

IMPACT OF TOOTH AGENESIS ON ORAL HEALTH-RELATED
QUALITY OF LIFE IN ADULTS

By

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A thesis submitted to the University of Birmingham for the degree of
MASTER OF SCIENCE (by research)

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December 2015

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Abstract

Aims: The aim of this cross-sectional survey was to evaluate the impact of tooth agenesis on adults and to investigate the effect of sex, age, race, social deprivation, severity of tooth agenesis, location of missing teeth and the presence of retained deciduous teeth on oral health-related quality of life (OHRQoL).

Method: A total of 71 adults (41 females and 30 males) with tooth agenesis, aged 16-30 years (mean 18.4 years, SD 2.8 years) were recruited from Birmingham Dental Hospital, United Kingdom. Friend controls were recruited for comparison with 15 subjects. All subjects completed the validated Oral Health Impact Profile (OHIP) 49-question questionnaire (OHIP-49). An age-matched control was derived from the 2009 Adult Dental Health Survey (ADHS).

Results: The mean number of missing teeth in subjects with tooth agenesis was 5.7 in the sample compared to the friend controls. In the sample compared to the ADHS control, the mean number of missing teeth was 5.4. Subjects with tooth agenesis had significantly higher scores in total OHIP-49 ($p=0.003$) and all domains except physical pain and handicap in comparison to a friend control. In comparison with the ADHS control, subjects with tooth agenesis had significantly higher scores in total OHIP-14 and all domains ($p<0.0001$). Reduced OHRQoL was seen in females (coefficient 0.2, 95% CI 0.03, 0.5, $p=0.023$), older patients (coefficient 0.04, 95% CI 0.01, 0.06, $p=0.004$) and in subjects with increased social deprivation. OHRQoL was minimally associated with the number of missing teeth and was not associated with the location of missing teeth or the presence of retained deciduous teeth.

Conclusions: Tooth agenesis can have a significant impact on OHRQoL in adults. This study furthers our understanding of the implications of tooth agenesis on OHRQoL and highlights the need for resources dedicated to the treatment of this patient group.

Acknowledgements

I would like to express my gratitude to the following:

Mrs Sheena Kotecha for overall guidance and supervision

Professor Thomas Dietrich for guidance and statistical support

Dr Vahid Ravaghi for statistical support

Mr John Turner for on going support

The University of Birmingham for generous funding and support

The staff at Birmingham Dental Hospital for their assistance with recruitment

The patients of Birmingham Dental Hospital and their nominated control participants for taking part in this study

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Chapter One
Literature Review

1. Literature review

1.1 Introduction

Tooth agenesis (hypodontia) is defined as the congenital absence of one or more teeth (Nunn *et al.*, 2003) and is the most common developmental dental anomaly (Larmour *et al.*, 2005). Patients presenting with tooth agenesis may report problems with dentofacial aesthetics, psychosocial handicap or functional difficulty (Goodman *et al.*, 1994). Treatment of tooth agenesis can be complex, protracted and often requires multidisciplinary care.

1.2 Prevalence

A range of figures for the prevalence of tooth agenesis have been reported. Prevalence varies depending on the country or racial group studied, as well as the age of patients. Very young patients may not show clinical or radiographic evidence of a developing tooth and older patients may have undergone previous extractions. Some studies do not use radiographs as part of their assessment and some include absent third molars, both of which can affect the prevalence figures (Larmour *et al.*, 2005). In addition, the prevalence of tooth agenesis amongst orthodontic patients may skew results, potentially over-representing anterior teeth due the associated effect on aesthetics and the consequent likelihood of seeking treatment.

1.2.1 Population differences

A wide range of prevalence is quoted, ranging from 4.4% in Latin America and the Caribbean, to 13.4% in Africa (Khalaf *et al.*, 2014). The prevalence of tooth agenesis in Europe was 7% (Khalaf *et al.*, 2014) and two English studies have reported the prevalence as 4.3% and 4.4% (Brook, 1974; Rose, 1966). The prevalence of tooth agenesis amongst orthodontically treated children is 11.3% (Fekonja, 2005).

1.2.2 Gender differences

Tooth agenesis is more prevalent in females, with a ratio of 3:2 (Brook, 1974).

1.2.3 Teeth involved

Tooth agenesis in the primary dentition is rare, with a prevalence reported at 0.3% of the UK population and no differences between males and females (Brook, 1974).

The third molar is the most commonly missing tooth, with a reported prevalence in a population study of 22.7% (Lynham, 1990), although it is the convention to exclude the third molar when considering a diagnosis of tooth agenesis.

A recent meta-analysis found that the mandibular second premolar was the most commonly missing tooth (Khalaf *et al.*, 2014), which is in agreement with evidence from the UK (Brook, 1974; Rose, 1966). Symons *et al.* (1993) found the mandibular second premolar was absent in 3.4% of individuals in Australia. The maxillary lateral incisor is the second most commonly absent tooth (Khalaf *et al.*, 2014). In some populations, the maxillary lateral incisor is the most commonly

missing tooth (Alvesalo and Portin, 1969; Cua-Benward *et al.*, 1992), with a reported prevalence between 1.1 and 4.3% (Alvesalo and Portin, 1969; Brook, 1974; Symons *et al.*, 1993).

Lower central incisors are occasionally missing, with prevalence rates higher in the southern Chinese population (Davis, 1987). Research suggests the absence of first molars is rare (Tan *et al.*, 2011).

1.2.4 Severity

Tooth agenesis can be categorised as mild (congenitally missing 1 or 2 teeth), moderate (congenitally missing 3 to 5 teeth) or severe (congenitally missing 6 or more teeth) (Khalaf *et al.*, 2014). The prevalence of mild, moderate and severe tooth agenesis is 81.6, 14.3 and 3.1% respectively (Khalaf *et al.*, 2014). Another term used to describe severe tooth agenesis is oligodontia, whereas anodontia is the congenital absence of all teeth (Nunn *et al.*, 2003). The prevalence of oligodontia is 0.3% in the UK population, but of patients with tooth agenesis attending a dental hospital, 58% had oligodontia and 32% had ten or more missing teeth (Brook, 1974).

More severe forms of tooth agenesis are more commonly associated with syndromes (Nieminen *et al.*, 2001) and so patients with severe tooth agenesis may require appropriate screening (Larmour *et al.*, 2005).

1.2.5 Patterns of tooth agenesis

Some authors have found bilateral tooth agenesis to be common (Brook, 1974; Tan *et al.*, 2011; Wong *et al.*, 2006), whereas others have found unilateral tooth

agenesis to be more common (Wisth *et al.*, 1974). Some studies have reported teeth on the right side of the dentition to be absent more frequently than the left side (Anweigi *et al.*, 2013a; Fekonja, 2005), whereas others have found that mandibular tooth agenesis is more common on the left (Arte *et al.*, 2001). In the maxilla, in unilateral tooth agenesis cases, research has found that the left and right side are equally affected (Arte *et al.*, 2001).

There are also differences between the maxilla and mandible, with maxillary teeth more commonly absent (Anweigi *et al.*, 2013a; Arte *et al.*, 2001; Fekonja, 2005).

Specific patterns of tooth agenesis exist in terms of teeth that are missing together. In cases with oligodontia, the most common pattern in the maxilla is missing lateral incisors, canines and premolars. In the mandible, the most common pattern is missing premolars (Tan *et al.*, 2011). Researchers investigating aetiology have studied groups of patients with incisor-premolar tooth agenesis and found missing canines, first and second molars to be rare (Arte *et al.*, 2001).

In general terms, the teeth that develop last in each tooth series, incisor, premolar and molar, tend to be most vulnerable to agenesis (Nieminen *et al.*, 2001).

1.3 Aetiology of tooth agenesis

A complex interplay between genetic, epigenetic and environmental influences during tooth formation can lead to anomalies of tooth number (Brook *et al.*, 2009). The congenital agenesis of teeth is a consequence of physical obstruction

or disruption of the dental lamina, space limitation, functional abnormalities of the dental epithelium or failure of initiation of the underlying mesenchyme (Nunn *et al.*, 2003). There are two main types of tooth agenesis: non-syndromic (familial) tooth agenesis and tooth agenesis associated with a syndrome. Non-syndromic tooth agenesis is the more common form (Cobourne, 2007).

1.3.1 Environmental factors

A number of environmental factors can cause tooth agenesis, such as early irradiation of tooth germs, hormonal and metabolic influences, trauma, osteomyelitis or the iatrogenic removal of a tooth germ (Nunn *et al.*, 2003). Cross-sectional studies have identified that environmental factors, such as maternal illness during pregnancy and low birth weight do not affect tooth number (Parkin *et al.*, 2009).

Due to the localised disturbance of the dental lamina, agenesis of the maxillary lateral incisor is common in the presence of a cleft. However, since agenesis of other teeth is common in patients with cleft lip and palate (CLP), an associated genetic element is also likely (Ranta, 1986).

1.3.2 Genetic Factors

There is now a large body of evidence confirming the genetic aetiology of tooth agenesis. Observational studies have evaluated the symmetry and familial tendency for tooth agenesis. Symmetrical tooth agenesis is common (Tan *et al.*, 2011) and suggests a common genetic cause, but symmetry between the maxillary and mandibular arches is uncommon, suggesting different mechanisms may be responsible in each arch (Brook, 1974; Tan *et al.*, 2011; Wong *et al.*,

2006). The prevalence of tooth agenesis amongst the siblings of affected children ranges from 8.4 to 29.1% and amongst their parents ranges from 20.4 to 37.6%. Both of these figures are higher than the prevalence in the general population, suggesting a strong genetic influence (Parkin *et al.*, 2009). Tooth agenesis has an equal maternal and paternal inheritance (Arte *et al.*, 2001).

When investigating incisor-premolar agenesis, the inheritance of this trait was shown to be autosomal dominant with 97% penetrance (Arte *et al.*, 2001). In contrast, other authors have found inheritance via autosomal recessive genes with complete penetrance, as the homeobox gene transcription factors MSX 1 and MSX 2 mutations did not appear in consanguineous individuals with tooth agenesis (Ahmad *et al.*, 1998). A mutation in PAX 9 is reported to be associated with oligodontia, specifically with missing posterior teeth (Cobourne, 2007; Nieminen *et al.*, 2001; Stockton *et al.*, 2000). More recently, the role of the gene WNT10A has been investigated. In an assessment of patients with non-syndromic oligodontia, 56% had WNT10A mutation. MSX 1, PAX 9 and AXIN 2 gene mutations were also present but much less common (van den Boogaard *et al.*, 2012).

The prevalence of tooth agenesis in different generations is not high enough to be caused by autosomal dominant single genes or an exclusive single gene. It seems most likely that a number of genes are involved at different gene loci and the interaction of these genes, in a certain environment, results in tooth agenesis (Parkin *et al.*, 2009; Tan *et al.*, 2011). This multifactorial aetiology accounts for cases of different missing teeth in affected individuals with the same mutation.

The likelihood of tooth agenesis also varies between families, reinforcing the theory that multiple genes are involved. There seems to be no significant association with the number or location of missing teeth in an affected individual with an affected parent, when compared to an affected individual with a parent that does not have tooth agenesis (Parkin *et al.*, 2009).

1.4 Syndromes associated with tooth agenesis

There are a large number of syndromes with tooth agenesis amongst the clinical features (Cobourne, 2007).

1.4.1 Cleft lip and palate

Individuals with CLP have a high prevalence of tooth agenesis compared with the general population, with the lateral incisor in the region of the alveolar cleft most susceptible. The maxillary lateral incisor is missing in 37% of individuals with CLP (Laatikainen and Ranta, 1994). The primary and permanent dentitions may be affected and as the severity of the cleft increases, the risk of maxillary lateral incisor agenesis increases (Ranta, 1986).

1.4.2 Ectodermal dysplasia

The ectodermal dysplasias (ED) are a group of conditions associated with tooth agenesis. Although there are 132 different clinical syndromes, there are two major types. In X-linked anhidrotic or hypohidrotic ED the sweat glands are absent or reduced in number, and in autosomal dominant hidrotic ED, the sweat glands are normal (Nunn *et al.*, 2003).

Severe ED can be life threatening and presents with abnormalities of ectodermal structures including the skin, hair, nails and sweat glands, as well as tooth agenesis. Milder cases may present only with tooth agenesis. Ellis van Creveld and incontinentia pigmenti are also classified with ED and may also present with tooth agenesis (Nunn *et al.*, 2003).

1.4.3 Down syndrome

Down syndrome is caused by trisomy of chromosome 21 and one common dental feature is tooth agenesis (Larmour *et al.*, 2005), with rates of up to 63% reported (Kumasaka *et al.*, 1997).

1.4.4 Van der Woude syndrome

Van der Woude syndrome follows an autosomal dominant inheritance pattern and is associated with CLP, tooth agenesis and paramedian lip pits (Larmour *et al.*, 2005). A high prevalence of tooth agenesis is reported (Ranta, 1986).

1.4.5 Other associated syndromes

Some other associated syndromes associated with tooth agenesis are: ADULT syndrome, limb mammary syndrome, Ehlers Danlos (Type VII) syndrome, Rieger syndrome (Type I) and Witkop syndrome (Cobourne, 2007).

1.5 Associated dental, skeletal and occlusal features

1.5.1 Morphology of teeth

The morphology of teeth may be altered in patients with tooth agenesis, with conical, tapered, microdont or peg-shaped upper lateral incisors reported

(Alvesalo and Portin, 1969; Arte *et al.*, 2001; Hobkirk *et al.*, 1994). There is evidence to show that the peg-shaped lateral incisor is a weaker expression of a gene causing tooth agenesis, whereas a slender lateral incisor appears not to be related to the same gene (Alvesalo and Portin, 1969). Microdontia is closely associated with tooth agenesis and patients with tooth agenesis have significantly smaller tooth dimensions in comparison to controls. The greatest differences are seen in the upper lateral incisor and lower central incisor (Brook *et al.*, 2009).

Evidence on the prevalence of incisor invaginations in patients with tooth agenesis is mixed, with some authors finding invaginations to be less common in a population with tooth agenesis (Arte *et al.*, 2001).

Taurodontism is a dental anomaly in which affected molars have an enlarged and elongated pulp chamber (Larmour *et al.*, 2005). Taurodontism has been identified in patients with tooth agenesis and the prevalence is three times higher than the general population (Arte *et al.*, 2001; Seow and Lai, 1989).

1.5.2 Palatally displaced canines

When patients with tooth agenesis are studied, it is evident that palatally displaced canines are more common, with the prevalence 4.5 times greater than a control population (Arte *et al.*, 2001). Equally, when patients with palatally displaced canines are investigated, the prevalence of tooth agenesis is greater than the control population (Pirinen *et al.*, 1996). The aetiology of canine impaction is disputed but one suggested theory is the guidance theory. A missing

or peg-shaped maxillary lateral incisor could theoretically predispose to maxillary canine impaction due to the lack of eruptive guidance (Becker, 1984).

1.5.3 Eruption and exfoliation of teeth

Research has found that patients with tooth agenesis are more susceptible to ectopic eruption of first permanent molars (Bjerklin *et al.*, 1992; Symons *et al.*, 1993), delayed tooth formation and delayed eruption of teeth (Ahmad *et al.*, 1998). Infraocclusion or ankylosis of primary molars is also more common in patients with tooth agenesis (Bjerklin *et al.*, 1992; Symons *et al.*, 1993).

1.5.4 Rotations of teeth

The frequency of rotated premolars is 3.5 times more common in patients with tooth agenesis than the general population (Arte *et al.*, 2001). In patients with missing teeth and no crowding, rotation of premolars and maxillary lateral incisors is more common when compared to a control group (Baccetti, 1998).

1.5.5 Transpositions

Canine-first premolar transposition is more common in patients with tooth agenesis than the general population. This most commonly occurs in those with missing maxillary lateral incisors, but is also more common in patients missing other teeth (Peck *et al.*, 1993).

1.5.6 Skeletal and occlusal features

Alveolar ridge development is dependent on the presence and eruption of teeth, therefore if teeth are absent, there will be reduced alveolar ridge development in

that region (Hobkirk *et al.*, 1994). If the missing teeth are maxillary lateral incisors, this can reduce anterior maxillary growth potential, resulting in a retrusive maxilla. This can then impact on the mandible, restricting growth and contributing to lower anterior crowding (Symons *et al.*, 1993). Researchers in the UK have found that anteroposterior skeletal pattern in patients with tooth agenesis is within the normal range, although as the severity of tooth agenesis increases, there is a greater tendency towards a class III relationship and reduction in maxillary-mandibular planes angle (MMPA) (Chung *et al.*, 2000). In Sweden, researchers have found that patients with tooth agenesis tend to have a retrognathic maxilla, reduced MMPA and upright upper and lower incisors. However, the soft tissue profile and aesthetics were not affected (Sarnas and Rune, 1983). A further study reported that tooth agenesis was more common in class II malocclusions than class I and III malocclusions, although there was agreement that class III malocclusions were associated with greater prevalence of absent maxillary teeth (Cua-Benward *et al.*, 1992).

In a cohort of orthodontically treated children, assessed retrospectively, patients with more severe tooth agenesis tended to have class III molars and an increased overbite (Fekonja, 2005).

1.6 Treatment of tooth agenesis

Management of tooth agenesis is commonly carried out by multidisciplinary teams and requires close liaison between the general dental practitioner, orthodontist, paediatric dentist, restorative dentist and oral surgeon (Nunn *et al.*, 2003). On the Index of Orthodontic Treatment Need (IOTN), extensive hypodontia with more than one missing tooth in any quadrant, requiring pre-

restorative orthodontics, scores 5h. Less extensive hypodontia scores 4h. Both of these scores fall into the 'needs treatment' categories (Brook and Shaw, 1989). Normative indices regularly used in the UK may not always correlate with treatment need of patients with tooth agenesis. Researchers in Newcastle compared Peer Assessment Rating (PAR), Index of Complexity, Outcome and Need (ICON) and Dental Aesthetic Index (DAI). It was found that the DAI may be sufficiently clinically sensitive for assessing whether or not to refer patients with missing teeth (Shelton *et al.*, 2008).

A number of factors should be taken into consideration when planning treatment for a patient with tooth agenesis (Carter *et al.*, 2003; Forgie *et al.*, 2005; Hobkirk *et al.*, 1995; Thind *et al.*, 2005). These include:

Patient factors

- Age
- Examination, work and social commitments
- Expectation
- Motivation
- Peer pressures

Skeletal factors

- Skeletal pattern and facial profile
- Skeletal development
- Amount of alveolar bone present

Dental factors

- Severity of tooth agenesis
- Eruption of teeth
- Root formation
- Position and condition of teeth present
- Degree of crowding
- Other associated dental features
- Relationship of the teeth to lip line

A major decision in treatment planning is whether to idealise, open or close tooth agenesis spaces.

1.6.1 Space closure

Space closure avoids the need for a prosthesis, which reduces long-term maintenance and is associated with better periodontal health. Space closure is preferred by patients, though is less favourable when canines of poor colour are moved into the lateral incisor position or the resulting symmetry is poor (Robertsson and Mohlin, 2000). Consideration can be given to canine crown recontouring, composite build-ups, single-tooth whitening, provision of lateral incisor crown torque and extrusion or gingival surgery to harmonise gingival margins (Rosa and Zachrisson, 2001). Attempting space closure in severe tooth agenesis cases may result in unwanted incisor retraction (Carter *et al.*, 2003). Space closure may also be slow and difficult due to reduced alveolar bone mass or because anchor units have reduced root area due to microdontia (Bergendal *et al.*, 1996).

1.6.2 Space opening

Space opening commits the patient to a permanent prosthesis but this may have functional and occlusal advantages in terms of canine guidance and buccal segment intercuspation (Balshi, 1993). Despite this, there is no significant difference in reported temporomandibular dysfunction between patients following space closure or space opening (Robertsson and Mohlin, 2000). Space closure may not be possible when tooth agenesis is severe, necessitating space to be idealised for prosthetic replacement. Space opening can be advantageous in some cases, for example, when maxillary lateral incisors are missing in a class III incisor case, as this helps to maintain a positive overjet. Space opening may also be preferred when maxillary lateral incisors are missing and the canines would make poor lateral incisors. The options available for prostheses follow restorative principles, with consideration being given to removable prostheses, fixed prostheses, implant-retained prostheses, adhesive fixed prostheses, composite build-ups or autotransplantation (Forgie *et al.*, 2005). If implants are being considered then sufficient space must be created, as well as ensuring root parallelism or divergence (Carter *et al.*, 2003; Jepson *et al.*, 2003). However, space opening for a prosthesis is associated with poorer periodontal indices, such as plaque and bleeding on probing scores (Robertsson and Mohlin, 2000).

Patients with tooth agenesis have a high risk of root resorption following orthodontic treatment, when assessed retrospectively prior to restorative intervention (Duedel *et al.*, 2009). This is unsurprising due to the large tooth movements sometimes required. Root resorption may impact on the post-orthodontic restorative prosthesis, occasionally precluding fixed bridge

placement. In some situations, maintenance of primary teeth may be appropriate depending on their prognosis. In the case of lower second primary molars, if they appear to have a good prognosis and are present at 20 years, the chance of long-term retention is high (Bjerklin and Bennett, 2000).

1.7 Quality of life

The World Health Organization (WHO) has defined quality of life (QoL) as an individual's perception of his or her position in life, in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns (World Health Organization, 1993). It is a broad ranging concept, which is affected in a complex way by a person's physical health, psychosocial state, level of independence, social relationships and relationship to salient features of their environment.

1.7.1 Health-related quality of life

The WHO defines health as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (World Health Organization, 1948). Health contributes to overall QoL and the impact of health and disease on QoL is known as health-related quality of life (HRQoL). HRQoL is a multidimensional concept with five domains: opportunity and resilience; health perception; functional states; impairments and disease and duration of life (Gift and Atchison, 1995).

A systematic review has found that poor oral status can affect HRQoL in some settings but further evidence is needed to support this (Naito *et al.*, 2006).

1.8 Oral health-related quality of life

Oral health was defined by the Department of Health (1994) as the standard of health of the oral and related tissues which enables an individual to eat, speak and socialise without active disease, discomfort or embarrassment and which contributes to general well-being. Oral health-related quality of life (OHRQoL) has also been defined as the impact of oral disorders on aspects of everyday life that are important to patients and persons, with those impacts being of sufficient magnitude, whether in terms of severity, frequency or duration, to affect an individual's perception of their life overall (Locker and Allen, 2007). OHRQoL makes up one aspect of HRQoL and takes into account how oral diseases or conditions affect the function and well being of a particular person from their own perspective (Rozier and Pahel, 2008).

OHRQoL encompasses multidimensional domains that include: survival of individual teeth and the dentition, absence of disease or symptoms, appropriate physical functioning, emotional well-being, satisfaction with oral health, perceptions of excellent oral health and absence of social or cultural disadvantage due to oral status. Physical functioning is associated with chewing, swallowing and the absence of pain, whereas emotional functioning is associated with smiling and social functioning is associated with normal roles (Gift and Atchison, 1995).

1.8.1 Relevance of oral health-related quality of life

Previously, the majority of the published healthcare research focused on outcomes related to clinical measures that were easily quantifiable, such as

treatment episodes (Laing *et al.*, 2010). As medical science has advanced, the incidence of disease has decreased and the focus of healthcare has evolved, aiming to drive prevention and retention of function (Gift and Atchison, 1995). Research in orthodontics has tended to focus on indices such as PAR scores or cephalometric measurements (Laing *et al.*, 2010; O'Brien *et al.*, 1998). However, research would suggest that a close relationship between clinical measures and patient perception of oral health status is unlikely (Allen *et al.*, 1999; de Oliveira and Sheiham, 2004; O'Brien *et al.*, 1998). To fully evaluate healthcare interventions outcome measures of importance to the patient, as well as the clinician need to be assessed. It is argued that the patient is the best person to judge his or her own HRQoL (Cunningham and Hunt, 2001).

Measuring HRQoL formally can aid in improving shared decision-making between patient and doctor, identify which patients are likely to benefit from an intervention and compare HRQoL before, during and after treatment (Rozier and Pahel, 2008). HRQoL measures are likely to be important in the future to justify treatment need, outcomes, determinants of health and provide evidence for publicly funded healthcare interventions (Cunningham and Hunt, 2001; Gift and Atchison, 1995; O'Brien *et al.*, 1998). O'Brien *et al.* (1998) have suggested that orthodontic treatment outcome should only be measured using a quality of life measurement .

1.9 Assessment of oral health-related quality of life

Most commonly, HRQoL is assessed using a self-completed questionnaire but telephone interviews and surrogate responders may be used (Cunningham and Hunt, 2001). HRQoL measures may be either generic or specific.

Generic measures provide a summary of HRQoL to form a single index measure or health profile, which allows different conditions or interventions to be compared. However, a generic measure may not be sensitive enough to detect changes as a result of oral disease or disease intervention and may contain questions that are irrelevant to a condition (Cunningham and Hunt, 2001).

Specific measures focus on a specific condition or disease and have a narrow focus so that they are sensitive to small, but clinically important changes in health. Specific measures do not allow comparisons across conditions and require both development and testing (Cunningham and Hunt, 2001).

1.9.1 Health-related quality of life generic measures

The SF-36 survey (Ware and Sherbourne, 1992) and EuroQol evaluation (Brooks, 1996) are examples of generic HRQoL measures.

Comparison of the SF-36 with the Oral Health Impact Profile (OHIP) generic OHRQoL measure has been performed. The SF-36 did not discriminate between the groups and is not likely to be sensitive to oral problems (Allen *et al.*, 1999). In contrast, when the OHIP and EuroQol were compared, both were found to have good discriminant validity. The OHIP was more sensitive to oral health factors, but the measures performed equally well for the main oral health factor, which was decayed teeth (Brennan and Spencer, 2005). However, tooth agenesis, spacing and aesthetics were not represented among the dental conditions that participants suffered from.

1.9.2 Oral health-related quality of life generic measures

The OHIP (Slade and Spencer, 1994) is the most commonly used generic OHRQoL measure, but a number of other valid and reliable measures have been developed for use in older adults. These include Social Impacts of Dental Disease (Cushing *et al.*, 1986), Subjective Oral Health Status Indicators (Locker and Miller, 1994), Dental Impact on Daily Living (Leao and Sheiham, 1996), Geriatric Oral Health Assessment Index (Atchison and Dolan, 1990), Dental Impact Profile (Strauss, 1996), Oral Health Related Quality of Life Measure (Kressin *et al.*, 1996) and Oral Health Related Quality of Life UK (OHRQoL-UK) measure (McGrath and Bedi, 2001).

The Child Oral Health Quality of Life (COHQoL) measure is made up of an age-specific Child Perception Questionnaires (CPQ), the Parental-Caregiver Perceptions Questionnaire (P-CPQ) and Family Impact Scale (Jokovic *et al.*, 2002). The CPQ has been used extensively in orthodontic patients, who are normally suited to the CPQ 11-14, which is aimed at 11-14 year-olds (Kotecha *et al.*, 2013; Laing *et al.*, 2010; Locker *et al.*, 2010; Seehra *et al.*, 2011), but has even been used in adolescents up to the age of 16 (Brosens *et al.*, 2013).

1.9.3 Oral health-related quality of life specific measures

A tooth agenesis-specific OHRQoL measure has recently been developed (Akram *et al.*, 2011) and its validity and reliability were tested whilst this present study was being performed (Akram *et al.*, 2013). The authors used qualitative methods to identify issues of importance to patients with tooth agenesis and used this to develop a condition-specific questionnaire. Twenty-two patients were assessed

in small focus groups and reported concerns were in relation to treatment, effect on daily activities, thoughts on appearance and reaction of other people (Akram *et al.*, 2011). This questionnaire was tested on patients aged 11-18, with a range of severity of tooth agenesis, at all stages in orthodontic treatment. It was found to be valid and reliable in this group (Akram *et al.*, 2013) but has not yet been used in older patients or tested more widely.

A condition-specific QoL measure has been developed for patients with severe dentofacial deformity requesting orthognathic treatment. It was developed through literature review and interviews with patients and clinicians and was reported to have good reliability and validity (Cunningham *et al.*, 2000; Cunningham *et al.*, 2002).

Klages *et al.* (2006) developed and tested a multi-item instrument for assessment of the psychosocial impact of dental aesthetic appearance, called the Psychosocial Impact of Dental Aesthetics Questionnaire (PIDAQ). While this may be a promising tool for orthodontic patients, patients with tooth agenesis may have other concerns that this measure may not be sensitive to, such as functional limitations.

1.9.4 Oral Health Impact Profile questionnaire

The OHIP was developed using the conceptual framework described by Locker (1988), which was based on the WHO classification of impairments, disabilities and handicaps (World Health Organization, 1980). In Locker's hierarchical framework, dental diseases cause impairment, which may result in functional

limitations or discomfort, lead to a disability (such as loss of function), or even a handicap (effect on capacity to work) (Locker, 1988).

Development of the OHIP began by obtaining 535 open-ended statements from 64 dental patients from private practice and dental hospital clinics. Participants were from South Australia and aged sixty or over. The statements obtained were reduced down to 46 based on content and ability to represent the conceptual model. Three questions based on handicap were added, since statements based on handicap were rare. The questionnaire developed contained 49 questions and is identified as the OHIP-49 (Slade and Spencer, 1994).

The OHIP-49 is divided into seven theoretical domains: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap. An example question is 'Have you been self-conscious because of your teeth, mouth or dentures?'. Responses are on a Likert scale with the following options: 'very often' (code 4), 'fairly often' (code 3), 'occasionally' (code 2), 'hardly ever' (code 1) or 'never' (code 0). Responses can be multiplied by the weighting for that individual question before summing weighted values to calculate overall score and domain scores. Weightings were calculated using Thurstone's method of paired comparisons and were used to reflect the severity of each impact. Reliability was tested with Cronbach's α using 122 repeat questionnaires at 20-month follow-up. All domains had good reliability except for handicap, in which reliability was moderate. Stability was evaluated in a test-retest of 46 subjects and six domains had good or excellent reliability. Reliability was poorer in the social disability domain. Due to the method by which the OHIP-49 was developed, it had good content validity. Social

impact correlated well with the need to visit a dentist, ensuring the OHIP-49 had good construct validity (Slade and Spencer, 1994). Validity and reliability has subsequently been confirmed in later research (Allen *et al.*, 1999; Jones *et al.*, 2004).

One advantage of the OHIP-49 is that the statements were derived from a patient group, and not from dental research. It is essential for an OHRQoL measure to assess the issues important to patients and so this patient-centred approach is important. However, the item reduction process and weightings derived were expert-centred (Locker and Allen, 2007).

As well as using weightings provided by Slade and Spencer (1994), there are other options for calculating overall and subscale scores. One option is additive, where a value is given to each response category in the Likert scale. These values range from “very often”, which is given a value of 4 to “never”, which is given a value of 0, and responses are summed to form the total score. A second option is a count of the number of impacts. Some authors class an impact as a response scored as “very often”, “fairly often” or “occasionally” (Brennan and Spencer, 2005), whereas other authors count an impact as a response scored as “very often” or “fairly often” (Locker and Slade, 1993). Comparison of the three methods of scoring found that the additive and weighted methods performed equally well and better than the method of counting the number of impacts (Allen *et al.*, 1999). The additive method is less complex than using the weighting method, does not compromise validity and may be more suitable at comparing groups (Locker *et al.*, 2001; Robinson *et al.*, 2003).

One of the downfalls of using a generic measure is that some items may be irrelevant to the population being studied, particularly in orthodontics where patients are generally fit and well (Cunningham and Hunt, 2001). A short form of OHIP was developed using secondary analysis of the data used in the development of the OHIP-49, bearing in mind that as the number of items used in a measure decreases, the reliability of the measure also decreases (Slade, 1997). The short-form OHIP-14 question measure (OHIP-14) retained the original concept of the OHIP-49 but items relating only to denture wearers or where 5% or more of responses were left blank or marked 'don't know' were eliminated. Internal reliability was high for the overall score and individual domains. In comparison with the OHIP-49, the OHIP-14 was as effective at detecting a difference between subgroups of older South Australians (Slade, 1997). The OHIP-14 is ideal for assessing OHRQoL in settings where only a limited number of questions can be administered (Slade, 1997).

The OHIP-49 and OHIP-14 have since been used extensively in non-tooth agenesis populations, including older patients (Locker and Slade, 1993; Slade and Spencer, 1994), young adults (Esperao *et al.*, 2010; Hassan and Amin, 2010; John *et al.*, 2003; Liu *et al.*, 2011a; Liu *et al.*, 2011b; Palomares *et al.*, 2012; Rusanen *et al.*, 2010; Silvola *et al.*, 2012) and adolescents (Feu *et al.*, 2010; Feu *et al.*, 2013; Masood *et al.*, 2013). The OHIP-49 has also been used successfully in adults with tooth agenesis (Anweigi *et al.*, 2013a; Hashem *et al.*, 2013; Meaney *et al.*, 2012).

It has been argued that generic OHRQoL measures such as the OHIP may not be suitable for orthodontic conditions, since the main concerns of orthodontic

patients are aesthetic, whereas the OHIP-49 and OHIP-14 focus on pain, discomfort and difficulty chewing (O'Brien *et al.*, 1998). The OHQoL-UK (McGrath and Bedi, 2001) includes questions that reflect the positive and negative impacts of OHRQoL and so can be useful when assessing the benefits of orthodontic treatment. The OHIP only measures negative impacts and so may be better for assessing OHRQoL prior to treatment (Liu *et al.*, 2011a).

1.9.5 Control groups in oral health-related quality of life research

Selecting a suitable control for patients with tooth agenesis can pose difficulties. Some previous studies have not included a control group (Anweigi *et al.*, 2013a; Locker *et al.*, 2010; Wong *et al.*, 2006). If a group with similar orthodontic need is used, no differences in OHRQoL may be evident (Laing *et al.*, 2010). A population with routine dental needs may be sourced (Hashem *et al.*, 2013) but this could be a poor control if they have missing anterior teeth or toothache, which have significant impacts on OHRQoL.

One option is to use a 'friend-control' (Rothman and Greenland 1998), selected by the participant. This control is convenient and generally well matched on ethnicity, education and age (Bunin *et al.*, 2011). However, the disadvantage is that the researchers do not select the control group, which has the potential to introduce confounding factors. To the authors' knowledge, this method of assigning a control has not been used in orthodontic research.

An alternative option is to use a historical control, such as the Adult Dental Health Survey (ADHS). The 2009 ADHS (Office for National Statistics. Social Survey Division, Information Centre for Health and Social Care, 2009) was the

fifth in a series of national dental surveys that have been carried out every decade since 1968. It aims to provide a profile of the dental health of adults in the UK and assess how this has changed over time. The 2009 ADHS collected data from two-stage cluster sampling of adults aged 16 and above in England, Wales and Northern Ireland. In two ten-week periods in 2009 and 2010, 11380 adults were interviewed and 6469 were examined. The OHIP-14 was used for the first time in the 1998 ADHS to assess OHRQoL of dentate adults. However, in the 2009 ADHS all dentate and edentate adults completed the OHIP-14.

It is important to ensure control groups are as similar as possible to the interventional group but in national surveys, there may be a shortage of local data and the sample may not be matched for age. In addition, the inclusion and exclusion criteria applied to the experimental group will not have been applied to the population studied in the control. This may introduce bias and confounders, which may affect the validity of the comparison (Gomm *et al.*, 2000).

1.10 Impact of oral conditions on oral health-related quality of life

The impact of a number of oro-facial and dental conditions on OHRQoL were compared by Jokovic *et al.* (2002), when the CPQ 11-14 was being tested. It was found that children with oro-facial conditions, such as cleft lip and palate, had the highest prevalence and severity of impacts on OHRQoL, in comparison with children with malocclusion and dental caries. As the number of carious surfaces increased, OHRQoL was more greatly affected. Of the oro-facial conditions assessed, isolated cleft lip or cleft palate affected OHRQoL the least, followed by unilateral CLP, then bilateral CLP (Jokovic *et al.*, 2002).

However, even though children with oro-facial conditions had the highest prevalence and severity of impacts OHRQoL, they were less likely to report that these impacts affected their lives overall. The authors suggest this may be because oro-facial conditions, such as CLP, are diagnosed at a young age and affected individuals have received long-term clinical and psychosocial care through the cleft team (Locker *et al.*, 2010).

In comparison with children seeking orthodontic treatment, Feu *et al.* (2010) found that children with poor dental health status, as measured on the Decayed, Missing, Filled Teeth (DMFT) scale, were statistically associated with poorer OHRQoL using OHIP-14.

1.10.1 Impact of malocclusion on oral health-related quality of life

The demand for cosmetic dentistry is increasing and aesthetics of the face and teeth have become increasingly important in popular culture. Dentofacial appearance can affect interpersonal relationships and perceived qualities such as friendliness, social class, intelligence and popularity from infancy to adulthood (Laing *et al.*, 2010). Attractive children are seen by others as likely to have more positive social behaviour and may even receive more positive treatment than their peers (Langlois *et al.*, 2000). As a result, deviation from ideal dentofacial aesthetics, especially in children, might adversely affect self-esteem and self-confidence, resulting in mockery from peers (Shaw *et al.*, 1991).

In 2009, a systematic review was undertaken to investigate the association between malocclusion, orthodontic treatment need and orthodontic treatment on QoL, HRQoL and OHRQoL (Liu *et al.*, 2009). Twenty-three papers were

included, although a meta-analysis could not be performed due to the heterogeneous methodologies. The majority of the research was cross-sectional and performed on children. The strength of the evidence was low, but did show an association between QoL and malocclusion or orthodontic treatment need.

Orthodontic treatment need is correlated with OHRQoL and research has found that children with normative treatment need had significantly greater impacts as measured on OHIP-14 (Feu *et al.*, 2010), with significant differences seen in patients with IOTN dental health component (dhc) grade 2 and above (Masood *et al.*, 2013). Masood *et al.* (2013) found that functional limitation, physical pain, physical disability, psychological disability and social disability were significant at IOTN dhc grade 3 and above, whereas handicap was only significant at IOTN dhc grade 5. Similar studies have found young adults with the need for orthodontic treatment scored more impacts in all domains (Liu *et al.*, 2011a) or in all domains except handicap (Hassan and Amin, 2010). Although severe malocclusion as measured on the IOTN has been shown to affect OHRQoL, severely compromised aesthetics is a better predictor of reduced OHRQoL in those seeking orthodontic treatment (Feu *et al.*, 2010). This correlates with research that found missing anterior teeth to be considered the most unattractive occlusal trait (Arrow *et al.*, 2011; Shaw, 1981).

A large cross-sectional study of 654 Japanese students found 40% had a malocclusion as measured on the IOTN and this contributed to impacts on daily performance. It was felt that this was conducive to psychological stress, especially interpersonal sensitivity and depression (Ekuni *et al.*, 2011). Self-perceived orthodontic treatment need has been assessed less often, but children

and adults who felt they had an orthodontic need had significantly greater impacts on the OHIP-14 (Feu *et al.*, 2010; Masood *et al.*, 2013).

Johal (2007) assessed the effect of increased overjet and spacing in the anterior dentition on OHRQoL in relation to a control. Both of these characteristics had a highly statistically significant effect on OHRQoL when rated by children and their caregivers. The authors therefore argue that malocclusion also affects the parent or guardian, rather than just the child. There was no significant difference between the two malocclusions (Johal *et al.*, 2007). Traebert and Peres (2007) found that malocclusion affected the OHRQoL of young Brazilian adults and occlusal traits including incisal crowding, anterior maxillary irregularity and increased overjet have the greatest impact. Amongst adults aged 16 to 64 with severe skeletal malocclusions, lateral crossbite, open bite, reverse overjet and class II molar relationships were associated with a significant increase in impacts on the OHIP-14 (Rusanen *et al.*, 2010).

As well as OHRQoL, researchers have looked at the influence of malocclusion on bullying and the consequent effect on self-esteem. In a cross-sectional study of 10 to 14-year olds, 12.8% of children were bullied at school, and these individuals were more likely to have a class II division 1 incisor relationship, an increased overjet, increased overbite and a higher IOTN aesthetic component (AC). Bullied participants had higher scores on CPQ and lower self-esteem, although it was unclear whether the negative impact on OHRQoL was due to malocclusion or bullying (Seehra *et al.*, 2011). A follow-up study found that the bullying had stopped in 78% of previously bullied individuals following the commencement of orthodontic treatment (Seehra *et al.*, 2013).

1.10.2 Impact of tooth agenesis on oral health-related quality of life of children

Historically, research has focussed on the prevalence and aetiology of tooth agenesis, but more recently the functional, psychosocial and emotional impacts have been investigated.

Common complaints in patients with tooth agenesis are missing teeth, spacing and appearance, whereas masticatory difficulties are rarely cited as the main complaint (Hobkirk *et al.*, 1994). In the development of a condition-specific OHRQoL measure for tooth agenesis (Akram *et al.*, 2011), children aged 11 to 18 were concerned by arch spacing and identified this as a reason for teasing and bullying. Other highlighted concerns were related to the size and colour of false teeth, dislike of removable dentures because of association with elderly people, size of teeth, difficulty obtaining well-fitting sports mouthguards and worries about the eventual loss of primary teeth where the successors were missing.

Wong *et al.* (2006) investigated OHRQoL in 25 children aged 11 to 15 in Hong Kong, using the CPQ 11-14. Participants had severe tooth agenesis, defined as 4 to 20 missing teeth. Tooth agenesis significantly affected OHRQoL, with all participants suffering one or more oral symptoms, 88% suffering functional limitations and 88% experiencing impacts on emotional well-being. There was a small but statistically significant association between the number of missing teeth and OHRQoL. When accounting for retained primary teeth, the impact of tooth agenesis on OHRQoL was stronger, suggesting that maintaining primary teeth was beneficial. However, since this study was cross-sectional, this relationship was an association, rather than causal. In addition, the tooth

agenesis group was not compared to a control and no sample size calculation was performed.

Locker (2010) investigated oligodontia amongst 11 to 14-year olds in Canada, also using the CPQ 11-14. Thirty-six individuals were studied and the population had 1 to 14 missing teeth. No sample size calculation was performed and there was no control for comparison. Seventy-seven per cent of the population experienced functional and psychological impacts either 'often' or 'everyday' and 88.9% had one or more impacts 'sometimes', 'often' or 'everyday' in the previous three months. Both of these prevalence figures were lower than those found by Wong *et al.* (2006). In contrast with Wong *et al.* (2006), correlations between total or domain scores and number of missing teeth were weak and non-significant. The authors felt this may be due to the lower number of missing teeth in this population studied, but accept that cultural differences may also have an effect (Locker *et al.*, 2010). In this study, children with oligodontia were found to have worse OHRQoL than children with caries or malocclusion, but better than children with orofacial conditions, such as CLP (Jokovic *et al.*, 2002). Conversely, Wong *et al.* (2006) found that severe tooth agenesis had a similar impact on the OHRQoL of children as orofacial conditions (Jokovic *et al.*, 2002), but this may also be related to the number of teeth participants were missing in each study.

Much of the research into OHRQoL in children with tooth agenesis has been performed without a control (Locker *et al.*, 2010; Wong *et al.*, 2006) whereas Laing *et al.* (2010) used an orthodontic control group. In this study, participants were aged 11 to 16 and the control group had an IOTN dhc score 4 or 5 to ensure their orthodontic treatment needs were comparable. No differences in

psychosocial impact were found between the two groups. The authors suggest this may be because both groups had concerns with their malocclusion, but for different reasons. Secondly, the study included patients with mild tooth agenesis, which may have less psychosocial impact than more severe tooth agenesis. Thirdly, adjacent teeth could have erupted into tooth agenesis spaces, improving aesthetics. Despite this, as the severity of posterior tooth agenesis increased, participants had greater functional limitations and there was tentative evidence that retained primary teeth were beneficial in terms of function (Laing *et al.*, 2010).

Kotecha *et al.* (2013) assessed the impact of tooth agenesis on the OHRQoL of 86 children aged 11 to 14. Participants had at least two missing teeth and were compared to an orthodontic group of patients with IOTN dhc score 2 or 3. Tooth agenesis had a significant effect on OHRQoL in terms of overall CPQ scores and all domain scores. However, there were no associations between the number of missing teeth and OHRQoL, although retained deciduous teeth may have accounted for this. Both of the studies that compared children with tooth agenesis to an orthodontic control group suggested that further research should include a non-orthodontic group (Kotecha *et al.*, 2013; Laing *et al.*, 2010).

1.10.3 Impact of tooth agenesis on oral health-related quality of life of adults

Meaney *et al.* (2012) performed qualitative research investigating the impact of tooth agenesis on ten adults aged 16 to 25. The study was performed in a dental hospital setting and the population consisted of males and females with mild, moderate or severe tooth agenesis. Key themes were identified and explored

using small focus groups in semi-structured interviews. The main motivation for treatment was to improve dental aesthetics and participants felt that treatment would make them less self-conscious and more comfortable. Participants were more aware of their appearance with age and having been first diagnosed aged 9 to 10, felt frustration with delays in starting treatment. As they transitioned into adulthood, participants had a better understanding of their condition and were more likely to make their own choices in relation to treatment. The OHIP-49 was also used prior to the qualitative interviews and scores ranged from 24 to 143. This was not explored further in the study.

The impacts of tooth agenesis and amelogenesis imperfecta on OHRQoL have been compared to a control using the OHIP-49. Ages ranged from 18 to 45 and patients in the tooth agenesis group had at least four teeth missing. The control group was sourced from a patient pool at the Dublin Dental Hospital, so patients were likely to need routine dental treatment only. No sample size calculation was performed prior to recruitment but 41 patients with tooth agenesis completed questionnaires. A *post hoc* sample size calculation was performed with a minimum important difference of six units on the OHIP scale and 41 patients gave their results a power of at least 90%. This study found statistically significant differences between the tooth agenesis and control groups, in all OHIP domains except handicap. The Rosenberg self-esteem scale found no differences in self-esteem between the groups but may not be a sufficiently sensitive measure, as it is generally used on individuals with severe facial disfigurement. Amelogenesis imperfecta had a greater effect on OHRQoL in comparison to tooth agenesis (Hashem *et al.*, 2013).

When studying mild, moderate and severe tooth agenesis, Anweigi *et al.* (2013a) investigated OHRQoL in 82 adults aged 16 to 34. Almost all participants had one or more impacts on the OHIP-49, although this was not compared to a control. Subjects were currently undergoing orthodontic treatment, but prior to restorative treatment. The number of missing teeth was a poor predictor of OHRQoL, but this may have been confounded by retained primary teeth, which were not recorded. The location of missing teeth was significantly associated with psychological discomfort, particularly anterior teeth. As age increased, adults with tooth agenesis considered themselves to have more impaired OHRQoL, more functional limitation and worse physical disability, although concerns with the aesthetics of missing anterior teeth seemed to reduce. Perceived functional limitation may increase with age due to a greater expectation from the dentition, or alternatively due to the progressive loss of retained primary teeth. This highlights the potential advantages in retaining primary teeth where possible (Anweigi *et al.*, 2013a).

1.10.4 Impact of other factors on oral health-related quality of life

When studying a population aged 15-25 years, research has found that malocclusion has the greatest effect on OHRQoL in the 15-18 years age group (Masood *et al.*, 2013). In research on restorative rehabilitation, younger adults were found to have higher neuroticism, whereas older adults were more psychologically stable (Al-Omiri and Karasneh, 2010).

There are notable sex differences in OHRQoL research. In general, females are more likely to report impacts than males and research has found this to be in the order of 2.6 times (Anweigi *et al.*, 2013a; de Oliveira and Sheiham, 2004; Esperao

et al., 2010; Feu *et al.*, 2010; Rusanen *et al.*, 2010). This includes females with tooth agenesis (Anweigi *et al.*, 2013a). Rusanen *et al.* (2010) found that females were more likely to report impacts in psychological and social dimensions. In contrast, some authors have found no difference in relation to sex (Masood *et al.*, 2013).

1.11 Effect of orthodontic treatment on oral health-related quality of life

A major reason cited for carrying out orthodontic treatment is to improve psychosocial well-being, although there is research that shows it does not have this effect (Shaw *et al.*, 1980). A twenty-year follow-up study showed that adults with visible malocclusion had similar social and psychological well-being in comparison to a control (Shaw *et al.*, 2007). However, this contrasts with research from Denmark, where adults with untreated, severe malocclusions were followed up fifteen years following initial assessment. These individuals continued to experience feelings of dissatisfaction with their teeth and memories of teasing persisted into adulthood (Helm *et al.*, 1985). Patients undergoing orthodontic treatment in 1981 had significantly higher self-esteem and satisfaction with life than those with unmet need when reassessed in 2001. However, these patients also had higher self-esteem prior to treatment, which may negate this difference. One potential flaw with this study was the large, but understandable attrition rate. In addition, the result may not be generalisable, since the orthodontic treatment provided in 1981 would vary significantly with contemporary orthodontic treatment (Shaw *et al.*, 2007).

Another long-term follow-up study performed in Australia found that orthodontic treatment may have a negative effect on life satisfaction and self-

esteem when followed up 17 years after treatment (Arrow *et al.*, 2011). This is compelling, but the reasons are not fully explored, the attrition rate was large and the control was not followed as a cohort but recruited at the 17-year follow-up. Missing teeth in the anterior region and molar antero-posterior relationship were associated with poorer OHRQoL in patients previously treated with fixed orthodontic appliances, particularly in the psychological discomfort domain. Self-esteem was significantly associated with the IOTN AC and OHRQoL was closely associated with life satisfaction and self-esteem (Arrow *et al.*, 2011).

Researchers have warned that studies investigating the effect of orthodontic treatment that are performed during adolescence can be unreliable as major life changes are occurring, which may mask changes in OHRQoL. This may be one of the reasons why research on psychosocial status has shown mixed results following orthodontic treatment (Hassan and Amin, 2010; O'Brien *et al.*, 1998). Studies on young adults may be more reliable since life changes occurring during puberty have subsided (Hassan and Amin, 2010).

In a large survey of 1675 adolescents aged 15 or 16, those that had completed orthodontic treatment reported fewer oral impacts on the OHIP-14 than those that were currently undergoing or had never had orthodontic treatment (de Oliveira and Sheiham, 2004). Children who received early orthodontic treatment with a Twin-block functional appliance reported higher self-concept and more positive childhood experiences in comparison to a control (O'Brien *et al.*, 2003). During orthodontic treatment, research has shown improvement in OHRQoL, functional limitation, emotional impact and social impact in children (Seehra *et al.*, 2013). Brosens (2013) also found that children one year into orthodontic

treatment scored significantly more highly in motivational questions than those that did not start treatment. However, there was an increase in CPQ scores, with significant increases in oral symptoms, functional limitations and social well-being. The authors suggest two possible reasons for this; children completed questionnaires immediately after appliance adjustment, when pain and discomfort is greatest, and treatment was with multiloop stainless steel archwires, which are associated with greater discomfort and poorer aesthetics. Children with higher self-esteem prior to treatment had less variability in OHRQoL during treatment. Feu *et al.* (2013) also found that OHRQoL reduced during orthodontic treatment, but upon completion of treatment there was a significant improvement compared to prior, and during treatment. Meaney *et al.* (2012) also found that psychosocial impacts, such as anxiety over appearance, can reduce when treatment nears completion.

When assessing patients previously identified as being bullied, 78% reported that bullying stopped once orthodontic treatment commenced. There were no differences between the self-esteem of bullied and non-bullied children, but bullied individuals had significantly greater scores on the CPQ subscales. The cessation of bullying may be in relation to a reduction in malocclusion but the authors accept that the relationship between malocclusion, bullying, self-esteem and OHRQoL are complex (Seehra *et al.*, 2013).

In comparison to pre-treatment, a prospective cohort study has found that adults with fixed appliances in-situ had significantly worse OHRQoL at twelve and eighteen months into treatment (Liu *et al.*, 2011b). There were no significant differences between these two time periods and there was no significant

handicap or physical disability throughout treatment. A large, controlled, cross-sectional study of young adults (Palomares *et al.*, 2012) found that adults treated with fixed orthodontic treatment had significantly greater OHRQoL when assessed six months following debond than untreated adults. The groups were similar at baseline and the main markers that had a greater negative impact on OHRQoL were severe malocclusions as measured on the IOTN dhc or worse aesthetic appearance as measured on the IOTN AC. In adults with tooth agenesis, OHRQoL may deteriorate during treatment (Anweigi *et al.*, 2013b). This may be because tooth agenesis spaces are opened during fixed appliance treatment, with detriment to aesthetics.

1.11.1 Effect of restorative treatment on oral health-related quality of life

Restorative dentistry may be the only treatment discipline required in cases involving tooth agenesis, or it may be the stage that follows comprehensive orthodontic treatment. If tooth agenesis spaces are opened then the options for restoring the space involve a removable prosthesis, fixed bridge, autotransplant or implant-supported restoration. Adolescents and young adults with tooth agenesis restored with resin-bonded bridges following orthodontic treatment have been compared with patients with tooth agenesis prior to restoration. Following restorative treatment, OHRQoL improved significantly in the restored group but deteriorated in the unrestored control group. It is possible that OHRQoL deteriorated in the control group as spaces were opened that may have been previously closed. The authors advise that patients with tooth agenesis should be advised that aesthetics may worsen during the orthodontic phase of

treatment, which may impact on OHRQoL, but that OHRQoL will improve following restorative treatment (Anweigi *et al.*, 2013b).

Adults with prosthetic rehabilitation have been compared with fully dentate, unrestored patients. Restorations included fixed prostheses, removable prostheses or both. Although patients with tooth agenesis that had been restored tended to be less satisfied than the fully dentate control, there were no significant differences in OHRQoL between the two groups. Interestingly only 6.2% of individuals with restorative rehabilitation were totally satisfied with their dentition, compared to 13.5% in the unrestored group. Furthermore, the position and type of prosthetic rehabilitation had no effect on OHRQoL when measured on Dental Impact on Daily Living (DIDL), OHIP and OHRQoL (Al-Omiri and Karasneh, 2010).

A small and uncontrolled cross-sectional study investigated the cementation of one to four implant-supported single crowns on patients with tooth agenesis. This was associated with a 75% reduction in impacts on the OHIP-49, greater biting force and increased masticatory ability, despite retained primary teeth being kept in until implant placement (Goshima *et al.*, 2010).

This research contrasts with literature on OHRQoL where subjects with removable prostheses tended to report greater impairment on OHRQoL, despite the similar age groups in both studies (John *et al.*, 2003).

In comparing fixed, tooth-borne prostheses with implant-supported prostheses in adults with tooth agenesis, patients were more satisfied by the aesthetic outcomes of implant-supported prostheses. Patients were more satisfied than

dental professionals with the outcome but restored patients with tooth agenesis still scored significantly more highly than patients without tooth agenesis. No patients received removable prostheses and due to the retrospective nature of this study, improvement in OHRQoL provided by the prostheses could not be assessed (Duedel *et al.*, 2009).

1.12 Aims of the study

The aim of this study is to investigate the impact of tooth agenesis on the OHRQoL of adults.

The null hypotheses were:

- i. There are no differences in the OHRQoL reported by adults with tooth agenesis compared to a friend-control sample or a control sample derived from the 2009 ADHS
- ii. There are no associations between OHRQoL and sex, age, ethnicity or social deprivation
- iii. There are no associations between OHRQoL in patients with tooth agenesis and the number of missing teeth, the location of missing teeth or the presence of retained deciduous teeth

Chapter 2

Method

2. Method

2.1 Study design

This study was a cross-sectional survey of adults presenting with tooth agenesis. OHRQoL was measured using a validated questionnaire and compared to two control groups. The first control group was selected by the participants with tooth agenesis, using the friend-control method. The second control group was a historic control, derived from the 2009 ADHS (Office for National Statistics, Social Survey Division, Information Centre for Health and Social Care, 2009).

Ethical approval was obtained from the West Midlands Black Country Research Ethics Committee (REC reference number 13/SC/0461). Research and Development approval was granted by Birmingham and the Black Country Clinical Research Network.

2.2 Study participants

All participants were recruited by the principal researcher (DH), between January 2014 and June 2015. Consecutive patients with tooth agenesis were recruited at Birmingham Dental Hospital, Birmingham Community Healthcare NHS Trust, from orthodontic new patient clinics, orthodontic treatment clinics, and multidisciplinary orthodontic-restorative clinics.

The inclusion criteria were:

- Aged 16 or above
- Tooth agenesis of two or more teeth excluding third molars, confirmed by clinical history and radiography

- English speaking
- Willing to participate in the study

The exclusion criteria were:

- Currently undergoing or previously undergone a course of extensive orthodontic or restorative dental treatment (this included fixed orthodontic appliances, fixed bridges or dental implants but excluded removable orthodontic appliances, removable dentures and simple restorations)
- Patients with cleft lip and palate
- Patients with craniofacial syndromes

2.3 Control groups

The first control group was recruited via the friend-control method (Rothman and Greenland 1998). Each participant with tooth agenesis was asked to choose a friend or colleague with the following inclusion criteria:

- Absence of tooth agenesis as far as the participant and friend-control were aware
- Aged 16 years or over and within 3 years of age of their friend or colleague
- Unrelated
- Same sex
- English speaking
- Willing to participate in the study

The friend-control group were subject to the same exclusion criteria as the tooth agenesis group.

The second control group was derived from the 2009 ADHS (Office for National Statistics. Social Survey Division, Information Centre for Health and Social Care, 2009).

2.4 Sample size calculation

The sample size was calculated to determine a minimum effect size of 0.5 for the difference in OHRQoL between the two groups, with α at 0.05. Sample sizes were calculated for power at the 80% and 90% levels.

To account for participants that failed to fully complete the questionnaire or failed to recruit a friend-control, it was decided to recruit an additional 10 per cent. At 80% power, the sample size calculation proposed a sample of 64 participants in each group, or 71 participants allowing for the 10% dropout rate. At 90% power, the calculation proposed a sample of 86 participants in each group, or 95 participants allowing for the 10% dropout rate.

2.5 Method

Consecutive patients with tooth agenesis were invited to participate in the study. The study was explained verbally and patients were given an invitation letter (Appendix 1) and an information sheet (Appendix 2). The information sheet outlined the purpose of the study, inclusion and exclusion criteria, and process for recruiting a friend-control. Patients who agreed to participate were given the written questionnaire or a link to the online version on the website

www.surveymonkey.com (SurveyMonkey Inc., Palo Alto, California, USA) (Appendix 3). All written questionnaires were uploaded onto SurveyMonkey by the principal investigator (DH). Subjects with tooth-agenesis were asked to nominate and obtain verbal consent from a friend-control, who was then emailed an invitation letter (Appendix 4) and information sheet (Appendix 5) with a link to the same online questionnaire. The information sheet included the inclusion and exclusion criteria. All subjects received a £10 shopping voucher as reward for completing the questionnaire. The ADHS control was derived from the 2009 ADHS (Office for National Statistics. Social Survey Division, Information Centre for Health and Social Care, 2009), which is available at: www.hscic.gov.uk/pubs/dentalsurveyfullreport09. Data from England was used and filtered to include only sex, age, ethnicity, IMD decile, OHIP-14 total score and domain scores. The ADHS control was then age-matched to the tooth agenesis sample. It was not possible to exclude subjects with tooth agenesis from the 2009 ADHS since this parameter was not recorded.

All subjects completed the validated OHIP-49 questionnaire (Slade and Spencer, 1994). The OHIP-49 is divided into seven domains: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap. The responses and associated codes are: 'never' (0), 'hardly ever' (1), 'occasionally' (2), 'fairly often' (3) and 'very often' (4).

The following socio-demographic details were recorded in the questionnaire:

- Age
- Sex
- Ethnicity

- Postcode

The postcode was used to obtain the patient's Index of Multiple Deprivation (IMD) Score using the Neighbourhood Statistics website (Office for National Statistics, 2011). The IMD provides a relative measure of social deprivation in comparison to other local areas in England. Lower-layer Super Output Areas are ranked from 1 (most deprived) to 32,482 (least deprived) (Department for Communities and Local Government, 2011). For this study, deciles were converted into quintiles due to the small number of subjects with tooth agenesis.

The following details were recorded from the clinical records using a data collection sheet (Appendix 6) to investigate the impact of these factors on OHRQoL:

- Total number of missing teeth
- Location of missing teeth
 - Anterior (incisors or canines)
 - Posterior (premolars or molars)
- Presence of retained deciduous teeth

2.6 Statistical analysis

All participants were assigned an anonymous identifier number to maintain confidentiality. Friend-controls were allocated an identifier that linked them to the appropriate participant with tooth agenesis. Data was then exported into a customised spreadsheet (Microsoft Excel 2011, Redmond, Washington, USA). The code scored by the participant for each question was summed to calculate the total OHIP-49 score and the seven domain scores. The number of impacts on

OHRQoL was calculated as the sum of the number of questions answered with 'occasionally', 'fairly often' or 'very often'. The OHIP-49 scores were used for comparison between the participants with tooth agenesis and the friend-control group. OHIP-14 scores were calculated from the OHIP-49 questions and used for comparison between participants with tooth agenesis and the ADHS group.

Data analysis was conducted using Stata Statistical Software: Release 14 (Statacorp. 2015, College Station, TX: Statacorp LP). The sample characteristics of the tooth agenesis and control groups were initially analysed using descriptive statistics. Differences in sample characteristics were then compared using the Chi-square test. The OHRQoL scores were tested for normality using qq plots. The OHIP scores were not normally distributed and consequently non-parametric statistical methods were used. Wilcoxon signed-rank or Mann-Whitney U tests were used to test for differences between the groups in overall OHIP scores, the seven domain scores and prevalence of impacts.

Negative binomial regression was used to investigate the association between OHRQoL and age, sex, ethnicity and social deprivation. Negative binomial regression was also used to investigate the association between OHRQoL and the number of missing teeth, location of missing teeth and presence of retained deciduous units, adjusting for age, sex, ethnicity and social deprivation. All statistical tests were two-sided and used a significance level of $p = 0.05$.

Chapter 3

Results

3. Results

3.1 Characteristics of the samples

Recruitment for the study began in January 2014 and was completed in June 2015. Participants with tooth agenesis completed a paper questionnaire on clinic or were given a link to an electronic version. All friend-controls completed the electronic version. In the timeframe available for the study, seventy-eight subjects with tooth agenesis were recruited. The majority of subjects were aged 16-18 years, and only a small number of subjects were aged over 30. The age range was therefore limited to 16 – 30 years for the tooth agenesis sample and both control groups. This resulted in a sample of 71 subjects with tooth agenesis. Of the 71 participants with tooth agenesis, 17 recruited a friend control. Two friend-controls were excluded since their ages were poorly matched to the subjects with tooth agenesis. The recruitment of 15 friend-controls from 71 recruits with tooth agenesis represents a response rate of 21.1%. The sample size calculation required 64 subjects in each group for 80% power. As a result, the comparison between the tooth agenesis group and the ADHS control met the sample size calculation. Due to the low response rate for recruitment of friend-controls, the comparison between the tooth agenesis group and the friend-control group did not meet 80% power.

Due to the small number of non-white subjects in the samples, ethnicity was divided into three groups: white (white British, white Irish and white other), South Asian (Indian, Pakistani, Bangladeshi) and Other.

Table 3. 1: Characteristics of the tooth agenesis and friend-control samples

Parameter	Group	
	Tooth agenesis	Friend-control
Number of participants	15	15
Sex, n (%)		
Male	5 (33.3)	5 (33.3)
Female	10 (66.7)	10 (66.7)
Age, mean (sd)	22.3 (9.7)	22.7 (9.7)
IMD quintile, n (%)		
1	2 (13.3)	2 (13.3)
2	3 (20.0)	2 (13.3)
3	0 (0.0)	3 (20.0)
4	5 (33.3)	1 (6.7)
5	5 (33.3)	7 (46.7)
Ethnicity, n (%)		
White	14 (93.3)	15 (100.0)
South Asian	0 (0.0)	0 (0.0)
Other	1 (6.7)	0 (0.0)
Missing teeth, mean (sd)	5.7 (2.7)	
Location of missing teeth, n (%)		
Anterior	10 (66.7)	
Posterior	12 (80.0)	
Retained deciduous teeth, n (%)	10 (66.7)	

Table 3.1 demonstrates the socio-demographic characteristics of the tooth agenesis and friend-control samples. Subjects with tooth agenesis were asked to recruit a friend-control of the same sex and age. Both groups consisted of 5 males and 10 females. The mean ages were 22.3 years in the tooth agenesis

group and 22.7 in the friend-control group. The friend-control method resulted in good matching of IMD and ethnicity. In this tooth agenesis sample, the mean number of missing teeth was 5.7. Amongst these patients, 10 were missing anterior teeth and 12 were missing posterior teeth. Ten patients with tooth agenesis had retained deciduous teeth.

Table 3. 2: Characteristics of the tooth agenesis and ADHS sample

Parameter	Group		p-value
	Tooth agenesis	ADHS	
Number of participants	71	999	
Sex, n (%)			0.671*
Male	30 (42.3)	448 (44.8)	
Female	41 (57.7)	551 (55.2)	
Age, mean (sd)	18.4 (2.8)	23.3 (4.6)	<0.001*
IMD quintile, n (%)			0.188*
1	23 (32.4)	214 (21.4)	
2	15 (21.1)	213 (21.3)	
3	10 (14.1)	232 (23.2)	
4	12 (16.9)	169 (16.9)	
5	11 (15.5)	171 (17.1)	
Ethnicity, n (%)			0.002*
White	52 (73.2)	854 (85.5)	
South Asian	14 (19.7)	77 (7.7)	
Other	5 (7.0)	68 (6.8)	
Missing teeth, mean (sd)	5.4 (3.5)		
Location of missing teeth, n (%)			
Anterior	51 (71.8)		
Posterior	33 (46.5)		
Retained deciduous teeth, n (%)	57 (73.1)		

* Chi-squared test. Significant p-values are indicated in bold.

Table 3.2 demonstrates the characteristics of the tooth agenesis and ADHS sample. This sample consisted of 71 participants with tooth agenesis (30 male, 41 female) and 999 individuals from the ADHS group (448 male, 551 female). The mean age was 18.4 years in the tooth agenesis group and 23.3 years in the ADHS group. There were significant differences between the groups with respect to age and ethnicity, with the tooth agenesis group being younger ($p < 0.001$) and consisting of more South Asian participants ($p = 0.002$). There were no significant differences in sex or social deprivation between the groups. The tooth agenesis group was missing a mean of 5.4 teeth, with 51 participants missing anterior teeth, 33 participants missing posterior teeth and 57 participants had retained deciduous teeth.

3.2 OHRQoL scores in subjects with tooth agenesis compared to friend-control

The individual item scores for the OHIP-49 were summed to produce a score for each domain. The domain scores were then summed to produce the total OHIP-49 score. The number of impacts was derived by summing the number of items that were answered with 'occasionally', 'fairly often' or 'very often'.

Table 3. 3: OHRQoL in subjects with tooth agenesis compared to friend-controls

OHIP-49 domain	Group		p-value
	Tooth agenesis	Friend control	
Functional limitation			0.003*
n	15	15	
Mean (sd)	11.1 (5.3)	4.5 (4.5)	
Median	12	3	
Range	2 - 18	0 - 14	
Physical pain			0.129*
n	15	15	
Mean (sd)	10.7 (6.8)	7.3 (4.2)	
Median	8	7	
Range	2 - 22	2 - 17	
Psychological discomfort			0.002*
n	15	15	
Mean (sd)	12.3 (6.4)	3.6(4.4)	
Median	13	2	
Range	1 - 20	0-14	
Physical disability			0.007*
n	15	15	
Mean (sd)	7.5 (5.5)	2.1 (2.6)	
Median	7	1	
Range	0 - 19	0 - 8	
Psychological disability			0.002*
n	15	15	
Mean (sd)	9.2 (7.3)	2.5 (3.2)	
Median	9	1	
Range	0 - 24	0 - 10	
Social disability			0.005*
n	15	15	
Mean (sd)	3.9 (3.2)	1.0 (1.7)	
Median	4	0	
Range	0 - 12	0 - 5	
Handicap			0.397*
n	15	15	
Mean (sd)	2.9 (4.0)	1.8 (3.2)	
Median	2	0	
Range	0 - 15	0 - 9	
Total			0.003*
n	15	15	
Mean (sd)	57.7 (33.5)	22.8 (18.4)	
Median	57	16	
Range	7 - 123	2 - 61	
Number of impacts			0.003*
n	15	15	
Mean (sd)	16.9 (10.3)	5.5 (5.2)	
Median	19	4	
Range	1 - 36	0 - 17	

* Wilcoxon signed-rank test. Significant p-values are indicated in bold.

Qq plots indicated that OHIP-49 scores were not normally distributed and therefore non-parametric tests were used. There were significant differences between subjects with tooth agenesis and their friend-controls for total OHIP-49 score ($p=0.003$) and number of impacts ($p=0.003$). There were also significant differences in functional limitation ($p=0.003$), psychological discomfort ($p=0.002$), physical disability ($p=0.007$), psychological disability ($p=0.002$) and social disability domains ($p=0.005$). There were no significant differences between the groups in the physical pain and handicap domains (Table 3.3).

Due to the small sample recruited with friend-controls, regression analyses were not undertaken.

3.3 OHRQoL scores in subjects with tooth agenesis compared to ADHS

The individual item scores for the OHIP-14 were summed to produce a score for each domain and the domain scores were summed to produce the total OHIP-14 score.

Table 3. 4: OHRQoL in subjects with tooth agenesis compared to ADHS control

OHIP-14 domain	Group		p-value
	Tooth agenesis	ADHS	
Functional limitation			<0.0001*
n	71	999	
Mean (sd)	1.1 (1.7)	0.2 (0.6)	
Median	0	0	
Range	0 - 7	0 - 5	
Physical pain			<0.0001*
n	71	999	
Mean (sd)	2.7 (2.2)	1.3 (1.8)	
Median	2	0	
Range	0 - 8	0 - 8	
Psychological discomfort			<0.0001*
n	71	999	
Mean (sd)	4.7 (2.8)	0.7 (1.6)	
Median	5	0	
Range	0 - 8	0 - 8	
Physical disability			<0.0001*
n	71	999	
Mean (sd)	1.2 (1.8)	0.3 (0.9)	
Median	0	0	
Range	0 - 8	0 - 7	
Psychological disability			<0.0001*
n	71	999	
Mean (sd)	3.7 (2.5)	0.6 (1.3)	
Median	4	0	
Range	0 - 8	0 - 8	
Social disability			<0.0001*
n	71	999	
Mean (sd)	1.4 (1.8)	0.3 (0.9)	
Median	1	0	
Range	0 - 8	0 - 8	
Handicap			<0.0001*
n	71	999	
Mean (sd)	1.6 (1.7)	0.2 (0.7)	
Median	1	0	
Range	0 - 6	0 - 8	
Total			<0.0001*
n	71	999	
Mean (sd)	16.3 (11.3)	3.5 (6.0)	
Median	16	1	
Range	0 - 50	0 - 37	

* Two sample Wilcoxon rank-sum (Mann-Whitney U) test. Significant p-values are indicated in bold.

Qq plots indicated that the OHIP-14 scores were not normally distributed and so non-parametric tests were used. There were very highly significant differences between subjects with tooth agenesis and the ADHS control for total OHIP-14 score ($p < 0.0001$) and all domain scores ($p < 0.0001$) (Table 3.4).

3.4 Regression Analyses

Table 3. 5: Negative binomial regression model 1. The association of OHRQoL with tooth agenesis.

	OHIP-14 domain															
	Functional limitation		Physical pain		Psychological discomfort		Physical disability		Psychological disability		Social disability		Handicap		Total	
	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value
Group																
ADHS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tooth agenesis	2.0 (1.2,2.8)	<0.001	0.7 (0.4,1.0)	<0.001	1.9 (1.4,2.4)	<0.001	1.4 (0.7,2.1)	<0.001	1.9 (1.4,2.4)	<0.001	1.6 (0.9,2.3)	<0.001	2.1 (1.4,2.8)	<0.001	1.5 (1.1,1.9)	<0.001

* Significant p-values are indicated in bold.

The negative binomial regression model 1 confirmed the highly statistically significant differences between the tooth agenesis and ADHS control group. The tooth agenesis group had higher impact on OHRQoL in total OHIP-14 (coefficient 1.5, 95% CI 1.1,1.9, $p < 0.001$) and all domains (Table 3.5).

Table 3. 6: Negative binomial regression model 2. OHRQoL associated with sex, age, social deprivation and race.

	OHIP-14 domain															
	Functional limitation		Physical pain		Psychological discomfort		Physical disability		Psychological disability		Social disability		Handicap		Total	
	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value
Sex																
Male	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Female	0.3 (-0.2, 0.7)	0.260	0.2 (-0.02,0.4)	0.076	0.4 (0.1,0.7)	0.007	0.09 (-0.3,0.5)	0.668	0.3 (0.05,0.6)	0.021	0.3 (-0.07,0.7)	0.107	0.3 (-0.1,0.8)	0.155	0.2 (0.03,0.5)	0.023
Age																
	-0.02 (-0.08,0.03)	0.426	0.03 (0.01,0.06)	0.001	0.04 (0.009, 0.07)	0.011	0.04 (-0.008,0.08)	0.105	0.03 (-0.005,0.06)	0.098	0.05 (0.003,0.1)	0.038	0.08 (0.02,0.1)	0.004	0.04 (0.01,0.06)	0.004
IMD																
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-0.3 (-0.6,0.04)	0.090	-0.2 (-0.4,0.1)	0.215	-0.2 (-0.6,0.2)	0.264	-0.3 (-0.9,0.3)	0.269	-0.3 (-0.8,0.09)	0.127	-0.3 (-0.9,0.3)	0.274	-0.7 (-1.3,0.002)	0.051	-0.3 (-0.6,0.07)	0.119
3	-0.1 (-0.5,0.2)	0.370	-0.07 (-0.3,0.2)	0.623	-0.07 (-0.5,0.3)	0.737	-0.2 (-0.8,0.4)	0.528	-0.4 (-0.8,0.03)	0.070	-0.3 (-0.9,0.3)	0.374	-0.2 (-0.9,0.4)	0.503	-0.1 (-0.5,0.2)	0.370
4	-0.3 (0.6,0.03)	0.080	-0.2 (-0.5,0.09)	0.174	-0.2 (-0.6,0.2)	0.360	-0.5 (-1.2,0.1)	0.122	-0.4 (-0.8,0.08)	0.107	-0.4 (-1.1,0.2)	0.197	-0.3 (-0.9,0.4)	0.448	-0.3 (-0.6,0.05)	0.098
5	-0.4 (-0.7,-0.04)	0.029	-0.3 (-0.6,-0.04)	0.027	-0.2 (-0.7,0.2)	0.284	-0.2 (-0.9,0.4)	0.508	-0.4 (-0.9,0.02)	0.062	-0.7 (-1.4,-0.06)	0.034	0.6 (-1.3,0.1)	0.120	-0.3 (-0.7,0.003)	0.052
Ethnicity																
White	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
South Asian	-0.1 (-0.5,0.3)	0.548	-0.2 (-0.5,0.1)	0.262	-0.3 (-0.8,0.2)	0.217	0.3 (-0.3,1.0)	0.327	-0.2 (-0.8,0.3)	0.376	-0.02 (-0.7,0.7)	0.964	0.006 (-0.7,0.8)	0.987	-0.1 (-0.5,0.3)	0.552
Other	-0.2 (-0.6,0.2)	0.333	-0.2 (-0.5,0.2)	0.374	-0.1 (-0.7,0.5)	0.731	-0.05 (-0.8,0.7)	0.892	-0.5 (-1.1,0.1)	0.137	-0.4 (-1.3,0.4)	0.305	-0.5 (-1.4,0.5)	0.308	-0.2 (-0.6,0.2)	0.384

* Significant p-values are indicated in bold.

Model 2 explored associations between OHRQoL and sex, age, social deprivation and ethnicity. Females were found to have significantly higher scores in total OHIP-14 (coefficient 0.2, 95% CI 0.03, 0.5, $p=0.023$) and in the psychological discomfort (coefficient 0.4, 95% CI 0.1, 0.7, $p=0.007$) and psychological disability domains (coefficient 0.3, 95% CI 0.05, 0.6, $p=0.021$). Older subjects had significantly higher total OHIP-14 score (coefficient 0.04, 95% CI 0.01, 0.06, $p=0.004$) and higher domain scores for physical pain (coefficient 0.03, 95% CI 0.01, 0.06, $p=0.001$), psychological discomfort (coefficient 0.04, 95% CI 0.009, 0.07, $p=0.011$), social disability (coefficient 0.05, 95% CI 0.003, 0.1, $p=0.038$) and handicap (coefficient 0.08, 95% CI 0.02, 0.1, $p=0.004$). When investigating the association between OHRQoL and age, the coefficient relates to a one year increase in age. Participants with reduced social deprivation scored significantly lower in the functional limitation (coefficient -0.4, 95% CI -0.7, 0.04, $p=0.029$), physical pain (coefficient -0.3, 95% CI -0.6, 0.04, $p=0.027$) and social disability domains (coefficient -0.7, 95% CI -1.4, 0.06, $p=0.034$). Social deprivation had a borderline significant association with total OHIP-14 score (coefficient -0.3, 95% CI -0.7, 0.003, $p=0.052$). No significant associations were found between ethnicity and OHRQoL (Table 3.6).

Table 3. 7: Negative binomial regression model 3. OHRQoL in subjects with tooth agenesis associated with the number of missing teeth, location of missing teeth and presence of retained deciduous teeth, adjusted for age, sex, social deprivation and ethnicity.

	Domain															
	Functional limitation		Physical pain		Psychological discomfort		Physical disability		Psychological disability		Social disability		Handicap		Total	
	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value	Coeff (CI)	p-value
Number of missing teeth	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	0.07 (-0.07,0.2)	0.300	0.04 (-0.04,0.1)	0.338	0.05 (0.0002,0.1)	0.049	0.01 (-0.1,0.2)	0.905	0.03 (-0.03,0.09)	0.379	0.02 (-0.1,0.1)	0.717	0.04 (-0.06,0.1)	0.441	0.05 (-0.02,0.1)	0.155
Anterior missing teeth																
None	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Missing	-0.8 (-1.8,0.3)	0.167	-0.3 (-0.8,0.3)	0.357	0.01 (-0.4,0.4)	0.957	-0.4 (-1.5,0.7)	0.496	0.1 (-0.3,0.6)	0.607	0.1 (-0.8,1.0)	0.818	0.3 (-0.4,1.1)	0.404	-0.1 (-0.6,0.4)	0.680
Posterior missing teeth																
None	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Missing	-1.1 (-2.2,0.1)	0.075	-0.07 (-0.7,0.5)	0.830	-0.1 (-0.6,0.3)	0.566	-0.7 (-1.9,0.6)	0.285	0.1 (-0.4,0.6)	0.674	-0.2 (-1.2,0.7)	0.670	-0.3 (-1.1,0.5)	0.458	-0.3 (-0.8,0.3)	0.373
Retained deciduous teeth																
None	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Retained	0.2 (-0.7,1.0)	0.682	0.02 (-0.5,0.5)	0.939	-0.3 (-0.7,0.01)	0.060	0.03 (-0.9,0.9)	0.949	-0.3 (-0.7,0.03)	0.072	-0.2 (-1.0,0.5)	0.516	0.007 (-0.6,0.7)	0.981	-0.2 (-0.7,0.2)	0.283

* Significant p-values are indicated in bold.

Model 3 explored associations between OHRQoL in subjects with tooth agenesis and the number of missing teeth, location of missing teeth and presence of retained deciduous teeth. The model was adjusted for age, sex, social deprivation and ethnicity. An increase in the number of missing teeth was associated with a small but significant increase in psychological discomfort (coefficient 0.05, 95% CI 0.0002, 0.1, $p=0.049$). For patients without retained deciduous teeth, there was a tendency towards an increase in psychological discomfort (coefficient -0.3, 95% CI -0.7, 0.01, $p=0.060$) and psychological disability (coefficient -0.3, 95% CI 0.7, 0.03, $p=0.072$), although the differences were not significant. The location of missing teeth was not associated with OHRQoL (Table 3.7).

Chapter 4

Discussion

4. Discussion

4.1 Discussion

A cross-sectional study was conducted to investigate OHRQoL in adults with tooth agenesis. Seventy-one subjects with tooth agenesis made up the sample, with a small female majority (Table 3.2). Fifteen subjects with tooth agenesis were compared to a friend-control and this group also consisted of a female majority (Table 3.1), which is typical of the orthodontic population (Shafi *et al.*, 2008). The mean number of missing teeth among all subjects with tooth agenesis was 5.4, with a range of 2 – 16 teeth (Table 3.2). The mean number of missing teeth among the fifteen subjects compared to the friend-control was 5.7, with a range of 2 – 12 teeth (Table 3.1). This was similar to a previous study performed in the same region, investigating tooth agenesis in children (Kotecha *et al.*, 2013). Amongst all subjects with tooth agenesis, 71.8% were missing anterior teeth, 46.5% were missing posterior teeth and 73.1% had retained deciduous teeth (Table 3.2). This was in close agreement with previous research (Anweigi *et al.* 2013a). The group of subjects with tooth agenesis that were compared to their friend-controls were missing anterior teeth in 66.7% of cases, posterior teeth in 80% and had retained deciduous teeth in 66.7% of cases (Table 3.1). This group had a higher proportion of missing posterior teeth in comparison to all subjects with tooth agenesis.

Patients who were currently undergoing, or had previously undergone, a course of extensive orthodontic or restorative dental treatment were excluded from the study, along with patients with cleft lip and palate and craniofacial syndromes to minimise confounding factors. Previous research has found that orthodontic

treatment, cleft lip and palate and craniofacial syndromes can affect OHRQoL (Arrow *et al.*, 2011; Brosens *et al.*, 2013; Jokovic *et al.*, 2002).

OHRQoL has been investigated in adults previously, using qualitative (Meaney *et al.*, 2012) and quantitative methods (Anweigi *et al.*, 2013a; Hashem *et al.*, 2013), however, these studies did not use an *a priori* power calculation. A sample size calculation was performed for this study, which used an effect size of 0.5, the minimum suggested for quality of life studies (Cohen, 1969). With α at 0.05, a sample size of 64 participants in each group was required for 80% power. An additional 10% were recruited to allow for dropouts, requiring 71 participants in each group for 80% power. The age range was limited to 16 – 30 years and following this, the 80% power sample size was met for the comparison between the tooth agenesis and ADHS control groups. This sample size was not met for the comparison between the tooth agenesis and friend-control groups.

The friend-control method (Rothman and Greenland 1998) was selected since it generally matches for ethnicity, education and age (Bunin *et al.*, 2011) and this assumption was supported in this study (Table 3.1). Subjects with tooth agenesis were asked to recruit a friend-control that was unrelated to them. Family members were not used since their OHRQoL could be influenced by family members with tooth agenesis. Participants were asked to ensure their friend-controls did not have tooth agenesis as far as they were aware.

Participants with tooth agenesis were also compared to ADHS data (Office for National Statistics. Social Survey Division, Information Centre for Health and Social Care, 2009). The same inclusion and exclusion criteria could not be applied to this historical control when the data was collected, which has the

potential to introduce bias and confounders (Gomm *et al.*, 2000). Subjects with tooth agenesis could not be excluded from the ADHS control since this data was not recorded. However, as the rate of tooth agenesis in the UK population is low (Brook, 1974; Rose, 1966), it was felt this would not prove a major confounding factor for OHRQoL in the ADHS group. In addition, it was felt that the subjects in the ADHS group would have a similar range of other dental features as the tooth agenesis group, such as malocclusion, which can affect OHRQoL. In this study, the group with tooth agenesis was well matched to the ADHS control for sex and social deprivation, but there were significant differences in age ($p < 0.001$) and ethnicity ($p = 0.002$) (Table 3.2). The group with tooth agenesis was significantly younger, which may be because older patients with tooth agenesis would more likely be referred to a dental hospital for restorative treatment rather than for joint orthodontic-restorative care, or alternatively managed in primary care (Table 3.2). There were significantly more South Asian subjects in the group with tooth agenesis compared to the ADHS sample (Table 3.2), which reflects the diverse ethnicity of the West Midlands region in comparison to England.

The OHIP-49 questionnaire (Slade and Spencer, 1994) was used for comparison between the subjects with tooth agenesis and their friend-controls. The OHIP-49 questionnaire has previously been used to measure OHRQoL in adults with tooth agenesis (Anweigi *et al.*, 2013a; Hashem *et al.*, 2013; Meaney *et al.*, 2012). However, the ADHS used the short form OHIP-14 (Slade, 1997) and therefore this questionnaire was used to compare subjects with tooth agenesis to the ADHS data. Both forms of the OHIP questionnaire have been shown to be valid and reliable (Slade and Spencer, 1994; Slade, 1997).

There are few studies that have investigated the impact of tooth agenesis on the OHRQoL of adults (Anweigi *et al.*, 2013a; Hashem *et al.*, 2013; Meaney *et al.*, 2012), although a slightly greater number of studies have tested a child population (Kotecha *et al.*, 2013; Laing *et al.*, 2010; Locker *et al.*, 2010; Wong *et al.*, 2006). This present study provides additional evidence that tooth agenesis has an impact on the OHRQoL of adults, which confirms the findings of other researchers (Anweigi *et al.*, 2013a; Hashem *et al.*, 2013; Meaney *et al.*, 2012). The median OHIP-49 score was 57 in subjects with tooth agenesis and 16 in the friend-control group (Table 3.3). The total OHIP-49 score for subjects with tooth agenesis was similar to that found by Hashem *et al.* (2013) but higher than that found by Anweigi *et al.* (2013a). A possible reason for this could be that Anweigi *et al.* (2013a) investigated subjects that were currently undergoing orthodontic treatment in preparation for restorative treatment. In the present study, all subjects completed questionnaires prior to any treatment, to reduce confounding factors. The total OHIP-49 score in the friend-control group in this study was lower than the control used by Hashem *et al.* (2013). This may be because Hashem *et al.* (2013) studied a control group of patients sourced from a dental hospital. These patients were therefore likely to have dental treatment need, which is a confounding factor for OHRQoL. There is no published research using the OHIP-14 questionnaire to measure the impact of tooth agenesis on adults, but the median score of 16 in this study is lower than patients of a similar age with orthodontic malocclusions (Masood *et al.*, 2013) but similar to orthognathic patients prior to starting treatment (Esperao *et al.*, 2010). When subjects with tooth agenesis were compared to the ADHS control, they had significantly higher scores for total OHIP-14 and across all domains (Table 3.4).

Subjects with tooth agenesis, compared to a friend-control, had significantly higher total OHIP-49 and all domain scores except physical pain and handicap (Table 3.3). In research investigating the impact of tooth agenesis on the OHRQoL of children, some authors have found significant differences to a control (Kotecha *et al.*, 2013) and others have found no difference (Laing *et al.*, 2010). The latter study used a control group with similar orthodontic treatment need to the subjects with tooth agenesis, whereas Kotecha *et al.* (2013) used a group with low orthodontic treatment need for comparison, which would be more representative of the general population.

Due to the small number of subjects recruited with the friend-control method, regression analysis was not performed on this sample. However, regression analyses were performed on the sample that was compared to the ADHS control. Negative binomial regression analysis confirmed that tooth agenesis was associated with increased scores in all domains and total OHIP-14 (Table 3.5). Females were found to have significantly higher scores in total OHIP-14 score as well as in the psychological discomfort and psychological disability domains (Table 3.6). This was partly in agreement with Anweigi *et al.* (2013a), who found females had higher scores in total OHIP-49 and all domains. Studies investigating patients without tooth agenesis have also found that orthodontic and orthognathic treatment need have greater impact on the OHRQoL of females (de Oliveira and Sheiham, 2004; Esperao *et al.*, 2010; Feu *et al.*, 2010; Rusanen *et al.*, 2010). Older patients were found to have significantly higher scores in the total OHIP-14 and in the physical pain, psychological discomfort, social disability and handicap domains (Table 3.6). Again this was partly in agreement with Anweigi

et al. (2013a), who found a significant difference in the physical pain domain and a trend towards impaired OHRQoL in the older age group, although this did not meet significance. Perceived poorer OHRQoL may increase with age due to a greater expectation from the dentition, or alternatively due to the progressive loss of retained primary teeth.

In subjects with tooth agenesis, reduced social deprivation was associated with reduced OHRQoL. Significant differences were measured in the IMD fifth quintile for the functional limitation, physical pain and social disability domains (Table 3.6). There was a borderline significant association between reduced social deprivation and total OHIP-14 score. The present study suggests that reduced social deprivation tends to protect against the impact of tooth agenesis on OHRQoL. This is in contrast with a study of children with tooth agenesis recruited from a similar population (Kotecha *et al.*, 2013), which found no association between social deprivation and OHRQoL. However, the subjects in this present study were older than the subjects in the study by Kotecha *et al.* (2013), which may account for these differences. No associations were found between ethnicity and OHRQoL in the group of subjects with tooth agenesis (Table 3.6), which agrees with the research by Kotecha *et al.* (2013).

Amongst subjects with tooth agenesis, an increase in the number of missing teeth was associated with a small but significant increase in psychological discomfort (Table 3.7). This was broadly in agreement with Anweigi *et al.* (2013a), who found that the number of missing teeth was not a good predictor of OHRQoL. One possible explanation for this could be that a missing upper lateral incisor may have more effect on OHRQoL than a number of missing posterior

teeth, because it is likely to cause visible spacing, which does have a significant effect on OHRQoL (Johal *et al.*, 2007). In research investigating OHRQoL in children with tooth agenesis, some investigators have found no effect from the number of missing teeth (Kotecha *et al.*, 2013; Locker *et al.*, 2010) and others have found that a greater number of missing teeth is associated with poorer OHRQoL (Laing *et al.*, 2010; Wong *et al.*, 2006). For those patients without retained deciduous teeth, there was a tendency towards an increase in psychological discomfort and psychological disability, although the differences were not significant (Table 3.7). This borderline significance is consistent with the research into children with tooth agenesis, where Kotecha *et al.* (2013) found no effect from retained deciduous teeth. In contrast, Wong *et al.* (2006) found that retained deciduous teeth improved OHRQoL. This may be because in the study by Wong *et al.* (2006), the most common missing teeth in the maxilla were lateral incisors and in the mandible were central incisors. Missing anterior teeth are considered one of the most unattractive occlusal traits (Arrow *et al.*, 2011; Shaw, 1981), so the retention of deciduous teeth in these areas could significantly improve appearance. In contrast, missing lower incisors were less common in the research by Kotecha *et al.* (2013), which studied children from a similar population to this study.

In the present study, the location of missing teeth was not associated with differences in total OHIP-14 or domain scores (Table 3.7), which agreed with research investigating OHRQoL in adults (Anweigi *et al.*, 2013a) and in children (Kotecha *et al.*, 2013; Laing *et al.*, 2010). This may be due to retained deciduous teeth, which may reduce the impact on function due to absent posterior teeth or

the impact on aesthetics due to missing anterior teeth. Anweigi *et al.* (2013a) found that missing anterior teeth had more impact on psychological discomfort than missing posterior teeth, although retained deciduous teeth were not recorded in this study.

It is recommended that a sample be recruited from a range of healthcare settings, to ensure the sample is representative of the population (Mays and Pope, 2000). However, tooth agenesis is uncommon in the general population and treatment can involve a multidisciplinary approach, resulting in a large proportion of cases being referred to the secondary care setting. As a result, population-based sampling would be challenging to perform for this study. In the timeframe available for this study, the sample size required for 80% power was met, suggesting the present study is sufficiently powered to investigate differences between the tooth agenesis and ADHS control. However, the ADHS control had significant differences to the tooth agenesis group in age and ethnicity, introducing potential bias and confounding factors. Recruitment of friend-controls was poor and failed to meet the sample size calculation. The study is underpowered for the comparison between the tooth agenesis and friend-control groups. This also prevented regression analysis to investigate the association of socio-demographic and dental factors with OHRQoL in this group. Although the friend-controls were well matched to the tooth agenesis group, they were not clinically examined, introducing another potential source of bias and confounding factors. The response rate for friend-controls was 21.1% and the additional 10% of participants recruited to allow for potential dropout was insufficient to account for this low response rate. The friend-control method has

previously been used in medical research (Ma *et al.*, 2004; Parikh-Patel *et al.*, 2002), but to the authors' knowledge, not in orthodontic research. The response rate in this present study was poor compared to the 62.6% response rate achieved by Parikh-Patel *et al.* (2002), despite an incentive being offered. However, difficulty in recruiting friend-controls has also been reported by Ma *et al.* (2004). Further research could be carried out to recruit a greater number of friend controls, perhaps with an alternative method of recruitment, or consideration given to using a different control group. Although OHRQoL has been investigated in adults previously, using qualitative (Meaney *et al.*, 2012) and quantitative methods (Anweigi *et al.*, 2013a; Hashem *et al.*, 2013), these studies did not use an a priori sample size calculation, and only Hashem *et al.* (2013) used a control group.

The OHIP questionnaires have limitations because they are generic OHRQoL measures that focus more on pain, discomfort and difficulty in mastication, rather than aesthetics, the most common cause of concern in orthodontic patients (O'Brien *et al.*, 1998). As a result, the OHIP measure may not be sensitive to detect issues experienced by patients with tooth agenesis. When this study was planned, a tooth agenesis-specific measure was being developed (Akram *et al.*, 2011) and subsequently this has been shown to be valid and reliable (Akram *et al.*, 2013). Once this measure has been used more widely in older patients, then it could be used in further research to determine the specific cause of the OHRQoL impact, although condition-specific measures do not allow comparisons between different conditions (Cunningham and Hunt, 2001). Qualitative techniques have also been used to investigate tooth agenesis (Akram

et al., 2011; Meaney *et al.*, 2012). These studies brought up themes associated with reduced OHRQoL that a generic measure such as OHIP may not be sensitive to, including arch spacing, perceived appearance of prosthetic teeth, perceived fit of removable dentures, potential loss of deciduous teeth and time spent waiting for multidisciplinary treatment (Akram *et al.*, 2011; Meaney *et al.*, 2012). This present study was cross-sectional in nature and there is a lack of longitudinal data on the effect of orthodontic treatment on patients with tooth agenesis. Longitudinal data is important since it can demonstrate causation, rather than just association. Longitudinal data is available on the association of OHRQoL with orthodontic treatment (de Oliveira and Sheiham, 2004; O'Brien *et al.*, 2003), combined orthognathic treatment (Esperao *et al.*, 2010; Murphy *et al.*, 2011; Silvola *et al.*, 2012) and restoration of patients with tooth agenesis (Goshima *et al.*, 2010). The limitations of this present study suggest that care should be observed when interpreting the results.

4.2 Conclusions

Tooth agenesis has a negative impact on the OHRQoL of adults, compared to the ADHS control group. Poorer OHRQoL was associated with females, older patients and increased social deprivation. OHRQoL was minimally associated with the number of missing teeth and was not associated with the location of missing teeth or presence of retained deciduous teeth.

The friend-control method proved effective at producing a well-matched control group, although the response rate was very low and any differences need to be interpreted with care.

Further research could be performed to recruit more friend-controls, perhaps using an alternative method of recruitment. The use of a tooth agenesis-specific measure would be beneficial to our understanding of the issues experienced by these patients and longitudinal testing could then give an indication of the potential effect of orthodontic and restorative treatment on the OHRQoL of patients with tooth agenesis.

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Appendices

Appendix 1: Invitation letter to participants with tooth agenesis

Version 1.2 20/11/2013

Dear

Invitation to take part in research to assess the impact of missing teeth on quality of life

My name is David Heads and I am an orthodontic trainee at Birmingham Dental Hospital. I am part of a team with the University of Birmingham undertaking research into the impact that naturally missing teeth has on adults.

We are asking you to be involved because we think you fit the criteria for our research. If you agree to take part, then you will need to complete a short online questionnaire that will take approximately 15 minutes to complete. You will also need to ask a friend or colleague to complete a similar questionnaire and once we have received both questionnaires then you will both receive a £10 gift voucher from Love2Shop.

All the information is enclosed with this letter. You do not have to take part if you do not wish to do so and this will not affect your upcoming care at Birmingham Dental Hospital. However we hope that you will choose to take part and help us to learn more about the impact that naturally missing teeth may have. Thank you for your help.

Yours sincerely,

David Heads, Specialist Registrar in Orthodontics

Appendix 2: Information sheet for participants with tooth agenesis

Version 1.4 20/11/2013

INFORMATION SHEET

The impact of tooth agenesis on oral health-related quality of life in adults

Why have I been invited to complete a questionnaire?

We are asking you to take part in a research project on the impact that naturally missing teeth have on adults over 16 years of age. You have been asked to take part because it was identified that you have naturally missing teeth after visiting Birmingham Dental Hospital.

What will happen to me if I take part?

If you agree to take part then you need to complete a short online questionnaire and choose a friend or colleague to complete a similar online questionnaire. Following this you will both be posted a £10 gift voucher from Love2Shop.

What happens next?

The questionnaire is accessible via the web link at the end of this information sheet and you will need to use the code provided for you. If you would prefer to complete a paper questionnaire, this can be arranged by emailing David Heads (d.heads@nhs.net).

You are able to partake in this research project if:

- You are aged 16 or over

- You have teeth naturally missing from birth (this excludes wisdom teeth or teeth removed by a dentist)
- You do not have cleft lip and palate
- You do not have any known craniofacial syndromes
- You are able to read and write in English
- You have not had or are currently undergoing a course of extensive orthodontic or restorative dental treatment
 - This includes fixed (train-track) braces, fixed bridges or dental implants
 - This does not include removable dentures or fillings

You will also need to choose another person to act as your control, who will need to complete a similar questionnaire and this person should be:

- A friend or colleague who is not related to you
- Aged over 16
- Aged within 3 years of you
 - i.e. up to 3 years older or up to 3 years younger
- Same gender as you
- Able to read and write in English
- Not have teeth naturally missing from birth to the best of your knowledge
 - This excludes wisdom teeth or teeth removed by a dentist
- Not have cleft lip and palate to the best of your knowledge
- Not have craniofacial syndromes to the best of your knowledge
- Not have had or be currently undergoing a course of extensive orthodontic or restorative dental treatment

- This includes fixed (train-track) braces combined with fixed bridges or dental implants
- This also includes fixed bridges or dental implants without fixed (train track) braces
- This does not include removable dentures, fillings, removable or fixed (train track) braces without fixed bridges or dental implants

You will need to provide the name and email address of your control in the online questionnaire so please discuss this with them first. If your control is not suitable then we will contact you.

Once you and your control have fully completed the questionnaires and we have ensured that your control is suitable, we will post you each a £10 gift voucher from Love2Shop. These vouchers must be posted out to two different names at two different addresses.

Do I have to take part?

No, if you don't want to participate then you do not need to complete the questionnaire. However your participation would be appreciated to contribute to this important research subject.

What happens to me after I take part?

If you want to receive information on the results of the trial we will send them to you by email. This will be available approximately 6 months after the results of the 93 participants have been tested with statistical analyses. All data collected

will be anonymous. The questionnaire data will be stored on an NHS encrypted memory stick for 6 months after the project is written up and then destroyed.

Other information and contact details

If you have any questions or difficulty completing the questionnaire you can contact me (David Heads).

This research is governed and supported by the University of Birmingham, will take place at Birmingham Dental Hospital and is being supervised by Professor T Dietrich (School of Dentistry), Mr J Turner and Sheena Kotecha (Orthodontic Department). The research has been reviewed by the NRES Committee South Central – Oxford C Research Ethics Committee.

If you have any queries or difficulties completing the questionnaire you can contact me:

David Heads (Orthodontic Specialty Registrar) Email: d.heads@nhs.net

If you want to complain you can contact:

Derrick De Faye (Patient experience officer) Tel: 0121 237 2836

Now follow this web link to the questionnaire:

<https://www.surveymonkey.com/s/JKSVM6>

Your unique identifier code is:

Thank you for reading and taking part!

David Heads

Appendix 3: Questionnaire (including consent, demographic details, OHIP-49, friend control details and contact details)

Consent

To ensure you understand the research, I want you to give consent to completing the questionnaire. You are required to answer "Yes" to each question if you are to consent to being in this trial.

If you answer "No" to any question, your questionnaire results will not be used and you will not receive your gift voucher. If you need to contact me to clarify anything then please email David Heads on: d.heads@nhs.net

* 1. I confirm that I have read the Information sheet provided for me.

- Yes
 No

* 2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving reason and without my treatment or legal rights being affected

- Yes
 No

* 3. I understand that the answers I give will be used anonymously as part of this research.

For those participants with naturally missing teeth, I understand that the relevant sections of my care record will be looked at by responsible individuals from Birmingham Dental Hospital or regulatory authorities, where it is relevant to this research (this includes postcode, information on missing teeth and presence of baby teeth).

Yes

No

* 4. I understand that the £10 gift voucher will only be posted out once my questionnaire is fully completed, my friend/colleague's questionnaire is fully completed and we both meet the criteria set out in the information sheet.

Yes

No

* 5. I agree to take part in this research

Yes

No

Participant number

Your participant number is provided for you by the research team and should be in the format H000 or C000

* 6. Please enter your unique identifier code here

Background information

* 7. What is your gender?

Female

Male

* 8. What is your date of birth?

(DD/MM/YYYY)

* 9. What is your ethnicity?

- White British
- White Irish
- White (other)
- Black African
- Indian
- Pakistani
- Bangladeshi
- Other Asian
- Black Caribbean
- Chinese
- Mixed (White and Black Caribbean)
- Mixed (White and Asian)
- Mixed (White and Black African)
- Mixed (other)
- Black (other)
- Arabic
- Other

* 10. What is your postcode?

Main questionnaire

* 11. Have you had difficulty chewing any foods because of problems with your teeth, mouth or dentures?

- | Never | Hardly ever | Occasionally | Fairly often | Very often |
|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

* 12. Have you had trouble pronouncing any words because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 13. Have you noticed a tooth that doesn't look right?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 14. Have you felt that your appearance has been affected because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 15. Have you felt that your breath has been stale because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 16. Have you felt that your sense of taste has worsened because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 17. Have you had food catching in your teeth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 18. Have you felt that your digestion has worsened because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 19. Have you felt that your dentures have not been fitting properly?

Never / Never worn dentures	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 20. Have you had painful aching in your mouth?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 21. Have you had a sore jaw?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 22. Have you had headaches because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 23. Have you had sensitive teeth, for example, due to hot or cold food or drink?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 24. Have you had toothache?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 25. Have you had painful gums?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 26. Have you found it uncomfortable to eat any foods because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 27. Have you had sore spots in your mouth?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 28. Have you had uncomfortable dentures?

Never / Never worn dentures	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 29. Have you been worried by dental problems?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 30. Have you been self conscious because of your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 31. Have dental problems made you miserable?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 32. Have you felt uncomfortable about the appearance of your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 33. Have you felt tense because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 34. Has your speech been unclear because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 35. Have people misunderstood some of your words because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 36. Have you felt that there has been less flavour in your food because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 37. Have you been unable to brush your teeth properly because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 38. Have you had to avoid eating some foods because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 39. Has your diet been unsatisfactory because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 40. Have you been unable to eat with your dentures because of problems with them?

Never / Never worn dentures	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 41. Have you avoided smiling because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 42. Have you had to interrupt meals because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 43. Has your sleep been interrupted because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 44. Have you been upset because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 45. Have you found it difficult to relax because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 46. Have you felt depressed because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 47. Has your concentration been affected because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 48. Have you been a bit embarrassed because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 49. Have you avoided going out because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 50. Have you been less tolerant of your spouse or family because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 51. Have you had trouble getting on with other people because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 52. Have you been a bit irritable with other people because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 53. Have you had difficulty doing your usual jobs because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 54. Have you felt that your general health has worsened because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 55. Have you suffered any financial loss because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 56. Have you been unable to enjoy other people's company as much because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 57. Have you felt that life in general was less satisfying because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 58. Have you been totally unable to function because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

* 59. Have you been unable to work to your full capacity because of problems with your teeth, mouth or dentures?

Never	Hardly ever	Occasionally	Fairly often	Very often
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

You're almost there!

60. What are your contact details ?

(These will only be used for posting out your £10 gift voucher and if I need to clarify an answer in your questionnaire. The details in this questionnaire are confidential and will not be shared)

Name	<input type="text"/>
Postal address	<input type="text"/>
Email address	<input type="text"/>
Telephone number	<input type="text"/>

* 61. Would you like to receive any information about the results of this research? Anonymous results can be emailed out once the trial is completed.

Yes

No

If yes, please enter email address below

62. For the participants with naturally missing teeth, please now select your friend or colleague as a control as outlined in the information sheet. Make sure you follow the guidance because if they are not matched to you, then I will need to ask you to select someone else. Please check with them, enter their details below and then they will then receive an email with a link to this questionnaire.

For the participants acting as the friend/colleague control, you have no need to answer this question as the questionnaire will not be sent to anyone else.

Name	<input type="text"/>
Email address	<input type="text"/>

You're done!

Thank you so much for completing this questionnaire. It will contribute greatly to this research project.

Kind Regards,

**David Heads
Orthodontic Registrar**

Appendix 4: Invitation letter to friend-controls

Version 1.2 20/11/2013

Dear (control),

Invitation to take part in research to assess the impact of missing teeth on quality of life

My name is David Heads and I am an orthodontic trainee at Birmingham Dental Hospital. I am part of a team with the University of Birmingham undertaking research into the impact that naturally missing teeth has on adults.

Your name and email address has been given to us by your friend/colleague because they feel you could act as a suitable control for our research. They should have discussed this with you.

If you agree to take part, then you will need to complete a short online questionnaire that will take about 15 minutes to complete. As long as you are suitably matched control and you both fully complete the questionnaires then you will both receive a £10 gift voucher from Love2Shop.

Once you have fully read the information sheet attached to this email, if you think you are suitable then follow the web link to complete the questionnaire, using the unique identifier code. If you don't think you are suitable, please email me back and I will contact your friend/colleague to choose another suitable control.

You do not have to take part if you do not wish to do so, but we hope that you will take part and help us to learn more about the impact that naturally missing teeth has on adults.

Follow this web-link to complete the questionnaire:
<https://www.surveymonkey.com/s/JKSVRM6>

Use this unique identifier code:

Thank you for your help.

Yours sincerely,

David Heads

Specialist Registrar in Orthodontics

Appendix 5: Information sheet for friend-controls

Version 1.3 20/11/2013

INFORMATION SHEET

The impact of tooth agenesis on oral health-related quality of life in adults

Why have I been invited to complete a questionnaire?

We are asking you to take part in a research project on the impact that naturally missing teeth have on adults over 16 years of age. You have been asked to take part as a control, which means you do not have any naturally missing teeth. Your details have been provided by a friend/colleague of yours and they should have discussed this with you in advance.

What will happen to me if I take part?

If you agree to take part then you need to complete a short online questionnaire. Once the questionnaire is fully completed and we have checked that you are suitable as a control to your friend or colleague, we will post you a £10 gift voucher from Love2Shop.

What happens next?

The questionnaire is accessible via the web link in this email and you will need to use the code provided for you. If you would prefer to complete a paper questionnaire, this can be arranged by emailing David Heads (d.heads@nhs.net).

You are able to partake in this research project if:

- You are aged 16 or over
- You are aged within 3 years of your friend/colleague
 - i.e. up to 3 years older or up to 3 years younger
- You are not related to your friend/colleague
- You are the same gender as your friend/colleague
- You do not have teeth naturally missing from birth
 - This excludes wisdom teeth or teeth removed by a dentist
- You do not have cleft lip and palate
- You do not have a craniofacial syndrome
- You have not had or are currently undergoing a course of extensive orthodontic or restorative dental treatment
 - This includes fixed (train track) braces combined with fixed bridges or dental implants
 - This also includes fixed bridges or dental implants without fixed (train track) braces
 - This does not include removable dentures, fillings, removable or fixed (train track) braces without fixed bridges or dental implants
- You are able to read and write in English

Once you and your friend/colleague have fully completed the questionnaires and we have ensured that you are suitably matched, we will post you each a £10 gift voucher from Love2Shop. These vouchers must be posted out to two different names at two different addresses.

Do I have to take part?

No, if you don't want to participate then you do not need to complete the questionnaire. However your participation would be appreciated since in research a control is required to compare results.

What happens to me after I take part?

If you want to receive information on the results of the trial we will send them to you by email. This will be available approximately 6 months after the results of the 93 participants have been tested with statistical analyses. All data collected will be anonymous. The questionnaire data will be stored on an NHS encrypted memory stick for 6 months after the project is written up and then destroyed.

Other information and contact details

If you have any questions or difficulty completing the questionnaire you can contact me (David Heads).

This research is governed and supported by the University of Birmingham, will take place at Birmingham Dental Hospital and is being supervised by Professor T Dietrich (School of Dentistry), Mr J Turner and Sheena Kotecha (Orthodontic Department). The research has been reviewed by the NRES Committee South Central – Oxford C Research Ethics Committee.

If you have any queries or difficulties completing the questionnaire you can contact me:

David Heads (Orthodontic Specialty Registrar) Email:

d.heads@nhs.net

If you want to complain you can contact:

Derrick De Faye (Patient experience officer) Tel: 0121 237

2836

Now follow the web link in the email to complete the questionnaire and use the unique identifier code provided.

Thank you for reading and taking part!

David Heads

Appendix 6: Tooth agenesis data collection proforma

Tooth agenesis data collection proforma

Demographic details

Patient number _____

Name _____

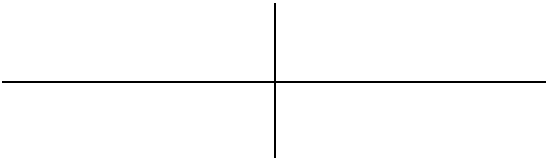
Date of birth _____

Sex _____

Postcode _____

Subject identifier _____

Dental characteristics

Missing teeth 

Number of missing teeth _____

Anterior missing teeth y/n

Posterior missing teeth y/n

Retained deciduous teeth y/n