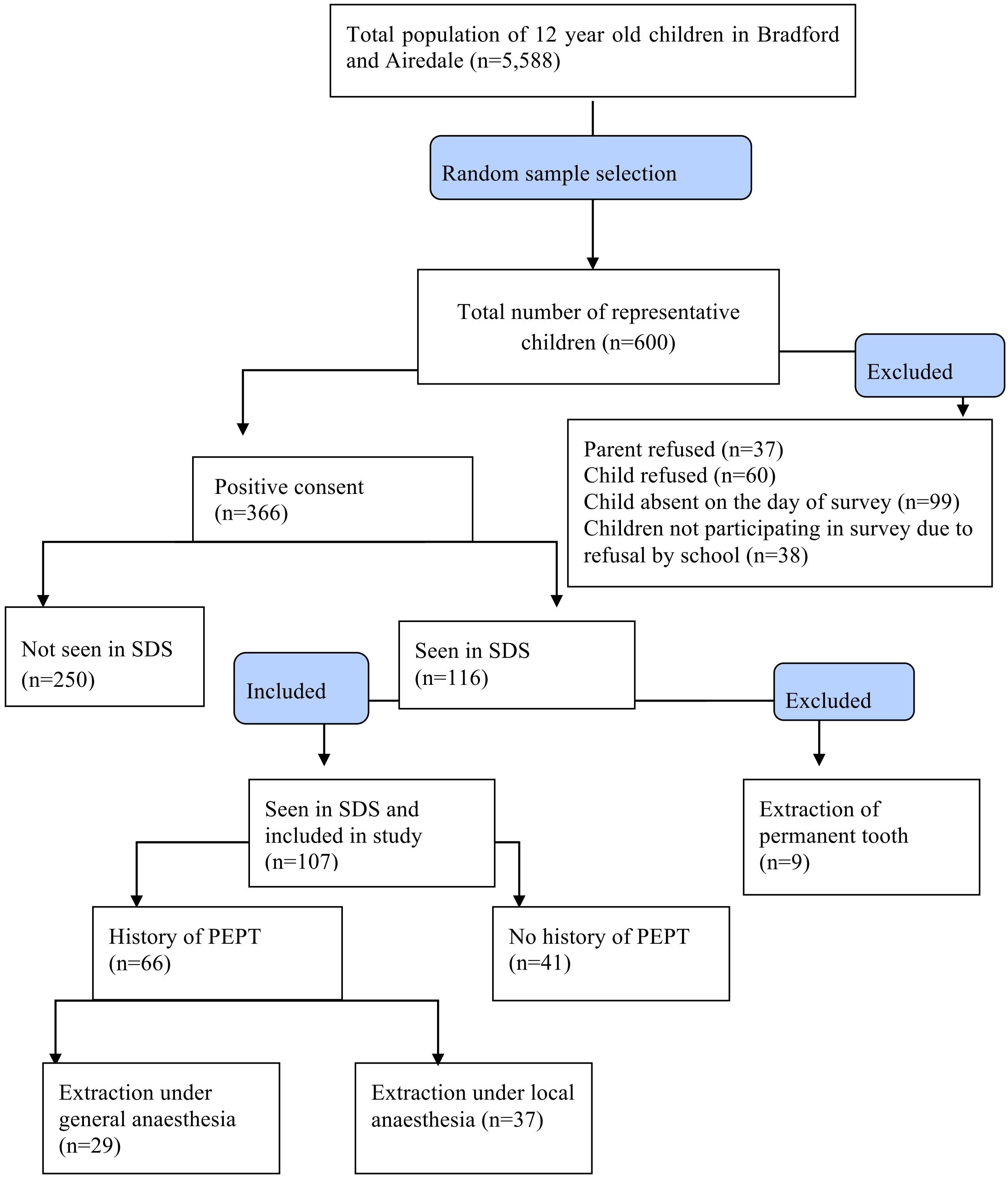
Figure 1. Flowchart of the number of the 12 year old children in Bradford and Airedale who were available for inclusion in this study of the orthodontic implications of premature extraction of primary teeth.



SDS- Salaried Dental Service; PEPT- premature extraction of primary tooth

Table 1. Information collected from 12 year old dental epidemiological survey and from retrospective dental notes in Bradford and Airedale Salaried Dental service (SDS).

Information from the 12 year old dental epidemiological survey	**Information from dental notes in Bradford and Airedale Salaried Dental Service (SDS)**
Age Gender Ethnicity Home postcode Date of dental survey DMFT Dental health component of modified Index of Orthodontic Treatment Need Aesthetic component of Index of Orthodontic Treatment Need	seen or not seen in SDS If seen in SDS: * Whether there was a history of premature extraction of a primary tooth/teeth or not * Whether extractions were carried out under general anaesthesia or local anaesthesia * Date of extraction/s * Number of tooth/teeth extracted * Tooth notation/s for extracted tooth/teeth

Table 2. Descriptive of patient groups 'seen in Salaried Dental Service' and 'not seen in Salaried Dental Service' by gender, ethnicity, dental health component and aesthetic component of modified Index of Orthodontic Treatment Need, age at examination of survey, DMFT and overall Index of Multiple Deprivation score.

	Children seen in Salaried Dental Service (n=116)	**Children not seen in Salaried Dental Service (n=250)**	p value
Gender n (%)	Male, n=65 (60.7%) Female, n=42 (39.3%)	Male, n=145 (58%) Female, n=105 (42%)	0.62
Ethnicity n (%)	White, n=23 (21.5%) Non-white, n=84 (78.5%)	White, n=160 (64%) Non-white, n=90 (36%)	0.001**
Dental Health Component n (%)	'No need', n=46 (43%) 'Need', n=61 (57%)	'No need', n=122 (48.8%) 'Need', n=128 (51.2%)	0.31
Aesthetic Component n (%)	'No need', n=88 (82.2%) 'Need', n=19 (17.8%)	'No need', n=217 (86.8%) 'Need', n=33 (13.2%)	0.26
Age at the time of survey in months Median (IQR)	148 (146-152)	150 (147-153)	0.01*
DMFT Median (IQR)	2 (0-3)	1 (0-2)	0.001**
Overall Index of Multiple Deprivation Median (IQR)	49.25 (36.06-60.95)	27.86 (17.84-48.03)	0.001*

* p<0.05, ** p<0.01

Table 3. Descriptive of patient groups according to orthodontic 'need' and 'no need' in children seen in Salaried Dental Service (n=107) and children who were seen in Salaried Dental Service and experienced premature extraction of primary tooth (PEPT) (n=66).

	Children with orthodontic 'need' (n=61)	**Children with orthodontic 'no need' (n=46)**
Gender n (%)	Male, n=35 (57.4%) Female, n=26 (42.6%)	Male, n=30 (65.2%) Female, n=16 (34.8%)
Ethnicity n (%)	White, n=15 (24.6%) Non-white, n=46 (75.4%)	White, n=8 (17.4%) Non-white, n=38 (82.6%)
DMFT Median (IQR)	2 (0-3)	1.5 (0-3)
Overall Index of Multiple Deprivation Median (IQR)	48.02 (25.37-61.94)	51.57 (40.92-60.05)
History of PEPT Yes/no	Yes, n= 37 (60.7%) No, n=24 (39.3%)	Yes, n=29 (63%) No, n=17 (37%)
For children seen in Salaried Dental Service and had history of PEPT (n=66)		
	Children with orthodontic 'need' (n=38)	**Children with orthodontic 'no need' (n=28)**
Number of teeth lost by PEPT Median (IQR)	6.5 (2-9)	4 (1-6)
Teeth lost under local anaesthesia v. general anaesthesia	Local anaesthesia, n=19 (50%) General anaesthesia, n=19 (50%)	Local anaesthesia, n= 18 (35.7%) General anaesthesia, n=10 (64.3%)
Maxillary v. mandibular tooth	Maxillary tooth, n=117 (53.9%) Mandibular tooth, n=100 (46.1%)	Maxillary tooth, n=58 (48.7%) Mandibular tooth, n=61 (51.3%)
Age at the time of PEPT in months Median (IQR)	79 (67-92)	80 (72-94)
Tooth type lost by PEPT	Anterior, n=49 (22.6%) First primary molar, n=84 (38.7%) Second primary molar, n=84 (38.7%)	Anterior, n=16 (13.4%) First primary molar, n=57 (47.9%) Second primary molar, n=46 (38.7%)

PEPT- Premature Extraction of Primary Tooth

Table 4. Multilevel results to investigate predictor variables to influence orthodontic 'need' in 107 children seen in Salaried Dental Service. The coefficient estimates of variables, their standard error (), odds ratio, 95% confidence interval of the odds ratio () and size of effect are given for the model.

	Variables		**Null Model**	**Random Intercept model with covariates**	**Odds ratio (CI)**	**Size of effect on orthodontic need**
Fixed effect			0.35(0.21)	0.09(1.27)		
Child level	Gender (ref Male)	Female v. Male		0.35(0.45)	1.42(0.58 to 3.45)	
	Ethnicity (ref White)	Others v. White		-0.46(0.53)	0.63(0.22 to 1.79)	
	Total teeth lost by premature extraction of primary tooth			0.16(0.08)	1.18(1.01 to 1.37)*	18%
Tooth level	Age at premature extraction of primary tooth			-0.01(0.01)	.96(0.12 to 8.59)	
	Tooth type (Maxillary or mandibular tooth)	Maxillary v. no extraction		0.11(2.27)	1.12(0.01 to 95.68)	
		Mandibular v. no extraction		0.12(2.28)	1.12(0.01 to 97.89)	
	Tooth type (second primary molar, first primary molar or anterior tooth)	Second primary molar v. no extraction		-0.12(0.41)	.89(0.4 to 1.2)	
		First primary molar v. no extraction		-0.16(0.40)	0.85(0.39 to 1.88)	
		Anterior tooth v. no extraction		0.0(0.0)	1(1 to 1)	
Random effect			2.6(0.59)	2.93(0.66)		

* Significant value (95% confidence interval does not include 0)

References

1. American Academy on Pediatric Dentistry Clinical Affairs Committee-Developing Dentition Subcommittee. Guideline on management of the developing dentition and occlusion in pediatric dentistry. *Pediatric Dentistry* 2008-2009;**30 (7 Suppl)**:184-95.

2. Fayle SA, Welbury RR, Roberts JF. British Society of Paediatric Dentistry: a policy document on management of caries in the primary dentition. *International Journal of Paediatric Dentistry* 2001;**11**(2):153-57.

3. Northway WM, Wainright RL, Demirjian A. Effects of premature loss of deciduous molars. The *Angle Orthodontist* 1984;**54**(4):295-329.

4. Linder-Aronson S. The effect of premature loss of deciduous teeth. A biometric study in 14 and 15 year-olds. *Acta Odontologica Scandinavica* 1960;**18**(2):101-22.

5. Richardson ME. The relationship between the relative amount of space present in the deciduous dental arch and the rate and degree of space closure subsequent to the extraction of a deciduous molar. *The Dental Practitioner and Dental Record* 1965;**16**(3):111-8.

6. Hoffding J, Kisling E. Premature loss of primary teeth: Part 1, its overall effect on occlusion and space in the permanent dentition. *Journal of Dentistry for Children* 1978;**45**:279-83.

7. Breakspear EK. Sequelae of early loss of deciduous molars. *Dental Record* 1951;**71**:127-34.

8. Ronnerman A, Thailander B. Alongitudinal study on the effect of unilateral extraction of primary molars. *Scandinavian Journal of Dental Research* 1977;**85**:362-72.

9. Pedersen J, Stensgaard K, Melsen B. Prevalence of malocclusion in relation to premature loss of primary teeth. *Community Dentistry and Oral Epidemiol*ogy 1978;**6**:204-09.

10. NHS Dental Epidemiology Programme for England. Oral Health Survey of 12 year old children in England, 2008/2009, National Protocol Sep 2008.

11. Burden DJ, Pine CM, Burnside G. Modified IOTN: an orthodontic treatment need index for use in oral health surveys. *Community Dentistry and Oral Epidemiology* 2001;**29**(3):220-5.

12. NHS Dental Epidemiology Programme for England. Oral Health Surveys of 5 year old children 2007/2008. Oct 2009 [cited; Available from: http://www.nwph.net/dentalhealth/reports/NHS_DEP_for_England_OH_Survey_5yr_2007-08_Report.pdf

13. Abu Aihaija ES, McSheny PF, Richardson A. A cephalometric study of the effect of extraction of lower first permanent molars. *Journal of Clinical Pediatric Dentistry* 2000;**24**(3):195-8.

14. Normando D, Cavacami C. The influence of bilateral lower first permanent molar loss on dentofacial morphology- a cehalometric study. *Dental Press Journal of Orthdontics* 2010;**15** (6):100-6.

15. Jalevik B, Moller M. Evaluation of spontaneous space closure and development of permanent dentition after extraction of hypomineralized permanent first molars. *International Journal of Paediatric Dentistry* 2007;**17**(5):328-35.

16. Brook PH, Shaw WC. The development of an index of orthodontic treatment priority. *European Journal of Orthodontics* 1989;**11**(3):309-20.

17. British Orthodontic Society. The Justification for Orthodontic Treatment. British Orthodontic Society, 12 Bridewell Place London EC4V 6AP: British Orthodontic Society, 12 Bridewell Place London EC4V 6AP; 2009.

18. NHS Dental Epidemiology Programme for England. Oral Health Survey of 12 year old Children 2008/ 2009 Nov 2010.

19. White DA, Morris AJ, Hill KB, Bradnock G. Consent and school-based surveys. *British Dental Journal* 2007;**202**(12):715-7.

20. Dyer TA, Marshman Z, Merrick D, Wyborn C, Godson JH. School-based epidemiological surveys and the impact of positive consent requirements. *British Dental Journal* 2008;**205**(11):589-92.

21. Tickle M, Blinkhorn AS, Milsom KM. The occurrence of dental pain and extractions over a 3-year period in a cohort of children aged 3-6 years. *Journal of Public Health Dentistry* 2008;**68**(2):63-9.

22. Owen DG. The incidence and nature of space closure following the premature extraction of deciduous teeth: a literature study. *American Journal of Orthodontics* 1971;**59**(1):37-49.

23. Clinch LM, Healy MJR. A longitudinal study of the results of premature extraction of deciduous teeth between 3-4 and 13-14 years of age. *Dental Practitioner* 1959;**9**:109-27.

24. Prendergast MJ, Beal JF, Williams SA. The relationship between deprivation, ethnicity and dental health in 5-year-old children in Leeds, UK. *Community Dental Health* 1997;**14**(1):18-21.

25. Bradford and Airedale Teaching Primary Care Trust. The oral health of 5 year old children living in Bradford and Airedale tPCT: Bradford and Airedale Teaching Primary Care Trust; 2006 2006.

26. Rabash J, Steele F, Browne W, Goldstein H. A user's guide to MLwiN. Centre for multilevel modelling, University of Bristol; 2009.

27. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *Journal of Clinical Epidemiology* 1996;**49**(12):1373-9.

28. Innes NP, Evans DJ, Stirrups DR. Sealing caries in primary molars: randomized control trial, 5-year results. *Journal of Dental Research* 2011;**90**(12):1405-10.

29. Drugan CS, Hamilton S, Naqvi H, Boyles JR. Inequality in uptake of orthodontic services. *British Dental Journal* 2007;**202**(6):E15; discussion 326-7.

30. Locker D. Disparities in oral health-related quality of life in a population of Canadian children. *Community Dentistry and Oral Epidemiology* 2007;**35**(5):348-56.

31. Mandall NA, McCord JF, Blinkhorn AS, Worthington HV, O'Brien KD. Perceived aesthetic impact of malocclusion and oral self-perceptions in 14-15-year-old Asian and Caucasian children in greater Manchester. *European Journal of Orthodontics* 2000;**22**(2):175-83.

32. Morris E, Landes D. The equity of access to orthodontic dental care for children in the North East of England. *Public Health* 2006;**120**(4):359-63.

33. Jamjoom MM, al-Malik MI, Holt RD, el-Nassry A. Dental treatment under general anaesthesia at a hospital in Jeddah, Saudi Arabia. *International Journal of Paediatric Dentistry* 2001;**11**(2):110-6.

34. Albadri S, Lee S, Lee G, Llewelyn R, Blinkhorn A, Mackie I. The use of general anaesthesia for the extraction of children's teeth. Results from two UK dental hospitals. *European Archives of Paediatric Dentistry* 2006;**7**(2):110-5.

35. Holt RD, Al Lamki S, Bedi R, Dowey JA, Gilthorpe M. Provision of dental general anaesthesia for extractions in child patients at two centres. *British Dental Journal* 1999;**187**(9):498-501.

Appendix XIII. Reporting sheet for 12-year-old survey of Bradford and Airedale district.

THE DENTAL OBSERVATORY

NHS Dental Epidemiology Programme

Oral Health Survey of 12 Year old Children 2008/09

Primary Care Trust Bradford & Airedale

Name of examiner (s) Keith Harrison / Carron Paige

Start/finish date of examination (dd/mm/yyyy-dd/mm/yyyy) 05-Mar-09 - 02-Jul-09

Number of children in school population aged 12 years 5,588.00

Total number of schools with 12-year-old children 28

Number of schools visited 27

Total number of children sampled 600

Number of children (consent) : parent withdrew child	37	**child absent when consent sought**	0		
child gave consent	366	**child refused consent**	60		
Number of children (examination) : examined	366	**absent**	99	**refused**	60

Please give answers rounded to 2 decimal places		**Standard**	**95% C.L. of Mean**	
	Mean	**Deviation**	**Lower**	**Upper**

DT	0.75	1.30	0.62	0.88
MT	0.11	0.45	0.06	0.16
FT	0.64	1.10	0.53	0.76
DMFT	1.50	1.79	1.32	1.69
Sealed teeth (code $T)	0.52	1.18	0.40	0.64
Sound teeth (including Sound and Sealed - code SS$T)	23.46	3.98	23.05	23.86

	Number	Percentage	Mean	Standard Deviation	95% C.L. of Me Lower	Upp r
With caries experience (DMFT >0)	206	56.00	2.67	1.60	2.45	2.89
With current dentinal decay (DT>0)	139	38.00	1.98	1.43	1.74	2.22

I confirm that this data was collected in accordance with the British Association for the Study of Community Dentistry guidelines (1992/93)

Signed Debra Clavin **Date :** **8-Jul-09**

Appendix XIV. Total number of children reported on the national survey for Bradford and Airedale (including extra school children).

Recorded School PCT Code	Child PCT Code	SCHOOL NAME	SCHOOL POSTCODE	Count Of Children
5J6 Calderdale	5NY	HIPPERHOLME AND LIGHTCLIFFE	HX3 8TL	3
5J6 Calderdale	5NY	THE BROOKSBANK SCHOOL SPORTS COLLEGE	HX5 0QG	1
5J6 Calderdale	5NY	THE NORTH HALIFAX GRAMMAR SCHOOL	HX2 9SU	4
5N1 Leeds	5NY	BENTON PARK HIGH	LS19 6LX	22
5N1 Leeds	5NY	PRINCE HENRYS GRAMMAR SCHOOL	LS21 2BB	3
5N1 Leeds	5NY	ST MARYS CATHOLIC	LS29 6AE	34
5N2 Kirklees	5NY	BIRKENSHAW MIDDLE SCHOOL	BD19 4BE	1
5N2 Kirklees	5NY	WHITECHAPEL MIDDLE SCHOOL	BD19 6HR	2
5NV North Yorkshire & York	5NY	3	BD23 1UQ	4
5NV North Yorkshire & York	5NY	4	BD23 1QL	26
5NV North Yorkshire & York	5NY	5	BD20 7RL	90
5NV North Yorkshire & York	5NY	6	BD23 5BS	1
5NV North Yorkshire & York	5NY	7	BD23 1PL	32
5NY Bradford & Airedale	5NY			363
Total				**586**

Appendix XV. Research Ethics Committee letter.

Bradford Research Ethics Committee
Top Floor
Extension Block
St Lukes Hospital

Chairman: **Professor Alan C Roberts**
OBE TD DL MPhil PhD DSc DTech LLD FLS FIBiol
Administrator: **Susan Jude**

Tel: 01274 365508 **Email:** susan.jude@bradfordhospitals.nhs.uk
Fax: 01274 365509 **Email:** alan.roberts@bradfordhositals.nhs.uk

3 March 2009 (Original lost Dec 08)

Dr J Godson
Deputy Director of Public Health/Consultant in Dental Public Health
University of Leeds
Department of Orthodontics
Level 6
Worsley Building
Clarendon Way
Leeds
LS2 9LU

Dear Dr Godson

Premature Loss of Primary Teeth and Orthodontic Treatment

Thank you for your letter dated 9 December 2008.
I can confirm that your proposal would be considered service evaluation/audit. Please see the guidance below from the NRES Consultation Group.

DIFFERENTIATING AUDIT, SERVICE EVALUATION AND RESEARCH
November 2006

RESEARCH	CLINICAL AUDIT	SERVICE EVALUATION
The attempt to derive generalisable new knowledge including studies that aim to generate hypotheses as well as studies that aim to test them.	Designed and conducted to produce information to inform delivery of best care.	Designed and conducted solely to define or judge current care.
Quantitative research – designed to test a hypothesis. Qualitative research – identifies/explores themes	Designed to answer the question: “Does this service reach a predetermined	Designed to answer the question: “What standard does this service achieve?”

following established methodology.	standard?"	
Addresses clearly defined questions, aims and objectives.	Measures against a standard.	Measures current service without reference to a standard.
Quantitative research -may involve evaluating or comparing interventions, particularly new ones. Qualitative research – usually involves studying how interventions and relationships are experienced.	Involves an intervention in use ONLY. (The choice of treatment is that of the clinician and patient according to guidance, professional standards and/or patient preference.)	Involves an intervention in use ONLY. (The choice of treatment is that of the clinician and patient according to guidance, professional standards and/or patient preference.)
Usually involves collecting data that are additional to those for routine care but may include data collected routinely. May involve treatments, samples or investigations additional to routine care.	Usually involves analysis of existing data but may include administration of simple interview or questionnaire.	Usually involves analysis of existing data but may include administration of simple interview or questionnaire.
Quantitative research - study design may involve allocating patients to intervention groups. Qualitative research uses a clearly defined sampling framework underpinned by conceptual or theoretical justifications.	No allocation to intervention groups: the health care professional and patient have chosen intervention before clinical audit.	No allocation to intervention groups: the health care professional and patient have chosen intervention before service evaluation.
May involve randomisation	No randomisation	No randomisation
ALTHOUGH ANY OF THESE THREE MAY RAISE ETHICAL ISSUES, UNDER CURRENT GUIDANCE:-		
RESEARCH REQUIRES R.E.C. REVIEW	AUDIT DOES NOT REQUIRE R.E.C. REVIEW	SERVICE EVALUATION DOES NOT REQUIRE R.E.C. REVIEW

I hope this helps clarify the situation.

Yours sincerely

Professor A Roberts
Chairman – Bradford Research Ethics Committee

Appendix XVI. Data collection proforma.

Proforma for PEPT research

1. PATIENT DEMOGRAPHS
Patient no:

DOB:

Male □ Female □

Ethnicity:

Postcode:

2. SURVEY INFO

Date of exam:

Teeth present:

DMFT:

DHC ortho need: □ No need □

Aesthetic component:

3. RETROSPECTIVE INFO

EXTRACTIONS: Yes □ No □

LA □ GA □

Date of extractions No of teeth Tooth number
i.
ii.
iii.
iv.

Any notes: