Dental Phenotypes and Parental Perspective of Quality of Life for Patients with Ectodermal Dysplasia and Isolated Hypodontia

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DECLARATION

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SUMMARY

This study aimed to compare the parental perspectives on OHRQoL impact and dental experience for children with ectodermal dysplasia (ED), severe isolated hypodontia (IH), and age and gender matched control groups; and to identify distinctive features to differentiate between children with ED and IH (both groups to be missing at least 6 permanent teeth).

A cross-sectional study of 86 children between 4 and 18-years old (mean age: 12.4-years old) with severe hypodontia (> 6 missing teeth) were recruited from the Dublin Dental University Hospital (DDUH) clinics. There were 29 children with ED and 57 children with IH and each case had an age and gender matched control, bringing the total sample to 172.

The Parental-Caregiver Perceptions Questionnaire (P-CPQ) portion of the Child Oral Health Quality of Life Questionnaire (COHQoL), including the global rating and Family Impact Scale (FIS), were used to gather information on parental perceptions of OHRQoL. A specifically designed questionnaire was used to collect information regarding the participants dental experiences as perceived by parents. Clinical examinations and existing clinical records were used to identify missing teeth and any associated dental abnormalities.

Nonparametric paired sample tests between ED cases and their matched controls revealed statistically significant differences ($p<0.05$) in all global rating, P-CPQ and FIS scores. Nonparametric paired sample tests between IH cases and their matched controls, revealed statistically significant differences ($p<0.05$) in global rating, in the overall score and in the emotional well-being and social well-being domains of the P-CPQ and in the parental emotional well-being

domain of the FIS and the overall total FIS score. In an unpaired analysis of the ED group compared to the IH group, the ED mean scores for functional limitations were significantly greater ($p < 0.001^{**}$). Spearman correlation revealed P-CPQ scores for males with ED, had a moderate correlation ($R_s = 0.576$; $p=0.001^{*}$) with functional limitations, oral symptoms ($R_s = 0.444$; $p=0.016^{*}$) and overall QoL ($R_s = 0.499$; $p= 0.006^{*}$).

Although the ED group had a higher prevalence of taurodontism, conical morphology and hypodontia of mandibular central and lateral incisors, canines and first and second molars, these features were still present in some IH cases.

The ED group reported the highest perceived number of appointments (20 or more dental visits; 58.6%), compared with the IH (26.3%) and the control groups (ED controls: 17.2%; IH controls: 15.8%).

Parents from the ED and IH groups reported the main information deficits were related to treatment timing and lack of explanation of the condition itself.

Conclusion

- Parents of children with ED and IH perceive a significant impact on QoL, for both the child and their family. Children with ED, in particular, have a greater perceived impact on function compared to children with IH.
- Parents perceived a greater impact on QoL for males with ED.
- There is no definite way to differentiate ED and IH based on dental features, but the presence of certain features may warrant further investigations.
- Children with ED undergo earlier and more extensive treatment.
- Parents want more education and communication from the clinician and want more involvement in the treatment planning process.

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ABBREVIATIONS

Child Oral Health Quality of Life Questionnaire		COHQoL	
Child Perception Questionnaire		CPQ	
Dublin Dental University Hospital		DDUH	
Early Childhood Oral Health Impact Scale		ECOHIS	
Ectodermal Dysplasia		ED	
Evaluating Measures of Patient-Reported Outcomes		EMPRO	
Family Impact Scale		FIS	
Hypohidrotic Ectodermal Dysplasia		HED	
Health-Related Quality of Life		(HRQoL)	
Health Service Executive (Ireland's Public Health System)		HSE	
Isolated Hypodontia		IH	
Lower Anterior Face Height		LAFH	
Maxillary		Max	
Mandibular		Mand	
National Foundation for Ectodermal Dysplasias		NFED	
Oral Health		OH	
Oral Health Impact Profile		OHIP	
Oral Health Related Quality of Life		OHRQoL	
Orthopantomogram		OPG	
Oral Health-Related Quality of Life for Patients with Hypodontia		OHRQoL-Hypodontia	
Parental-Caregiver Perceptions Questionnaire		P-CPQ	
Quality of Life		QoL	
Statistical Package for Social Sciences		SPSS	
Tallaght University Hospital / St. James's Hospital Joint Research Ethics Committee		JREC	
Tooth Agenesis Code		TAC	
Tooth-Site Absence		TSA	
Upper Right	Upper Left	UR	UL
Lower Right	Lower Left	LR	LL

Introduction

Hypodontia is defined as the congenital absence of one or more teeth, ranging in severity from mild to severe, including the total absence of tooth formation (Goodman et al., 1994; Hobkirk et al., 1980; Schalk-van der Weide et al., 1992; Vastardis, 2000). Hypodontia can occur in the absence of other conditions, known as isolated hypodontia (IH). Hypodontia can also be associated with a syndrome, Ectodermal dysplasia (ED) being the most common. ED is a diverse group of congenital conditions affecting two or more ectodermal structures (Ulm et al., 1998).

The diagnosis of both ED and IH is ideally based on genetic analysis which formed the basis of the current recommended classification for ED (Wright et al., 2019). There is extremely high variability in the expression of a mutation, even within families (Dreesen et al., 2014), therefore dental phenotypes may be more applicable and useful in the dental management of these populations.

It has been suggested that sufficient distinctive dental phenotypic features exist between ED and IH to distinguish between the two conditions (Dhamo et al., 2018). Hypodontia patterns and presence of other dental anomalies are significant components of the phenotypes for both ED and IH, particularly as other manifestations of ED may be very mild. Patterns of hypodontia can be quite variable and difficult to convey, with exponential combination possibilities. The tooth agenesis code (TAC) was developed by Van Wijk and Tan in 2006 to analyse hypodontia patterns using a binary system (Van Wijk et al., 2006), potentially allowing easier analysis and translation of pattern data within and between studies. Generating more inter-relatable data on the patterns of hypodontia, both isolated and syndromic, may be beneficial not only for research,

but may also be valuable in treatment planning and potentially may contribute to the generation of a more standardised treatment protocol in the future.

Currently, the management of hypodontia for both ED and IH is very varied (Filius et al., 2016), even within institutions there is a lack of consistency in the care provided for these patients, often resulting in frustration among patients and parents (Gill et al., 2015). Both conditions are also associated with numerous other dental anomalies, such as malocclusions, taurodontism and microdontia. These anomalies can complicate management, highlighting the importance of the entire phenotype and not just the number of missing teeth.

Severe hypodontia, both isolated and syndromic and its management, can have a significant impact on a child's oral health-related quality of life (OHRQoL) (Anweigi et al., 2013; Kotecha et al., 2013). It has been shown that children can self-report from as young as 5/6 years-old (Barbosa et al., 2008; Zaror et al., 2019). However, parents are ultimately the principal decision makers when it comes to dental intervention and their perception of their child's OHRQoL is likely to have the biggest influence on dental management (Jokovic et al., 2003; Parsons et al., 1999; Stricker, 1970). Therefore, knowledge of parental perceptions on the impact of hypodontia and its management would be very valuable for both conditions.

The present study explores parental perspectives on the OHRQoL impact and dental experience for children with ED, IH and age and gender-matched controls. It also looks to compare the number, location (both clinically and radiographically), and patterns of hypodontia in these children. The prevalence of associated dental anomalies for children with ED and children with severe IH (missing at least 6 permanent teeth) were also explored.

1 LITERATURE REVIEW

1.1 Hypodontia

1.1.1 Definition

Hypodontia is the congenital absence of one or more primary or permanent teeth excluding the third molar (Goodman et al., 1994; Hobkirk et al., 1980; Schalk-van der Weide et al., 1992; Vastardis, 2000). It is classified by the number of missing teeth (Larmour et al., 2005). Mild hypodontia is generally understood as missing one or a few teeth; severe hypodontia, also known as oligodontia, as missing six or more teeth; and anodontia as having no teeth (Hobkirk et al., 1980; Schalk-van der Weide et al., 1992). In the present study, the term hypodontia will be used to describe any missing teeth and severe hypodontia will be used to specifically describe 6 or more missing teeth.

1.1.2 Prevalence

In the permanent dentition, the reported prevalence of hypodontia varies between 2.6% to 14.7% (Table 1-1), with the prevalence, generally, being higher in females compared to males (Gábris et al., 2006; Hagiwara et al., 2016; Kielan-Grabowska et al., 2019; Larmour et al., 2005; Polder et al., 2004). In Europe, the prevalence is thought to be approximately 5.5% and the UK has been reported to have a prevalence of about 4-4.5% (Brook, 1974; Polder et al., 2004; Rose, 1966). However, the prevalence of hypodontia in Ireland remains unclear. O' Dowling et al. conducted a retrospective study of 3056 radiographic records from an Irish orthodontic population. Of the 3056 children, 354 had hypodontia of one or more teeth, a prevalence of 11.5% (incorrectly reported as 11.3%) (O'Dowling et al., 1990). A more recent Health Service Executive (HSE) audit of the Irish

public orthodontic waiting list from 2013 reported a hypodontia prevalence of 4.8%, based on 291 patients (Meade et al., 2013).

In the permanent dentition, the mandibular second premolars and the maxillary lateral incisors are the most frequently missing teeth in Caucasian populations, with prevalence ranges of 2.91%–3.22% and 1.55%–1.78% respectively (Larmour et al., 2005; Polder et al., 2004). The first molars and maxillary central incisors are considered the most stable teeth, only absent in up to 0.04% of cases (Polder et al., 2004) (Table 1-2) (Fournier et al., 2018) (Table 1-3). Fournier et al. estimated the average percentage of hypodontia of each tooth type based on 101 genetic-related articles, which represented both IH and syndromic patients and subsequently allocated the tooth types into three groups based on the frequency of hypodontia (Table 1-3). The three groups were; common, less common and rare. The results of Fournier's analysis are in keeping with previous prevalence studies, but also showed that these values varied depending on the individual genetic mutation (Fournier et al., 2018).

The primary dentition tends to be less affected with the lateral incisors of both arches most frequently affected with reported prevalence rates of between 0.5-2.4% (Larmour et al., 2005). The absence of primary teeth is highly associated with missing permanent successors (Larmour et al., 2005; Nik-Hussein, 1989; Polder et al., 2004; Rushmah, 1992). Mild hypodontia is the most common presentation, with as many as 80% of hypodontia patients only missing 1 or 2 teeth (Fournier et al., 2018; Larmour et al., 2005; Polder et al., 2004).

Severe hypodontia has a prevalence of less than 1%, with reports as low as 0.25% in European populations (Larmour et al., 2005) and may present as an isolated condition or as part of a syndrome (Hobkirk et al., 1980).

Table 1-1: A sample of hypodontia prevalence studies from 1936 to 2020.

Author	Country	Age (years)	Sample size	Prevalence (%)
(Dolder, 1936)	Switzerland	6-15	10,000	3.4%
(Grahnén, 1956)	Sweden	11-14	1,006	6.1%
(Glenn, 1961)	USA	3-16	777	5.1%
(Gimnes, 1963)	Norway	6-15	36,000	4.5%
(Castaldi et al., 1966)	Canada	6-9	457	4.2%
(Blayney et al., 1967)	USA	12-14	11,713	3.8%
(Davies, 1968)	Australia	12-14	2,170	6.3%
(Egermark-Eriksson et al., 1971)	Sweden	10-16	3,327	6.3%
(Haavikko, 1971)	Finland	5-13	1,041	8%
(Hundstadbraten, 1973)	Norway	7-14	1,295	10.1%
(Thilander et al., 1973)	Sweden	7-13	5,459	6.1%
(Bachmann, 1974)	Switzerland	9-10	8,694	7.7%
(Brook, 1974)	UK	11-14	1,115	4.4%
(Thompson et al., 1974)	Canada	6-12	1,191	7.4%
(Wisth et al., 1974)	Norway	9	813	6.8%
(Bergstrom, 1977)	Sweden	8-9	2,589	7.4%
(Magnusson, 1977)	Iceland	8-16	1,116	7.9%
(RØlling, 1980)	Denmark	9-10	3,325	7.8%
(Davis, 1987)	Hong Kong	12	1,093	6.9%
(Lo Muzio et al., 1989)	Italy	7-14	1,529	5.2%
(al-Emran, 1990)	Saudi Arabia	13-14	500	4%
(Lynham, 1990)	Australia	16-26	662	6.3%
(O'Dowling et al., 1990)	Ireland	7-17	3,056	11.5%
(Aasheim et al., 1993)	Norway	7-10	1,953	6.5%
(Salama et al., 1994)	Saudi Arabia	5-10	1,300	2.6%
(Johannsdottir et al., 1997)	Iceland	6-7	396	5%
(Bäckman et al., 2001)	Sweden	7	739	7.4%
(Thilander et al., 2001)	Colombia	5-17	4,724	3%
(Ng'ang'a et al., 2001)	Kenya	8-15	615	6.3%
(Nordgarten et al., 2002)	Norway	18	9,532	4.5%
(Silva Meza, 2003)	Mexico	9-20	668	2.7%
(Abu Alhaija et al., 2005)	Jordan	13-15	1,003	6%
(Fekonja, 2005)	Slovenia	~12	212	11.3%
(Albashaireh et al., 2006)	Jordan	16-45	1,045	5.5%
(Endo et al., 2006)	Japan	5-15	3,358	8.5%
(Gábris et al., 2006)	Hungry	6-18	2,219	14.7%
(Sisman et al., 2007)	Turkey	9-36	2,413	7.5%
(Küchler et al., 2008)	Brazil	6-12	1167	4.8%
(Maatouk et al., 2008)	Tunisia	12-18	262	13.4%
(Yamaguchi et al., 2008)	Japan	13-42	3,683	5.8%
(Goya et al., 2008)	Japan	3-17	2,072	9.4%
(Harris et al., 2008)	USA	12-18	1700	5.2%
(RØlling et al., 2009)	Denmark	9-12	8,138	7.4%
(Celikoglu et al., 2010)	Turkey	10-25	3,341	4.6%
(Gomes et al., 2010)	Brazil	10-15	1,049	6.3%

(Tallón-Walton et al., 2010)	Spain	6-83	1,518	7.3%
(Vahid-Dastjerdi et al., 2010)	Iran	9-27	1,751	9.1%
(Behr et al., 2011)	Bavaria	5-44	1,353	12.6%
(Kim, 2011)	Korea	9-30	3,055	11.3%
(Lee et al., 2011)	Korea	14-35	3,133	5.7%
(Gupta et al., 2011)	India	14+	1,123	4.2%
(Amini et al., 2012)	Iran	1-20	3,374	5.2%
(Cantekin et al., 2012)	Turkey	8-14	1,291	6.2%
(Sheikhi et al., 2012)	Iran	7-25	2,422	10.9%
(Shetty et al., 2012)	India	13-15	2,469	8%
(Fekonja, 2015)	Slovenia	Adult	2,546	6.9%
(Hagiwara et al., 2016)	Japan	16-18	9,584	3.9%
(Gokkaya et al., 2015)	Turkey	11-20	1,236	7%
(Park et al., 2017)	Korea	6-12	4,611	3.4%
(Gracco et al., 2017)	Italy	9-16	4,006	9%
(Sola et al., 2018)	Spain	7-11	2,500	3.5%
(Kielan-Grabowska et al., 2019)	Poland	6-15	674	11.6%
(Aras et al., 2020)	Turkey	9-16	1,036	6.6%

Table 1-2*:* Frequency of hypodontia by tooth-type. Adapted from (Polder et al., 2004).

Frequency	**Teeth (in descending order of most prevalent)**	**Prevalence %**
Common	1. Mand 2nd premolar 2. Max lateral incisor 3. Max 2nd premolar	1.5–3.1%
Less Common	4. Mand central incisor 5. Mand lateral incisor & Max 1st premolar 6. Max Canines & Mand 2nd molar	0.1–0.3%
Rare	7. Max 2nd molar & Max 1st molar 8. Mand Canines 9. Mand 1st molar & Max central incisor	0.01–0.04%

Table 1-3: Frequency of hypodontia per tooth-type estimated from the analysis of 101 genetic-related articles, based on 522 patients. Table compiled from (Fournier et al., 2018).

	Tooth-Type	% Frequency of Hypodontia
Common		
1.	Max 2nd Premolar	61.57%
2.	Mand 2nd Premolar	55.52%
3.	Max Lateral Incisor	50.77%
Less Common		
4.	Mand Central Incisor	49.90%
5.	Mand 2nd Molar	42.39%
6.	Max 1st Premolar	41.87%
7.	Max 2nd Molar	40.73%
8.	Mand Lateral Incisor	34.52%
Rare		
9.	Max 1st Molar	29.64%
10.	Max Canine	27.05%
11.	Mand 1st Premolar	24.75%
12.	Mand 1st Molar	22.58%
13.	Mand Canine	17.23%
14.	Max Central Incisor	10.61%

1.1.3 Isolated Hypodontia (IH)

Hypodontia that occurs in isolation, without any other signs or symptoms is referred to as Isolated Hypodontia (IH), regardless of the number of missing teeth. This study refers to the term IH to describe non-syndromic patients who are missing 6 or more permanent teeth.

1.1.4 Syndromic Hypodontia

Hypodontia is associated with numerous syndromes and conditions; including ED, Down's syndrome, Hemifacial Microsomia and Van der Woude syndrome. It has been reported that hypodontia of canines, first molars and maxillary central incisors is rare (Fournier et al., 2018; Symons et al., 1993). Absence of multiple teeth, and these teeth in particular, may indicate an underlying syndrome and should always be considered in the diagnostic workup (Cobourne, 2007).

1.1.5 Diagnosis

Diagnosis of hypodontia is usually made radiographically with the absence of any sign of tooth formation or calcification (Aasheim et al., 1993; Bartzela et al., 2013; Chung et al., 2008; Dhamo et al., 2018; Toshiya Endo et al., 2006). A final diagnosis of hypodontia and classification of hypodontia severity, should not be made before the age of 9 years-old, as the formation of the second premolars can begin as late as 9–10 years-old, particularly for boys (Wisth et al., 1974). It is well documented that hypodontia is associated with delayed dental development (Bailit et al., 1968; Dhamo et al., 2016; Garn et al., 1970; Haavikko, 1971; Schalk van der Weide et al., 1993) and delayed exfoliation of primary teeth is often the prompt for further investigation. It may also be suspected due to a positive family history or diagnosis of a hypodontia-related condition/ syndrome such as ED, cleft lip and palate or Down Syndrome. However, hypodontia is often an incidental finding during a routine dental examination.

1.1.6 Aetiology

Odontogenesis is a continuous, extremely complex and advanced process with no defined beginning or end-points that is coordinated by “sequential and reciprocal interactions between the epithelial and mesenchymal tissues” (Thesleff, 2003). Any mistakes in this process may lead to abnormalities in tooth morphology, tooth number, as well as complete cessation of tooth development.

There is a tendency towards a strong family history for both ED and IH and it should be included as part of the diagnostic process. Both ED and IH have various modes of inheritance and can be autosomal dominant, autosomal recessive, sex-linked or a de-novo mutation, with very varying degrees of expression. However, the aetiology of hypodontia is complex and thought to be

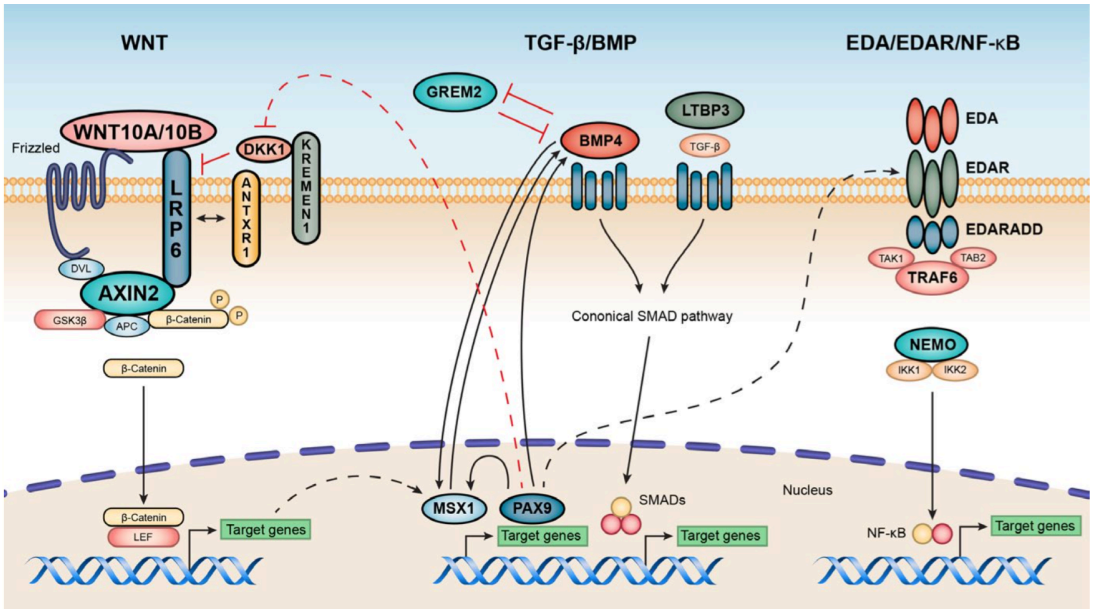
multifactorial involving not only genetic factors such as mutations in PAX9, MSX1, and EDA but also environmental factors like infection, hormonal and metabolic imbalances, drugs, and localised interruption of the dental lamina (e.g. cleft lip and palate patients) (Brook, 1984, 2009; Larmour et al., 2005). Brook (2009) suggested that the timing, extent and duration of an environmental insult was more significant than the actual insult itself.

1.1.7 Genetics

Even when environmental factors are considered, there is no denying the significant influence genetic mutations have on the developing dentition.

There are five main families of signalling molecules which regulate organ development in all animals; bone morphogenetic protein (BMP), hedgehog (HH), fibroblast growth factor (FGF), ectodysplasin (EDA) and wingless-related integration site WNT (Balic et al., 2015). These pathways have feedback loops which are interconnected and mutually dependent (Yu et al., 2019) (Figure 1-1). Relevant pathways need to respond in the correct manner and dose, at the correct time and in the correct place to allow the process to run smoothly. While blocking any one of these signalling pathways results in arrested or abnormal tooth development, both WNT and EDA are of particular importance in the development of teeth (Balic et al., 2015; Bei, 2009).

Figure 1-1: Three hypodontia-associated signalling pathways, WNT, BMP and EDA. Reproduced from (Yu et al., 2019).



WNT

WNT pathway is considered the most important for both initiation and regulation of teeth and other organs. It is involved in all stages of tooth development (Thesleff et al., 1997). Animal studies have shown that blocking or activating this pathway results in hypodontia and hyperdontia respectively (Balic et al., 2015; Järvinen et al., 2018; Thesleff, 2006).

Mutations in the WNT10A gene are reported to be the most common cause of hypodontia. WNT10A and other WNT pathway mutations combined are thought to be responsible for as many as half of human hypodontia cases, including both IH and ED (Arte et al., 2013; Mues et al., 2014; Yin et al., 2015). WNT is thought to mostly affect lateral incisors and second premolars, rarely affect first molars and mandibular canines and least of all the upper central incisors (Fournier et al., 2018).

EDA

EDA is required specifically for the development of teeth and other organs developing from the ectodermal epithelium covering the surface of the embryo, such as hair and certain glands (Balic et al., 2015). The EDA gene was initially identified as the gene associated with hypohidrotic ectodermal dysplasia (HED). HED mutations tend to block the function of the entire EDA gene, which can result in severe hypodontia affecting all tooth types (Kere et al., 1996). A systematic review by Fournier et al. showed that even though the maxillary central incisors were least likely to be missing, they were still absent in 41.18% of patients (Fournier et al., 2018).

EDA mutations can also cause IH and are usually associated with severe hypodontia. Furthermore, this form of mutation has been shown to most likely cause hypodontia of the anterior teeth, while rarely affecting molars (Fournier et al., 2018).

EDAR

EDAR is the EDA receptor and mutations tend to cause severe hypodontia in most cases. EDAR most commonly affects lateral incisors and mandibular central incisors, while rarely affects molars or maxillary central incisors (Fournier et al., 2018).

EDAR-associated death domain (EDARADD)

Similarly, EDARADD presents mostly as severe hypodontia and in contrast to EDAR, commonly results in hypodontia of molars and premolars (Fournier et al., 2018).

Homeobox Genes

Homeobox genes are a large family of about 235 similar functional genes that regulate the development of numerous body structures during embryonic development (Genetics Home Reference, 2018). MSX1, AXIN2, and PAX9 are Homeobox genes and mutations of these genes are known to be involved in hypodontia. These genes encode for transcription factors, meaning they bind to and control the activity of other genes, being particularly involved in the initiation and morphogenetic stages of odontogenesis (Fournier et al., 2018; Genetics Home Reference, 2018).

MSX1 is more commonly associated with severe or syndromic hypodontia and less common with mild hypodontia (Fournier et al., 2018). This mutation appears to predominantly present with hypodontia of premolars and sometimes molars (Fournier et al., 2018). PAX9 mutations are nearly always associated with missing molar and premolar teeth and occasionally some incisor teeth (Fournier et al., 2018). AXIN2, also known as a regulator of the WNT signalling pathway, generally involves a wider range of tooth types and it tends to be related to syndromic severe hypodontia more often than IH (Fournier et al., 2018). A mutation in AXIN2 has also been described in association with colorectal cancer in adults (Clendenning et al., 2019; Fournier et al., 2018). This is an important finding for clinicians treating patients with hypodontia, particularly if a positive family history of colorectal cancer exists.

As the required level of expression for each gene varies throughout the odontogenic process, Fournier et al. hypothesised that it may be possible for other genes to compensate for some of the deficits in a mutation. This hypothesis may also explain the variability in phenotypes and why only certain teeth are

missing, particularly when there is more than one mutation present (Fournier et al., 2018).

Given that there is such high variability in the expression of a mutation even within families (Dreesen et al., 2014), dental phenotypes may be more clinically applicable for the dental management of patients with ED and IH.

1.2 Ectodermal Dysplasia

1.2.1 Definition

Ectodermal Dysplasia (ED) is the most common syndrome associated with hypodontia (Ulm et al., 1998). It is defined as a diverse group of congenital conditions affecting two or more ectodermal structures such as skin, hair, nails, teeth and sweat glands, with more than 200 conditions identified under the umbrella of Ectodermal Dysplasia (Irvine, 2009).

1.2.2 Prevalence

ED is considered rare with few and contradictory prevalence reports in the literature. Generally, studies have been based on either small geographical clusters or theoretical estimates (Nguyen-Nielsen et al., 2013). The National Foundation for Ectodermal Dysplasias (NFED) estimate that approximately 3.5 per 10,000 people are affected by ED (National Foundation for Ectodermal Dysplasias website, n.d.). With a current Irish population of approximately 4.9 million (Ireland Population (2020) - Worldometer, n.d.) this may translate to 1700 people with ED in Ireland.

Hypohidrotic ectodermal dysplasia (HED) is the most common form of ED and is estimated to occur in 1 per 20,000 live-births (Genetics Home Reference, 2019; Nguyen-Nielsen et al., 2013). From an Irish perspective, this would equate to

approximately 246 people with HED in Ireland. X-Linked HED (XLHED) is the most prevalent form of HED, making up approximately 70%, with both the autosomal dominant and recessive HED being much rarer (Nguyen-Nielsen et al., 2013; Priolo et al., 2001). XLHED primarily affects males with variable phenotypic expression in heterozygous female carriers, with little or no manifestations compared to their male counterparts (Nguyen-Nielsen et al., 2013; Tarpey et al., 2007). This variability may be due to skewed X-inactivation (Van den Veyver, 2001).

1.2.3 Clinical Manifestations

ED can affect any ectodermal structures, most commonly presenting with hypodontia, dry eczematous skin, reduced or essentially absent ability to sweat, sparse hair, dystrophic nails and frequent nose bleeds due to a lack of mucus. ED can also affect the mammary, thyroid and lacrimal glands, the lacrimal duct, thymus, cornea, and the conjunctiva (Irvine, 2009). There have also been reports of reduced mucus glands in the respiratory and gastrointestinal tracts (Reed et al., 1970; Siegel et al., 1990) and therefore, it is not surprising that an increased incidence of allergic rhinitis and nasal obstruction in ED individuals has been reported (Mehta et al., 2007).

1.2.4 Classification

Traditionally, ED has been classified by phenotype and mode of inheritance (Freire-Maia et al., 1988; Pinheiro et al., 1994). A new classification for ED was proposed by an international advisory group in 2017, suggesting that ED should be organised according to the phenotypic features, Online Mendelian Inheritance in Man (OMIM) number, mode of inheritance, genetic mutation, and associated

genetic pathways (e.g., EDA, WNT, TP63 “tumour protein p63”) or structure (Wright et al., 2019) (Figure 1-2).

Figure 1-2: Organisation of ED conditions based on molecular pathways (Wright et al., 2019).

OMIM number	Syndrome name(s)	Gene	Distinguishing features
EDA/NFKappaB pathway			
305100	Hypohidrotic ectodermal dysplasia; ED1; Christ-Siemens-Touraine syndrome	Ectodysplasin A; *EDA* (300451)	Hypohidrosis, hypotrichosis, hypodontia, smooth dry skin, craniofacial dysmorphology, periorbital pigmentation
129490	Hypohidrotic ectodermal dysplasia 10A	Ectodysplasin A Receptor; *EDAR* (604095) or *EDARADD* (606603)	Hypohidrosis, hypotrichosis, hypodontia, smooth dry skin, craniofacial dysmorphology, periorbital pigmentation
224900	Hypohidrotic ectodermal dysplasia 10B	Ectodysplasin A Receptor; *EDAR* (604095) or *EDARADD* (606603)	Hypohidrosis, hypotrichosis, hypodontia, smooth dry skin, craniofacial dysmorphology, periorbital pigmentation
308300	Incontinentia Pigmenti; IP	*IKBKG* (300248)	Short stature, cataract, microphthalmia, hypodontia, extra ribs, breast aplasia, staged skin involvement, nail dystrophy, atrophic hair
300291	Ectodermal dysplasia and immunodeficiency 1: EDAID1	*IKBKG* (300248)	Hypohidrosis, hypotrichosis, morbidity/mortality secondary to immunodeficiency
WNT pathway			
305600	Focal dermal hypoplasia, Goltz syndrome	*PORCN* (300651)	Short stature, facial asymmetry, narrow auditory canals, hearing loss, oral papillomas, hypodontia, syndactyly, sparse hair, skin atrophy
257980	Odontoonychodermal dysplasia; OODD	*WNT10A* (606268)	Sparse eyebrows, severe hypodontia, smooth tongue, hyperhidrosis, hyperkeratosis, dystrophic nails, sparse eyebrows, thin hair
224750	Schopf-Schulz-Passarge syndrome	*WNT10A* (606268)	Hypodontia, eyelid cysts, keratoderma, hypoplastic nails, hypotrichosis
TP63 pathway			
103285	Acro-dermato-ungual-lacrimal-tooth syndrome (ADULT syndrome)	*TP63* (603273)	Lacrimal obstruction, hypodontia, dysplastic teeth, breast hypoplasia, ectrodactyly, thin skin, dysplastic nails
106260	Ankyloblepharon-ectodermal defects-cleft lip/palate (AEC; Hay-Wells syndrome)	*TP63* (603273)	Scalp erosions, conductive hearing loss, maxillary hypoplasia, lacrimal duct atresia, hypotrichosis, ankyloblepharon, cleft lip, hypodontia
129400	Rapp-Hodgkin syndrome	*TP63* (603273)	Short stature, maxillary hypoplasia, hearing loss, cleft l/p, hypodontia, syndactyly, thin skin, hypohidrosis

Conditions were included in accordance with the definition of ED and clustered depending on their molecular aetiology. However, if conditions were of unknown aetiology, they were grouped with ED’s of similar phenotype (Wright et al., 2019).

1.3 Ectodermal Dysplasia and Isolated Hypodontia

1.3.1 Associated Dental Features

Hypodontia is one of the most common anomalies of dental development and ED is the most common syndrome associated with hypodontia (Ulm et al., 1998; Vastardis, 2000). They are both frequently associated with additional

abnormalities in tooth development and eruption. The following associated features are reflective of both IH and ED.

Skeletal Features

Patients with severe hypodontia, including those with ED, are said to have a slight tendency towards a reduced lower anterior facial height and a class 3 skeletal relationship (Acharya et al., 2010; Avelar Fernandez et al., 2018). This tends to become more significant with increasing hypodontia severity, especially when more than one tooth type is missing (Acharya et al., 2010; Chung et al., 2000).

Dental Features

Patients with hypodontia, both ED and IH, often have teeth that are abnormal in shape and size, with delayed or abnormal eruption frequently reported. There is also an increased prevalence of retained primary teeth, infraocclusion, taurodontism and failure of alveolar bone growth.

Morphological Abnormalities

The association between hypodontia and microdontia is well documented in the literature (Baccetti, 1998; Baum et al., 1971; Garn et al., 1970). The maxillary lateral incisors are most frequently affected, even in cases of mild hypodontia. With increasing severity of hypodontia and in syndromic associated cases, a more general microdontia of the entire dentition is seen (Brook et al., 2009). Dhamo et al. showed that individuals with ED were 7 times more likely to have morphological abnormalities when compared to IH (Dhamo et al., 2018).

In ED, morphological abnormalities primarily occur in the incisors, canines and first molars of both arches (Prager et al., 2006). There tends to be a generalised microdontia, with an increased incisal convergence of the incisors, canines and

sometimes the molars. This convergence results in the anterior teeth having a conical appearance and a 'bud-like' shape for molars (Bergendal, 2014; Prager et al., 2006; Reyes-Reali et al., 2018).

Impaction and Transposition

Hypodontia is associated with a higher frequency of eruption anomalies, with teeth either becoming ectopic or migrating to a different location and becoming transposed. Peck found that when the maxillary lateral incisors were missing or microdontic in size, the maxillary canines were 13 times more likely to be ectopic (Peck et al., 1996). It has been proposed that this occurs due to the loss of eruption guidance for the maxillary canines (Becker, 1984). Hypodontia patients are also reported to experience a high frequency of canine/ first premolar transposition (Bourzgui et al., 2012; Peck et al., 1996, 1993). Similarly, there are multiple case reports of impacted and transposed teeth in patients with ED (Bilge et al., 1995; Guler et al., 2005; Yenisey et al., 2004).

Taurodontism

Taurodontism is "an apical extension of the pulp chamber in a tooth with multiple roots" (Schalk-Van Der Weide et al., 1993). Subsequently, taurodont teeth have enlarged and elongated pulp chambers and comparatively shorter roots.

There is an increased frequency of taurodontism in patients with hypodontia and in patients with ED (Crawford et al., 1991; Kan et al., 2010; Schalk-Van Der Weide et al., 1993; Seow et al., 1989). Seow et al. in 1989 and Kan et al. in 2010, reported prevalence rates of 35% and 36% respectively, for patients with hypodontia.

The cause of taurodontism is uncertain. A popular theory suggests taurodontism is the result of a disruption in developmental homeostasis, delaying the

invagination of Hertwig's epithelial root sheath (Witkop et al., 1988). As Hertwig's epithelial root sheath is an ectodermal derivative, the association between taurodontism and anomalies of ectodermally derived structures in conditions such as ED and IH is not unexpected and supported by both clinical and molecular studies (Hu et al., 2007; Kan et al., 2010; Seow et al., 1989; Wright et al., 2008).

Retention of Primary Teeth

The presence of primary teeth beyond the expected age of exfoliation (retained primary teeth) is commonly associated with hypodontia of the permanent successors (Kotecha et al., 2013). In that situation, retaining the primary tooth is generally beneficial to a young patient; providing better aesthetics and function, maintaining space, preventing tilting or drifting of adjacent teeth and most importantly, preserving alveolar bone for future prosthetic/ implant care (Kotecha et al., 2013). It has been estimated that up to 25% of the alveolar ridge width is lost within 3 years following extraction of a retained primary mandibular molar in a patient with hypodontia of the successor (Ostler et al., 1994).

Tooth-Site Absences

When comparing patient groups with hypodontia, the retention of primary teeth could be a confounding factor masking the real impact of hypodontia, particularly in comparison to those without retained primary teeth. Patients with ED tend to have a higher prevalence of primary tooth hypodontia and as such, are much less likely to have retained primary teeth (Schnabl et al., 2018). Raziee et al. recorded the presence of a clinically edentulous site instead of radiographical absence to allow for the presence of retained primary teeth. This represented a site that contained neither a primary nor a permanent tooth (Raziee et al., 2019). Each

quadrant is said to have 7 tooth-sites (assuming 3rd molars are excluded from the assessment). If, for example, site 3 in the upper right quadrant contains neither a primary nor permanent tooth it is recorded as an edentulous site, but if site 3 contains a primary or permanent tooth, it is recorded as occupied. This approach was proposed in an attempt to provide a more accurate representation of the actual number of teeth present in the patient's mouth at the time of examination, irrespective of whether the tooth was primary or permanent.

Infraocclusion

Unfortunately, retained primary teeth sometimes become ankylosed and infraoccluded. This is particularly problematic when there is hypodontia of the successor. Infraocclusion may be progressive and result in tilting of the adjacent teeth. Submergence of the primary tooth below the gingiva is also possible, resulting in a large bony defect in the area. Messer and Cline classified mild infraocclusion as being; at least 1mm below the occlusal plane, as judged from the two nearest non-ankylosed teeth in the same quadrant, and above the interproximal contact; with moderate as being within the occluso-gingival margins of interproximal contact; and severe as being below the interproximal contact point (Messer et al., 1980).

1.4 Patterns of Hypodontia

1.4.1 Literature

Dhamo et al suggested that sufficient distinctive phenotypic features exist between ED and severe IH (Dhamo et al., 2018). She proposed that missing second permanent molars, having abnormally shaped incisors and canines and delayed dental development of approximately one year of the permanent teeth present, could discriminate ED from severe IH (Dhamo et al., 2018).

Schalk-van der Weide (1994) previously implied that phenotypic features could be a reliable indicator of syndromic or isolated hypodontia. It was suggested that if the most stable teeth are missing, or if there is a large number of missing teeth, ED may be likely and the patient should be assessed carefully for other phenotypic features (Schalk-van der Weide et al., 1994). Tan reported a reasonable number of common patterns between IH participants (Tan et al., 2011). However, other studies that have looked at IH have suggested that the presentation of patterns is too heterogeneous (Créton et al., 2007; Dreesen et al., 2014).

1.4.2 Tools

1.4.3 Tooth Agenesis Code (TAC)

Analysis methods, such as the Tooth Agenesis Code, can be helpful in pattern analysis, particularly when you consider there are more than 4 billion possible pattern combinations (Van Wijk et al., 2006). In 2006, Van Wijk and Tan developed a method called the tooth agenesis code (TAC), which identifies tooth agenesis codes using a binary system (Van Wijk et al., 2006). TAC assigns a specific value to each missing tooth and generates a unique value for each tooth agenesis pattern. Assuming wisdom teeth are excluded, seven teeth can be either present or missing in each quadrant, with the possibility of 128 unique combinations or patterns in each quadrant.

TAC allows investigators to assess the prevalence of certain patterns, to compare the symmetry of those patterns and to easily and clearly represent different phenotypes (Van Wijk et al., 2006). TAC is a tool to translate these findings, allowing for easier data analysis and comparison with other investigators (Van Wijk et al., 2006).

Figure 1-3: Example of TAC (Van Wijk et al., 2006)

	Right upper jaw (q1)								Left upper jaw (q2)							
A	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
B	128	64	32	16	8	4	2	1	1	2	4	8	16	32	64	128
A	48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
	Right lower jaw (q4)								Left lower jaw (q3)							

1.5 Early Dental Intervention

The diagnosis of ED can occur at a very young age, particularly if there is a positive family history. In addition, children with ED are more likely to be missing primary teeth (Schnabl et al., 2018).

The National Foundation for Ectodermal Dysplasia (NFED) encourage early dental treatment to enhance general health through both good nutrition, and improved aesthetics. Prosthetic intervention for a child as young as 2 or 3 years-old has been suggested and advocated by the NFED. Early intervention is thought to encourage normal development of speech, function, facial support and improved TMJ function, as well as the physical, emotional and psychosocial benefits (Hickey et al., 2001; National Foundation for Ectodermal Dysplasias, 2003).

Early intervention typically involves the fabrication of dentures (Chokhachi et al., 2019; Hickey et al., 2001; Nunn et al., 2003; Schnabl et al., 2018). However, treatment is contingent upon the child's cooperation and parents must be informed of the difficulties associated with a prosthesis in a growing child such as; initial speaking difficulties, dietary limitations, the burden of multiple appointments for adjustments and prosthesis replacement due to continued growth. Bone atrophy, due to prolonged prothesis wear, may also become a significant issue, particularly if implants are to be considered in later years. There

are many factors that contribute to alveolar bone loss, including the use of prosthesis. Intensive/ prolonged use, unstable occlusal conditions and immediate dentures have all been associated with alveolar bone loss (Atwood, 1957, 1962). It is also important to consider that development of the alveolar bone occurs in conjunction with tooth bud formation, so in areas without tooth bud formation, the formation of alveolar bone is already deficient (National Foundation for Ectodermal Dysplasias, 2003). Accurate record taking or necessary adjustments may be challenging in a young child, potentially resulting in accelerated bone loss and therefore compromising long-term treatment plans.

Early dental intervention is less common in IH patients. This may be due to a lower prevalence of altered morphology and primary tooth hypodontia, therefore delaying the need for dental management.

It is crucial to regularly assess the patient's individual desired dental outcome, expectations, and overall psychosocial status prior to any prosthodontic care (Hickey et al., 2001).

1.6 Management of Children with Severe Hypodontia

Management of children with ED and IH will always include prevention of caries and a spectrum of interventions ranging from; no additional treatment; to space maintenance; removable prosthesis, e.g. dentures; fixed prosthesis, e.g. conventional bridges, resin-bonded bridges; anterior composite restorations; multi-stage or single-stage orthodontics; and implants (Chokhachi et al., 2019; Gill et al., 2015; Schnabl et al., 2018). Their management can require complex multi-disciplinary care and if started at a young age can lead to prolonged treatment times, resulting in a substantial appointment burden to the patient and their family (Gill et al., 2015).

At present, there is no standardised management approach for severe hypodontia, in either ED or IH (Filius et al., 2016). In the paediatric population, generation of a standardised approach to care for children is particularly challenging due to the high variability in presentation and the inherent issue that children are continuously growing and changing. Consequently, their clinical presentation and treatment need is subject to constant change (Hvaring, 2017). Studies on the management of severe hypodontia, both ED and IH, are mainly of poor quality, often being case reports or series (Filius et al., 2016). This lack of quality is most likely attributed to the low prevalence of severe hypodontia and adversely affects the clinician's ability to formulate an evidence-based standardised approach (Filius et al., 2016). Even an international expert panel for the rehabilitation of children with ED found it difficult to come to a consensus, highlighting the complexity of this condition and its management (Klineberg et al., 2013). Standardisation of treatment protocols for other patient groups such as cleft lip and palate has been achieved, resulting in favourable outcomes (Shaw et al., 1992). This demonstrates both the possibility and feasability of achieving a standardised, patient focused system of care and is encouraging for those affected by severe hypodontia, including those with ED (Barber et al., 2018).

1.7 Oral Health-Related Quality of Life (OHRQoL)

1.7.1 Definitions

Quality of Life (QoL)

The World Health Organisation (WHO) defines QoL as an "individual's perception of their 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." It is an expansive model influenced by the individuals psychosocial state, and their

environment (“WHO | WHOQOL: Measuring Quality of Life,” 2014). This concept materialised from the gradual realisation that traditional clinical health measures were insufficient and need to be supplemented by more holistic methods to obtain a more accurate reflection of well-being (Locker et al., 2007). This approach acknowledges the desire to not only survive, but to thrive. However, it is important to recognise that health and QoL are distinct entities. The ‘disability paradox’ is a good example where an individual who suffers from a chronic illness may report a good QoL in spite of serious and persistent limitations (Albrecht et al., 1999; Locker et al., 2007).

Oral Health (OH)

Oral health is defined by the WHO as “a state of being free from chronic mouth and facial pain, oral and throat cancer, oral infection and sores, periodontal (gum) disease, tooth decay, tooth loss, and other diseases and disorders that limit an individual’s capacity in biting, chewing, smiling, speaking, and psychosocial wellbeing” (WHO/Europe | Disease prevention - Oral health, n.d.).

Oral Health-Related Quality of Life (OHRQoL)

OHRQoL is 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 et al., 2007). A fundamental element of OHRQoL involves recognising that the patient’s perspectives and priorities are of equal importance to that of the clinician and should be considered when planning and delivering care (Kotecha et al., 2013).

1.8 Measures of Children's Oral Health-Related Quality of Life

OHRQoL instruments facilitate the evaluation of the overall impact of oral disorders. In recent years a number of OHRQoL instruments have been developed for children and adolescents. Age is an important factor when assessing OHRQoL in children. There are instruments designed for young children, aged 0–6 years such as the; Early Childhood Oral Health Impact Scale (ECOHIS); Scale of Oral Health Outcomes for 5-year-old children (SOHO-5); Michigan Oral Health-Related QoL scale (Michigan- OHRQoL); Oral Health-related Early Childhood Quality of Life tool (OH-ECQoL); and the Dental Discomfort Questionnaire (DDQ) (Zaror et al., 2019).

There are instruments designed for those aged 7–18 years, such as the; Child Perceptions Questionnaire 8–10 (CPQ8–10) and 11–14 (CPQ11– 14); Child Oral Health Impact Profile (Child-OHIP); Child Oral Impact on Daily Performance Index (Child-OIDP); Child Dental Pain Questionnaire (Child-DPQ); Dental Free-time Trade-Off Scale (DFTO); Impact of Fixed Appliances Questionnaire (IFAQ); Malocclusion Impact Questionnaire (MIQ); and the Oral Health-Related Quality of Life for Patients with Hypodontia (OHRQoL-Hypodontia) (Zaror et al., 2019).

And finally, there are instruments designed for children of all ages (0–18 years), including the; Family Impact Scale (FIS); Parental-Caregiver Perceptions Questionnaire (P- CPQ); Pediatric Oral Health-Related Quality of Life (POQL); and the Pediatric Quality of Life Inventory™ Oral Health Scale™ (PedsQL-OHTM) (Zaror et al., 2019).

With multiple instruments now available it's important that they are evaluated and shown to capture what they have set out to measure (Locker et al., 2007; Zaror et al., 2019). Zaror et al. conducted a systematic review in 2019 of the

available instruments assessing the OHRQoL in children and adolescents and evaluated them using the Evaluating Measures of Patient-Reported Outcomes (EMPRO) tool.

ECOHIS was found to be the most complete instrument and despite being originally developed to assess the impact of dental caries, it is currently considered a universal OHRQoL instrument for children under 6-years old (Zaror et al., 2019). CPQ, Child-OIDP, Child-OHIP also scored well, which is consistent with a previous systematic review by Gilchrist in 2014, and FIS had the best EMPRO evaluation for children of any age, along with P-CPQ and POQL.

However, Zaror's EMPRO evaluation did suggest that further research is necessary for the condition-specific instruments, such as malocclusion and hypodontia, as they did not score as well overall as the generic instruments (Zaror et al., 2019).

1.8.1 OHRQoL- Hypodontia

OHRQoL- Hypodontia was developed by a UK study in 2011 to assess the important issues and the impact of IH on patients OHRQoL (Akram et al., 2011). Five focus groups, held over the course of 6 months, were used to identify key areas of concern for hypodontia patients, involving patients at different stages of treatment. The questionnaire was designed for children with IH, aged 11 to 18 years-old, and was formulated from the issues raised by 22 IH patients during the focus groups using saturated thematic analysis. Four main themes were identified; treatment; effect on daily activities (e.g. function, speech and oral hygiene); thoughts on appearance; and the reaction of other people. The response options for the questionnaire were a five-level Likert scale, including: strongly agree; agree; do not agree or disagree; disagree; strongly disagree. The

next phase of the study was assessing the ease of administration of the questionnaire and this was tested by 10 hypodontia patients, aged between 11 and 15 years-old and included the time taken to complete the questionnaire, readability, and questions that were misunderstood or left unanswered.

As neither the experts nor the 10 patients that took part in this phase of the study raised any objections while testing the questionnaire and because the questions were derived from the data obtained from focus groups, the authors concluded that the questionnaire had good face and content validity. The systematic review by Zaror et al. did find that the OHRQoL- Hypodontia was well rated for conceptual model, reliability, and validity, but due to poor scores in responsiveness and interpretability they advised further research was required. Although the OHRQoL- Hypodontia was produced specifically to target areas that are particularly relevant and important to children with hypodontia, given that children with syndromic hypodontia were excluded, that the questionnaire has only been tested for children aged 11-16 years old and that the questionnaire was designed to report the perspective of the children themselves and not the perspectives of parents, it was felt that for these reasons this tool would not be appropriate for use in this study.

1.8.2 Child Oral Health Quality of Life Questionnaire (COHQoL)

The Child Oral Health Quality of Life Questionnaire (COHQoL) contains four components; the Child Perception Questionnaire (CPQ) 8-10 and 11-14 years-old; global rating; Parental-Caregiver Perception Questionnaire (P-CPQ); and the Family Impact Scale (FIS).

1.8.3 Child Perception Questionnaire (CPQ)

This tool was developed to measure the OHRQoL of children, with the aim of being sensitive to children's cognitive, emotional, and social development (Jokovic et al., 2003). CPQ has specific age versions including 8-10 and 11-14 years-old, therefore allowing the use of the same instruments throughout childhood and adolescence (Zaror et al., 2019). This is of particular importance as the instrument was intended to be used as an outcome measure in clinical trials and evaluation studies, therefore sensitivity to change is necessary (Jokovic et al., 2003; Locker et al., 2007). CPQ has shown to be both a valid and reliable tool (Gilchrist et al., 2014; Zaror et al., 2019) and has been validated for several orofacial disorders, such as caries (Shin et al., 2015), enamel defects (Marshman et al., 2005), malocclusion (O'Brien et al., 2006, 2007) and craniofacial disorders (Jokovic et al., 2002; Wogelius et al., 2009).

1.8.4 Parental-Caregiver Perception Questionnaire (P-CPQ)

The P-CPQ forms one component of the COHQoL. Developed as an adjunct to the CPQ's, it measures the impact on the child from the parent's perspective (Jokovic et al., 2003). P-CPQ was designed for children between 6 and 14 years old, but the psychometric features have been evaluated on children from 3 years-old and upwards (Zaror et al., 2019).

The use of parents as proxies for their children has suffered much criticism in the literature, with concerns regarding the accuracy of responses, particularly regarding older children (Jokovic et al., 2003).

Despite the criticisms, parental reports are valuable. Ultimately parents make the decisions regarding their child and their perceptions can have a significant

influence on their child's management (Parsons et al., 1999), resulting in their "needs" and preferences fuelling healthcare, as seen commonly in orthodontic patients (Jokovic et al., 2003; Stricker, 1970). The P-CPQ authors suggest that the parental reports provide supplemental and complementary information, giving a more comprehensive overview of a child's health and well-being (Jokovic et al., 2003).

Development of P-CPQ

The P-CPQ and CPQ were designed in a very similar manner with the conceptual framework for both questionnaires developed through a review of existing child HRQoL measures (Jokovic et al., 2003). The authors identified four health domains including; oral symptoms, functional limitations, emotional well-being, and social well-being (Jokovic et al., 2003). A selection of 46 items were adapted from existing questionnaires and comprehensively reviewed by 17 clinicians and 41 parents of child patients (Jokovic et al., 2003). Thirty-three items were selected for the final questionnaire using an item impact study (Jokovic et al., 2004). The impact method highlights the items that are rated most frequently and that are most important to the target population, while also improving the ability to detect small changes (Locker et al., 2007).

Structure of P-CPQ

The P-CPQ contains 33 questions in total with 6 in the oral symptoms' domain; 8 in functional limitations; 8 in emotional well-being; and 11 in social well-being. The questions relate to the frequency of events in the previous three months, with the response options being: never= 0, once or twice= l, sometimes= 2, often= 3, every day or almost every day= 4. A "don't know" response is also included because the participant is reporting on another individual (Jokovic et al., 2003).

Global ratings of the child's overall well-being are obtained through a five-point response scale from 'excellent' to 'poor' for oral health and from 'not at all' to 'very much' for well-being (Jokovic et al., 2003).

1.8.5 Family Impact Scale (FIS)

The Family Impact Scale (FIS) was developed as another component of the COHQoL and looks to depict the impact of the child's condition on the family. It considers the effects on family finances, family interactions and the subjective hardship experienced by parents (Locker et al., 2002). Subsequently, it is only included in the P-CPQ due to the sensitive nature of its content (Locker et al., 2002). FIS contains 14 questions and was developed in conjunction with P-CPQ. Four domains were identified during its development; parental and family activities, containing 5 items; parental emotions, containing 4 items; family conflict, containing 4 items; and financial burden, which has 1 item (Locker et al., 2002). The response options for this scale are the same as for P-CPQ (as stated above). Similar to CPQ and P-CPQ, validation has been achieved for paediatric, orthodontic and craniofacial anomaly groups (Barbosa et al., 2009; Locker et al., 2002).

1.8.6 Oral Health Impact Profile (OHIP)

The OHIP was based on the International Classification of Impairments, Disabilities and Handicaps (ICIDH); a manual of disease consequences published by the WHO. OHIP was designed to assess the 'social impact' of oral conditions that cause oral dysfunction, discomfort and disability, with the intention to provide a measure of self-perceived oral health (Locker et al., 2007). Response weighting was based on an expert panel comprised of individuals with a dental background and as such, may not be reflective of patients' priorities (Carr et al.,

2001; Locker et al., 2007). Although OHIP aims to be patient centred, some of the elements of the tool are more suggestive of an expert-centred measure of subjective oral health (Locker et al., 2007). In a 2018 systematic review by Barber et al., OHIP was found to be the most popular measurement tool used for hypodontia (Barber et al., 2018). A child and a short version of OHIP, COHIP and OHIP-14 respectively, also exist.

1.8.7 Child Oral Health Impact Profile (COHIP)

COHIP was designed to assess OHRQoL for children aged between 8-15 years. It was developed and validated by an international study in the USA and Canada in 2007 (Broder et al., 2007). The study reports that COHIP consists of two questionnaires; one for children and one for parents, however the methodology seems to suggest that the same questionnaire was given to both the parent and the child. The development of COHIP was based on Jokovic's methodology for the CPQ and not on the OHIP, as the name suggests. The initial item pool was generated from Jokovic's 2002 study, (Jokovic et al., 2002) with the use of similar health domains and following a similar design protocol. It included the involvement of both clinicians and parents in its development and also the use of impact studies. This differs from the adult OHIP which was based on response weighting by dental professionals.

1.9 Impact of Hypodontia on Oral Health-Related Quality of Life

As well as the physical limitations (poor body temperature control, hearing issues, chewing difficulties, abnormal speech, and skin and eye infections), children with ED may also face emotional, social and behavioural challenges related to their self-image (Kohli et al., 2011; Locker et al., 2005). Severe hypodontia as its own entity, has a substantial impact on oral health-related quality of life (Anweigi et

al., 2013; Kotecha et al., 2013). A 2017 Norwegian adult study reported that those affected by ED and IH had both an increased prevalence and higher levels of anxiety (Saltnes et al., 2017). Using the shortened version of the OHIP (OHIP-14), they also found that these adults had significantly poorer OHRQoL when compared to controls. The poorest OHRQoL scores were observed for those suffering with dry mouth and wearing removable dentures (Saltnes et al., 2017).

Some studies have claimed that there is a higher level of impact on females (Anweigi et al., 2013; Kohli et al., 2011). However, one must consider the risk of reporter bias, as males may be less likely to voice their concerns.

The number and location of missing permanent teeth have not been shown to be a good predictor of OHRQoL (Anweigi et al., 2013; Kotecha et al., 2013). As seen in other areas of OHRQoL, other factors may contribute to the impact such as social-economic status (SES), the home environment, parenting styles, and emotional maturity (Locker, 1992). However, location of missing teeth has been shown to be a good predictor of psychological discomfort (Anweigi et al., 2013). The predominant impact seems to be appearance-related, but it has been suggested that functional impacts may increase with age for both ED and IH individuals (Anweigi et al., 2013; Kohli et al., 2011), with the presence or retention of primary teeth likely moderating the impact of both of these factors (Anweigi et al., 2013). Therefore, whenever possible, it is important to advocate for the retention of primary teeth. Another theory in relation to primary tooth hypodontia, particularly for children with ED, is that older children have had to deal with functional problems over a longer period and may be more conscious of chewing difficulties with more independent food choices and increased social awareness (Kohli et al., 2011).

The functional implications are controversial in the literature. In 1994, Hobkirk et al. conducted a retrospective study of 451 children with hypodontia and found that children were mostly concerned with aesthetics and the spacing between teeth. Functional issues were only noted in 8.7% of patients' complaints, suggesting that functional difficulties are uncommon for patients with severe hypodontia (Hobkirk et al., 1994). Both Wong et al., and Locker et al. used the CPQ to assess OHRQoL for children with severe hypodontia aged 11–15 years (Locker et al., 2010; Wong et al., 2006). In contrast to Hobkirk, they concluded that severe hypodontia did significantly impact on function (Locker et al., 2010; Wong et al., 2006). Anweigi et al. used the Oral Health Impact Profile (OHIP) to assess OHRQoL, for hypodontia patients aged between 16 and 34 years-old and also agreed that there was a significant impact on function (Anweigi et al., 2013). Dueled et al. also found inferior OHIP scores in dentally rehabilitated hypodontia patients when compared to the fully dentate control group (Dueled et al., 2009). However, despite many negative impacts, individuals with severe hypodontia have been shown to have a better OHRQoL when compared to children with oro-facial syndromes, such as cleft lip and palate (Locker et al., 2010).

1.10 Conclusion

When considering hypodontia patterns, the literature on TAC is inconsistent and mainly reports on IH and syndromes, such as cleft-lip and palate, Pierre Robins, Downs syndrome and rarely specifically ED. The majority of TAC studies have concluded that TAC patterns alone, are too heterogeneous in nature. Hypodontia patterns are only part of the picture (phenotype), as both ED and IH are also complicated by numerous other dental anomalies, such as malocclusions, microdontia and taurodontism. Studies that have considered the entire phenotype

have suggested possible distinctive features between syndromic hypodontia (generally including multiple syndromes) and IH. Few studies have compared the specific phenotypic features of ED and severe IH. Therefore, exploring the phenotypic features, could prove more beneficial than comparing hypodontia patterns alone, particularly for the overall management of these conditions. Studies have confirmed the lack of consistency in the management of hypodontia (Filius et al., 2016). Furthermore, there are few studies comparing the QoL in ED and IH, and even fewer report on the parental perceptions (Kohli et al., 2011; Kotecha et al., 2013; Raziee et al., 2019). Parents are the primary decision-makers and therefore their perceptions of their child's QoL will have a major influence on their child's dental management. A better understanding of parent's perceptions on OHRQoL and further knowledge of the dental phenotypes of ED and IH, including hypodontia and other dental anomalies may provide clinicians with a better understanding of these complex conditions and therefore facilitate a more standardised approach to management.

2 AIMS AND HYPOTHESIS

2.1 Aim

The aim of this study is to compare the parental perspectives on OHRQoL impact and dental experience for children with ectodermal dysplasia (ED), severe isolated hypodontia (IH); and age and gender matched control groups and to identify distinctive features which differentiate between IH and ED (both groups to be missing at least 6 permanent teeth).

2.2 Primary Outcome

- Evaluate the parental perception of OHRQoL in patients with ED, IH and age and gender matched control groups and associated variables, using the validated Parental-Caregiver Perceptions Questionnaire (P-CPQ).

2.3 Secondary Outcomes

2.3.1 Comparisons between all groups (ED, IH and control groups):

- Evaluate the family impact in ED, IH and control groups using the validated Family Impact Scale (FIS) questionnaire and overall oral well-being using the global rating and their respective correlation to the P-CPQ score.
- Evaluate the general demographics between all groups.
- Evaluate the clinical and radiographical features.
- Compare variables related to dental experience as reported by the parents, such as age of first dental visit, number of overall dental visits, parental concerns and the child's behaviour among children with ED, IH and control groups.

2.3.2 Comparisons between two groups (ED and IH groups):

- Compare the location, tooth-type and number of missing teeth including total number of clinically missing tooth-units by site in each patient and associated variables between ED and IH.
- Evaluate the pattern of missing teeth using the Tooth Agenesis Code (TAC) analysis between the groups (ED and IH).
- Evaluate the relevant clinical and radiographical features between ED and IH groups (the presence of conical teeth, microdontia, infraocclusion, aesthetic restorations, enamel defects (hypomineralisation/ hypoplasia), taurodontism, denture use and the age of the patient on delivery of first denture).

3 MATERIAL AND METHODS

3.1 Ethical Approval

Tallaght University Hospital / St. James's Hospital Joint Research Ethics Committee (JREC) granted ethical approval for this study (Appendix 1).

3.2 Study Design and Sample Calculation

This cross-sectional study was written in accordance with the guidelines of the 'Strengthening the reporting of observational studies in epidemiology' (STROBE Statement).

G*Power is a stand-alone power analysis program for statistical tests frequently used in social and behavioural research (Erdfelder et al., 1996; Faul et al., 2007). G*Power 3.1 software (Universität Düsseldorf version 3.1.) was used for sample size calculation in this study where comparisons of distributions of counts between three groups (ED, IH, and controls); across 2 categories of a variable were planned using chi-square goodness of fit tests (Faul et al., 2007). Assuming a medium effect related to group, an alpha error rate of 0.05, and power of 0.80; a minimal sample size of 108 (36 in each group) would be necessary. Ideally each of the groups should be of equal size, however the rare prevalence of ED, in particular would make this difficult to achieve.

Patients that attended the clinics of the Dublin Dental University Hospital (DDUH) were invited to participate in the study. Only those who fulfilled the eligibility criteria were included (Tables 3-1 and 3-2) and classified according to their condition: ED, IH and control.

Table 3-1: Inclusion criteria for all groups

Isolated Group	ED Group	Age and Gender Matched Control Groups
Non-syndromic medical history	Confirmed diagnosis of Ectodermal Dysplasia	Healthy and a non-syndromic medical history
Under 18 years of age	Under 18 years of age	Under 18 years of age and age: gender required
Confirmed diagnosis of 6 or more missing permanent teeth (excluding third molars)	Confirmed diagnosis of 6 or more missing permanent teeth (excluding third molars)	Intact primary and permanent dentition (i.e. no missing teeth- excluding third molars)

Table 3-2: Exclusion criteria for all groups.

Isolated Group	ED Group:	Age and Gender- Matched Control Group:
Diagnosis of a syndrome	Unconfirmed diagnosis of ED	Diagnosis of a syndrome
Over 18 years of age	Over 18 years of age	Over 18 years of age or age: gender not required
Fewer than 6 permanent teeth missing	Fewer than 6 teeth missing	Congenitally missing any teeth (excluding third molars)
Inability to provide consent	Inability to provide consent	Inability to provide consent
Incomplete records and decline of invitation for examination	Incomplete records and decline of invitation for examination	Incomplete records and decline of invitation for examination

3.2.1 Recruitment

Phase 1: Ectodermal Dysplasia and Isolated Hypodontia Participants

A gatekeepers was appointed from the DDUH Division 1 administrative department. Eligible candidates attending clinics of the DDUH were invited to participate in this study and given an information pack; containing an invitation letter and an information leaflet as well as consent and assent forms (Appendix

2). If after two weeks, no response was received from the eligible candidates (i.e. no receipt of the consent form) they were then telephoned by the gatekeeper. Informed written consent was obtained from each participant's legal guardian and where applicable an informed written assent or consent (with respect to participants aged 18 years old) was also obtained.

Phase 2: Control Participants

Once the participants with ED and IH had been recruited, a list of required age and gender combinations was formulated. Children attending the DDUH for caries or orthodontic management were included in the study. Children were excluded if they had a significant oral condition such as; a developmental dental disorder (e.g. Amelogenesis imperfecta) or a significant dental trauma (e.g. avulsion, intrusion, lateral luxation, complicated crown fracture, root fracture, particularly if involving the permanent dentition). DDUH staff and students were made aware of the project and reminded on a regular basis throughout the project to create awareness. Written copies of the inclusion and exclusion criteria, the required age and gender combinations and information packs were provided at the beginning of every paediatric and orthodontic clinic, encouraging that, if clinicians came across a patient who they felt may fulfil the inclusion criteria, they asked the patient and their parent if they would be happy to be contacted regarding research and were subsequently provided with information packs. The recruitment process then followed the same protocol as outlined above in Phase 1 (Appendix 3).

3.2.2 Confidentiality

All participants were allocated a unique identifier code and hard copies of all consent forms data collection sheets and iPad were stored in a secure locker in DDUH. All electronic data was password protected on a DDUH desktop.

3.3 Training and Calibration

Two examiners were trained for data collection using a pictorial Microsoft Office PowerPoint presentation (Dr. Emily Crossan and Dr. Shkre Agkhre). The datasheet was piloted on children attending the paediatric dental clinic and subsequently modified based on the feedback prior to commencement of the study to ensure ease of use and accurate recording of required data (Marshall, 2005). A reference table was attached to all datasheets to aid examiners (Appendix 4) and all examinations included extra-oral and intra-oral clinical photographs to ensure reliability and comparability to other studies (Kopycka-Kedzierawski et al., 2007; McLaren et al., 2017; Park et al., 2019; Subbalekshmi et al., 2017).

As a training exercise and to increase reliability between examiners the first 10 individuals were examined twice; once by each of the principal examiners (Dr. Emily Crossan, Dr. Shkre Agkhre). Differences were discussed until a consensus was reached between examiners. Following this, 10 random participants were scored by each examiner and then compared in a Kappa analysis. The following examination outcome variables were included in the Kappa analysis; including skeletal relationship, assessment of LAFH, occlusion, overbite, overjet, presence of crossbite or open bite, the presence of caries, restorations, aesthetic restorations, hypodontia, microdontia, conical morphology, hypomineralisation, hypoplasia, infraocclusion and taurodontism (Appendix 7).

The TAC tool was used in accordance with the instructions provided on the TAC website, with multiple trial excel worksheets constructed to ensure correct excel data format and use of the TAC tool.

3.3.1 Data Collection

Clinical examinations together with any existing clinical records including clinical photographs and radiographs were provided for all participants. This included Orthopantomograms (OPGs) which were utilised to identify patterns of missing teeth and any associated dental abnormalities. All data were recorded on a datasheet and then tabulated in Excel files.

3.3.2 Examinations

A standard full dental assessment, including medical and dental history was provided for each participant and recorded on a coded datasheet (Appendix 4).

Extraoral clinical examination included presence or absence of ED features, such as sparse hair, orthodontic skeletal relationship and assessment of lower anterior face height. Intra-oral clinical examination included orthodontic examination, dental charting with codes for caries, restorations and other dental anomalies such as abnormal shape, hypomineralisation or infraocclusion. Clinical photographs, both extra-oral and intra-oral, were taken for each participant to ensure reliability and as a reference. The diagnosis of hypodontia was made radiographically by the absence of a tooth, tooth bud or calcification and a negative extraction history. A recent OPG (within the last 2 years), was required for radiographic examination. OPG's were available for most participants from pre-existing dental records in the DDUH. OPGs taken in other dental institutes were requested with the patient's legal guardian's permission. Radiographs were

only taken when clinically necessary. No OPGs were taken for control participants.

3.3.3 Collection of Outcome Variables

Dry skin and Eczema

Dry skin was recorded if the skin on the patient's face, neck or hands appeared dry and flaky in conjunction with patient history.

Eczema was recorded if an erythematous rash was noted on the patient's face, neck or hands in conjunction with patient history.

Dry eyes

Dry eyes were recorded if the patient/ parent reported a history of excess or diminished tear-secretion, if they reported dry eyes and / or the need for lubricating eye drops was noted in the patient history.

Sparse hair/ eyebrows and Abnormal nails

Sparse hair or eyebrows and abnormal nails were noted if reported by the patient/ parent during the history. Photos were also taken to compare with textbook images of hypotrichosis and onychodysplasia.

Abnormal sweating

Abnormal sweating was recorded if a history of excess or diminished sweat-secretion was reported by the patient/ parent.

Skeletal Classification

Patients skeletal classification was noted as Class I/ II/ III and determined by assessing facial convexity; straight, convex or concave using zero median

(mentally dropping a true vertical line from the bridge of the nose) (González-Ulloa et al., 1968) and bimanual palpation (Kettle's method) in natural head posture (Cobourne et al., 2010).

Lower Anterior Face Height

Total anterior face height extends from soft tissue nasion to soft tissue menton and the lower anterior face height extends from subnasale to soft tissue menton (Johnston et al., 2005). Lower anterior face height was recorded in this study as normal if assessed to be 50-55% of the total anterior face height and increased or reduced if greater than or less than 50-55% respectively (Johnston et al., 2005).

Molar Occlusion

Molar occlusion was evaluated according to Angles classification, by clinical examination (Cobourne et al., 2010):

- **Class I:** Occlusion of the mesiobuccal cusp of the upper first molar with the buccal groove of the lower first molar.
- **Class II**: Occlusion of the mesiobuccal cusp of the upper first molar anterior to the buccal groove of the lower first molar.
- **Class III:** Occlusion of the mesiobuccal cusp of the upper first molar posterior to the buccal groove of the lower first molar.

Incisor Relationship

Incisor relationship was recorded as per the British Standard's Institute classification (Littlewood et al., 2019):

- **Class I:** Lower incisors occlude with or are immediately below the upper central incisor's cingulum.
- **Class II**: Lower incisor edges are posterior to the upper incisor's cingulum.
    - **Class II, div 1:** Upper incisors are proclined, creating an increased overjet.
    - **Class II, div2:** Upper incisors are retroclined.
- **Class III**: Lower incisor edges are anterior to the upper incisor's cingulum. The overjet may be reversed.

Overjet

Overjet was measured in millimetres with a standard metal examination ruler from the incisal of the most prominent maxillary central incisor to the labial of mandibular central incisors when in full intercuspation (Cobourne et al., 2010).

Overbite

The total height of the mandibular incisors overlapped by the maxillary incisors when in full intercuspation was recorded as a percentage (Cobourne et al., 2010).

Crossbite

A crossbite was noted when there was a "discrepancy in the buccolingual relationship of the upper and lower teeth" (Littlewood et al., 2019).

Anterior Open Bite

An anterior open bite was recorded when there was no vertical overlap of the upper and lower incisors when the teeth were in occlusion (Littlewood et al., 2019).

Hypomineralisation

Hypomineralisation was characterised by a demarcated qualitative defect of the enamel, presenting as an abnormality in translucency, and may be white, yellow or brown in colour (Weerheijm et al., 2001).

Hypoplasia

Hypoplasia was defined as a quantitative enamel defect presenting as pits, grooves or larger areas of reduced enamel thickness (Federation Dentaire International (FDI), 1992; Ghanim et al., 2015).

Caries

Caries was recorded if frank cavitation, with visual caries into dentine was detected in either a primary or permanent tooth ("WHO | World Health Statistics 2013," 2013).

Restorations

A restoration was recorded if one or more permanent restorations as a result of previous caries were noted, without any current caries anywhere on a primary or permanent tooth ("WHO | World Health Statistics 2013," 2013).

Aesthetic Restorations

An aesthetic restoration was recorded if one or more permanent restorations were present as a result of any reason *other than* for the treatment of caries in a primary or permanent tooth, i.e. morphological restoration e.g. restoration of conical or infraoccluded teeth.

Infraocclusion

Infraocclusion was recorded as mild, moderate or severe as per Messer and Cline's classification for both primary and permanent teeth (Messer et al., 1980).

Mild: At least 1mm below the occlusal plane, as judged from the two nearest non-ankylosed teeth in the same quadrant, and above the interproximal contact.

Moderate: Within the occluso-gingival margins of interproximal contact.

Severe: Below the interproximal contact point.

Hypodontia

The diagnosis of hypodontia was made radiographically by the absence of a tooth, tooth bud or calcification development (Aasheim et al., 1993; Bartzela et al., 2013; Chung et al., 2008; Dhamo et al., 2018; Toshiya Endo et al., 2006) and a negative extraction history recorded on the datasheet for permanent teeth only.

Tooth-Site Absences (TSA)

Quadrants were divided up into 7 sites (excluding the 3rd molars). A TSA was recorded if the site contained neither a primary nor permanent tooth (Raziee et al., 2019). If the site contained either a primary or permanent tooth it was recorded as occupied. TSA's were recorded in an attempt to allow for the presence of any retained primary teeth.

Abnormal Crown Morphology

Teeth, both primary and permanent, were recorded as microdont if they were wider cervically than occlusally (Bäckman et al., 2001; Grahnén, 1956; Küchler et al., 2008) and primary or permanent teeth that converged to a point occlusally

were subcategorised as conical (Bergendal, 2014; Prager et al., 2006; Reyes-Reali et al., 2018).

Taurodontism

A taurodont tooth is enlarged vertically, with the pulp chamber extending apically below the cementoenamel junction (CEJ) at the expense of the roots and is diagnosed radiographically (Terezhalmy et al., 2001). In this study, taurodontism was recorded if a fully developed permanent multi-rooted (molar) tooth displayed an enlarged pulp chamber extending apically on the OPG. Specifically, If the length from the lowest point of the occlusal end of the pulp chamber (Point A on Figure 3-1) to the furcation (Point B on Figure 3-1) was greater than or equal to half of the length from the lowest point of the occlusal end of the pulp chamber (Point A on Figure 3-1) to the root apices (Point C on Figure 3-1), the tooth was considered to be taurodontic (AB ≥ half of AC) (Witkop et al., 1988).

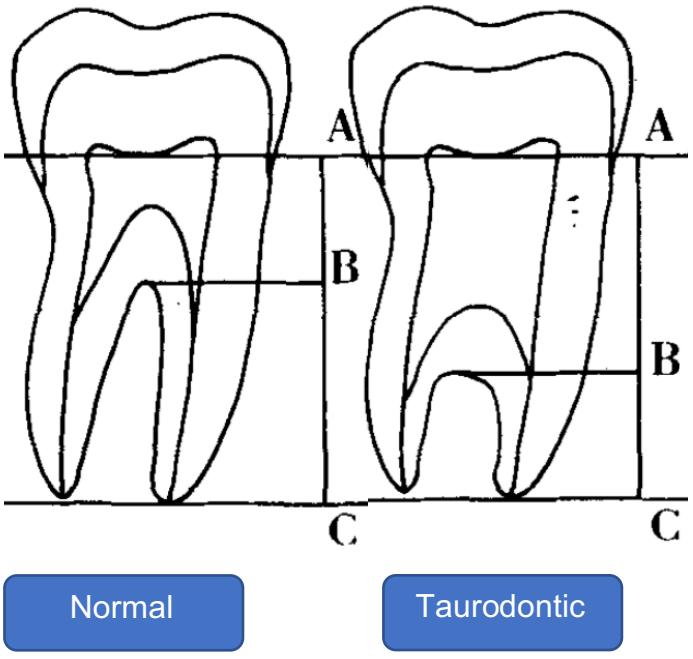


Figure 3-1: Taurodontism

***A** = lowest point of occlusal end of pulp chamber; **B**= furcation level; **C**= root apices (Schalk-Van Der Weide et al., 1993; Witkop et al. 1988).*

TAC analysis

A separate Excel file was created denoting the presence or absence of each tooth, excluding 3rd molars. These files were then uploaded to the TAC data analysis tool website, as per the instructions provided on the website (http://www.toothagenesiscode.com/). The TAC data analysis tool generates the hypodontia patterns present in the sample and the frequency of each pattern by assigning a unique hypodontia code to each pattern.

3.4 Questionnaires

3.4.1 P-CPQ and FIS

The P-CPQ and FIS were utilised to gauge parent's perception of their child's oral health related quality of life (OHRQoL) and the impact on their family (Appendix 5). The P-CPQ contains 33 questions, covering four domains; oral symptoms, functional limitation, emotional well-being and social well-being. FIS has 14 items with four domains; parental and family activities, parental emotions, family conflict, and financial burden. The responses dictate the frequency of each issue; never = 0, once/ twice= 1, sometimes= 2, often= 3, and everyday/ almost every day = 4. A don't know option is also available, as the parent may not be aware of certain circumstances in their child's life or other family members. Each domain is scored individually and then totalled to give an indication of the OHRQL impact.

3.4.2 Specifically Designed Background Questionnaire

A specifically designed background questionnaire was formulated to gain relevant information not captured by the P-CPQ and FIS (Appendix 6). This questionnaire focused on the parent's perception of their child's dental experience to date, including what attributes they value the most when it comes

to their child's dental health and their perception of the number of dental visits their child has attended.

The questionnaire was piloted 3 times and subsequently altered in the paediatric postgraduate clinic of the DDUH to ensure ease of understanding among the general population and accurate collection of the intended data (Marshall, 2005).

3.4.3 Questionnaire Data Collection

All questionnaires including the global rating, P-CPQ, FIS and the specifically designed background questionnaire were transferred to Survey Monkey ™. Parents self-completed all questionnaires on a password protected iPad while their child was being examined. The participants' unique identifying code, age, gender and the relationship of the guardian (e.g. mother or father) were also recorded.

3.5 Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS® for Mac, Version 26.0, SPSS Inc., Chicago, IL, USA). Chi-square or Fisher's Exact analyses were performed, as appropriate, for case (ED/IH)/ control variables and case (ED)/ case (IH) variables. McNemar paired analyses were also performed, as appropriate, for case/ control variables to leverage the study design. The Bonferroni corrected critical p-value of 0.017 for statistical significance was considered to manage the increased probability of making Type I errors from multiple comparisons between the cases and controls for the two conditions, and then between the cases themselves. In analysis of the clinical features between ED and IH, reference groups were altered to allow for all Odds Ratio's to be represented as OR>1 for easier interpretation. For

quantitative variables, following normality testing and interpretation of histograms, it was established that all relevant data were not normally distributed and non-parametric paired and independent samples tests were used as appropriate (e.g. Wilcoxon signed-rank test; Mann-Whitney U test). Spearman correlations were carried out for variables related to global score, P-CPQ and FIS.

4 RESULTS

4.1 General Participant Characteristics

One hundred and seventy-four patients were invited to participate in the study. The majority invited had IH (135) however 73 of these patients declined to participate and 5 were excluded, as they were missing fewer than 6 teeth. Fifty-seven individuals with IH remained and were included in the study (25 females and 32 males, with a mean age of 13.4 years).

Thirty-nine individuals with ED were invited to participate, 6 declined to participate and 4 were excluded as they were missing fewer than 6 teeth. The remaining 29 were included in the study, (9 females and 20 males, with a mean age of 10.5 years). The total sample with complete data was 86 and is summarised in Figure 4-1. Age and gender-matched controls were recruited for each participant and OPG's were not available for 6 control participants. Most participants were Caucasian (83.1%), aged between 4 and 18-years old (mean age: 12.4-years old) (Table 4-1).

A positive family history of ED was only found in the ED group (65.5%; N=19). A positive family history of IH was found in all groups, with the majority represented in the IH (54.4%; N= 31) and ED (31%; N= 9) groups (Table 4-1).

An inter-examiner analysis showed good agreement between examiners with Kappa scores greater than 0.8 for all of the following examination variables, including skeletal relationship, assessment of LAFH, occlusion, overbite, overjet, presence of crossbite or open bite, the presence of caries, restorations, aesthetic restorations, hypodontia, microdontia, conical morphology, hypomineralisation, hypoplasia, infraocclusion and taurodontism (Appendix 7).

Figure 4-1: Distribution of candidates.

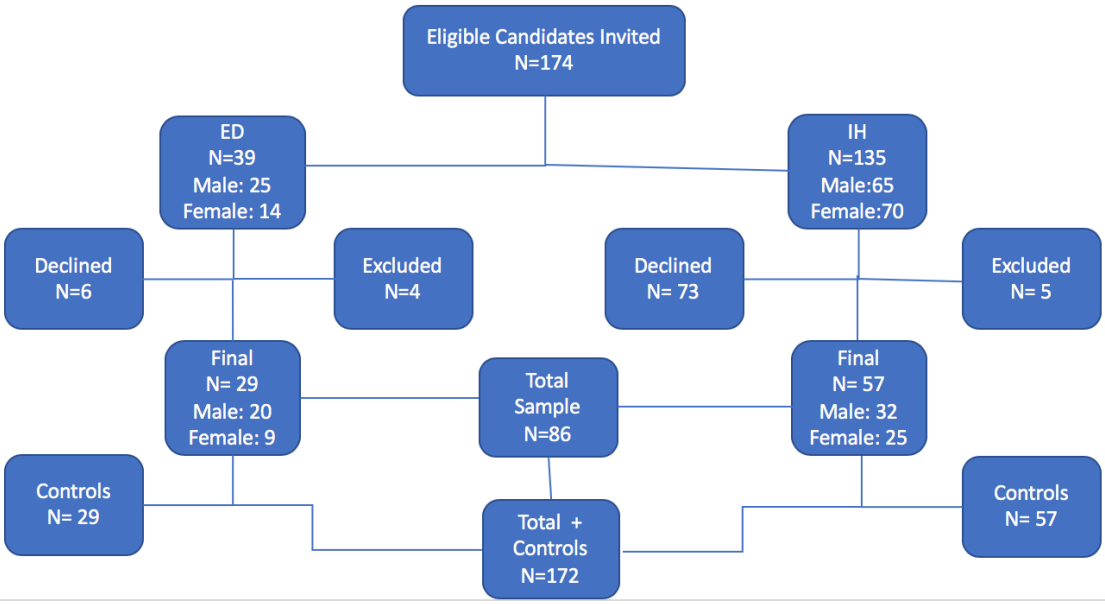


Table 4-1: Prevalence of general sample demographics.

Assessment	ED (29)	ED Controls (29)	IH (57)	IH Controls (57)	Total Sample (172)
Gender N (%)					
Female	9 (31%)	9 (31%)	25 (43.9%)	25 (43.9%)	68 (39.5%)
Male	20 (69%)	20 (69%)	32 (56.1%)	32 (56.1%)	104 (60.5%)
Age (Continuous)					
Mean (SD)	10.45 (3.68)	10.45 (3.68)	13.4 (2.98)	13.4 (2.98)	12.41 (3.49)
Median	11	11	14	14	13
Ethnicity N (%)					
Caucasian	24 (82.8%)	21 (72.4%)	53 (93%)	45 (78.9%)	143 (83.1%)
Other	5 (17.2%)	8 (27.6%)	4 (7%)	12 (21.1%)	29 (16.9%)
p-value	0.345		0.031*		-
Behaviour/ Sensory disorder (ASD, Dyspraxia, etc) N (%)					
No	27 (93.1%)	27 (93.1%)	52 (91.2%)	54 (94.7%)	160 (93%)
Yes	2 (6.9%)	2 (6.9%)	5 (8.8%)	3 (5.3%)	12 (7%)
p-value	1.00		0.716		-
ED Family History N (%)					
No	10 (34.5%)	29 (100%)	57 (100%)	57 (100%)	153 (89%)
Yes	19 (65.5%)	0 (0%)	0 (0%)	0 (0%)	19 (11%)
p-value	<0.001*		-		-
IH Family History N (%)					
No	20 (69%)	28 (96.6%)	26 (45.6%)	53 (93%)	127 (73.8%)
Yes	9 (31%)	1 (3.4%)	31 (54.4%)	4 (7%)	45 (26.2%)
p-value	0.005*		<0.001*		-
Questionnaire completed by N (%)					
Mother	20 (69%)	20 (69%)	45 (78.9%)	39 (68.4%)	124 (72.1%)
Father	9 (31%)	9 (31%)	12 (21.1%)	18 (31.6%)	48 (27.9%)
p-value	1.00		0.202		-
Fisher's Exact *p-value <0.05					

4.2 Clinical Assessment

4.2.1 Clinical Features

The clinical findings are reported in Tables 4-2 and 4-3. The ED group had significantly lower prevalence of caries and of hypomineralisation and far fewer restorations (due to caries) when compared to both the ED controls and the IH group (Tables 4-2 and 4-3). In the current sample, the IH group were 3 times more likely to have caries (OR: 3.00; CI: 1.06-8.47).

In contrast, the ED group showed a significantly higher prevalence of taurodontism, conical morphology and aesthetic restorations when compared to the IH group (Table 4-2). The ED group were almost 57 times more likely to have a conically shaped tooth and 79 times more likely to have a taurodont tooth (OR: 79.33; CI: 9.61-655.01) than the IH group (OR: 56.45; CI: 11.63-274.04) (Table 4-2).

The IH group were shown to have the highest prevalence of infraocclusion, present in 36.8% of the sample, this was statistically significant when compared to the IH controls (Table 4-3), but not in comparison to the ED group (Table 4-2). Infraocclusion was significantly greater in the ED group when compared to their controls (Table 4-3).

Features such as sparse hair and abnormal nails and sweating were only present in the ED group, with the ED group being almost 291 times more likely to present with sparse hair and abnormal sweating (OR: 290.88; CI: 16.087-5259.82) than the IH group (Table 4-2). In contrast, dry skin, eczema, dry eyes and dry mouth were reported in all groups, however with the ED group representing the majority prevalence (Table 4-3).

The ED group were almost 13 times (OR:12.80; CI: 3.96-41.40) more likely to wear a denture than the IH group, with 55.2% of the ED group wearing a denture compared to 8.8% of the IH group and 0% in the control groups (Table 4-2). Of those wearing dentures (n=21), the median age at first denture for the ED group was approximately 4-years old compared to 14-years old in the IH group. Regarding number of dentures, those in the ED group had a median of three dentures overall compared to just one in the IH group (Figures 4-2; 4-3).

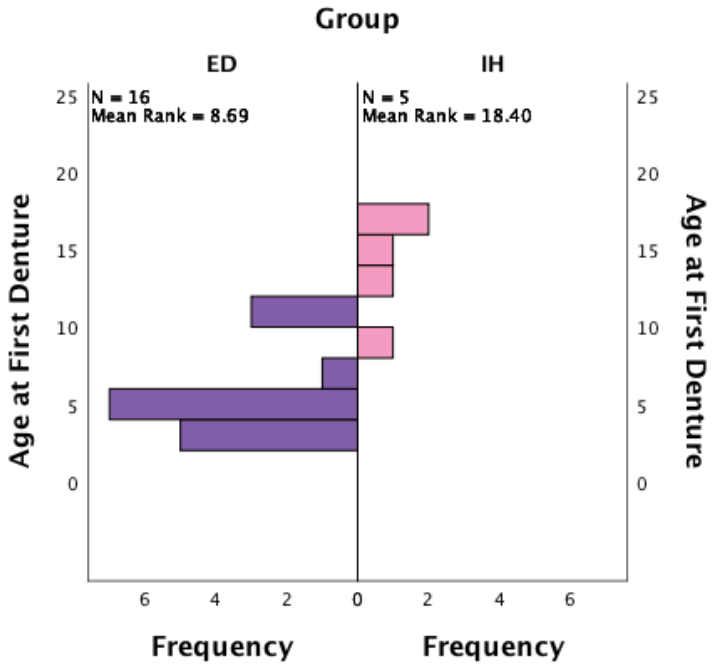


Figure 4-2: Distribution of age at first denture in ED group (purple) and IH group (pink) (Mann-Whitney U test, p-value= 0.002)*

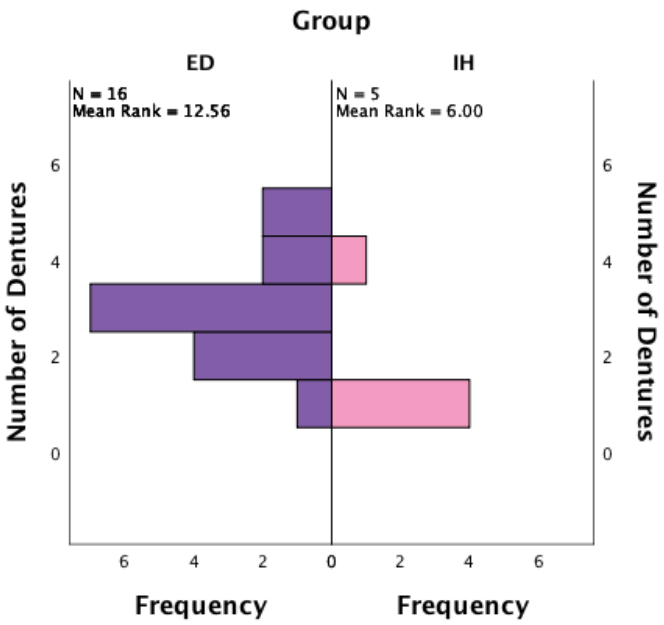


Figure 4-3: Distribution of number of dentures in ED group (purple) and IH group (pink) (Mann-Whitney U test p-value= 0.033)*

Table 4-2: Prevalence of clinical features in ED and IH groups.

Assessment	ED (29)	IH (57)	p-value	OR 95% CI	OR *(Ref)*
Caries N (%) 1º and 2º Teeth					
No	23 (79.3%)	32 (56.1%)			
Yes	6 (20.7%)	25 (43.9%)	0.034*	3.00 (1.06-8.47)	ED
Restorations N (%) 1º and 2º Teeth					
No	21 (72.4%)	29 (50.9%)			
Yes	8 (27.6%)	28 (49.1%)	0.056	2.53 (0.97-6.66)	ED
Microdont N (%) 1º and 2º Teeth					
No	11 (37.9%)	22 (38.6%)			
Yes	18 (62.1%)	35 (61.4%)	0.952	1.03 (0.41-2.58)	IH
Conical N (%)1º and 2º Teeth					
No	2 (6.9%)	46 (80.7%)			
Yes	27 (93.1%)	11 (19.3%)	<0.001**	56.45 (11.63-274.04)	IH
Aesthetic Restorations N (%) 1º and 2º Teeth					
No	10 (34.5%)	50 (87.7%)			
Yes	19 (65.5%)	7 (12.3%)	<0.001**	13.57 (4.51-40.81)	IH
Infraoccluded N (%) Only noted in 1º Teeth					
No	21 (72.4%)	36 (63.2%)			
Yes	8 (27.6%)	21 (36.8%)	0.391	1.53 (0.58-4.01)	ED
Hypomineralised N (%) 1º and 2º Teeth					
No	26 (89.7%)	42 (73.7%)			
Yes	3 (10.3%)	15 (26.3%)	0.085	3.01 (0.82-11.73)	ED
Taurodontism N (%) 2º Molar Teeth only					
No	12 (41.4%)	56 (98.2%)			
Yes	17 (58.6%)	1 (1.8%)	<0.001**	79.33 (9.61-655.01)	IH
Wearing Denture N (%)					
No	13 (44.8%)	52 (91.2%)			
Yes	16 (55.2%)	5 (8.8%)	<0.001**	12.80 (3.96-41.40)	IH
ED Features N (%)					
Dry skin					
No	8 (27.6%)	44 (77.2%			
Yes	21 (72.4%)	13 (22.8%)	<0.001**	8.88 (3.20-24.71)	IH
Eczema					
No	15 (51.7%)	47 (82.5%)			
Yes	14 (48.3%)	10 (17.5%)	0.003**	4.39 (1.62-11.90)	IH
Dry eyes					
No	16 (55.2%)	54 (94.7%)			
Yes	13 (44.8%)	3 (5.3%)	<0.001**	14.63 (3.70-57.77)	IH
Dry mouth					
No	15 (51.7%)	55 (96.5%)			
Yes	14 (48.3%)	2 (3.5%)	<0.001**	25.67 (5.25-125.59)	IH
Sparse hair/ eyebrows					
No	8 (27.6%)	57 (100%)			
Yes	21 (72.4%)	0 (0%)	<0.001**	290.88 (16.087-5259.82)	IH
Abnormal nails					
No	16 (55.2%)	57 (100%)			
Yes	13 (44.8%)	0 (0%)	<0.001**	94.09 (5.31-166	IH
Abnormal sweating					
No	8 (27.6%)	57 (100%)			
Yes	21 (72.4%)	0 (0%)	<0.001**	290.88 (16.087-5259.82)	IH
Fisher's Exact *p-values <0.05 and ***the Bonferroni corrected critical*** ** p-values <0.017 OR = Odds Ratio; CI= Confidence Interval					

Table 4-3: Prevalence of clinical characteristics in ED, IH and Control groups.

Assessment	**ED (29)** N (%)	**ED (29) Controls** N (%)	**IH (57)** N (%)	**IH Controls (57)** N (%)	**Total Sample (172)** N (%)
Caries 1º and 2º Teeth					
No	23 (79.3%)	14 (48.3%)	32 (56.1%)	36 (63.2%)	105 (61%)
Yes	6 (20.7%)	15 (51.7%)	25 (43.9%)	21 (36.8%)	67 (39%)
Fisher's Exact	p= 0.014**		p= 0.445		-
McNemar	p= 0.035*		p= 0.556		-
Restorations 1º and 2º Teeth					
No	21 (72.4%)	15 (51.7%)	29 (50.9%)	28 (49.1%)	93 (54.1%)
Yes	8 (27.6%)	14 (48.3%)	28 (49.1%)	29 (50.9%)	79 (45.9%)
Fisher's Exact	p= 0.104		p= 0.851		-
McNemar	p= 0.180		p= 1.000		-
Microdont 1º and 2º Teeth					
No	11 (37.9%)	28 (96.6%)	22 (38.6%)	51 (89.5%)	112 (65.1%)
Yes	18 (62.1%)	1 (3.4%)	35 (61.4%)	6 (10.5%)	60 (34.5%)
Fisher's Exact	p <0.001**		p <0.001**		-
McNemar	p <0.001**		p <0.001**		-
Infraocclusion Only noted in 1º Teeth					
No	21 (72.4%)	28 (96.6%)	36 (63.2%)	53 (93.0%)	138 (80.2%)
Yes	8 (27.6%)	1 (3.4%)	21 (36.8%)	4 (7%)	34 (19.8%)
Fisher's Exact	p= 0.025*		p <0.001**		-
McNemar	p= 0.039*		p <0.001**		-
Hypomineralisation 1º and 2º Teeth					
No	26 (89.7%)	17 (58.6%)	42 (73.7%)	43 (75.4%)	128 (74.4%)
Yes	3 (10.3%)	12 (41.4%)	15 (26.3%)	14 (24.6%)	44 (25.6%)
Fisher's Exact	p= 0.007**		p= 0.830		-
McNemar	p= 0.022*		p= 1.000		-
Hypoplasia 1º and 2º Teeth					
No	28 (96.6%)	29 (100%)	55 (96.5%)	56 (98.2%)	168 (97.7%)
Yes	1 (3.4%)	0 (0%)	2 (3.5%)	1 (1.8%)	12 (7%)
Fisher's Exact	p= 1.000		p= 1.000		-
McNemar	p= 1.000		p= 1.000		-
Taurodontism 2º Molar Teeth only					
No	12 (41.4%)	24 (82.8%)	56 (98.2%)	50 (87.7%)	142 (82.6%)
Yes	17 (58.6%)	5 (17.2%)	1 (1.8%)	7 (12.3%)	30 (17.4%)
Fisher's Exact	p= 0.001**		p= 0.061		-
McNemar	p= 0.004*		p= 0.070		-
Prevalence of ED Features					
Dry skin					
No	8 (27.6%)	21 (72.4%)	44 (77.2%	39 (68.4%)	112 (65.1%)
Yes	21 (72.4%)	8 (27.6%)	13 (22.8%)	18 (31.6%)	60 (34.9%)
Fisher's Exact	p= 0.001**		p= 0.293		-
McNemar	p= 0.002**		p= 0.405		-
Eczema					
No	15 (51.7%)	23 (79.3%)	47 (82.5%)	47 (82.5%)	132 (76.7%)
Yes	14 (48.3%)	6 (20.7%)	10 (17.5%)	10 (17.5%)	40 (23.3%)
Fisher's Exact	p= 0.027*		p= 1.000		-
McNemar	p= 0.057		p= 1.000		-
Dry eyes					
No	16 (55.2%)	29 (100%)	54 (94.7%)	55 (96.5%)	154 (89.5%)
Yes	13 (44.8%)	0 (0%)	3 (5.3%)	2 (3.5%)	18 (10.5%)
Fisher's Exact	p <0.001**		p= 1.000		-
McNemar	p <0.001**		p= 1.000		-
Dry mouth					
No	15 (51.7%)	29 (100%)	55 (96.5%)	56 (98.2%)	155 (90.1%)
Yes	14 (48.3%)	0 (0%)	2 (3.5%)	1 (1.8%)	17 (9.9%)
Fisher's Exact	p <0.001**		p= 1.000		-
McNemar	p <0.001**		p= 1.000		-

Sparse hair/ eyebrows					
No	8 (27.6%)	29 (100%)	57 (100%)	57 (100%)	151 (87.8%)
Yes	21 (72.4%)	0 (0%)	0 (0%)	0 (0%)	21 (12.2%)
Fisher's Exact	p <0.001**		-		-
McNemar	p <0.001**		-		-
Abnormal nails					
No	16 (55.2%)	29 (100%)	57 (100%)	57 (100%)	159 (92.4%)
Yes	13 (44.8%)	0 (0%)	0 (0%)	0 (0%)	13 (7.6%)
Fisher's Exact	p <0.001**		-		-
McNemar	p <0.001**		-		-
Abnormal sweating					
No	8 (27.6%)	29 (100%)	57 (100%)	57 (100%)	151 (87.8%)
Yes	21 (72.4%)	0 (0%)	0 (0%)	0 (0%)	21 (12.2%)
Fisher's Exact	p <0.001**		-		-
McNemar	p <0.001**		-		-
Total Number of ED Features					
Mean (SD)	4.03 (1.99)	0.48 (0.79)	0.49 (0.83)	0.5 (0.80)	1.11 (1.72)
Median	4	0	0	0	0
Mann Whitney U	p <0.001**		p= 0.601		-
Wilcoxon	p <0.001**		p= 0.684		-
*** p-values <0.05 and ** p-values <0.017**					

4.2.2 Orthodontic Features

The orthodontic findings are reported in Tables 4-4 and 4-5. A normal LAFH (50-55%) was present in most participants in all groups. A reduced LAFH was present more often in the ED group when compared to both IH and control groups (Tables 4-4 and 4-5). The ED group had equal numbers of class 2 and class 3 facial profiles, however the prevalence of class 3 was considerably higher when compared to the prevalence in IH and control groups (Tables 4-4 and 4-5). A class 2 facial profile was the most common in both the IH and control groups, with class 3 being the least common (Table 4-5). Similarly, class 2 incisor and molar relationships were the most common in both the IH and control groups. The ED group had equal number of class 2 and class 3 incisor relationships and much the same numbers for class 2 and class 3 molar relationships (Incisor: N=8:8; Molar: N=10:9; Class 2:3 respectively). The presence of an anterior open-bite and a crossbite were similar in all groups.

Table 4-4: Prevalence of orthodontic features in ED and IH groups

Assessment	**ED (29)** N (%)	**IH (57)** N (%)
Facial Profile		
Class 1	5 (17.2%)	20 (35.1%)
Class 2	12 (41.4%)	21 (36.8%)
Class 3	12 (41.4%)	16 (28.1%)
Chi-Square	p= 0.196	
LAFH		
Normal	20 (69%)	44 (77.2%)
Reduced	8 (27.6%)	2 (3.5%)
Increased	1 (3.4%)	11 (19.3%)
Chi-Square	p= 0.001**	
Incisor Relationship		
Class 1	0 (0%)	9 (15.8%)
Class 2	8 (27.6%)	28 (49.1%)
Class 3	8 (27.6%)	19 (33.3%)
No Incisor Relationship	13 (44.8%)	1 (1.8%)
Chi-Square	p <0.001**	
Molar Relationship		
Class 1	1 (3.4%)	13 (22.8%)
Class 2	10 (34.5%)	27 (47.4%)
Class 3	9 (31%)	12 (21.1%)
No Molar Relationship	9 (31%)	5 (8.8%)
Chi-Square	p= 0.008**	
Anterior Open-bite		
No	23 (79.3%)	53 (93%)
Yes	6 (20.7%)	4 (7%)
Fisher's Exact	p= 0.080	
Crossbite		
No	21 (72.4%)	39 (68.4%)
Yes	8 (27.7%)	18 (31.6%)
Fisher's Exact	p= 0.703	
Overjet		
Mean (SD)	0.59 (1.8)	2 (2.3)
Median	0	2
Mann Whitney U	p <0.001**	
Overbite		
Mean (SD)	9.62 (26.5)	38.7 (42.3)
Median	0	40
Mann Whitney U	p <0.001**	
*** p-values <0.05 and ** p-values <0.017**		

Table 4-5: Prevalence of orthodontic features in ED, IH and control groups.

Assessment	ED (29) N (%)	ED Controls (29) N (%)	IH (57) N (%)	IH Controls (57) N (%)
Facial Profile				
Class 1	5 (17.2%)	7 (24.1%)	20 (35.1%)	22 (38.6%)
Class 2	12 (41.4%)	19 (65.5%)	21 (36.8%)	26 (45.6%)
Class 3	12 (41.4%)	3 (10.3%)	16 (28.1%)	9 (15.8%)
Chi-Square	p= 0.026*		p= 0.274	
LAFH				
Normal	20 (69%)	16 (55.2%)	44 (77.2%)	38 (66.7%)
Reduced	8 (27.6%)	3 (10.3%)	2 (3.5%)	1 (1.8%)
Increased	1 (3.4%)	10 (34.5%)	11 (19.3%)	18 (31.6%)
Chi-Square	p= 0.006**		p= 0.391	
Incisor Relationship				
Class 1	0 (0%)	7 (24.1%)	9 (15.8%)	15 (26.3%)
Class 2	8 (27.6%)	18 (62.1%)	28 (49.1%)	36 (63.2%)
Class 3	8 (27.6%)	3 (10.3%)	19 (33.3%)	6 (10.5%)
No Incisor Relationship	13 (44.8%)	1 (3.4%)	1 (1.8%)	0 (0%)
Chi-Square	p <0.001**		p= 0.009**	
Molar Relationship				
Class 1	1 (3.4%)	11 (37.9%)	13 (22.8%)	24 (42.1%)
Class 2	10 (34.5%)	17 (58.6%)	27 (47.4%)	26 (45.6%)
Class 3	9 (31%)	1 (3.4%)	12 (21.1%)	7 (12.3%)
No Molar Relationship	9 (31%)	0 (0%)	5 (8.8%)	0 (0%)
Chi-Square	p <0.001**		p= 0.019*	
Anterior Open-bite				
No	23 (79.3%)	26 (89.7%)	53 (93%)	55 (96.5%)
Yes	6 (20.7%)	3 (10.3%)	4 (7%)	2 (3.5%)
Fisher's Exact	p= 0.470		p= 0.679	
Crossbite				
No	21 (72.4%)	23 (79.3%)	39 (68.4%)	40 (70.2%)
Yes	8 (27.7%)	6 (20.7%)	18 (31.6%)	17 (29.8%)
Fisher's Exact	p= 0.539		p= 0.839	
Overjet mm				
Mean (SD)	0.59 (1.8)	4.28 (3.0)	2 (2.3)	3.61 (2.51)
Median	0	4	2	3
Mann Whitney U	p <0.001**		p= 0.006**	
Overbite %				
Mean (SD)	9.62 (26.5)	38.79 (33.7)	38.7 (42.3)	37.21 (31.8)
Median	0	30	40	30
Mann Whitney U	p <0.001**		p= 0.785	
*** p-values <0.05 and ** p-values <0.017**				

4.3 Hypodontia

There was a total of 1194 missing permanent teeth in the IH and ED groups, combined (N= 86) (Table 4-6). The distribution of missing permanent teeth was similar from right to left, with generally larger differences between the maxillary and mandibular arches. The second premolars were the most commonly missing teeth, missing in 93% of participants and with similar distributions in all quadrants (Max: 80.8%; Mand: 76.7%; UR: 82.6%; UL: 79.1%; LR:77.9%; LL:75.6%). The next most commonly absent teeth were the maxillary first premolars (Max: 67.4%; UR: 66.3%; UL:68.6 %) and the maxillary lateral incisors (Max: 67.4%; UR: 68.6%; UL: 66.3%), with equal frequency (Table 4-6).

Table 4-6: Distribution of missing permanent teeth across the maxillary and mandibular arches according to tooth type in all participants, N=86.

Tooth	**Maxillary** N(%)	**Mandibular** N(%)	**Total** N
Central Incisor	19 (11.0%)	103 (59.9%)	122
Lateral incisor	116 (67.4%)	85 (49.4%)	201
Canine	36 (43.6%)	54 (31.4%)	129
First Premolar	116 (67.4%)	89 (51.7%)	205
Second Premolar	139 (80.8%)	132 (76.7%)	271
First Molar	65 (37.8%)	50 (29.1%)	115
Second Molar	73 (42.4%)	78 (45.3%)	151

4.3.1 IH Group

The total number of missing permanent teeth in the IH group was 609, with a maximum of 23 and a minimum of 6 missing teeth. There was an average of 10.68 (s.d.= 4.41) missing permanent teeth, with 75.4% of the IH group missing between 6 and 11 teeth (Figure 4-4).

The second premolars were by far the most commonly missing, absent in 95% (N=54) of the participants in the IH group (UR: 80.7%; UL: 77.2%; LR: 75.4%; LL: 75.4%), followed by the maxillary first premolars (UR: 61.4%; UL: 59.6%) and the maxillary lateral incisors (UR: 51.38%; UL: 50.8%). The IH group had hypodontia of the anterior teeth in 77%, which on average affected 30% of the anterior teeth. The maxillary central incisors were not missing in any participants in the IH group (Table 4-7).

4.3.2 ED Group

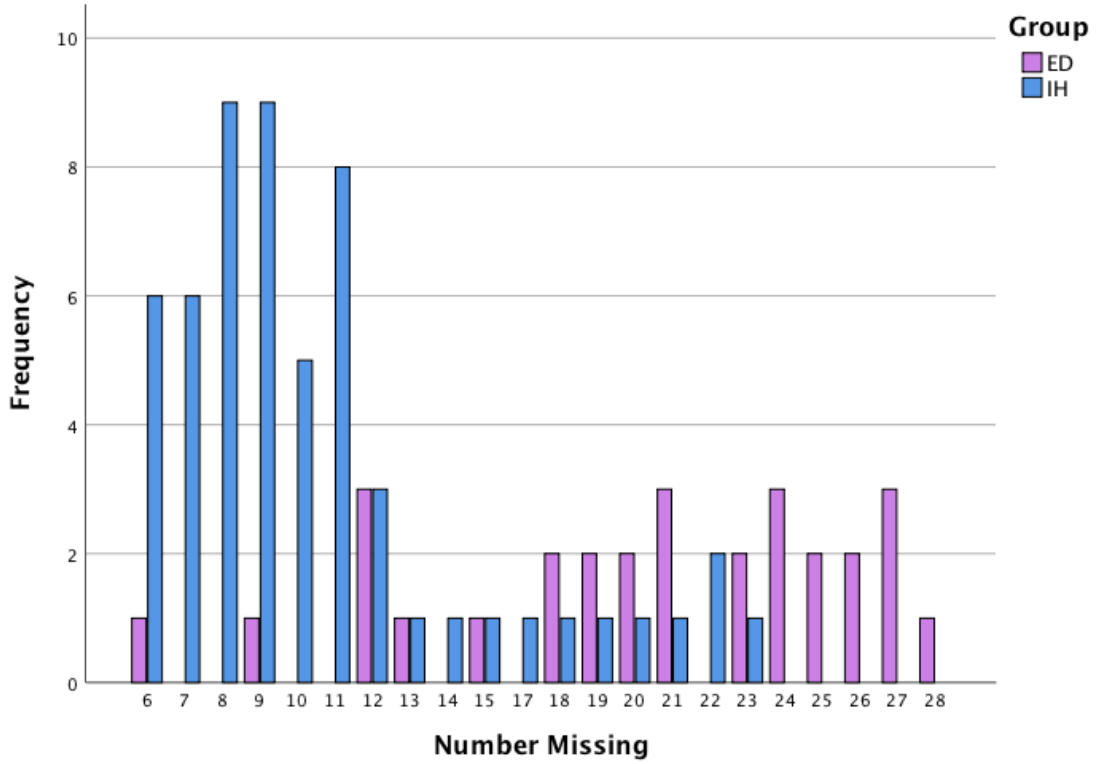
The total number of missing teeth in the ED group was 585, with a maximum of 28 and a minimum of 6 missing teeth. There was an average of 20.17 (s.d.= 5.85) missing teeth with 72% of participants in the ED group having between 6 and 24 missing teeth (Figure 4-4).

The lower central incisors were the most commonly missing in the ED group and were missing for all participants (Mand: 100%; LR: 100%; LL: 100%), followed by the maxillary lateral incisors missing in all but one participant (Max: 96.6%; UR: 96.5%; UL: 96.5%) and then the mandibular lateral incisors (Mand: 87.9%; LR: 89.7%; LL: 86.2%), the second premolars (Max: 84.5%; Mand: 79.3%; UR: 86.2%; UL: 82.8%; LR: 82.8%; LL: 75.9%), first premolars (Max: 81.0%; Mand: 75.9%; UR: 75.9%; UL: 86.2%; LR: 79.3%; LL: 72.4%) and the second molars (Max: 77.6%; Mand: 69.0%; UR: 79.3%; UL: 75.9%; LR: 65.5%; LL: 72.4%). All tooth-types were affected by hypodontia in the ED group, with the maxillary central incisors being the least common, missing in n=19 (10 right; 9 left)(32.8%). The ED group had hypodontia of the anterior teeth in 100%, which on average affected 48% of the anterior teeth.

Table 4-7: Distribution of missing permanent teeth across the maxillary and mandibular arches according to tooth type in IH and ED groups.

Tooth	IH Maxillary N(% n/114 x100)	ED Maxillary N(%n/58x100)	IH Mandibular N(%n/114 x100)	ED Mandibular N(%n/58x100)
Central Incisor	0 (0%)	19 (32.8%)	22 (38.6%)	58 (100%)
Lateral incisor	60 (52.6%)	56 (96.6%)	34 (29.8%)	51 (87.9%)
Canine	39 (34.2%)	36 (62.1 %)	20 (17.5%)	34 (58.6%)
First Premolar	69 (60.5%)	47 (81.0%)	45 (39.5%)	44 (75.9%)
Second Premolar	90 (78.9%)	49 (84.5 %)	86 (75.4%)	46 (79.3%)
First Molar	34 (29.8%)	31 (53.4%)	21 (18.4%)	29 (50.0%)
Second Molar	28 (24.6%)	45 (77.6%)	38 (33.3%)	40 (69.0%)

Figure 4-4: Frequency of a given number of missing permanent teeth.



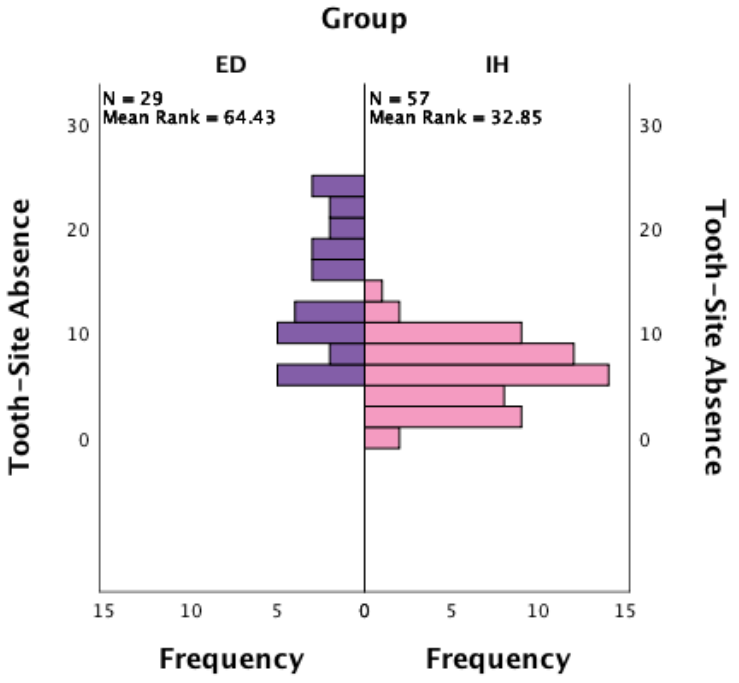
4.3.3 Tooth-Site Absences (TSA)

The median number of tooth-site absences, total number of missing teeth and total number of anterior missing teeth were all significantly greater in the ED group when compared to the IH group (Table 4-8). The distribution of TSA's is depicted in Figure 4-5 and clearly demonstrates the disparity between the groups.

Table 4-8: Descriptive analysis of hypodontia related variables in ED and IH groups.

Group	ED (29)	IH (57)	Mann Whitney U
Tooth-site absences			
Mean (SD)	13.41 (5.97)	5.77 (3.11)	p <0.001*
Median	11	6	
Total missing teeth			
Mean (SD)	20.17 (5.96)	10.68 (4.45)	p <0.001*
Median	21	9	
Anterior missing teeth			
Mean (SD)	8.76 (2.79)	3.47 (3.33)	p<0.001*
Median	9	2	

Figure 4-5: Frequency of the tooth-site absences in ED and IH groups.



Dentures

Descriptive analysis of variables related to wearing a denture are displayed in Table 4-9. There was a similar distribution of denture wearers in both genders (Females: 20.6%; Males: 26.9%). For those wearing dentures in the IH group, there was a median number of 9 TSA's compared to 17.5 in the ED group and 16 overall. A minimum of 8 TSA's for those wearing a denture was found.

Table 4-9: Variables related to wearing a denture.

	No denture	Tooth-site absences (TSA)		Wearing a denture	Tooth-site absences (TSA)		Range
Group	**N (%)**	Mean (SD)	Median	**N (%)**	Mean (SD)	Median	
IH	52 (91.2%)	5.42 (3.02)	6	5 (8.8%)	9.40 (1.14)	9	8-11
ED	13 (44.8%)	8.92 (3.50)	8	16 (55.2%)	17.06 (5.01)	17.5	9-23
All	65 (75.6%)	6.12 (3.40)	6	21 (24.4%)	15.24 (5.50)	16	8-23
Gender							
Female	27 (79.4%)	6.04 (2.81)	6	7 (20.6%)	9.43 (0.79)	10	8-10
Male	38 (73.1%)	6.18 (3.80)	6	14 (26.9%)	18.14 (4.37)	18.5	9-23

4.3.4 IH TAC

Quadrant 1 (UR) had 24 unique patterns; quadrant 2 (UL) had 26 unique patterns; quadrant 3 (LL) had 29 unique patterns; and quadrant 4 (LR) had 28 unique patterns. There were 37 unique patterns in the maxilla, 43 unique patterns in the mandible and 54 unique patterns in the entire dentition overall. The most common maxillary and mandibular patterns are displayed in figures 4-6 and 4-7, with the blank spaces representing hypodontia of the relevant teeth.

Figure 4-6: First most common IH TAC patterns per arch.

Index	TAC = q1.q2	Freq.	e17	e16	e15	e14	e13	e12	e11	e21	e22	e23	e24	e25	e26	e27
1	24.24	6														

Index	TAC = q4.q3	Freq.	e47	e46	e45	e44	e43	e42	e41	e31	e32	e33	e34	e35	e36	e37
1	24.24	6														

Figure 4-7: Second most common IH TAC patterns per arch.

Index	TAC = q1.q2	Freq.	e17	e16	e15	e14	e13	e12	e11	e21	e22	e23	e24	e25	e26	e27
2	112.112	5														

Index	TAC = q4.q3	Freq.	e47	e46	e45	e44	e43	e42	e41	e31	e32	e33	e34	e35	e36	e37
2	16.16	4														

4.3.5 ED TAC

Quadrant 1 (UR) had 16 unique patterns quadrant 2 (UL) had 18 unique patterns, quadrant 3 (LL) had 17 unique patterns and quadrant 4 (LR) had 16 unique patterns. There were 25 unique patterns in the maxilla, 20 unique patterns in the mandible and 29 unique patterns in the entire dentition overall. The most common maxillary and mandibular patterns are displayed in figures 4-8 and 4-9 with the blank spaces representing hypodontia of the relevant teeth.

Figure 4-8: First most common ED TAC patterns per arch.

Index	TAC = q1.q2	Freq.	e17	e16	e15	e14	e13	e12	e11	e21	e22	e23	e24	e25	e26	e27
1	94.94	3														

Index	TAC = q4.q3	Freq.	e47	e46	e45	e44	e43	e42	e41	e31	e32	e33	e34	e35	e36	e37
1	127.127	7														

Figure 4-9: Second most common ED TAC patterns per arch.

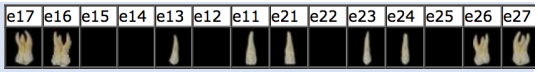
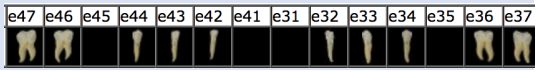
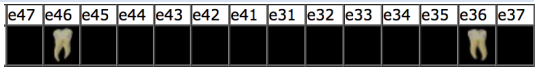
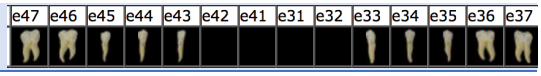
Index	TAC = q1.q2	Freq.	e17	e16	e15	e14	e13	e12	e11	e21	e22	e23	e24	e25	e26	e27
2	127.127	2														

Index	TAC = q4.q3	Freq.	e47	e46	e45	e44	e43	e42	e41	e31	e32	e33	e34	e35	e36	e37
2	123.123	2														

4.3.6 Common Patterns

The TAC tool does not allow differentiation between different patient groups and therefore comparison of common TAC patterns between ED and IH was conducted manually, with three patterns that occurred in both the ED and IH groups displayed in Table 4-10. These patterns mostly occurred just once in each group. There were no common patterns between ED and IH groups when comparing the entire dentitions.

Table 4-10: Three TAC patterns that were common to both ED and IH groups.

Location	TAC	Frequency		Missing Teeth (FDI)	Illustrations of TAC
		ED	**IH**		
Maxillary TAC	2.2	1	1	12, 22	
	26.18	1	1	15, 14, 12, 22, 25	
	94.94	3	1	17, 15, 14, 13, 12, 22, 23, 24, 25, 27	
Mandibular TAC	17.17	1	1	45, 41, 31, 35	
	95.95	2	1	47, 45, 44, 43, 42, 41, 31, 32, 33, 34, 35, 37	
	3.3	1	1	42, 41, 31, 32	

4.4 P-CPQ Questionnaire Results

4.4.1 Results for ED, IH and Control groups

The majority of all questionnaires were completed by mothers (Table 4-1). The paired and unpaired analyses of the mean global scores and the mean P-CPQ scores are displayed in Tables 4-11, 4-12; and 4-13, 4-14, respectively. A higher score in global rating and P-CPQ correlates overall to a poorer QoL. Following normality tests and inspection of histograms, it was established that the global

rating, P-CPQ and FIS data were not normally distributed. Multiple transformations were attempted to produce a more normal distribution of the score data. However, these transformations were unsuccessful and nonparametric tests were used for data analysis. The ED group scored the highest in the global rating and in P-CPQ across the board, followed by the IH group, with the controls scoring the lowest in all categories. Nonparametric paired sample tests between ED cases and their matched controls, to account for age and gender confounding, revealed statistically significant differences ($p<0.05$) in all global and P-CPQ scores.

Nonparametric paired sample tests between IH cases and their matched controls, to account for age and gender confounding, revealed statistically significant differences ($p<0.05$) in global rating and in emotional well-being and social well-being in the P-CPQ. Statistically significant differences were not evident in oral symptoms or functional limitations.

When compared to IH, the ED group had a slightly higher mean score in the global rating, however this was not statistically significant. For the P-CPQ, when the ED group was compared to the IH group, the only significant difference was for functional limitations. The P-CPQ mean scores in relation to a family history of IH were consistently higher across all domains with a positive family history, however these differences were only significant for social well-being and the overall total score. P-CPQ mean scores in relation to a family history of ED for the ED group, given that this was the only group with a positive history, showed consistently lower mean scores across all domains with a positive family history, however these differences were not statistically significant.

Table 4-11: Descriptive paired analysis of mean Global Scores for all groups.

Variables	**Global Scores** Min-Max	**Global Scores** Mean (SD)	**Global Scores** Median	**p-value**
ED Group				Wilcoxon
ED Control (29)	2-7	4.34 (1.29)	4	
ED (29)	2-10	5.97 (1.90)	6	0.005**
IH Group				Wilcoxon
IH Controls (57)	2-9	4.70 (1.93)	4	
IH (57)	2-10	5.58 (2.00)	6	0.015**
*p<0.05; ** p<0.017				

Table 4-12: Descriptive unpaired analysis of mean Global scores.

Variables	**Global Scores** Min-Max	**Global Scores** Mean (SD)	**Global Scores** Median	**p-value**
ED and IH Groups				Mann Whiney U
IH (57)	2-10	5.58 (2.00)	6	0.575
ED (29)	2-10	5.97 (1.90)	6	
Family History of Hypodontia				Mann Whiney U
No (127)	2-10	5.10 (1.92)	5	0.521
Yes (45)	2-9	5.27 (1.99)	5	
Family History of ED				Mann Whiney U
No (153)	2-10	5.07(1.94)	5	0.152
Yes (19)	2-9	5.74 (1.82)	6	
*p<0.05; ** p<0.017				

Table 4-13: Descriptive paired analysis of mean P-CPQ scores for all groups.

Variables	**Oral Symptoms** Mean (SD)	**Functional Limitations** Mean (SD)	**Emotional Well-being** Mean (SD)	**Social Well-being** Mean (SD)	**Total P-CPQ** Mean (SD)
ED Group					
Control (29)	3.07 (2.90)	3.28 (5.30)	1.86 (3.56)	2.41 (4.71)	10.62 (14.28)
ED (29)	5.45 (4.63)	11.79 (7.71)	8.0 (9.08)	7.93 (9.76)	33.17 (28.46)
Wilcoxon	p=0.025*	p <0.001**	p=0.002**	p=0.002**	p <0.001**
IH Group					
Control (57)	4.02 (3.43)	3.49 (4.51)	3.04 (4.26)	3.75 (4.97)	14.30 (14.47)
IH (57)	4.18 (3.80)	5.39 (6.07)	7.02 (8.31)	6.74 (7.30)	28.89 (22.37)
Wilcoxon	p=0.867	p=0.123	p=0.008**	p=0.006**	p <0.001**
*p<0.05; ** p<0.017					

Table 4-14: Descriptive unpaired analysis of mean P-CPQ scores.

Variables	Oral Symptoms Mean (SD)	Functional Limitations Mean (SD)	Emotional Well-being Mean (SD)	Social Well-being Mean (SD)	Total P-CPQ Mean (SD)
ED and IH Groups					
IH (57)	4.18 (3.80)	5.39 (6.07)	7.02 (8.31)	6.74 (7.30)	28.89 (22.37)
ED (29)	5.45 (4.63)	11.79 (7.71)	8.0 (9.08)	7.93 (9.76)	33.17 (28.46)
Mann Whiney U	p= 0.143	p <0.001**	p=0.561	p=0.822	p=0.528
Wearing a denture					
No (151)	4.10 (3.74)	4.86 (6.07)	4.84 (7.21)	5.16 (7.06)	21.05 (22.04)
Yes (21)	4.53 (3.78)	10.53 (7.58)	6.21 (5.87)	5.68 (6.50)	26.95 (19.98)
Mann Whiney U	p=0.027*	p <0.001**	p=0.079	p=0.188	p=0.017**
IH Family History					
No (127)	4.18 (3.80)	5.39 (6.07)	7.02 (8.31)	6.74 (7.30)	28.89 (22.37)
Yes (45)	5.45 (4.63)	11.79 (7.71)	8.0 (9.08)	7.93 (9.76)	33.17 (28.46)
Mann Whiney U	p=0.226	p=0.397	p=0.198	p=0.015**	p=0.049*
ED Family History in ED group only					
No (10)	7.20 (5.75)	14.20 (7.76)	11.40 (12.96)	12.20 (13.44)	45.00 (38.54)
Yes (19)	4.53 (3.78)	10.53 (7.58)	6.21 (5.87)	5.68 (6.50)	26.95 (19.98)
Mann Whiney U	p= 0.138	p=0.308	p=0.573	p=0.247	p=0.377
*p<0.05; ** p<0.017					

Correlations between P-CPQ and hypodontia-related variables

Spearman correlations between P-CPQ mean scores and hypodontia-related variables, displayed in Tables 4-15 to 4-18, revealed at best weak correlations. The IH group had the only statistically significant results. They showed weak correlations for functional limitations, emotional and social well-being and overall total P-CPQ scores in all considered hypodontia-related variables; missing anterior teeth, total missing teeth, TSA's and wearing a denture.

Table 4-15: Correlations between P-CPQ and Missing Anterior Teeth

	Oral Symptoms		Functional Limitations		Emotional Well-being		Social Well-being		Total P-CPQ	
Group	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value
ED	-0.067	0.730	0.134	0.489	-0.141	0.466	-0.061	0.754	-0.024	0.901
IH	0.204	0.127	0.296	0.025*	0.329	0.013*	0.334	0.011*	0.374	0.004*

R_s = Spearman's rho; *p<0.05

Table 4-16: Correlations between P-CPQ and Total Missing Teeth

	Oral Symptoms		Functional Limitations		Emotional Well-being		Social Well-being		Total P-CPQ	
Group	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value
ED	-0.026	0.895	0.185	0.337	-0.102	0.597	0.015	0.938	0.124	0.523
IH	0.067	0.622	0.321	0.015*	0.334	0.011*	0.318	0.016*	0.322	0.012*

R_s = Spearman's rho; *p<0.05

Table 4-17: Correlations between P-CPQ and TSA's

	Oral Symptoms		Functional Limitations		Emotional Well-being		Social Well-being		Total P-CPQ	
Group	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value
ED	0.247	0.196	0.342	0.070	0.038	0.846	0.021	0.914	0.272	0.154
IH	0.166	0.217	0.301	0.023*	0.272*	0.041*	0.297	0.025*	0.345	0.009*

R_s = Spearman's rho; *p<0.05

Table 4-18: Correlations between P-CPQ and wearing a denture

	Oral Symptoms		Functional Limitations		Emotional Well-being		Social Well-being		Total P-CPQ	
Group	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value
ED	0.175	0.363	0.208	0.280	0.000	1.000	-0.071	0.714	0.133	0.493
IH	0.211	0.116	0.238	0.074	0.367	0.005*	0.356	0.007*	0.379	0.004*

R_s = Spearman's rho; *p<0.05

Correlations between P-CPQ and age

A moderate correlation of R_s = 0.449 (p<0.001*) was found for the IH group between increasing age and oral symptoms (Table 4-19). No other statistically significant correlations were found.

Table 4-19: Correlations between P-CPQ and age

	Oral Symptoms		Functional Limitations		Emotional Well-being		Social Well-being		Total P-CPQ	
Group	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value
IH age	0.449	<0.001*	0.148	0.270	0.189	0.160	0.061	0.655	0.230	0.085
ED age	0.199	0.301	0.143	0.458	0.202	0.295	0.211	0.273	0.251	0.189

R_s = Spearman's rho; *p<0.05

Correlations between P-CPQ and gender

Statistically significant moderate correlations were found for the ED group between males and oral symptoms; R_s = 0.444 (p=0.016*), functional limitations; R_s = 0.576 (p=0.001*), and total overall score; R_s = 0.499 (p= 0.006*) (Table 4-20). For the IH group, there were weak correlations between being female and all domains except for functional limitations. However, none of these correlations reached statistical significance.

Table 4-20: Correlations between P-CPQ and gender

	Oral Symptoms		Functional Limitations		Emotional Well-being		Social Well-being		Total P-CPQ	
Group	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value	R_s	p-value
IH gender	-0.254	0.056	0.010	0.942	-0.119	0.380	-0.119	0.379	-0.088	0.514
ED gender	0.444	0.016*	0.576	0.001*	0.292	0.124	0.359	0.055	0.499	0.006*

R_s = Spearman's rho; *p<0.05
Negative correlation = females
Positive correlation = males

4.4.2 FIS Results

The mean FIS scores for ED, IH and respective controls are displayed in Table 4-21 to 4-22. Similar to the P-CPQ scores, the ED group scored the highest in FIS in all categories, followed by the IH group, with the controls scoring the lowest overall. Nonparametric paired sample tests between ED cases and their matched controls, to account for age and gender confounding, revealed statistically significant differences ($p<0.05$) in all FIS scores. However, for the IH and their control group and the IH compared to ED group the only significant differences were for parental emotional well-being and the total FIS score. Statistically significant differences were not evident in family activities, family conflict, and financial burden scores.

A family history of IH showed significant differences for parental emotional well-being. However, a family history of ED failed to reach any statistical significance when considering the ED group, which was the only group with a positive family history of ED.

Table 4-21: Descriptive paired analysis of mean FIS scores for all groups.

Variables	**Activities** Mean (SD)	**Emotional** Mean (SD)	**Conflict** Mean (SD)	**Financial** Mean (SD)	**Total** FIS Mean (SD)
ED Group					
Control (29)	2.72 (3.52)	0.52 (1.30)	0.72 (1.58)	0.17 (0.468)	4.14 (5.91)
ED (29)	6.07 (4.94)	3.41 (2.53)	2.62 (2.95)	0.83 (1.00)	12.93 (10.38)
Wilcoxon	p= 0.006**	p<0.001**	p= 0.006**	p= 0.004**	p<0.001**
IH Group					
Control (57)	2.44 (2.57)	0.35 (0.61)	1.11 (2.09)	0.37 (0.79)	4.16 (5.10)
IH (57)	3.89 (3.77)	1.49 (1.79)	1.56 (2.11)	0.44 (0.78)	7.39 (6.85)
Wilcoxon	p= 0.053	p<0.001**	p= 0.173	p= 0.640	p= 0.009**
*p<0.05; ** p<0.017					

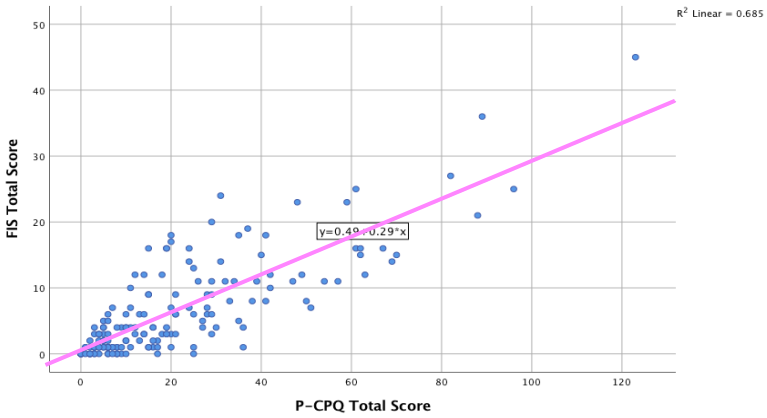
Table 4-22: Descriptive unpaired analysis of mean FIS scores.

Variables	**Activities** Mean (SD)	**Emotional** Mean (SD)	**Conflict** Mean (SD)	**Financial** Mean (SD)	**Total** FIS Mean (SD)
ED and IH Groups					
IH (57)	3.89 (3.77)	1.49 (1.79)	1.56 (2.11)	0.44 (0.78)	7.39 (6.85)
ED (29)	6.07 (4.94)	3.41 (2.53)	2.62 (2.95)	0.83 (1.00)	12.93 (10.38)
Mann Whiney U	p= 0.056	<0.001**	p= 0.062	p= 0.053	p= 0.009**
Family History of IH					
No	3.48 (4.01)	1.09 (1.92)	1.48 (2.39)	0.46 (0.83)	6.51 (8.02)
Yes	3.87 (3.18)	1.64 (1.93)	1.36 (1.84)	0.38 (0.72)	7.24 (6.14)
Mann Whiney U	p= 0.113	p= 0.030*	p= 0.795	p= 0.660	p= 0.093
Family History of ED in ED group only					
No	7.10 (6.56)	4.20 (3.62)	4.10 (2.30)	1.00 (1.16)	16.40 (14.49)
Yes	5.53 (3.95)	3.00 (1.70)	1.84 (1.83)	0.74 (0.93)	11.11 (7.23)
Mann Whiney U	p= 0.769	p= 0.735	p= 0.138	p= 0.573	p= 0.636
*p<0.05; ** p<0.017					

Correlation between P-CPQ and FIS

Scores from the P-CPQ and FIS overall were strongly correlated, with R_s = 0.789; <0.001*, correlation between the QoL instruments, as depicted in Figure 4-10.

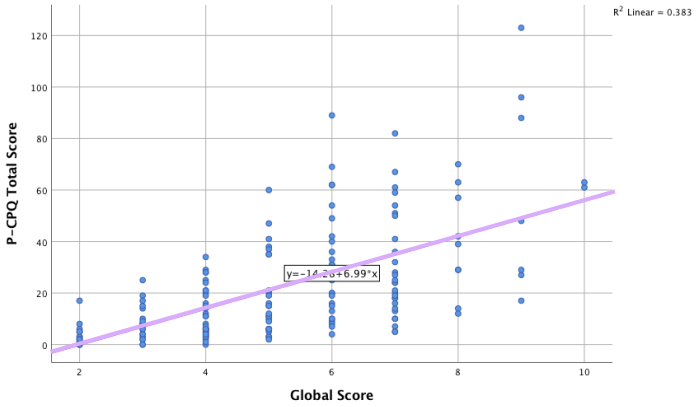
Figure 4-10: Dot-plot correlation between P-CPQ and FIS.



Correlation between P-CPQ and Global Rating

Scores from the P-CPQ and global rating overall were also moderate-strongly correlated with R_s = 0.663; <0.001*, correlation between the QoL tools, as displayed in Figure 4-11.

Figure 4-11: Dot-plot correlation between global scores and P-CPQ.



"Don't Know" (DK) Responses in P-CPQ

Overall, parents used the "Don't Know" (DK) response to answer 4.4% of the P-CPQ and FIS questions. This increased to 5.6% when FIS responses were excluded. Both the ED and IH groups had higher numbers of DK responses, 7.5% and 9.7% respectively, when compared to controls (2.2%) (Table 4-23).

Table 4-23: "Don't Know" responses for P-CPQ and FIS.

Features	Controls (86) N	ED (29) N	IH (57) N	Total (172) N
P-CPQ				
Oral Symptoms	24	3	19	46
Function	15	12	35	62
Emotional	9	14	39	62
Social	15	43	89	147
P-CPQ Total	63	72	182	317
% of Total P-CPQ Questions	2.2%	7.5%	9.7%	5.6%
FIS				
FIS Total	10	9	19	38
P-CPQ + FIS	73	81	201	355
% of Total P-CPQ + FIS Questions	1.8%	5.9%	7.5%	4.4%

4.5 Specifically Designed Background Questionnaire

The specially designed questionnaire results are detailed in Table 4-24. The mean age for a child's first dental visit was lowest in the ED group, 3.24 years (SD± 2.23) (Figure 4-12 and Table 4-24). The main motivation for attending the dentist initially for both the IH and control groups was 'Nothing in particular/ general check -up'. In contrast, the main motivation in the ED group was 'Missing teeth' (Figure 4-13 and Table 4-24). The majority of all participants first attended their local Health Service Executive (HSE- public service) dentist (Table 4-24).

In a list of factors related to their child's teeth/mouth: 'function, speech, how the teeth look, reaction of other children, reaction of other parents, being self-conscious'; both the IH and control groups ranked appearance ('How the teeth look') as the most important feature, whereas the ED group ranked 'Function' as the most important (Table 4-24). All groups agreed that the 'Reaction of other parents' was the least important factor.

When asked if their child was self-conscious about their teeth/ mouth, 65.5% of the ED group, 61.4% of IH group 34.5% of the ED control group and 57.9% of the IH control group reported they believed their child was self-conscious (Table 4-24). The concern about their teeth presented at a median age of 6 for the ED group, age 10 for the IH group and ages 9 and 10 for the ED and IH control groups respectively (Figure 4-14).

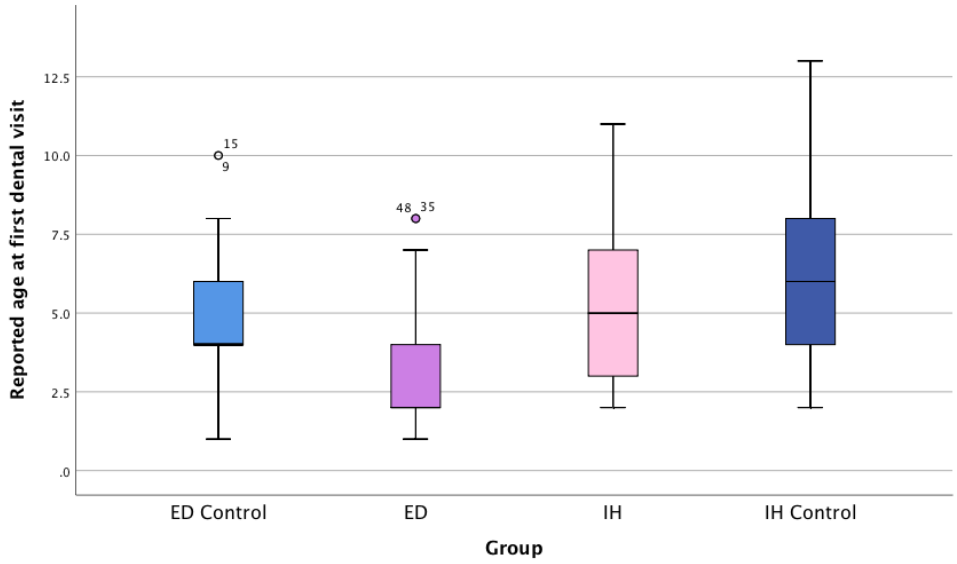


Figure 4-12: Age at first dental visit.

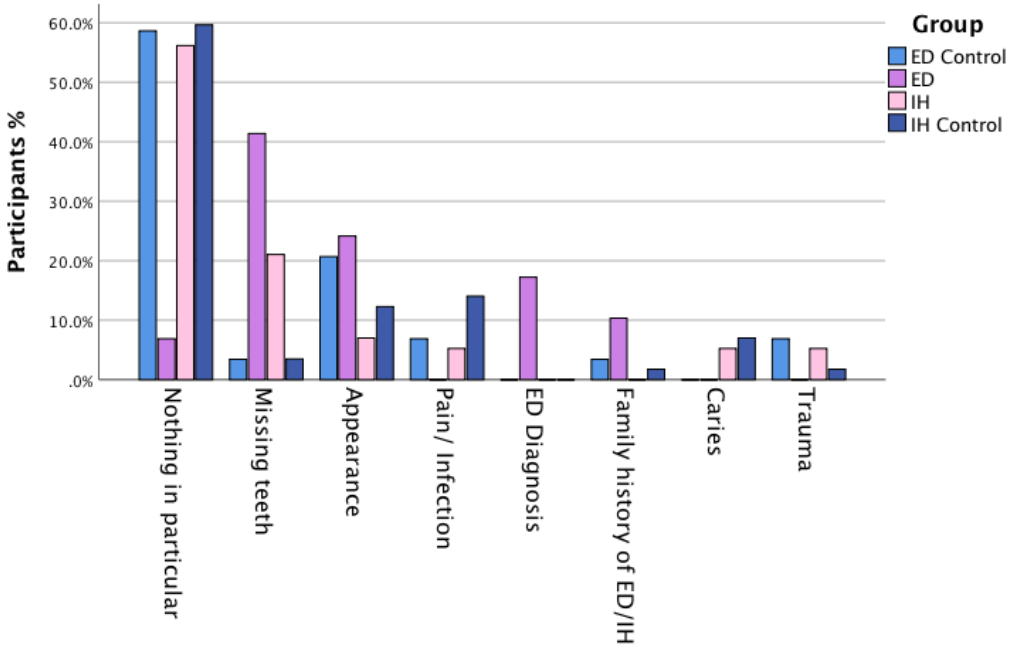


Figure 4-13: Motivation for first attending the dentist

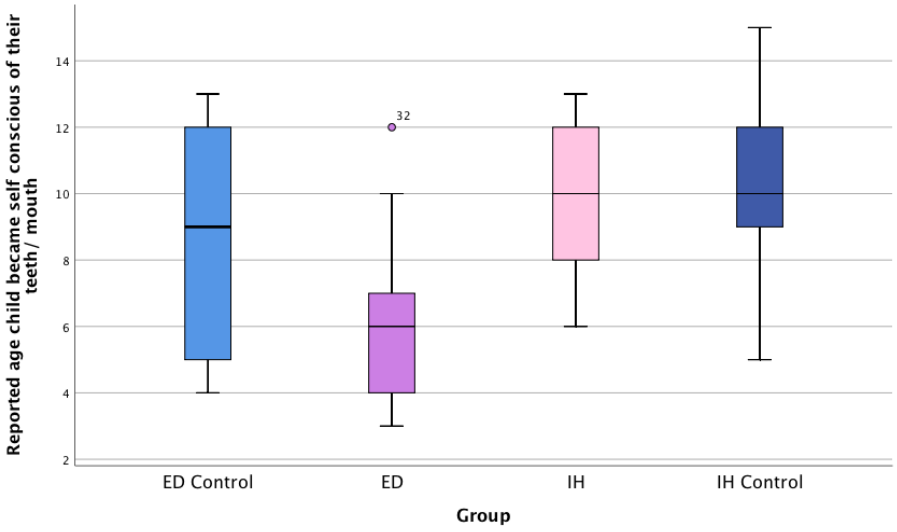


Figure 4-14: Reported age child became self-conscious with respect to their mouth.

The majority of parents in all groups reported their children were cooperative for dental treatment. For those who reported a lack of cooperation, the main reason given in all groups was dental anxiety, followed by being ‘too young’ for dental treatment, again in all groups.

The majority of the ED group reported ‘20 or more dental visits’ (58.6%), with none reporting ‘5 or less dental visits’. Similarly, the majority of the IH group reported attending between ‘10-20 dental visits’ (43.9%) and ‘20 or more dental visits’ (26.3%), with only 3.5% reporting ‘5 or less dental visits’. In contrast, the control groups, were more divided and mostly reported attending between ‘5-10 dental visits’ and ‘10-20 dental visits’ (Table 4-24).

The majority of both control and IH groups reported the dentist as their main source of information about their child’s mouth/ teeth. Similarly, the ED group reported they mainly received information from the dentist, but they also reported receiving information from the internet, support groups, family/ friends and their dermatologist.

When asked about issues regarding information provision, parents from both IH and ED groups reported that information related to treatment timing was deficient, as well as an inadequate explanation of the condition itself.

Finally, when asked ‘if they could start the treatment over again, what would they change’, the majority in all groups reported they would ‘not change anything’, followed by ‘start treatment earlier’.

Table 4-24: Descriptive analysis for Specifically Designed Questionnaire

	ED (29)	ED Controls (29)	IH (57)	IH Controls (57)
Q1: Age at first dental visit				
Min-Max	1-8	1-10	2-11	2-13
Mean (SD)	3.24 (2.23)	4.79 (2.19)	5.19 (2.27)	6.19 (2.63)
Median	2	4	5	6
Wilcoxon	p= 0.008**		p= 0.015**	
Mann Whitney U	p= 0.004**		p= 0.050*	
Q2: Motivation for attending N (%)				
Nothing in particular	2 (6.9)	17 (58.6%)	32 (56.1%)	34 (59.6%)
Missing teeth	12 (41.4%)	1 (3.4%)	12 (21.1%)	2 (3.5%)
How the teeth look	7 (24.1%)	6 (20.7 %)	4 (7%)	7 (12.3%)
Pain/ Infection	0 (0%)	2 (6.9%)	3 (5.3%)	8 (14%)
ED diagnosis	5 (17.2%)	0 (0%)	0 (0%)	0 (0%)
Family history ED/ IH	3 (10.3%)	1 (3.4%)	0 (0%)	1 (1.8%)
Caries	0 (0%)	0 (0%)	3 (5.3%)	4 (7%)
Trauma	0 (0%)	2 (6.9%)	3 (5.3%)	1 (1.8%)
Q3: First dentist N (%)				
Local GDP	4 (13.8%)	14 (48.3%)	15 (26.3%)	21 (36.8%)
Local HSE	13 (44.8%)	12 (41.4%)	36 (63.2%)	29 (50.9%)
Paediatric Dentist	5 (17.2)	0 (0%)	4 (7%)	0 (0%)
DDUH	5 (17.2)	3 (10.3%)	2 (3.5%)	7 (12.3%)
Crumlin CHI Dental Service	2 (6.9%)	0 (0%)	0 (0%)	0 (0%)
Q4: Qualities ranked most and least important by parents N (%)				
(a) Function				
Most	11 (37.9%)	11 (37.9%)	15 (26.3%)	18 (31.6%)
Least	6 (20.7%)	3 (10.3%)	4 (7%)	6 (10.5%)
(b) Speech				
Most	5 (17.2%)	1 (3.4%)	4 (7%)	8 (14%)
Least	1 (3.4%)	1 (3.4%)	11 (19.3%)	2 (3.5%)
(c) Reaction of other children				
Most	1 (3.4%)	2 (6.9%)	0 (0%)	0 (0%)
Least	0 (0%)	2 (6.9%)	4 (7%)	7 (12.3%)
(d) Reaction of other parents				
Most	3 (10.3%)	1 (3.4%)	2 (3.5%)	3 (5.3%)
Least	15 (51.7%)	20 (69%)	34 (59.6%)	34 (59.6%)
(e) Child being self-conscious				
Most	3 (10.3%)	1 (3.4%)	15 (26.3%)	8 (14%)
Least	5 (17.2%)	2 (6.9%)	0 (0%)	1 (1.8%)
(f) How the teeth look				
Most	6 (20.7%)	13 (44.8%)	21 (36.8%)	19 (33.3%)
Least	2 (6.9%)	1 (3.4%)	4 (7%)	7 (12.3%)
Q5: Self-conscious N (%)				
No	10 (34.5%)	19 (65.5%)	22 (38.6%)	24 (42.1%)
Yes	19 (65.5%)	10 (34.5%)	35 (61.4%)	33 (57.9%)
McNemar	p= 0.049*		p= 0.815	
Chi-square	p= 0.018*		p= 0.703	
Q5b: Age they became self-conscious				
Mean (SD)	6.11 (2.58)	8.44 (3.50)	9.9 (2.48)	10.28 (2.71)

Median	6	9	10	10
Wilcoxon	p= 0.104		p= 0.801	
Mann Whitney U	p= 0.107		p= 0.609	
Q6: Perceived number of appointments				
Less than 5 visits	0 (0%)	4 (13.8%)	2 (3.5%)	9 (15.8%)
5-10 visits	6 (20.7%)	10 (34.5%)	15 (26.3%)	19 (33.3%)
10-20 visits	6 (20.7%)	10 (34.5%)	25 (43.9%)	20 (35.1%)
20 or more visits	17 (58.6%)	5 (17.2%)	15 (26.3%)	9 (15.8%)
Chi-square	p= 0.004*		p= 0.073	
Q7: Cooperative N (%)				
No	4 (13.8%)	2 (6.9%)	9 (15.8%)	5 (8.8%)
Yes	22 (75.9%)	27 (93.1%)	48 (84.2%)	50 (87.7%)
Sometimes	3 (10.3%)	0 (0%)	0 (0%)	2 (3.5%)
Q7b: Reasons for lack of cooperation N (%)				
Dental anxiety	3 (10.3%)	1 (3.4%)	4 (7%)	5 (8.8%)
ASD	1 (3.4%)	0 (0%)	0 (0%)	0 (0%)
Too young	3 (10.3%)	0 (0%)	4 (7%)	2 (3.5%)
Didn't want to wear a denture	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)
Dentist lacked experience with children	0 (0%)	1 (3.4%)	0 (0%)	0 (0%)
Q8: Information source N (%)				
Dentist	15 (51.7%)	28 (96.6%)	54 (94.7%)	55 (96.5%)
Family/ Friends	3 (10.3%)	1 (3.4%)	2 (3.5%)	1 (1.8%)
Dermatologist	2 (6.9%)	0 (0%)	0 (0%)	0 (0%)
Support Group	3 (10.3%)	0 (0%)	0 (0%)	0 (0%)
Doctor	0 (0%)	0 (0%)	0 (0%)	1 (1.8%)
Internet	6 (20.7%)	0 (0%)	1 (1.8%)	0 (0%)
Q8b: Did you receive enough information? N (%)				
No	5 (17.2%)	5 (17.2%)	11 (19.3%)	2 (3.5%)
Yes	24 (82.8%)	24 (82.8%)	46 (80.7%)	55 (96.5%)
Q9 Information provision issues N (%)				
Too much information too soon	0 (0%)	2 (6.9%)	2 (3.5%)	1 (1.8%)
Treatment timing	2 (6.9%)	1 (3.4%)	3 (5.3%)	0 (0%)
Treatment options	0 (0%)	0 (0%)	1 (1.8%)	1 (1.8%)
Condition not explained	3 (10.3%)	0 (0%)	2 (3.5%)	0 (0%)
Cost and funding	0 (0%)	0 (0%)	1 (1.8%)	0 (0%)
Q 10: Would you change anything? N (%)				
Nothing	24 (82.8%)	17 (58.6%)	37 (64.9%)	33 (57.9%)
Start treatment earlier	5 (17.2%)	10 (34.5%)	16 (28.1%)	19 (33.3%)
Waited until older	0 (0%)	0 (0%)	1 (1.8%)	1 (1.8%)
More focus on better home care	0 (0%)	1 (3.4%)	0 (0%)	2 (3.5%)
More involved in decision making	0 (0%)	1 (3.4%)	1 (1.8%)	0 (0%)
Private care	0 (0%)	0 (0%)	2 (3.5%)	2 (3.5%)
*** p-values <0.05 and ** p-values <0.017**				

5 DISCUSSION

Few recent studies have investigated the parental perceptions of OHRQoL for ED and IH groups and even fewer have reported on their findings (Kohli et al., 2011; Kotecha et al., 2013; Raziee et al., 2019). This cross-sectional study included 86 sets of participants and parents overall, 57 with IH and 29 with ED. Each participant had a control matched for age and gender. Control participants were also recruited from DDUH clinics, so that cases could be compared with patients of a similar background of hospital-based care. The DDUH is a tertiary care centre, as well as a teaching hospital and receives referrals for individuals with developmental dental conditions from all over Ireland. In this study, the majority of the participants were Caucasian at 83%, Table (4-1), which would be fairly reflective of the ethnic population of Dublin in 2020, with approximately 90% of the population being Caucasian, and almost identical to the figures for Ireland according to the 2016 Irish census (82.2%) (Central Statistics Office, 2016; Dublin Population 2020 (Demographics, Maps, Graphs), 2020).

5.1 Clinical Features

The ED group had the lowest prevalence of caries and restorations (due to caries), which was somewhat of an unexpected finding given that xerostomia and wearing a denture are likely to increase a patient's caries risk and approximately 50% of the ED group reported symptoms of a dry mouth and also wore a denture.

In keeping with the current literature, the ED group showed the highest prevalence of taurodontism, conical morphology, microdontic morphology and aesthetic restorations (Bergendal et al., 2016; Crawford et al., 1991; Dhamo et al., 2018; Prager et al., 2006; Rasmussen, 1999; Reyes-Reali et al., 2018).

Taurodontism was present in 58% of the ED group in this study, which is comparable with the literature (Bergendal et al., 2016; Crawford et al., 1991). Contrastingly, only 1 participant (1.8%) in the IH group presented with taurodontism, which is considerably lower than what would have been expected, given previous reports of around 30-35%. (Kan et al., 2010; Schalk-Van Der Weide et al., 1993; Seow et al., 1989). A conical tooth-morphology was present in 93% of the ED group compared to 19% in the IH group. Dhamo et al. had a similar finding of 17.1% in the IH group, but reported a lower prevalence of conical teeth (63.6%) in the ED group.

There was a considerable difference in the prevalence of denture use (55.2% of ED group; 8.8% of IH group; 0% of control group; Table 4-3). For the ED group, the increased number of TSA's meant that they were provided with their first dentures much earlier (approx. 4-years old compared to 14-years old in the IH group). This difference of 10 years results in a considerable difference in the required intervention, with those in the ED group having a median of three dentures compared to just one in the IH group (Figures 4-2 and 4-3).

5.2 Orthodontic Features

The orthodontic findings in this study are in agreement with the current literature. A slight tendency towards a skeletal class 3 relationship and a reduced lower anterior facial height (LAFH) have been reported in association with severe hypodontia (Acharya et al., 2010; Avelar Fernandez et al., 2018). The ED group in this study presented with equal numbers of skeletal class 2 and class 3 relationships, however the ED group had more class 3 relationships when compared to the IH and control groups, with a class 3 relationship being the least

common in both IH and control groups. Similarly, a reduced LAFH was present more often in the ED group when compared to both IH and control groups.

5.3 Hypodontia

The most commonly missing teeth were the second premolars, missing in 95% of the IH group, confirming previous reports (Larmour et al., 2005; Polder et al., 2004). Although all participants in the ED and IH groups were all classified as having severe hypodontia, participants in the ED group were missing 2 times more teeth than that of the IH group. The maxillary central incisors were the least commonly missing teeth in both groups but were still missing in 32.8% of the ED group.

Dhamo et al. proposed that missing second permanent molars could potentially be one of the phenotypic indicators to discriminate ED from severe IH (Dhamo et al., 2018). Second molars were missing in approximately 73% of the ED group compared to 29% of the IH group. However, similarly large differences existed between the mandibular central and lateral incisors, canines and first molars in both groups. Schalk-van der Weide's suggestion that ED should be considered if the most stable teeth are missing, or in those missing a large number of teeth, may be more fitting than Dhamo's hypothesis (Schalk-van der Weide et al., 1994). In addition to the hypodontia of the second molars, Dhamo et al. also suggested that the presence of abnormally-shaped incisors and canines and a one year delayed dental development of the present teeth could potentially be phenotypic indicators of ED. It is reasonable to suggest that a combination of these theories should be considered and subsequently prompt further investigation; including the presence of conical teeth, 1-year delayed development, hypodontia of the more "stable teeth", particularly the maxillary

central incisor, missing large numbers of teeth (particularly greater than 10) and taurodontism.

5.3.1 TAC Patterns

TAC has been reported to allow easy comparison of hypodontia patterns (Van Wijk et al., 2006). The TAC tool generates codes to represent the hypodontia pattern using a binary system (Van Wijk et al., 2006). TAC was employed in this study in the hope that it would be a helpful adjunct for hypodontia pattern analysis.

The literature for TAC is controversial. In a sample of 92 patients with severe IH, Tan reported that the six most common patterns represented half of all the patterns and concluded that TAC allowed easier data analysis. (Tan et al., 2011). However, given that Tan is the second author on the original TAC paper, author bias must be considered.

Other IH studies have suggested that the presentation of patterns is too heterogeneous (Créton et al., 2007; Dreesen et al., 2014). Créton reported that no single overall pattern occurred more than twice and Dreesen reported that in a sample of 77 patients with severe IH, there were 75 unique tooth agenesis patterns (Créton et al., 2007; Dreesen et al., 2014). This study had similarly heterogeneous findings in both the IH and ED groups, with 54 unique overall patterns in 57 participants in the IH group and 29 unique overall patterns in 29 participants in the ED group.

Dhamo et al. also utilised TAC for both ED and IH however the findings are only presented in table format and are not discussed (Dhamo et al., 2018). The tables display 2 common patterns per arch and then overall for each group with no indication if there were any common patterns between the ED and IH groups.

This may be attributed to the TAC tool's inability to allow comparisons between different cohorts. This is a major limitation of the tool as it means that any comparisons between different cohorts must be done manually, which given the high variability in pattern codes is a large undertaking and is very time consuming. Although the concept and potential of TAC is strong, ultimately for this study, TAC provided no additional information or benefit. The inability of the TAC tool to allow differentiation between groups in a single sample, in particular, is a major drawback of the index.

5.4 P-CPQ Questionnaire

Parental perceptions are particularly important in paediatric dentistry given the nature of the inherent triadic relationship that exists between parent, child and paediatric dentist and the significant influence parents have on dental management.

The P-CPQ questionnaire has been validated for many different oral conditions and therefore was deemed suitable for use in this study . Furthermore, it has been used in many different countries facilitating cross-study comparability. The P-CPQ questionnaire was specifically designed to investigate the parental perceptions of the impact of oral conditions on their children and outperformed a hypodontia-specific QoL instrument in a recent systematic review (Zaror et al., 2019).

Previous studies have used linear regression to analyse COHQoL scores (Kotecha et al., 2013; Laing et al., 2010; Raziee et al., 2019). For this study, the global rating, P-CPQ and FIS scores were not normally distributed and scatterplots showed very weak (R-squared<0.2) linear relationships with explanatory variables of interest. Attempts to transform the data to achieve

normality were unsuccessful and did not improve the strength of the linear relationships. Therefore, with the key assumption unmet, linear regression was not carried out.

Other studies have used Poisson regression, however a Poisson regression is only suitable for count data and although the studies state that they treated the data as count data, there is no description of how they transformed the scores (continuous data) into count data (Abanto et al., 2012; Bendo et al., 2014; Dantas-Neta et al., 2016).

O'Brien et al. carried out a logistic regression for CPQ scores. Logistic regression is used for binary outcomes while CPQ scores, like the P-CPQ scores, are continues outcomes, casting doubt on the suitability of the regression used (O'Brien et al., 2006).

Parents from both the ED and IH groups reported significant impacts on QoL when compared to the control groups. These findings are in agreement with the literature that severe hypodontia, both syndromic and isolated, have a substantial impact on OHRQoL (Anweigi et al., 2013; Kotecha et al., 2013; Locker et al., 2010; Saltnes et al., 2017; Wong et al., 2006).

Anweigi et al. and Kohli et al. showed that functional impacts increased with age for both IH and ED individuals respectively. Interestingly in this study, only oral symptoms scores increased with age for the IH group, with no other correlations reaching statistical significance. It should be noted that a different OHrQoL instrument (OHIP) was used in the study by Anweigi et al. OHIP does cover similar domains to P-CPQ and CPQ and therefore results can be compared with this study's findings. Furthermore, OHIP is reported by the children themselves

but it has been shown that parent perceptions correlate well with their children, with no significant differences reported (Jokovic et al., 2003; Kohli et al., 2011).

These studies also reported a higher level of impact to females (Anweigi et al., 2013; Kohli et al., 2011). Anweigi et al. reported a higher impact for females across the board for an IH cohort, whereas this study only found weak correlations between being female and mean P-CPQ scores, with none of these correlations reaching statistical significance. Kohli et al. found a significantly greater impact on emotional well-being for female participants with ED in their study. However, this study found that males had a moderate correlation (R_s = 0.576; p=0.001*) with functional limitations, oral symptoms (R_s = 0.444; p=0.016*) and overall QoL (R_s = 0.499; p= 0.006*) and no statistically significant correlation with emotional well-being. These findings may reflect a more accurate clinical picture as males are more likely to have a more pronounced presentation of ED compared to females and so it is reasonable to surmise that they may incur more of an impact when compared to females. It should be noted that the majority of participants with ED were male (n=20; 69%) and this may have influenced the results. The gender inequality in the ED sample is a limitation of this study, but not unexpected given the nature of the genetic inheritance of ED and the gender distribution is similar to that of Kohli et al. (Kohli et al.: 63%, n=22 males and 37%, n=13 females; This study: 69%, n=20 males and 31%, n=9 females). However, it is also important to remember that these findings reflect the parental perceptions of QoL impact and as such, may account for these differences.

Overall, previous studies have shown that the number and location of missing permanent teeth are not good predictors of OHRQoL (Anweigi et al., 2013; Kotecha et al., 2013; Raziee et al., 2019), with the exception of psychological

discomfort, which Anweigi et al. showed was impacted by hypodontia of anterior teeth. This study found only weak correlations between P-CPQ mean scores and hypodontia-related variables, which were only statistically significant for the IH group.

5.4.1 FIS

FIS provides an indication of the overall impact on the family and FIS scores are strongly correlated with P-CPQ scores, meaning that parents who reported a higher impact on QoL in the P-CPQ were also likely to report a higher impact on their family and vice versa. This study highlights the significant impact both conditions have on the child's family, particularly for those with ED, and perhaps the need for clinicians to be mindful of this when providing care for a child with ED or IH. This is consistent with other orofacial conditions such as cleft lip and palate, which has also been shown to have a significant impact on the child's family (Agnew et al., 2020). Similarly, parents of children with other long-term conditions can also feel frustrated and emotionally challenged (Smith et al., 2015). It is important to note that the DDUH and the HSE (Ireland's public health system) subsidise dental treatment for children with severe hypodontia, therefore helping to mitigate the financial burdens of dental treatment for children with ED and IH, potentially reducing any financial barriers to dental treatment, that families may face. This is likely to account for the lack of significance in the financial burden domain for both ED and IH in this study.

5.4.2 Dealing with "Don't Know" (DK) Responses in P-CPQ

Most OHRQoL measures do not offer "don't know" (DK) responses. However, a DK option is valuable in questionnaires requiring the participant to report on issues relating to another individual. "Forced responses are invalid and increase

random error" (Jokovic et al., 2004). In OHIP, DK responses can be included, but are rarely used however if used, they are entered as missing values. If there are more than nine missing values, the questionnaire is excluded from the sample (Slade, 1997).

The P-CPQ questionnaire includes the option to respond DK for all questions except for the global rating (questions 1 & 2). The issue of DK responses was addressed in a 2004 study by Jokovic, using two study groups to assess four adjustment methods; 1) deletion from sample, 2) item means (for the entire sample) imputation, (3) replacement with a zero, and (4) adjustment, imputation of mean value for the items that were not answered with DK. The authors concluded that all methods of adjustment were equally appropriate, however, they cautioned that the use of the first method (deletion from the sample) may lead to the loss of valuable data and may weaken studies with small sample sizes (Jokovic et al., 2004). A study by Marshman et al. had similar results, concluding that all four approaches were acceptable, with only minor variations reported (Marshman et al., 2007). The replacement approach demonstrated a superior performance, with the highest internal consistency found. Contrastingly, the exclusion method adversely affected the validity of the questionnaire (Marshman et al., 2007). Subsequently, the replacement approach (with a zero) was utilised in this study.

5.5 Specifically Designed Background Questionnaire

This questionnaire provided additional insight. Interestingly, some parents from the ED and IH groups felt they received insufficient explanation of the condition itself. This was a surprising finding but highlights the importance of clear communication between the clinician, the patient and their parents. This deficit

has also been noted in association with other long-term conditions (Smith et al., 2015). The initial consultation should involve an assessment of the family's knowledge and understanding so that information can be provided that is appropriate and tailored to the patient's needs. Parents from both the ED and IH groups reported insufficient information related to treatment timing. This highlights the need to include parents in the treatment planning process with the possibility of an individualised timeline or guide of the stages of treatment, particularly for ED and IH patients who have a long and potentially complicated road of dentistry ahead.

Parents reported that children with ED attended the dentist earlier, mainly due to concern regarding missing teeth and reported the highest burden of patient visits. Their parents perceived that they become self-conscious much younger than any other group and value function over aesthetics.

Parents of children with IH were more concerned with aesthetics over function and also reported a high attendance burden, but generally reported that their child became self-conscious later in childhood, when compared to the ED group.

The specifically designed questionnaire has not been validated, however it has revealed valuable information on parental perceptions not covered by the P-CPQ. Knowing where parents place value and where and when they perceive problems, such as self-consciousness, is a key component to understanding a parent's perspective and is an area that would greatly benefit from further research.

5.6 Strengths and Limitations and Future Research

This research provides insight into the parental perceptions of OHRQoL for patients with severe hypodontia related to ED and IH, which is especially relevant for dentists serving the Irish population of children with severe hypodontia. From a paediatric dentistry perspective, having an understanding of parental viewpoints and areas of concern is fundamental to the successful planning and provision of care for these patient groups. Children affected by ED and IH are unique patient cohorts who will often present with a greater burden of care and treatment complexity in their lifetime. Factors which can influence dental management and shape outcomes must be considered. As a parent's perception of their child's OHRQoL is likely to have the strongest influence on dental management, an understanding their perceptions is of great value to clinicians. Other studies have acknowledged this finding, including those using P-CPQ, however data is often only reported in relation to its correlation to the child's data.

This study also provides insights into the parent's perception of appointment burdens, their priorities and their perception of their child's self-consciousness and raises awareness of the dental phenotypes associated with ED and IH. Use of the specifically designed questionnaire in this study highlighted several issues, including the importance of parent education and involving parents in the treatment planning, so that they understand the management process. Therefore, validation of this questionnaire on the parental perspectives of their child's dental experience would be valuable in future studies.

A prospective study following patients and parents, and incorporating questionnaires throughout their journey from first assessment through adolescence and into adulthood, would provide great insight and could be very

valuable for future research and inform decision making in the area of service provision.

Dental treatment for children with severe hypodontia is currently subsidised by public funds in Ireland, reducing any effect of financial burden and should be considered when interpreting this data.

There is also a risk of participation bias in this study, particularly in the IH group, due to the high numbers of patients who declined to participate in the study. Our small sample size may also be a limitation.

Another recognised limitation may be that many of the participants did not receive treatment in the DDUH. For those who live in different counties of Ireland, treatment is mainly carried out locally, with only treatment planning or progress reviews being provided in the DDUH. This may also be considered a strength of the study, in that the participants involved represented the four corners of Ireland and not just one area, strengthening the generalisability of the data.

During data collection, OPG's were not available for 6 of the control participants. This is a limitation of the study; however, it is uncommon for OPG's to be taken at such a young age (ages 4, 5, 6, 7) unless an anomaly or pathology is suspected. It is unlikely that these 6 control participants would have influenced the questionnaire results, if they did have undiagnosed hypodontia, given that they would be unaware of the anomaly. This limitation may have influenced the prevalence rates for taurodontism in the control groups.

6 CONCLUSIONS

- Parents of children with ED and IH perceive a significant impact on QoL, for both the child and their family. Children with ED, in particular, have a greater perceived impact on function compared to children with IH.
- There was a moderate correlation of P-CPQ scores for males with ED and increased functional limitations, increased oral symptoms and overall increased impact on QoL.
- There is no definite way to differentiate ED and IH based on dental features, however, the presence of certain features such as the presence of conical teeth, hypodontia of the more ‘stable teeth’, particularly the maxillary central incisor, missing large numbers of teeth (particularly greater than 10) and taurodontism may warrant further investigations.
- Children with ED undergo earlier and more extensive treatment.
- Clinicians also need to consider the additional treatment burden that comes with early intervention, particularly for children with ED and weigh it up against the potential benefits for each individual child, ideally by involving both parent and child in the process.
- Parents want more education and communication from the clinician and want more involvement in the treatment planning process.

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7 APPENDICES

Appendix 1: Ethical Approval Letters

Tallaght University Hospital | Ospidéal Ollscoile Thamhlachta

An Academic Partner of Trinity College Dublin

SJH/AMNCH Research Ethics Committee Secretariat
researchethics@tuh.ie

Ms Emily Crossan,
DDUH,
Lincoln Place,
Dublin 2

23rd October 2019

Re: Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients versus patients with ectodermal dysplasia

REC Reference: 2019-10 List 37 (08)
Previous REC Reference: 2018-07 (3)
(Please quote reference on all correspondence)

EudraCT Number: N/A

Date of Valid Submission to REC: 23.09.2019
Date of Ethical Review: 18.10.2019
R&I application Number: N/A

Dear Ms Crossan,

Thank you for your correspondence in which you submitted an amendment for the above named study.

The Chairman has reviewed the documentation you submitted and approved this amendment.

The following documents were reviewed:

- Amendment request form, dated 23.09.2019
- Invitation letter
- PIL and CF
- Assent form

Applicants must submit an annual report for ongoing projects and an end of project report upon completion of the study. It is the responsibility of the researcher/research team to ensure all aspects of the study are executed in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018. ***Additionally, please note for documents submitted for GDPR purposes that the REC and the Chair are not confirming that you're documents are GDPR compliant, they are approving the document from an ethical perspective.***

Yours sincerely,

Sadhbh O'Neill

REC Officer – Dr Sadhbh O'Neill - SJH/TUH Research Ethics Committee

SJH/TUH Research Ethics Committee Secretariat
email: researchethics@tuh.ie

Tallaght University Hospital | Ospidéal Ollscoile Thamhlachta
An Academic Partner of Trinity College Dublin

Dr. Anne O'Connell
Consultant in Paediatric Dentistry
Dublin Dental University Hospital
Lincoln Place
Dublin 2

31st August 2018

Re: Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients versus patients with ectodermal dysplasia
REC Reference: 2018/07/03 / 2018-08 List 30 (4)
(Please quote reference on all correspondence)

Dear Dr. O'Connell,

Thank you for your correspondence in which you sent in a response to the Committee's letter which detailed the Committee's queries and concerns in relation to the submission of the above referenced research study.

The Chairman has reviewed your response on behalf of the Committee, is happy all issues are dealt with satisfactorily and now gives full ethical approval for the study to proceed.

Yours sincerely,

Secretary
SJH/TUH Research Ethics Committee

Appendix 2: Participant Invitation, Information, Consent and Assent:

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

OSPIDÉAL DÉADACH BHAILE ÁTHA CLIATH
DUBLIN DENTAL HOSPITAL

Invitation Letter

New Research Project: Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients versus patients with ectodermal dysplasia.

Dear Parent/ Guardian,

I would like to invite you and your child to take part in a new research study taking place in the Dublin Dental University Hospital.
I am researching the different patterns of missing teeth in children, with **and** without Ectodermal Dysplasia (a group of conditions that affects teeth, hair, nails and sweat glands) and looking at the development of teeth that **do grow**.

You have been contacted because your child attends the Dublin Dental University Hospital or is a member of the Irish Division of the Ectodermal Dysplasia Society.

To participate in this study, we need your permission to access details in your child's dental records, such as their age, gender, date and age at presentation, dental charting, x-rays, photos, notes, number of visits, type and cost of treatment.

In addition, your child will be invited for a dental assessment in the Dublin Dental University Hospital, which may include an x-ray if clinically necessary and you will be asked to fill in questionnaires regarding the dental treatment your child has received to date.

More information can be found in the enclosed information leaflet, as well as a consent form. If you would be happy to participate in this study, we would ask you to please contact Katie Lombard at katie.lombard@dental.tcd.ie or at **01 612 73 03** to arrange an assessment in the Dublin Dental University Hospital.

By participating in this research, you will help us to achieve a better understanding of the patterns of missing teeth and determine the best way to plan dental services to care for children with missing teeth.
If you have any further questions please contact Katie Lombard at
katie.lombard@dental.tcd.ie or at **01 612 73 03**.
If you do not wish to take part, this will not affect your child's future treatment.

Many Thanks,
Emily.

Dr. Emily Crossan
Postgraduate student in Paediatric Dentistry,
Dublin Dental University Hospital,
Lincoln Place,
Dublin 2.

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

OSPIDÉAL DÉADACH BHAILE ÁTHA CLIATH
DUBLIN DENTAL HOSPITAL

Patient Information

Research Title:

Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients versus patients with ectodermal dysplasia.

Dublin Dental University Hospital.
Division of Public and Child Dental Health.
Researchers: Dr. Emily Crossan, Postgraduate in Paediatric Dentistry.
Dr. Anne O'Connell, Associate Professor/ Consultant in Paediatric Dentistry.
Dr. Michael O'Sullivan, Associate Professor/Consultant in Restorative Dentistry.

Hypodontia is when a tooth or teeth fail to form in the jaw (missing teeth).

- It is the most common developmental dental problem.
- Hypodontia can present; by itself or as part of a syndrome.
- **Ectodermal Dysplasia (ED)** is a group of conditions affecting; teeth, hair, nails, skin, and sweat glands. It is very commonly associated with lots of missing teeth.

This project aims to explore the different patterns of missing teeth in children, to look at the dental treatment they received and to understand how parents feel about their child's dental treatment.

Why have my child and I been invited to take part in this study?

- You have been invited to take part in this study because your child attends the Dublin Dental University Hospital or is a member of the Irish Division of the Ectodermal Dysplasia Society.

If I decide not to take part, will this affect my child's future dental care?

- No. You and your child do not have to take part. Participating in the study is voluntary, and will not affect your child's future treatment.

What will happen if I agree to take part?

- If you are happy to take part in the research, the following details will be collected from your child's records:
  Age, gender, date and age at presentation, dental charting, radiographs, photos, notes, number of visits, and type of treatment.
- You will be asked to fill in questionnaires regarding the dental treatment your child has received to date.
- Your child will be invited for a dental assessment in the Dublin Dental University Hospital, which may include an x-ray if clinically necessary. We would ask you to please contact Katie Lombard at katie.lombard@dental.tcd.ie or at **01 612 73 03** to arrange an assessment in the Dublin Dental University Hospital.

Can I withdraw from the study?

- Yes.
- If you volunteer for the study but later decide you do not wish to participate, that's ok. You may quit at any time and this will not affect your child's future treatment.
- All records will be completely and permanently removed from the study.

Will our information be kept confidential?

- Yes.
- Your identity and the identity of your child will be kept confidential. Your names or personal information will not be disclosed to anyone outside of the study and will not be published.
- All records will be coded and any computerised data will be stored on a password-protected computer with restricted access

Are there any risks involved?

- No.
- There are no potential risks associated with participating in this study.

Is there any compensation?

- No. This is not possible, as this is a research study.
- There are no anticipated direct benefits on an individual basis. However, it is hoped that the information gained from this research will benefit children in the future.

Has this research been approved by an Ethics Committee?

- Yes. The study has been granted ethical approval by Tallaght Hospital / St. James's Hospital Joint Research Ethics Committee (REC).

What will the data be used for:

- The study will form part of a thesis for a postgraduate Doctorate Degree.
- The findings may be presented to dental colleagues or published in relevant dental journals.

Further Information:

If you have any further questions about the study, participating in the study, or your rights, please feel free to contact Katie Lombard at katie.lombard@dental.tcd.ie or **01 612 73 03.**

Thank you for your time and consideration.

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

OSPIDÉAL DÉADACH BHAILE ÁTHA CLIATH
DUBLIN DENTAL HOSPITAL

Consent Form

Title of Research Study:
Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients versus patients with ectodermal dysplasia.

If you have any further questions about the study, participating in the study, or your rights, please feel free to contact Katie Lombard at katie.lombard@dental.tcd.ie or at **01 612 73 03**

PLEASE TICK YOUR RESPONSE IN THE APPROPRIATE BOX

- I have read and understood the Participant Information. YES ☐ NO ☐
- I have had the opportunity to ask questions and discuss the study. YES ☐ NO ☐
- I have received satisfactory answers to all my questions YES ☐ NO ☐
- I have received enough information about this study YES ☐ NO ☐
- I freely and voluntarily agree for my child to be part of this research study. YES ☐ NO ☐
- I give permission for the data from my child's dental records to be included in this research, which will be published in the relevant dental literature. YES ☐ NO ☐
- I agree to attend for examination, in the Dublin Dental University Hospital, for this study. Additional dental X-Rays may be required for diagnosis (to assess the number and location of missing teeth) but not for research purpose only. YES ☐ NO ☐
- I understand that I am free to withdraw my child from the study at any time without giving a reason and without this affecting my child's future care. YES ☐ NO ☐
- I would like to receive a copy of this signed agreement? YES ☐ NO ☐

If you are happy for you and your child to participate in this research study, please sign below and please bring this form with you when you attend the Dublin Dental University Hospital.

Child's Name:

Legal Guardian's Signature: _____ Date: _____

Legal Guardian's Name in print: _____ Email: _____

Investigator's Signature: Date:

Investigator's Name in print: _____

Assent Form

Title of Research Study:

Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients verses patients with ectodermal dysplasia.

TO BE COMPLETED BY CHILDREN 8-YEARS AND OLDER.
PLEASE TICK YOUR RESPONSE IN THE APPROPRIATE BOX

- This study and this assent form have been explained to me. YES □ NO □
- I have had the opportunity to ask questions and discuss the study. YES □ NO □
- I have received satisfactory answers to all my questions. YES □ NO □
- I have received enough information about this study. YES □ NO □
- I freely and voluntarily agree to be part of this research study. YES □ NO □
- I give permission for the data from my dental records to be included in this research, which will be published in the relevant dental literature. YES □ NO □
- I agree to attend for examination in the Dublin Dental University Hospital Additional dental X-Rays may be required for diagnosis (to determine number and location of missing teeth) but not for research purpose only. YES □ NO □
- I understand that I am free to withdraw from the study at any time without giving a reason and without this affecting my future care. YES □ NO □

Child's Signature: _____ Date: _____

Child's Name in print: _____

Investigator's Signature: _____ Date: _____

Investigator's Name in print: _____

Appendix 3: Control Invitation, Information, Consent and Assent

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

OSPIDÉAL DÉADACH BHAILE ÁTHA CLIATH
DUBLIN DENTAL HOSPITAL

Invitation Letter

New Research Project: Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients versus patients with ectodermal dysplasia.

Dear Parent/ Guardian,

I would like to invite you and your child to take part in a new research study taking place in the Dublin Dental University Hospital.
I am researching the different patterns of missing teeth in children, with **and** without Ectodermal Dysplasia (a group of conditions that affects teeth, hair, nails and sweat glands) and looking at the development of teeth that **do grow**.

You have been contacted because your child is not missing any teeth.

To participate in this study, we need your permission to access details in your child's dental records, such as their age, gender, date and age at presentation, dental charting, x-rays, photos, notes, number of visits, type and cost of treatment.

In addition, your child will be invited for a dental assessment in the Dublin Dental University Hospital, which may include an x-ray if clinically necessary and you will be asked to fill in questionnaires regarding the dental treatment your child has received to date.

More information can be found in the enclosed information leaflet, as well as a consent form. If you would be happy to participate in this study, we would ask you to please contact Katie Lombard at katie.lombard@dental.tcd.ie or at **01 612 73 03** to arrange an assessment in the Dublin Dental University Hospital.

By participating in this research, you will help us to achieve a better understanding of the patterns of missing teeth and determine the best way to plan dental services to care for children with missing teeth.
If you have any further questions please contact Katie Lombard at katie.lombard@dental.tcd.ie or at **01 612 73 03**.
If you do not wish to take part, this will not affect your child's future treatment.

Many Thanks,
Emily.

Dr. Emily Crossan
Postgraduate student in Paediatric Dentistry,
Dublin Dental University Hospital,
Lincoln Place,
Dublin 2.

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
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OSPIDÉAL DÉADACH BHAILE ÁTHA CLIATH
DUBLIN DENTAL HOSPITAL

Patient Information

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Dublin Dental University Hospital.
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Researchers: Dr. Emily Crossan, Postgraduate in Paediatric Dentistry.
Dr. Anne O'Connell, Associate Professor/ Consultant in Paediatric Dentistry.
Dr. Michael O'Sullivan, Associate Professor/Consultant in Restorative Dentistry.

Hypodontia is when a tooth or teeth fail to form in the jaw (missing teeth).

- It is the most common developmental dental problem.
- Hypodontia can present; by itself or as part of a syndrome.
- **Ectodermal Dysplasia (ED)** is a group of conditions affecting; teeth, hair, nails, skin, and sweat glands. It is very commonly associated with lots of missing teeth.

This project aims to explore the different patterns of missing teeth in children, to look at the dental treatment they received and to understand how parents feel about their child's dental treatment.

Why have my child and I been invited to take part in this study?

- You have been invited to take part in this study because your child is not missing any teeth.

If I decide not to take part, will this affect my child's future dental care?

- No. You and your child do not have to take part. Participating in the study is voluntary, and will not affect your child's future treatment.

What will happen if I agree to take part?

- If you are happy to take part in the research, the following details will be collected from your child's records:
  Age, gender, date and age at presentation, dental charting, radiographs, photos, notes, number of visits, and type of treatment.
- You will be asked to fill in questionnaires regarding the dental treatment your child has received to date.
- Your child will be invited for a dental assessment in the Dublin Dental University Hospital, which may include an x-ray if clinically necessary. We would ask you to please contact Katie Lombard at katie.lombard@dental.tcd.ie or at **01 612 73 03** to arrange an assessment in the Dublin Dental University Hospital.

Can I withdraw from the study?

- Yes.
- If you volunteer for the study but later decide you do not wish to participate, that's ok. You may quit at any time and this will not affect your child's future treatment.
- All records will be completely and permanently removed from the study.

Will our information be kept confidential?

- Yes.
- Your identity and the identity of your child will be kept confidential. Your names or personal information will not be disclosed to anyone outside of the study and will not be published.
- All records will be coded and any computerised data will be stored on a password-protected computer with restricted access

Are there any risks involved?

- No.
- There are no potential risks associated with participating in this study.

Is there any compensation?

- No. This is not possible, as this is a research study.
- There are no anticipated direct benefits on an individual basis. However, it is hoped that the information gained from this research will benefit children in the future.

Has this research been approved by an Ethics Committee?

- Yes. The study has been granted ethical approval by Tallaght Hospital / St. James's Hospital Joint Research Ethics Committee (REC).

What will the data be used for:

- The study will form part of a thesis for a postgraduate Doctorate Degree.
- The findings may be presented to dental colleagues or published in relevant dental journals.

Further Information:

If you have any further questions about the study, participating in the study, or your rights, please feel free to contact Katie Lombard at katie.lombard@dental.tcd.ie or **01 612 73 03.**

Thank you for your time and consideration.

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PLEASE TICK YOUR RESPONSE IN THE APPROPRIATE BOX

- I have read and understood the Participant Information. YES ☐ NO ☐
- I have had the opportunity to ask questions and discuss the study. YES ☐ NO ☐
- I have received satisfactory answers to all my questions YES ☐ NO ☐
- I have received enough information about this study YES ☐ NO ☐
- I freely and voluntarily agree for my child to be part of this research study. YES ☐ NO ☐
- I give permission for the data from my child's dental records to be included in this research, which will be published in the relevant dental literature. YES ☐ NO ☐
- I agree my child will attend for examination in the Dublin Dental University Hospital, for this study. YES ☐ NO ☐
- I understand that I am free to withdraw my child from the study at any time without giving a reason and without this affecting my child's future care. YES ☐ NO ☐
- I would like to receive a copy of this signed agreement? YES ☐ NO ☐

If you are happy for you and your child to participate in this research study, please sign below and please bring this form with you when you attend the Dublin Dental University Hospital.

Child's Name: _____

Legal Guardian's Signature: _____ Date: _____

Legal Guardian's Name in print: _____ Email: _____

Investigator's Signature: _____ Date: _____

Investigator's Name in print: _____

Assent Form

Title of Research Study:

Identifying patterns of hypodontia in the primary and permanent dentitions of non-syndromic hypodontia patients verses patients with ectodermal dysplasia.

TO BE COMPLETED BY CHILDREN 8-YEARS AND OLDER.
PLEASE TICK YOUR RESPONSE IN THE APPROPRIATE BOX

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- I have had the opportunity to ask questions and discuss the study. YES ☐ NO ☐
- I have received satisfactory answers to all my questions. YES ☐ NO ☐
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- I give permission for the data from my dental records to be included in this research, which will be published in the relevant dental literature. YES ☐ NO ☐
- I agree to attend for examination in the Dublin Dental University Hospital YES ☐ NO ☐
- I understand that I am free to withdraw from the study at any time without giving a reason and without this affecting my future care. YES ☐ NO ☐

Child's Signature: _____ Date: _____

Child's Name in print: _____

Investigator's Signature: _____ Date: _____

Investigator's Name in print: _____

Patient ID.

Date: __/__/__.

Hypodontia Assessment Form

Gender: M ☐ **F** ☐ **DOB:**__/__/__. **Ethnicity:** _____. **ED Diagnosis Y/N :**____**Medical History:**_____.

Please circle relevant features: Asthma Hay fever Nosebleeds Aspiration _____.

Family History: Mum ☐ Dad ☐ Brother ☐ Sister ☐ Other ☐ Please specify anomaly: _____.

Previous extractions or dental trauma? Please specify:_____.

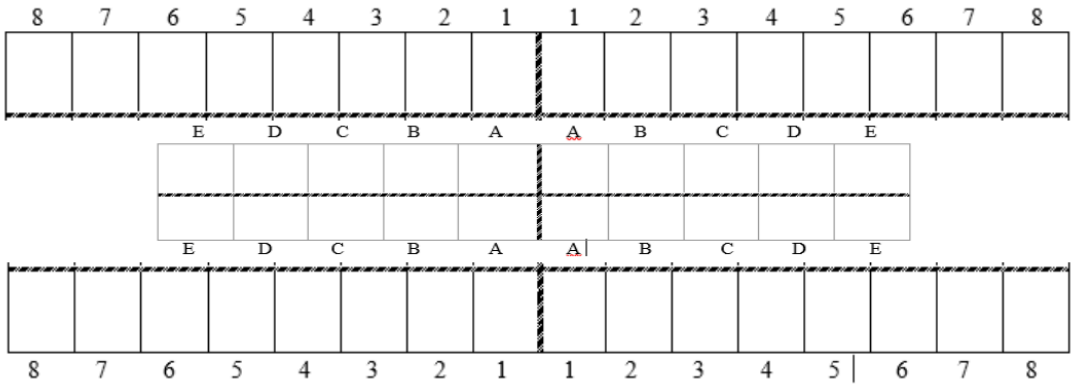
Wearing prosthesis? Please specify type and age of prosthesis and number of prosthesis:_____.

ED Features: Please circle relevant features: Dry skin, Eczema, Dry eyes Dry mouth Sparse hair/eyebrows Abnormal nails Abnormal Sweating

Facial Profile Class I ☐ Class II ☐ Class III ☐ **Lower anterior Face Height:** Normal 50-55% ☐ Reduced< 50% ☐ Increased > 55% ☐

Classification: Molar: Left ☐ Right ☐ Incisors ☐ Overbite % ☐ Overjet mm ☐ Anterior Open Bite ☐ Cross-bite:Y/N ☐ If Y, Specify:_____.

Clinical Charting Please Circle Teeth Present.



Teeth in Occlusion

Legend
- ✓ =Normal
- • =Restoration
- A. = Aesthetic Restoration
- 0. = Caries
- 1. = Congenitally Missing
- 2. = Conical
- 3. = Microdont
- × = Removed/ Lost

Infraocclusion
- ↓ A=Mild
- ↓ B= Moderate
- ↓ C=Severe

HP = Hypoplasia
HM = Hypomineralisation

Emily Crossan

1

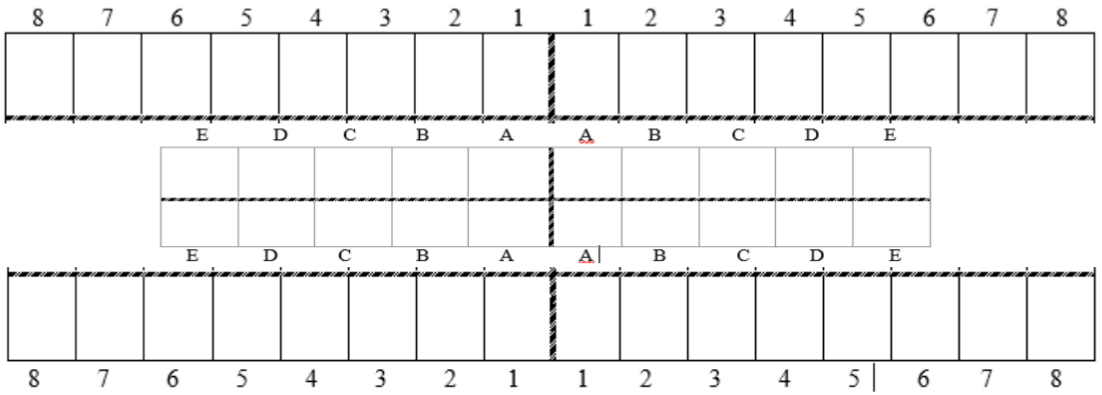
Appendix 4: Datasheet

Patient ID.

Date: ___/___/___.

Hypodontia Assessment Form

Radiographic Findings:



Legend

✓ =Normal
• =Restoration
A. = Aesthetic Restoration
0. = Caries
1. = Congenitally Missing
2. = Conical
3. = Microdont
✖ = Removed/ Lost
Infraocclusion
↓ A=Mild
↓ B= Moderate
↓ C=Severe
AR = Abnormal Resorption

Delayed Development (Y/N) ☐ If Y, Specify:_____.

OPG: Taken Today: (Y/N) ☐ If N, please specify date of exposure:___/___/___. Patient age on this date:____. Number of OPG's:_____.

Checklist:

☑ **Assessment form completed and checked for:**
- **Caries.**
- **Restorations.**
- **Congenitally missing teeth.**
- **Microdontia.**
- **Abnormal shape – conical teeth.**
- **Infraocclusion.**
- **Taurodontism.**
- **Hypoplastic/ Hypomineralised teeth.**
- **Abnormal resorption.**

☑ **Photographs taken using background: Total = 9**

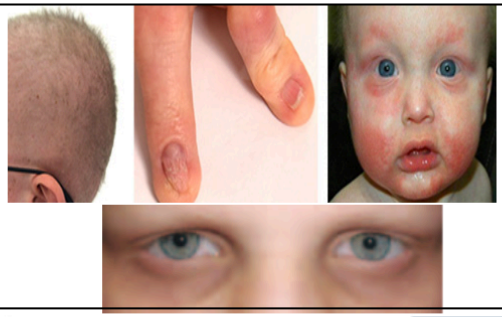
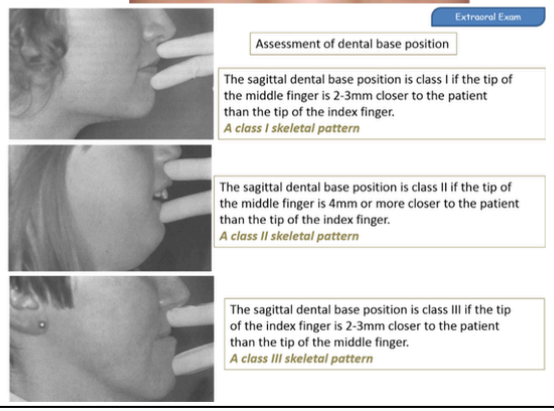
➔ **E/O**
- **Portrait (No glasses)**
- **Profile (No glasses)**
- **Hands (To include finger nails)**
- **Smile**

➔ **I/O**
- **Straight**
- **R+L Buccal (Use buccal mirror if possible)**
- **Max and Mand Occlusal**

Patient ID.

Date: ___/___/___.

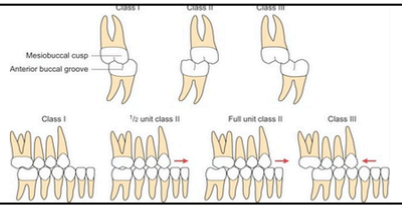
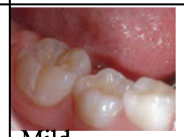
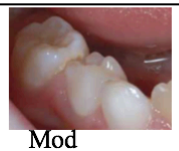
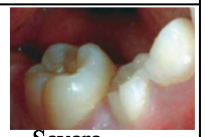
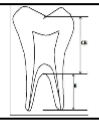
Hypodontia Assessment Form

Section	Action	Example
Family History	Please write the number of siblings or other relatives affected, Please specify anomaly.	Brother 4 Sister 5 Ectodermal dysplasia/ Isolated.
ED Features:	Please circle appropriate features to indicate presence of: ☐ Dry skin/ eczema, particularly on the face. ☐ Patient complaint of dry eyes, please note in comments section any pronounced dark circles around the eyes. ☐ Dry mouth: Clinically- matte appearance of tongue or oral mucosa +/- mirror sticking to mucosa. ☐ Sparse hair/eyebrows. ☐ Abnormal, dystrophic nails. ☐ Reduced/ non-ability to sweat. (Ask if any problems sweating / over – heating).	
Ortho Facial Profile	Please indicate if class I, II, or III by ticking the relevant box. Class I: Straight profile Class II: Convex Class III: Concave	
Dental Classification	Please indicate if class I, II, or III by writing the respective numeral. **Class I:** MB cusp of the upper 6 occludes with the buccal groove of the lower first molar.	I/ II/ III Angles Classification.

Patient ID.

Date: ___/___/___.

Hypodontia Assessment Form

	Class II: MB cusp of the upper first molar occludes <u>anterior</u> to the buccal groove of the lower first molar. **Class II, div 1**: Upper incisors are tilted <u>outwards</u>, creating an overjet. **Class II, div2**: Upper incisors are <u>labially</u> inclined. **Class III**: MB cusp of the upper first molar occludes <u>posterior</u> to the buccal groove of the lower first molar.	
Overbite (%)	Please write percentage in adjacent box	40%
Overjet (mm)	Please write measurement in adjacent box	4mm
Cross-bite	Please indicate presence or absence (Y/N) and specify	Isolated anterior cross-bite 52 +82
Teeth in Occlusion	Please indicate in adjacent box	6 3 3 6 6 3 3 6
OPG	Please indicate if taken on same day as exam and if not please note the exposure date and age of the patient on that date.	N, 13/09/17 Patient age: 7
Delayed Development	Please indicate delayed or normal chronological development in adjacent box	7 year old patient with un-erupted FPM's
Anomalies	Please indicate presence of anomalies in relevant Table: ✓ = Normal. 1 = Microdont. **H** = Hypodontia • = Restoration. 2 = Conical **HM** = Hypomineralisation 0 = Caries. 3 = Congenitally missing. **AR** = Abnormal Resorption	3 3 2 3 2 2 3 • 2 3 3 3 1 2 3 2 2 3 2 3 3
Infraocclusion	**Messer and Cline 1980 Classification:** ↓ **a= Mild:** Between occlusal surface and interproximal contact, less than 2mm. ↓ **b= Moderate:** Within occluso-gingival margins of interproximal contact. ↓ **c= Severe:** Below interproximal contact point. McGeown & O'Connell 2014	   Mild Mod Severe McGeown & O'Connell 2014.
Taurodontism	Molars with apical enlargement of the pulp chamber.	

Appendix 5: COHQoL Questionnaires (Global rating, P-CPQ and FIS)

Your child is: Response options: Male/ Female

Your child's age is: _____years old

Questionnaire completed by: _____

Participant ID: _____

Global Rating

Response options provided for all questions (1&2): Excellent/ Very good/ Good/ Fair/ Poor

1. How would you rate the health of your child's teeth, lips, jaws and mouth?
2. How much is your child's overall well-being affected by the condition of his/her teeth, lips, jaws or mouth?

P-CPQ

Response options provided for all questions (1-33): Never/ Once or twice/ Sometimes/ Often/ Every-day or almost every-day/ Don't know.

1. During the last 3 months, how often has your child had: Pain in the teeth, lips, jaws or mouth?
2. During the last 3 months, how often has your child had: Bleeding gums?
3. During the last 3 months, how often has your child had: Sores in the mouth?
4. During the last 3 months, how often has your child had: Bad breath?
5. During the last 3 months, how often has your child had: Food stuck in the roof of the mouth?
6. During the last 3 months, how often has your child had: Food caught in or between the teeth?

7. During the last 3 months, how often has your child had: Difficulty biting or chewing foods such as fresh apple, corn on the cob or firm meat?
8. During the last 3 months, because of his/ her teeth, lips, mouth, or jaws, how often has your child: Breathed through the mouth?
9. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had trouble sleeping?
10. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had difficulty saying any words?
11. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Taken longer than others to eat a meal?
12. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had difficulty drinking or eating hot or cold foods?
13. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had difficulty eating foods he/she would like to eat?
14. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had diet restricted to certain types of food (e.g. soft food)?
15. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child been: Upset?
16. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child been: Irritable or frustrated?
17. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child been: Anxious or fearful?
18. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Missed school (e.g. pain, appointments, surgery)?

19. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Had a hard time paying attention in school?
20. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted to speak or read out loud in class?
21. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted to talk to other children?
22. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Avoided smiling or laughing when around other children?
23. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Worried that he/she is not as healthy as other people?
24. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Worried that he/she is different than other people?
25. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Worried that he/she is not as good-looking as other people?
26. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Acted shy or embarrassed?
27. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Been teased or called names by other children?
28. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Been left out by other children?
29. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted or been unable to spend time with other children?

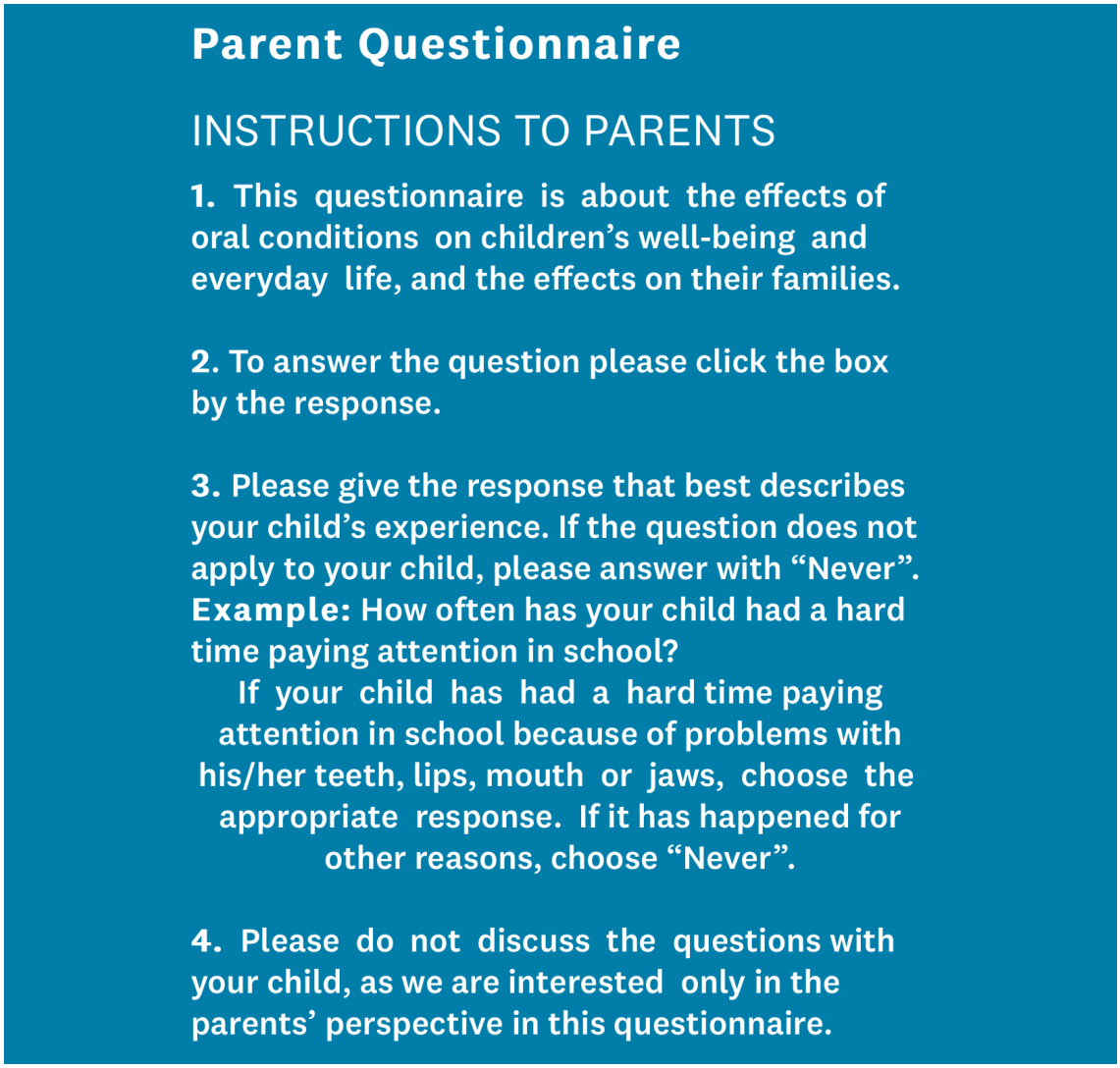
30. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted or been unable to participate in activities such as sports, clubs, drama, music, school trips?
31. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Worried that he/she has fewer friends?
32. During the last 3 months how often has your child: Concerned what other people think about his/her teeth, lips, mouth or jaws?
33. During the last 3 months how often has your child: Asked questions by other children about his/her teeth, lips, mouth or jaws?

FIS

Response options provided for all questions (1-14): Never/ Once or twice/ Sometimes/ Often/ Every-day or almost every-day/ Don't know.

1. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member: Been upset?
2. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member: Had sleep disrupted?
3. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member: Felt guilty?
4. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member: Taken time off work (e.g. pain, appointments, surgery)?
5. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member: Had less time for yourself or the family?

6. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member: Worried that your child will have fewer life opportunities (e.g. for dating, getting married, having children, getting a job he/she will like)?
7. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member: Felt uncomfortable in public places (e.g. stores, restaurants) with your child?
8. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Been jealous of you or others in the family?
9. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Blamed you or another person in the family?
10. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Argued with you or others in the family?
11. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Required more attention from you or others in the family?
12. During the last 3 months, how often has the condition of your child's teeth, lips, mouth or jaws: Interfered with family activities at home or elsewhere?
13. During the last 3 months, how often has the condition of your child's teeth, lips, mouth or jaws: Caused disagreement or conflict in your family?
14. During the last 3 months, how often has the condition of your child's teeth, lips, mouth or jaws: Caused financial difficulties for your family?


Parent Questionnaire
INSTRUCTIONS TO PARENTS
1. This questionnaire is about the effects of oral conditions on children's well-being and everyday life, and the effects on their families.
2. To answer the question please click the box by the response.
3. Please give the response that best describes your child's experience. If the question does not apply to your child, please answer with "Never".
Example: How often has your child had a hard time paying attention in school?
If your child has had a hard time paying attention in school because of problems with his/her teeth, lips, mouth or jaws, choose the appropriate response. If it has happened for other reasons, choose "Never".
4. Please do not discuss the questions with your child, as we are interested only in the parents' perspective in this questionnaire.

*** 1. How would you rate the health of your child's teeth, lips, jaws and mouth?**

- ○ Excellent
- ○ Very good
- ○ Good
- ○ Fair
- ○ Poor

*** 2. How much is your child's overall well-being affected by the condition of his/her teeth, lips, jaws or mouth?**

- ○ Not at all
- ○ Very little
- ○ Some
- ○ A lot
- ○ Very much

*** 3. During the last 3 months, how often has your child had:**
Pain in the teeth, lips, jaws or mouth?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 4. During the last 3 months, how often has your child had: Bleeding gums?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 5. During the last 3 months, how often has your child had: Sores in the mouth?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 6. During the last 3 months, how often has your child had: Bad breath?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 7. During the last 3 months, how often has your child had:**
Food stuck in the roof of the mouth?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 8. During the last 3 months, how often has your child had:**
Food caught in or between the teeth?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 9. During the last 3 months, how often has your child had:**
Difficulty biting or chewing foods such as fresh apple, corn on the cob or firm meat?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 10. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Breathed through the mouth?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 11. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had trouble sleeping?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 12. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had difficulty saying any words?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 13. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Taken longer than others to eat a meal?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 14. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had difficulty drinking or eating hot or cold foods?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 15. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had difficulty eating foods he/she would like to eat?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 16. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Had diet restricted to certain types of food (e.g. soft food)?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 17. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child been:**
Upset?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 18. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child been:**
Irritable or frustrated?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 19. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child been:**
Anxious or fearful?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 20. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Missed school (e.g. pain, appointments, surgery)?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 21. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Had a hard time paying attention in school?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 22. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted to speak or read out loud in class?**

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 23. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted to talk to other children?**

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 24. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Avoided smiling or laughing when around other children?**

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 25. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Worried that he/she is not as healthy as other people?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 26. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child? Worried that he/she is different than other people?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 27. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Worried that he/she is not as good-looking as other people?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 28. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Acted shy or embarrassed?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 29. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Been teased or called names by other children?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 30. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Been left out by other children?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 31. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted or been unable to spend time with other children?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 32. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Not wanted or been unable to participate in activities such as sports, clubs, drama, music, school trips?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 33. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Worried that he/she has fewer friends?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 34. During the last 3 months how often has your child:**
Concerned what other people think about his/her teeth, lips, mouth or jaws?

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 35. During the last 3 months how often has your child:**
Asked questions by other children about his/her teeth, lips, mouth or jaws?

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 36. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member:**
Been upset?

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 37. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member:**
Had sleep disrupted?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 38. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member:**
Felt guilty?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 39. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member:**
Taken time off work (e.g. pain, appointments, surgery)?

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 40. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member:**
Had less time for yourself or the family?

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 41. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member:**
Worried that your child will have fewer life opportunities (e.g. for dating, getting married, having children, getting a job he/she will like)?

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 42. During the last 3 months, because of your child's teeth, lips, mouth or jaws, how often have you or another family member:**
Felt uncomfortable in public places (e.g. stores, restaurants) with your child?

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 43. During the last 3 months, because of his/her teeth, lips, mouth, or jaws, how often has your child: Been jealous of you or others in the family?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 44. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Blamed you or another person in the family?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 45. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Argued with you or others in the family?**

- ○ Never
- ○ Once or twice
- ○ Sometimes
- ○ Often
- ○ Everyday or almost everyday
- ○ Don't know

*** 46. During the last 3 months, because of his/her teeth, lips, mouth or jaws, how often has your child: Required more attention from you or others in the family?**

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 47. During the last 3 months, how often has the condition of your child's teeth, lips, mouth or jaws: Interfered with family activities at home or elsewhere?**

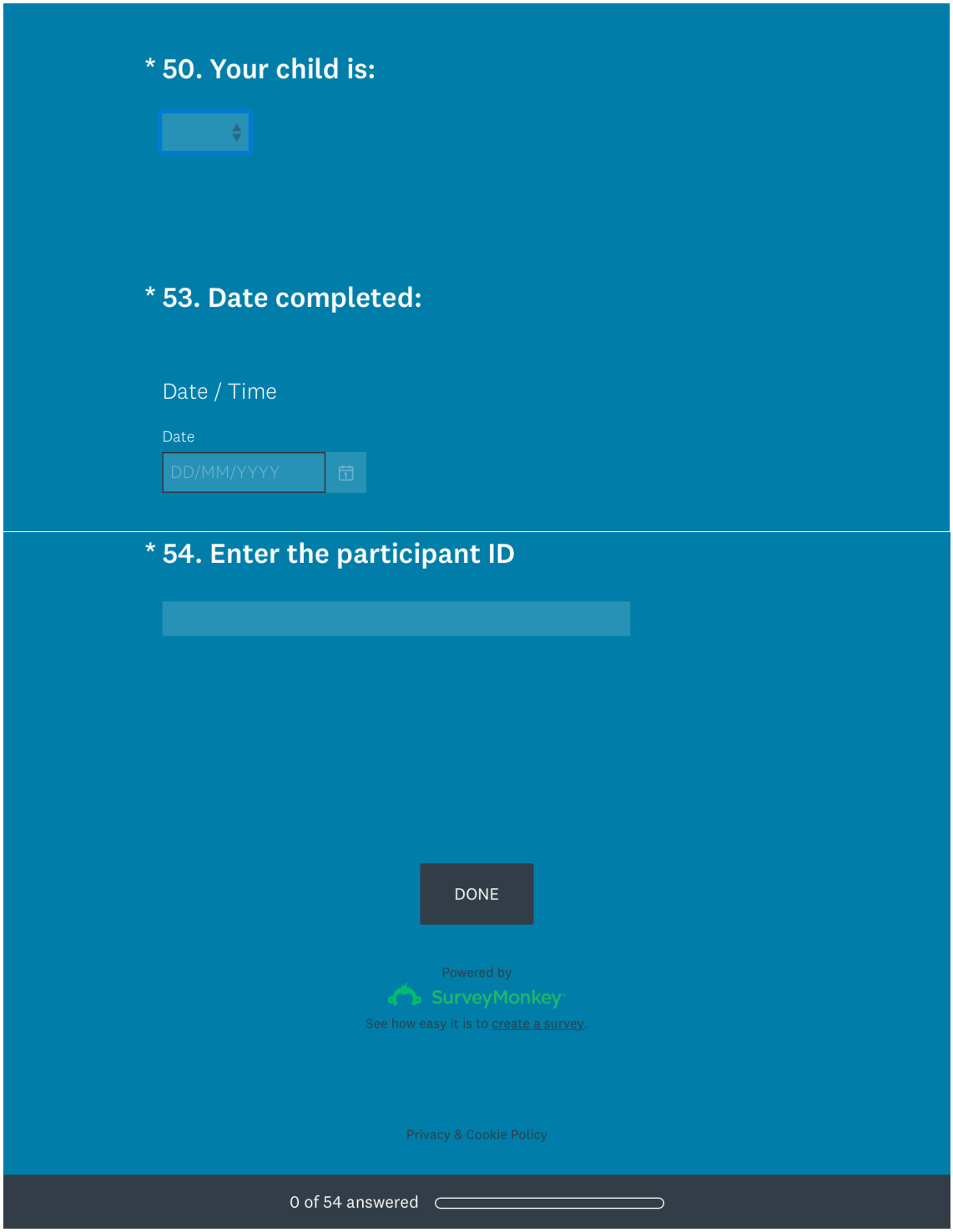
- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

*** 48. During the last 3 months, how often has the condition of your child's teeth, lips, mouth or jaws: Caused disagreement or conflict in your family?**

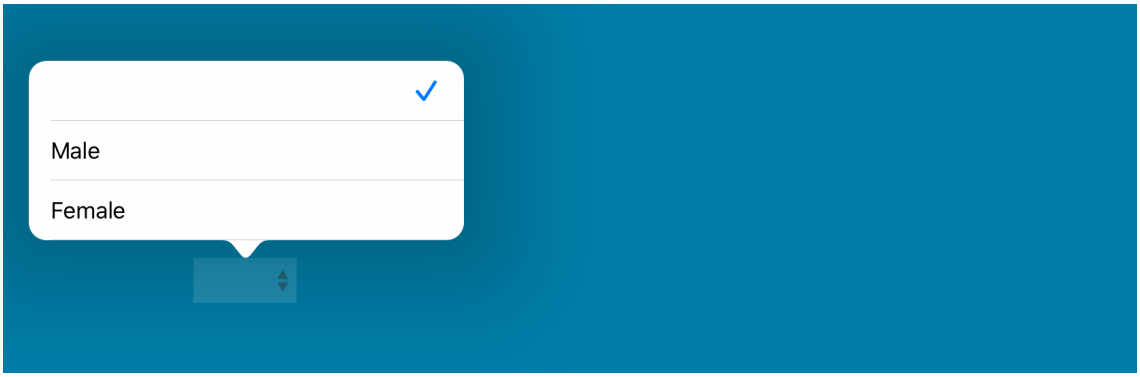
- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know

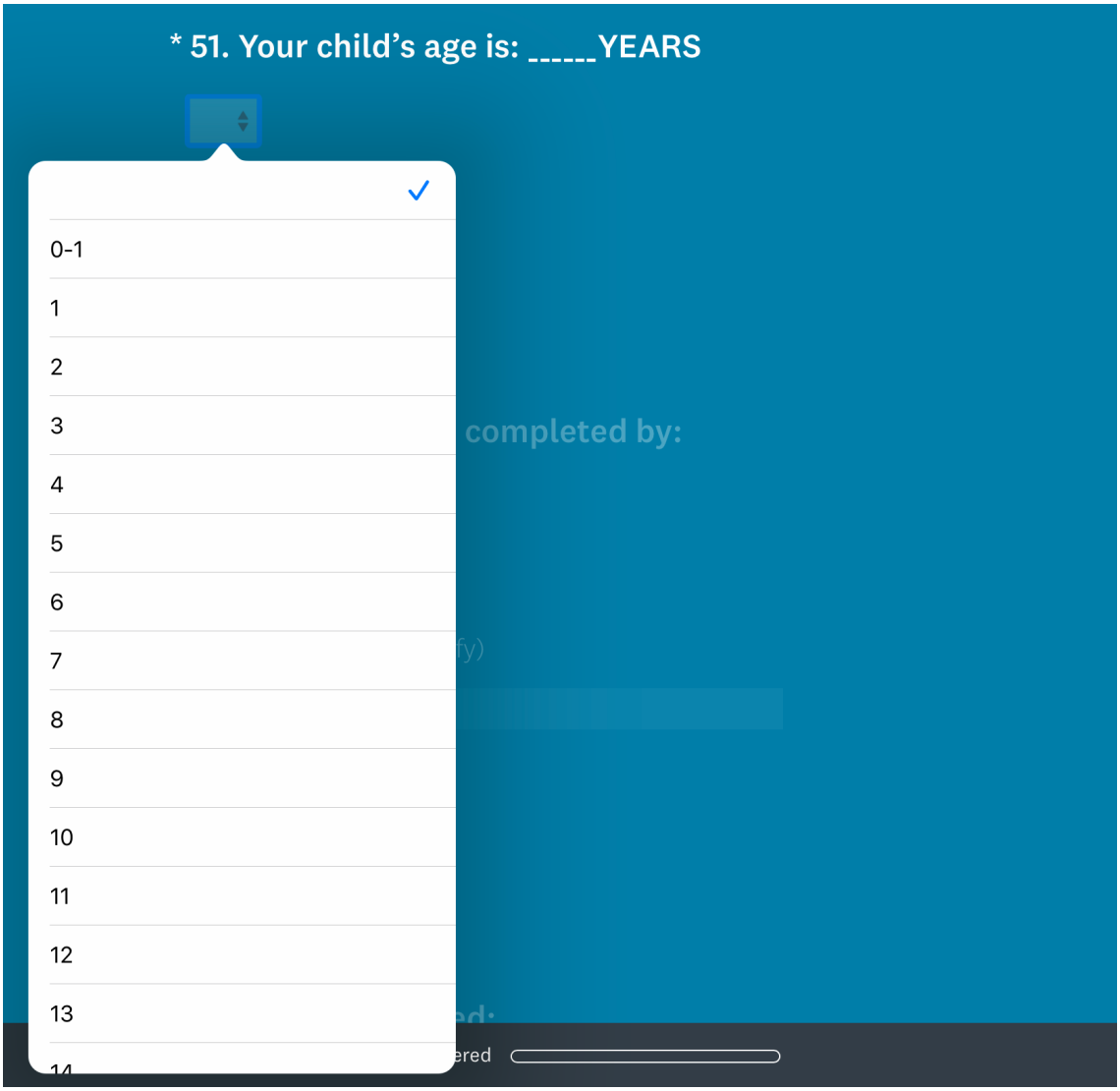
*** 49. During the last 3 months, how often has the condition of your child's teeth, lips, mouth or jaws: Caused financial difficulties for your family?**

- Never
- Once or twice
- Sometimes
- Often
- Everyday or almost everyday
- Don't know


* 50. Your child is:
* 53. Date completed:
Date / Time
Date
DD/MM/YYYY
* 54. Enter the participant ID
DONE
Powered by
SurveyMonkey
See how easy it is to create a survey.
Privacy & Cookie Policy
0 of 54 answered

Example of response formats for gender and age:





Appendix 6: Specifically Designed Questionnaire

Participant ID: _____

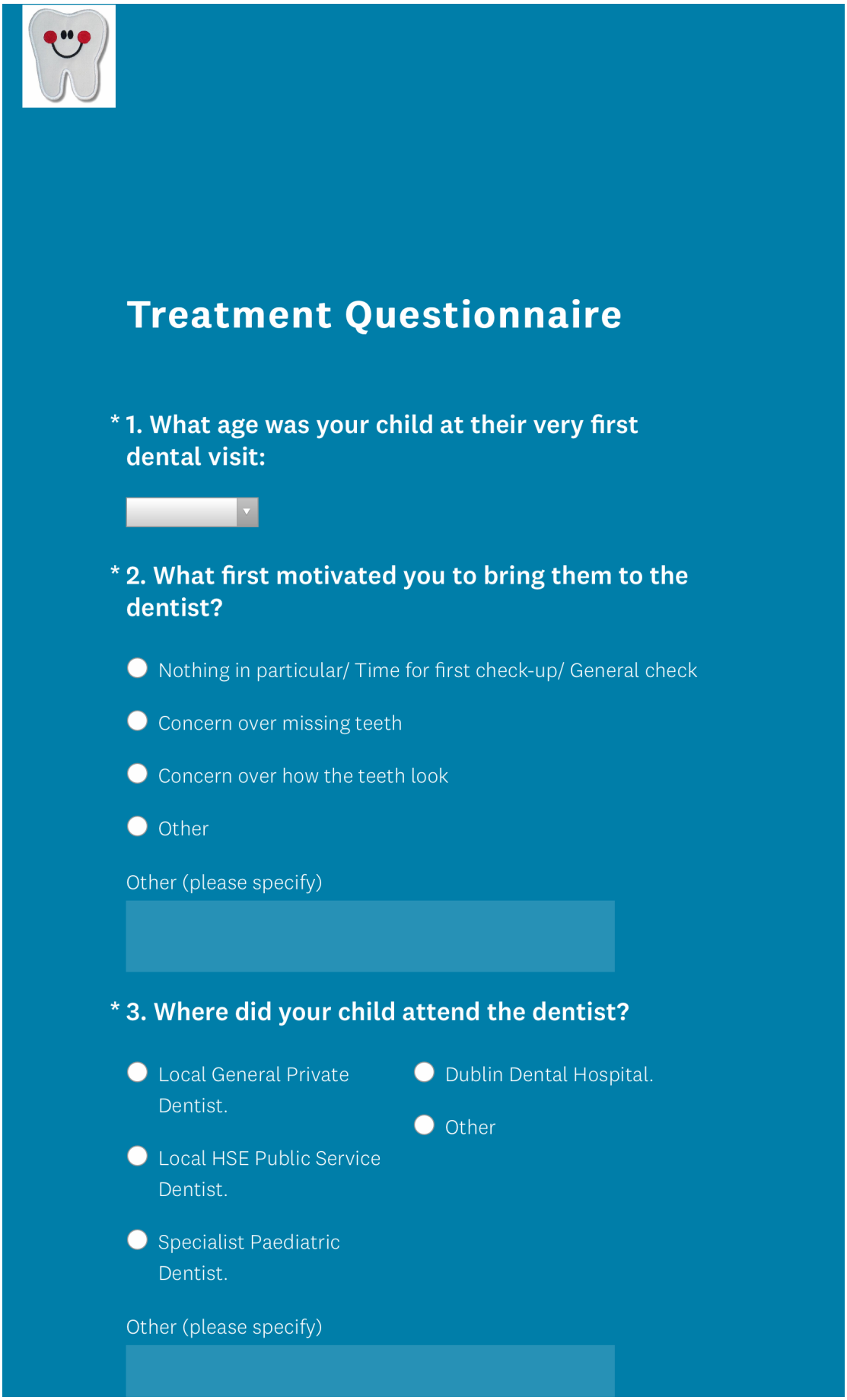
1. What age was your child at their very first dental visit:
2. What first motivated you to bring them to the dentist?
3. Where did your child attend the dentist?
4. What concerned you most about your child's teeth? Please Rank from 1 - 6 (1 being of most concern and 6 of least concern) *List of options: Function (Ability to eat food); Speech; Reaction of other children; Reaction of other parents; Your child's reaction (self-conscious about teeth); How the teeth look.*
5. In your opinion, has your child ever been self-conscious about their teeth?

   If yes, please specify at what age?
6. How many dental visits has your child had? *Response options: Less than 5 visits/ 5-10 visits/ 10-20 visits/ 20 or more visits.*
7. Was your child cooperative for dental visits?

   If you answered 'No', Why do you think your child was not cooperative?
8. Where did you get information about your child's dental condition?

   Did you receive enough information?
9. Please specify what additional Information needed:
10. If you could start from the beginning again, what would you change?

Screenshots of Specifically Designed Questionnaire on iPad



Treatment Questionnaire

*** 1. What age was your child at their very first dental visit:**

*** 2. What first motivated you to bring them to the dentist?**

- Nothing in particular/ Time for first check-up/ General check
- Concern over missing teeth
- Concern over how the teeth look
- Other

Other (please specify)

*** 3. Where did your child attend the dentist?**

- Local General Private Dentist.
- Local HSE Public Service Dentist.
- Specialist Paediatric Dentist.
- Dublin Dental Hospital.
- Other

Other (please specify)

*** 4. What concerned you most about your child's teeth?**
Please Rank from 1 - 6 (1 being of most concern and 6 of least concern)

- Function (Ability to eat food)
- Speech.
- Reaction of other children.
- Reaction of other parents.
- Your child's reaction (self-conscious about teeth).
- How the teeth look.

*** 5. In your opinion, has your child ever been self-conscious about their teeth?**

- Yes.
- No.

If yes, at what age?

*** 6. How many dental visits has your child had?**

- Less than 5 visits.
- 5-10 visits.
- 10-20 visits.
- 20 or more visits.

*** 7. Was your child cooperative for dental visits?**

- Yes.
- No.
- Sometimes.

Sometimes. Please Specify:

8. If you answered 'No', Why do you think your child was not cooperative?

- ○ Too young, not worried yet about the missing teeth.
- ○ Dentist lacked experience of dealing with children.
- ○ Did not want to wear a denture.
- ○ Other
- ○ Growing out of dentures very fast. (Too many dentures needed).

Other (please specify)

*** 9. Where did you get information about your child's dental condition?**

- ○ Dentist
- ○ Support Group
- ○ Internet
- ○ Other
- ○ Friends

Other (please specify)

*** 10. Did you receive enough information?**

- ○ Enough.
- ○ Need more

Need more. Please Specify

*** 11. If you could start from the beginning again, would you:**

- ○ Change nothing.
- ○ Start dental treatment earlier.
- ○ Wait and start treatment when your child was older and more cooperative for treatment.
- ○ Other

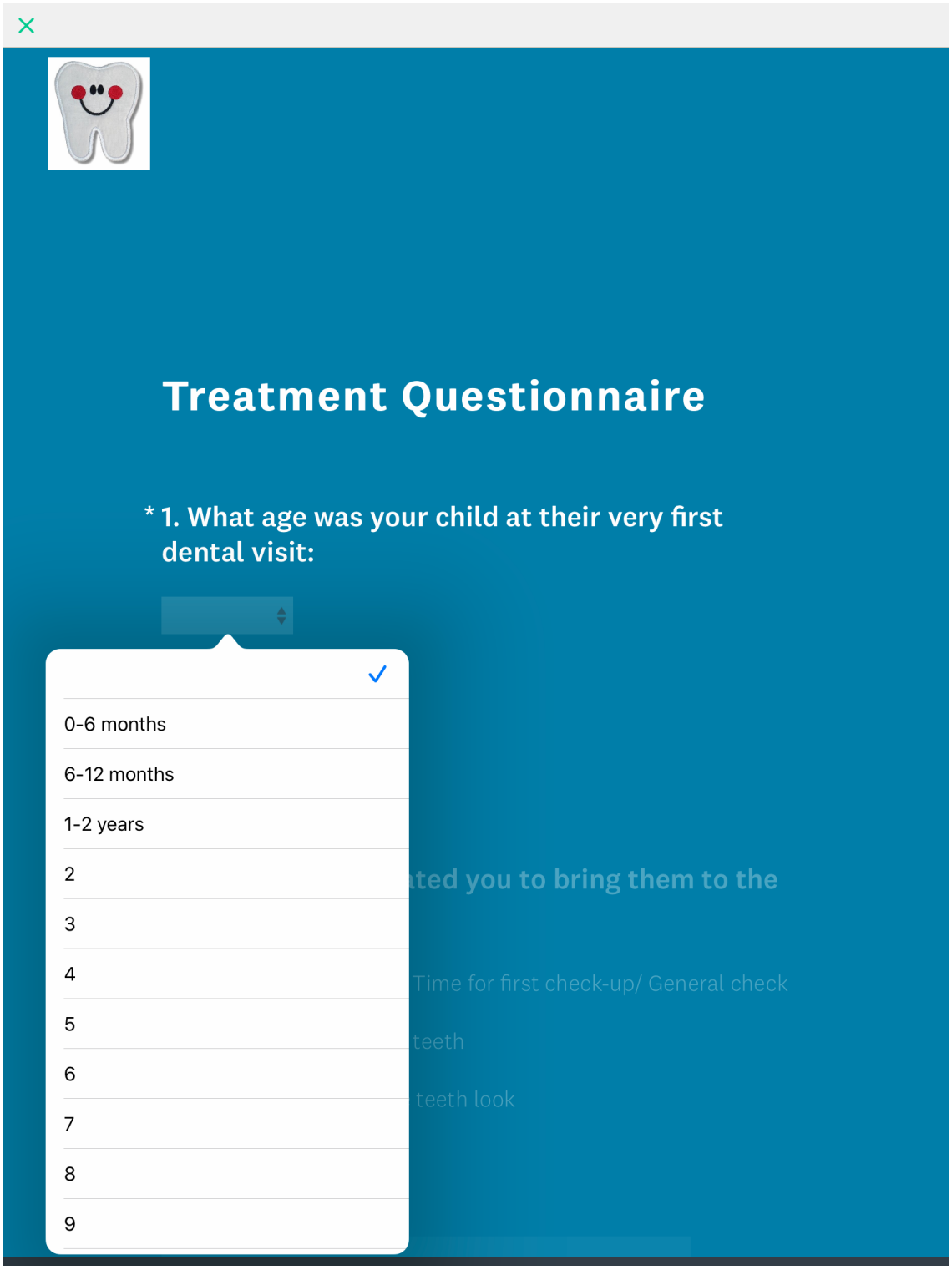
Other. (Please specify)

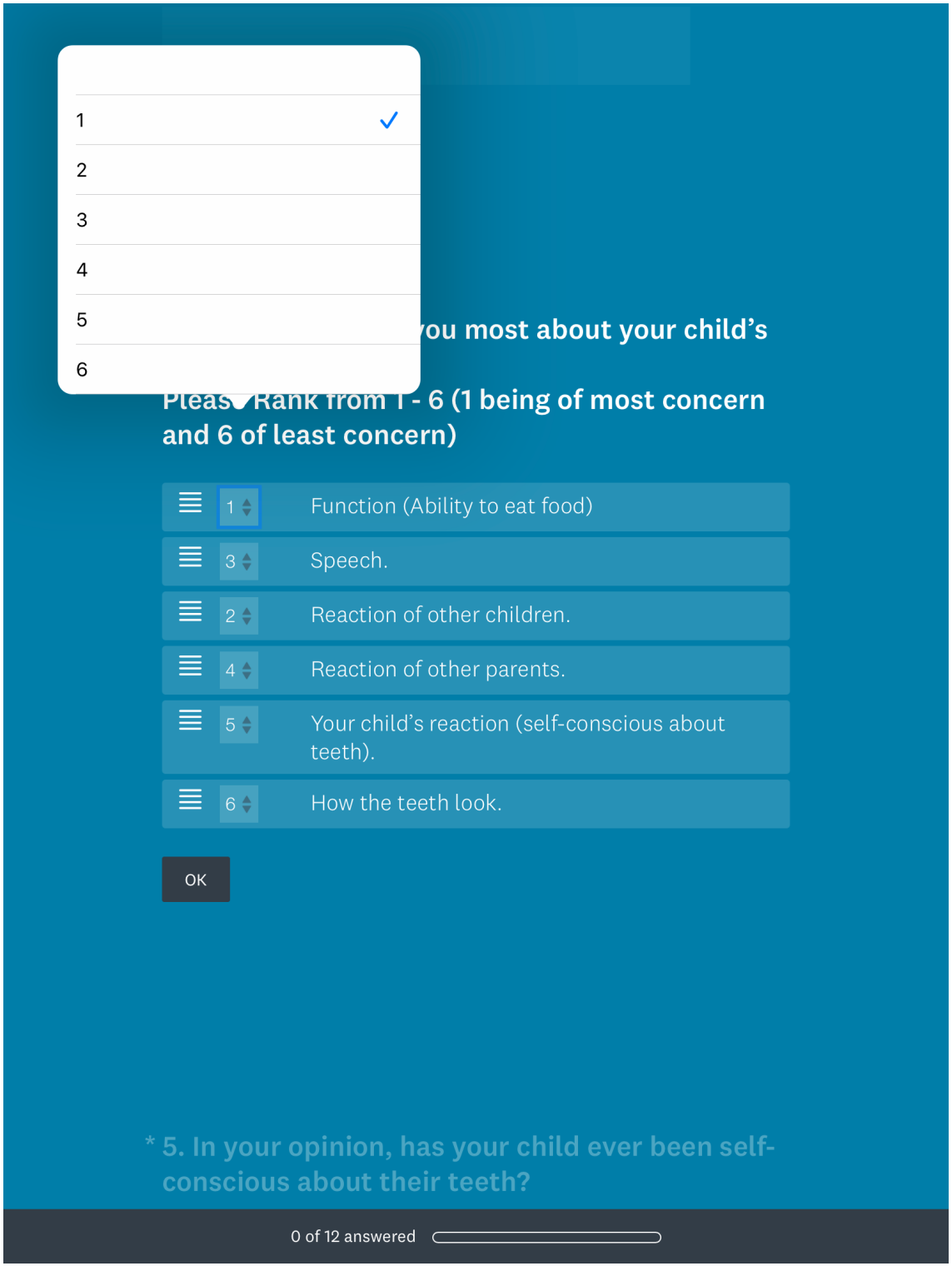
*** 12. Please enter your participant ID:**

DONE

0 of 12 answered

Examples of response format for Specifically Designed Questionnaire




1
2
3
4
5
6
ou most about your child's
Pleas Rank from 1 - 6 (1 being of most concern and 6 of least concern)
1 Function (Ability to eat food)
3 Speech.
2 Reaction of other children.
4 Reaction of other parents.
5 Your child's reaction (self-conscious about teeth).
6 How the teeth look.
OK
* 5. In your opinion, has your child ever been self-conscious about their teeth?
0 of 12 answered

Appendix 7: Clinical Examination Inter-Examiner Kappa Scores

Outcome Variable	Kappa Score
Facial Profile	0.80
LAFH	1.00
Molar Occlusion	1.00
Incisor Occlusion	1.00
Overjet	1.00
Overbite	1.00
AOB	1.00
Crossbite	1.00
Restorations	1.00
Aesthetic Restorations	1.00
Caries	1.00
Conical	1.00
Microdont	1.00
Infraocclusion	1.00
Hypomineralisation	1.00
Hypoplastic	1.00
Taurodontism	1.00
Abnormal Resorption	1.00