Child-reported outcomes for the aesthetic management of molar incisor hypomineralisation

PG student: Mrs Noren N Hasmun
Supervisors: Professor Helen D Rodd
Dr Mario Vettore
Dr Claire Elcock

Academic Unit of Oral Health, Dentistry and Society
School of Clinical Dentistry
University of Sheffield
United Kingdom

The University Of Sheffield.

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Abstract

Background
Molar Incisor Hypomineralisation (MIH), with a global prevalence of 12-14%, is one of the most common developmental defects of enamel (DEE) to affect children. The condition is associated with considerable functional and aesthetic problems with visible incisor opacities potentially having a negative impact on children's social interaction and self-esteem. This prospective clinical study is the first to evaluate the impact of minimally invasive dental treatments, aimed at improving the appearance of enamel opacities associated with MIH, on children's oral health-related quality of life and overall well-being.

Aim
This study aimed to explore the relationships between socio-demographics, clinical status and oral health-related quality of life (OHRQoL) in children with MIH who received aesthetic treatment for their incisor opacities.

Materials and methods
This clinical study involved children, aged 7-16 years, referred to a UK Dental Hospital for management of permanent anterior teeth enamel opacities of reported cosmetic concern. Following ethical approval, participants completed a number of validated questionnaires, primarily the C-OHIP-SF19, Harter's Self-Perception Profile for Children (SPPC) and the Friends and Family Test, prior to any intervention (T_0). Treatment regimens included: microabrasion, resin infiltration (Icon™, DMG), tooth whitening, composite resin restoration or a combination of treatments. The recruitment, treatment and subsequent visits were conducted from June 2017 to October 2018. Children were reviewed after one (T_1) and six (T_2) months, completing the questionnaires each time. Clinical photos were taken at each time point. Change in children's OHRQoL and self-concept at T_0, T_1 and T_2 were analysed using the Friedman's Two Way Analysis of Variance by Rank and Wilcoxon Signed Rank tests. Links between predictors, the socio-emotional wellbeing domain of C-OHIP-SF19 and children's OHRQoL were assessed using structural equation modelling and were underpinned by a theoretical model of HRQoL proposed by Wilson and Cleary.

Results
Of 111 children initially invited, 103 consented to participate and 86 were reviewed at 6-months (83% completion rate). They had a mean age of 11-years (range 7-15), 60% were female and the majority (92%) were White British/Northern European. Most children (56%) received a combination of microabrasion and Icon™. Children were very positive about the treatment they had received (100% likely to recommend their care to friends and family). The total and all C-OHIP-SF19 domain scores were significantly increased following treatment, indicating substantial improvement in OHRQoL (p<0.001). In addition, there was a significant change in the SPPC, Physical Appearance subscale scores, reflecting children's perceptions that they looked better following treatment (p<0.001). Within the Wilson and Cleary model, a higher number of anterior teeth requiring aesthetic treatment was linked to lower socio-emotional wellbeing scores at T_2 (ß=-0.179, p<0.01). Greater need for orthodontic treatment at baseline was related to worse OHRQoL at T_2 (ß=-0.154,p<0.05). Higher self-concept at baseline was significantly associated with higher OHRQoL and socio-emotional wellbeing at baseline (ß=0.460,p<0.01 and ß=0.254,p<0.05). Self-

concept at baseline indirectly predicted socio-emotional wellbeing at six-months follow-up, via socio-emotional wellbeing at baseline (ß=0.197, p<0.01).

Conclusions
This is the first study to explore and demonstrate the simultaneous effects of clinical status, self-concept, socio-emotional wellbeing and children's OHRQoL following simple aesthetic treatment for incisor opacities associated with MIH. Whilst minimal interventions for incisor opacities undoubtedly improve children's OHRQoL, a number of complex psychosocial factors and clinical confounders may influence this overall outcome.

Publications and presentations

A number of publications, abstracts and conference presentations have been given relating to this body of work as listed below.

Peer reviewed papers

Hasmun N, Lawson J, Vettore MV, Elcock C, Zaitoun H, Rodd H. Change in oral health-related quality of life following minimally invasive aesthetic treatment for children with molar incisor hypomineralisation: a prospective study. *Dent J.* 2018. 6(4),61;https://doi.org/10.3390/dj6040061

Large JF, Hasmun N, Lawson JA, Elcock C, Vettore, MV, Rodd, HD. What children say and clinicians hear: accounts relating to incisor hypomineralisation of cosmetic concern. *Eur Arch Paediatr Dent.* 2019. doi: 10.1007/s40368-019-00465-1

Walshaw E, Noble F, Conville R, Hasmun N, Lawson J & Rodd H. 'Molar incisor hypomineralisation and dental anomalies: a random or real association?' *Int J Paediatr Dent*, 2019. https:// doi: 10.1111/ipd.12601. [Epub ahead of print]

Conference presentations and abstracts

European Academy of Paediatric Dentistry (EAPD) Lugano, June 2018

Hasmun N, Lawson J, Vettore M, Elcock C, Rodd H. The impact of aesthetic interventions for incisor opacities on children's self- concept and oral health-related quality of life.

Lawson J, Hasmun N, Zaitoun, H, Rodd, H. Children's perspectives following micro-invasive techniques for enamel opacities of cosmetic concern.

Large J, Hasmun N, Lawson J, Elcock C, Rodd H. What children say and clinicians hear: accounts relating to incisor opacities of cosmetic concern (Winner of the EAPD Young Scientist Award).

Rodd H, Lawson J, Large J, Yesudian G, Hasmun N. White spots and brown marks: descriptors and diagnosis of MIH by general dental practitioners.

International Association for Dental Research (IADR) London, July 2018

Hasmun N, Vettore M, Zaitoun H, Elcock C, Rodd H. Interventions for children's incisor opacities: do they make a difference?

International Association Paediatric Dentistry (IAPD) Cancun, July 2019

Hasmun N, Vettore M, Elcock C, Rodd H. Determinants of socio-emotional wellbeing and oral health-related quality of life over time for children with Molar Incisor Hypomineralisation.

Walshaw E, Noble F, Conville R, Lawson JA, Rodd H
Do children with Molar Incisor Hypomineralisation also have other dental anomalies?

British Society Paediatric Dentistry (BSPD) Birmingham, September 2019

Lawson JA. Timms L, Hasmun N, Rodd H. Assessment of clinical outcomes for the aesthetic improvement of incisor opacities.

British Orthodontic Conference (BOC) Glasgow, September 2019

Walmshaw E, Noble F, Lawson JA, Conville R, Hasmun N, Rodd H. Molar incisor hypomineralisation and hypodontia: a random or real association?

Frequently used abbreviations

AC	Aesthetic Component
AI	Amelogenesis Imperfecta
AMOS	Analysis of Moment Structures
BMPs	Bone morphogenetic proteins
CEJ	Cemento-enamel junction
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CI	Confidence Interval
C-OHIP-SF19	Children Oral Health Impact Profile Short Form 19
COHRQoL	Child oral health-related quality of life
C-OIDP	Child Oral Impacts on Daily Performances
CPQ	Child Perception Questionnaire
CPP-ACP	Casein Phosphopeptide-Amorphous Calcium Phosphate
DDE	Developmental Defects of Enamel
DEJ	Dentino-enamel Junction
DHC	Dental Health Component
dmft	Decayed, missing, filled, teeth (primary dentition)
DMFT	Decayed, Missing, Filled, Teeth (permanent dentition)
EAPD	European Academy Paediatric Dentistry
ECOHIS	Early Childhood Oral Health Impact Score
EDI	Enamel Defects Index
EEE	External enamel epithelium
FFT	Friends and Family Test
FGFs	Fibroblast growth factors
FPM	First Permanent Molars
GCM	Growth Curve Model
HCl	Hydrochloric acid
H_3PO_4	Phosphoric acid
HRQoL	Health-Related Quality of Life
HSPM	Hypomineralised second primary molars
ICC	Intraclass Correlation Coefficient
IEE	Inner enamel epithelium
IMD	Index of Multiple Deprivation
IOTN	Index of Orthodontic Treatment Need
mDDE	Modified Developmental Defects of Enamel
MHSI	Molar Hypomineralisation Severity Index
MIH	Molar Incisor Hypomineralisation
ML	Maximum likelihood
NaOCL	Sodium hypochloride
NHS	National Health Service
OHRQoL	Oral Health Related Quality of Life
QoL	Quality of Life

PEB	post-eruptive breakdown
PI	Permanent Incisor
RI	Reflective index
RMSEA	Root Mean Square Error of Approximation
SD	standard deviation
SEM	Structural Equation Modeling
SES	Socio-economic status
SHH	Sonic hedgehog
SI	Stratum intermedium
SPPC	Self-Perception Profile for Children
SR	Stellate reticulum
SSC	Stainless steel crown
T_0	Baseline
T_1	One-month follow-up visit
T_2	Six-month follow-up visit
VAS	Visual Analogue Scale
WHO	World Health Organisation

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Chapter 1

Introduction

1.1 Background

Molar incisor hypomineralisation (MIH) is one of the most common developmental defects of enamel (DDE), presenting global clinical and public concern. It is characterised by changes in the colour, lucency and composition of enamel. It has considerable diversity in appearance, presenting with white, yellow or brown opacities of different sizes. The condition affects any number of the first permanent molars and usually involves one or more of the permanent incisors, which are mineralising at around the same time as the molars. However, the incisors are usually less severely affected than the first permanent molars and post eruptive breakdown of enamel is rarely seen on the hypomineralised incisors. Of much greater concern to young patients and parents is the poor aesthetics of these affected anterior teeth. The psychosocial impacts relating to the appearance of MIH have been little investigated despite increasing recognition of the importance of this aspect in determining an individual's oral health-related quality of life (OHRQoL) and overall wellbeing.

In recent years, researchers have shown an interest in the management of hypomineralised incisors. Several treatment approaches have been adopted to improve the aesthetics of these teeth, which present with a variety of different coloured opacities. The use of topical remineralisation products such as fluoride varnish and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP 'Tooth Mousse'), as well as approaches such as microabrasion, resin infiltration, tooth whitening, and composite resin restorations have all been described in the literature, but with a poor level of evidence for outcomes. To date, most papers published in this area have been case reports. Very few quantitative studies have been carried out to assess the effectiveness of these commonly used minimally invasive dental treatments in improving the aesthetic appearance of MIH incisors.

Therefore, there is still insufficient data to support the use of these dental treatments to reduce to visibility of enamel opacities on MIH incisors in children. Furthermore, no study has been conducted to assess the impact of aesthetic treatment to conceal the visibility of enamel opacities relating to MIH affected incisors on children's oral health related quality of life and their overall wellbeing.

This clinical study will be the first to evaluate children's perceptions of the success of clinical interventions to camouflage the appearance of enamel opacities on their MIH incisors and its impact on their quality of life. This study will also consider how relationships between oral clinical measures, sociodemographic characteristics, psychological factors, OHRQoL and overall QoL may interrelate to predict any improvement in children's OHRQoL and health related quality of life (HRQoL) following clinical interventions to improve incisor aesthetics in MIH.

1.2 Outline of thesis

The literature review, provided in chapter two, will set the context for this study by describing the underlying principles of enamel formation and the range of developmental defects of enamel (DDE) that are most commonly seen. There will then be a focus on MIH with discussion on the various treatment regimens that are in clinical use. The final part of the literature review will support the methods used in the study design and will consider the instruments used to measure children's OHRQoL and the theoretical framework on which this study is based.

Chapter three will be a brief overview of the study's aims and objectives.

The subsequent chapter (four) will describe the participants and the study design. Details will be given about ethical approvals, recruitment and assessment of participants, and will be followed by the treatments and follow up regimens they received for visible enamel opacities on their permanent anterior teeth. The baseline and follow-up measures that they completed will be presented. This chapter will also provide an explanation of the statistical approaches used.

The first part of results chapter (five) will present the participants' general demographic information such as gender, age, and postcode, as well as clinical

variables such a severity of MIH and caries status, which may all impact on OHRQoL. Details about the specific treatment regimens received will also be included. Following this, patient-reported outcomes will be described at baseline, one- and six-months follow up. Finally, the statistical model will be presented, which explores any change in child-reported OHRQoL and predictors of this relationship.

In chapter six, a discussion of the results will be provided, considering the strengths and limitations of the study and the ways in which the findings add to the existing body of knowledge, The clinical and social relevance of the study will be appraised. Priorities for future research in this field will be proposed.

In the final chapter (seven), a summary of the conclusions from this study will be presented.

For completeness, the appendix section will include all measures and ethics-related documentation pertaining to this clinical study.

Chapter 2
Literature review

2.1. Introduction

As this research essentially focuses on the management of abnormal enamel, albeit from the child's perspective, it is important that the clinician has a sound understanding of the underlying processes that contribute to both normal and abnormal enamel formation. The aetiology, presentation, and clinical outcomes of incisor opacities, are hugely variable and this is a continuing area of increasing interest and knowledge. The following sections will describe enamel formation in detail, with reference to key *in vivo* and *in vitro* studies.

2.2 Amelogenesis

Mature enamel is the hardest and most highly mineralised tissue in human and mammalian teeth. Approximately 96% of enamel composition (by weight) is made up minerals (predominantly calcium hydroxyapatite crystals) and the remaining 4% is occupied by organic material (mainly proteins and lipids) and water (Robinson et al., 1995, Simmer and Fincham, 1995, Bath-Balogh and Fehrenbach, 2006).

Amelogenesis, or enamel formation, occurs in the extracellular space between dentine and the odontoblast cell layer. It is a lengthy and complex process and commences during the bell stage of tooth development (Elhennawy et al., 2017). This process involves a series of programmed physiological and chemical events including gene expression, protein secretion, protein folding and assembly, mineral growth, and protein degradation.

Amelogenesis has been divided into three distinct stages (Ronnholm, 1962, Smith and Nanci, 1995, Robinson et al., 1998, Hu et al., 2007, Alaluusua, 2010) as follows:

a. The secretory phase: which is when the enamel matrix is secreted, achieves its full thickness and begins its mineralisation
b. The transition phase: which is marked by major secretion of amelogenin and is regarded as an early maturation phase
c. The maturation phase: which is when organic materials such as proteins are eliminated and the final high mineral content is acquired.

The stages will be discussed in detail in the subsequent sections.

2.2.1 Pre- secretory stage

Before the secretory stage takes place, a pre-secretory stage, which involves cytodifferentiation of mantle dentine, deposition of predentine matrix, initial mineralisation of the predentine matrix, and transformation from pre-ameloblasts to ameloblasts must occur. Amelogenesis begins only after mineralisation of predentine has started.

2.2.2 Secretory stage

During the secretory stage, large amounts of enamel matrix are laid down at the extracellular space along the mineralisation front apparatus (Simmer and Hu, 2001, Hu et al., 2007). Soon after the initial formation of enamel, the distal end of the ameloblasts becomes specialised and appear folded to form the secretory face of the Tomes' processes, which aligns to the dentine enamel junction (DEJ). The aprismatic enamel layer will become the basis of the interdigitating portions of the Tomes' processes. Each enamel rod is a secretory product of Tomes' processes from a single ameloblast, so the organisation of the enamel rod and inter-rod enamel is exclusively determined by each Tomes' process (Simmer and Hu, 2001, Hu et al., 2007, Bartlett, 2013). Each Tomes' process consists of a 'base' and 'tip' processes. The enamel proteins which form the inter-rod enamel are deposited from the 'base' process while the 'tip' process is involved in the enamel rod formation (Bartlett, 2013). A second secretory site becomes active within the Tomes' processes which controls growth of the length and width of the enamel rods (Smith and Nanci, 1995). The newly formed enamel crystals are

partially mineralised. The enamel crystals are comprised mainly of proteins and carbohydrates, and only a small amount of calcium hydroxyapatite. Approximately 10,000 to 40,0000 of the parallel enamel crystals will be packed together to form an enamel rod and each ameloblast is responsible for creating one enamel rod (Bartlett, 2013). The enamel crystals elongate near the mineralisation front apparatus and grow by the amount of crystal deposited incrementally each day. The amount of crystal varies, depending on a variety of systemic factors and is manifested structurally as rod cross-striations (Simmer and Fincham, 1995). During this time, protein trace elements are either re-absorbed by the secretory ameloblasts or may accumulate in the inter-rod. Here they grow progressively and become organised parallel to each other as ameloblasts move away from the dentine surface. Mineral crystallites, developing between the enamel rods (inter-rods), may have more limited lengths, but they are always positioned spatially to be at angles relative to enamel rod crystallites (Bartlett, 2013). The secretory ameloblasts move vertically away from the dentine as they secrete the enamel matrix at the rods and inter-rods growth sites and the enamel layer increases in thickness (Smith and Nanci, 1995).

The secretory ameloblasts secrete three major enamel proteins: amelogenin (80%); ameloblastin (5%), and enamelin (3-5%). The cells also secrete enamel proteinases (enamelysin, matrix metalloproteinase-20 [MMP-20]), which are subsequently responsible for the degradation of enamel proteins (Brookes et al., 1995, Simmer et al., 2012, Bartlett, 2013). In normal enamel formation, the secretory activity of ameloblasts gradually decreases once the full thickness of enamel has been deposited. Once the secretory activity falls below the threshold required for maintaining the apical portion of the Tomes' processes, a thin aprismatic enamel layer will be produced. The final product of this stage is a partially mineralised enamel crystal which comprises approximately 10-20% of the mineral content and the remaining portion is occupied by enamel matrix proteins and water (Alaluusua, 2010). The narrow innermost enamel layer is slightly more highly mineralised than the outer two-thirds of the matrix.

Any disturbances during the secretory stage will result in quantitative defect with formation of hypoplastic enamel which will be discussed in further detail in a subsequent section (Simmer and Hu, 2001, Hu et al., 2007).

2.2.3 Transitional stage

During this next stage, the tall columnar ameloblasts cells undergo further histological changes. Their length shortens by half and the long Tomes' processes shrink and are no longer in contact with the enamel surface. The inner structure of the ameloblasts also undergoes major reformation, with the nucleus positioned more centrally, and the previously condensed linearly arranged endoplasmic reticulum acquires a more disordered appearance (Robinson, 2014). The enamel surface is smooth and coated by the thin aprismatic enamel layer (Bartlett, 2013). The secretory activity decreases but is not terminated, and the types of proteins secreted are different from proteins secreted during the secretory stage (Reith, 1970, Hu et al., 2007, Moradian-Oldak, 2013, Robinson, 2014).

Degradation of enamel matrix proteins, primarily amelogenins, occurs through enzymatic function of MMP-20. MMP-20 (Sidaly et al., 2015). Extracellular protein Kallikrein 4 (KLK-4: a serine protease that degrades the organic matrix) facilitates further degradation of enamel matrix proteins. KLK-4 transforms the huge protein molecules to small peptides and amino acids and accelerates their removal from the extracellular tissue through the ruffle-ended part of the ameloblast cells (Brookes et al., 1995, Robinson et al., 1995, Robinson, 2014). Degradation of enamel matrix proteins becomes evident throughout the transitional phase and halfway through maturation phases where the enamel proteins are replaced by water, producing a highly hydrated and porous tissue (Smith et al., 1989, Robinson, 2014). At this stage, amelotin (AMTN) is secreted as a part of the new basal membrane and enamel hydroxyapatite crystals stop growing in length (Hu et al., 2007). This marks the beginning of the maturation phase and any disruption during this process may cause retention of organic materials (proteins) and results in hypomineralised enamel (Jedeon et al., 2013, Sidaly et al., 2015). The Tomes' processes completely disappear at the end of the transitional stage.

2.2.4 Maturation stage

As the maturation stage commences, the ameloblast cells undergo further morphological changes, becoming shorter and wider. The key event of maturation is a dramatic increase in mineral content (due to influx of mineral ions

into the enamel crystals) and the degradation of matrix protein. Removal of matrix protein is essential for crystal growth as proteins would inhibit crystal growth (Robinson et al., 1995). Degradation of enamel proteins through proteolytic degradation occurs twice, firstly during secretory stage facilitated by MMP-20 and then in the transitional/maturation stage, which is mediated mainly by the serine protease Kallikrein-4 (KLK-4). Rapid deposition of minerals on the side of hydroxyapatite crystals becomes evident following removal of these proteins, and maturation growth also accelerates from inside to the outer surface as ions enter from the ameloblast layer (Simmer and Hu, 2001, Robinson, 2014). During maturation stage, the pH dropped significantly from 7.0 to more acidic, 6.5. Robinson (2014) suggested that pH changes possibly due to hydroxyl ions being removed when hydroxyapatite crystals grow or protons were pumped into enamel through ruffle ended ameloblasts (Robinson, 2014)

Gradually, the fluid which substitutes the organic matrix during transitional stage is displaced as the volume of crystallites increases and results in a less hydrated, less porous and harder enamel (Robinson, 2014). Further degradation of small peptides and amino acids is believed to be achieved by ameloblasts through their ruffle-ended tufts (Robinson, 2014). However, it is not clear whether these diffuse out of the tissue or are actively removed. Hu (2007) proposed that the entire mineralisation phase of human permanent teeth takes about 3-6 years and this includes mineral deposition and enamel hardening which is regulated by ameloblasts (Hu et al., 2007). The narrow outer layer of enamel mineralises very slowly during the middle and late stages of maturation. It is the last part of the tissue to mature and the tooth may be actually erupting before this part completes its mineralisation. Therefore, it appears clinically as white porous enamel, though this may only be visible microscopically, and its mineralisation continues post-eruptively (Robinson, 2014). Less mineralised enamel on newly erupted teeth is porous and permeable, thus enables mineral ions from saliva such as calcium and fluoride diffuse and incorporate into enamel and eventually promotes mineralisation of outer layer of enamel.

Any physiological or environmental disturbances that occur during the maturation stage of amelogenesis will result in the formation of ‘soft’ or hypomineralised enamel of normal thickness. Once the enamel is fully mature, the ameloblasts stop modulating and undergo regression (Smith and Nanci, 1995).

2.2.5 Inorganic composition of enamel

During amelogenesis, ameloblasts undergo transformation histologically and chemically. The calcium hydroxyapatite crystals of enamel have a chemical formula of $Ca_{10}(PO_4)_6(OH)_2$, which primarily consists of a large amount of acid phosphate (HPO_4^{2-}), carbonate (CO_3^{2-}), sodium (Na^+), and fluoride (F^-) and other ions that closely pack in the hydroxyapatite crystals (Simmer and Fincham, 1995). On average, the extremely long and wavy hydroxyapatite crystals are 50-70nm in width and 25-30nm in thickness, extending from the dentino-enamel junction (DEJ) to the enamel surface (Robinson et al., 1995). Aoba (1996) described the chemical properties of hydroxyapatite crystals during amelogenesis as calcium-deficient, acid phosphate-rich carbonatoapatites and this composition changes substantially throughout this complex process. The main content of this inorganic material is as described below.

Scanning electron microscope analysis of enamel shows that acid phosphate (HPO_4^{2-}) is found mainly at the outer layer of secretory enamel and its composition decreases from 22% to 11% in deeper enamel layers. The net movement of mineral can occur only when the concentration of the mineral is higher in the fluid surrounding the hydroxyapatite crystals than inside the hydroxyapatite crystals itself. Since the concentration of HPO_4^{2-} is high in the fluid, huge amounts of HPO_4^{2-} diffuse into the growing tip of the hydroxyapatite crystals which later convert to phosphate ions (PO_4^{3-}) to form stronger crystallites, as it loses its protons throughout amelogenesis (Simmer and Fincham, 1995). The enamel fluid surrounding the dental enamel hydroxyapatite crystals also contains high concentrations of carbonate and magnesium ions, both of which seem to modulate the mineralisation process (Aoba, 1996). Upon interaction with water molecules, these minerals diffuse into the hydroxyapatite crystals and form stronger crystallites (Simmer and Fincham, 1995). Carbonate ions, being the second-most prevalent inorganic content in enamel comprises 3-4% of the hydroxyapatite crystals mainly seen at the DEJ region and its concentration decreases towards the enamel surface (Robinson et al., 1995). Carbonate ions become incorporated into the hydroxyapatite crystals mostly by replacing the phosphate ions (85 to 90%) and hydroxyl ions (10-15%, mainly at the DEJ region) making the apatite more permeable to fluid and modify its physical properties in terms of crystal size and shape (Robinson et al., 1995, Simmer and Fincham, 1995). During the early secretory phase, the concentration of carbonate

is relatively high because ameloblasts are actively forming the crystallites and secrete carbonate starting from the DEJ, and this process is completed towards the outer enamel surface (Robinson et al., 1995). On average the mean ratio of calcium to phosphorus (Ca:P) in normal enamel is 1:8.

Fluoride is initially acquired during the secretory stage of enamel development and the absorption continues during transition and maturation stages and after the ameloblasts have ceased their function. It is interesting to note that selective fluoride uptake is optimum during transitional and early maturation phase and may affect the ameloblasts, enamel structure and the risk of subsequent enamel caries (Robinson, 2014). Some of this fluoride is incorporated into the growing enamel hydroxyapatite crystals whilst some diffuses back out of the enamel. A recent review suggested that these free fluoride ions (F^-) are important in pH regulation during amelogenesis (Ji et al., 2018). Fluoride is believed to induce protons release, which in turn decreases pH in the cell microenvironment. This acidic microenvironment stimulates the upregulation of ion transporters, reduces the pH further and upregulating the expression of bicarbonate transporters (Ji et al., 2018). This results in the release of a large amount of bicarbonate from ameloblasts, which may neutralise the pH to form a microenvironment that accelerates hydroxyapatite crystals formation (Ji et al., 2018). This acidic environment also enhances diffusion of fluoride ions (F^-) into ameloblasts and may induce change in amelogenin structure and function. Indeed, the retention of F^- induces a series of pathological changes, including abnormality of crystal formation, leading to dental fluorosis (Robinson et al., 1995, Ji et al., 2018).

The concentration of fluoride in normal human enamel is relatively low, but its concentration increases with systemic consumption of fluoride. Fluoride ions incorporate into the enamel hydroxyapatite crystals by substituting the hydroxyl ions and form fluorohydroxyapatite, which alters the physical properties of the crystals. Fluorohydroxyapatite is more stable and able to withstand acid attacks better than is normal hydroxyapatite or fluoroapatite (Robinson et al., 1995, Simmer and Fincham, 1995). Fluoride concentrations are significantly higher in the outer enamel surface than the inner surface because the immature surface enamel is porous and more permeable so is able to absorb more fluoride from enamel. This happens mainly prior to tooth eruption but following completion of mineralisation (Robinson et al., 1995).

The concentration of magnesium is relatively low in normal enamel because of its inability to incorporate into the enamel hydroxyapatite lattice (Simmer and Fincham, 1995). Its concentration is about 0.4% of mineral content in DEJ and the concentration declines towards the outer enamel surface. Magnesium plays an important role in inhibiting hydroxyapatite growth however and reduces its crystallinity. The presence of magnesium and carbon in the enamel hydroxyapatite lattice is associated with high protein enamel and which is hypomineralised (Robinson et al., 1995).

2.2.6 Enamel appearance

Enamel thickness is approximately 2.5mm and 2.0mm at the cusp tips and incisal edges of the teeth respectively and it gradually thins towards the cervical region. Very thin enamel is observed at the cervical region where enamel and cementum meet. In general, enamel is white in colour, glossy, semi-translucent in the incisal and occlusal regions, and becomes more yellow in the cervical region. The colour and translucency of enamel corresponds to its thickness and the colour of the underlying dentine. With ageing, enamel becomes darker (due to thinning and increased visibility of the dentine), has a reduced permeability and increased organic content.

One of the characteristics of mineralised tissues such as enamel and dentine is light-scattering properties. When enamel is exposed to a visible light, the surface and subsurface of normal enamel will absorb and reflect the light, and emit fluorescence. The amount of light absorbed by the enamel determines the shade of the tooth. The optical properties of mineralised tissues can be measured accurately using high-resolution imaging devices, quantifying a parameter called the ‘refractive index’ (RI), which serves as an indicator of the tissues’ light-scattering properties (Hariri et al., 2013). Scattering occurs at interfaces between substances such as enamel, water and air, as they all have different refractive indices (RI) (Subramaniam et al., 2014). The RI of enamel, water and air are reported to be 1.62-1.65, 1.33 and 1.00, respectively (Kidd and Fejerskov, 2004, Paris et al., 2013).

Alterations in enamel translucency can be an indicator of underlying pathology, for example, a ‘white spot lesion’ in early dental caries is seen because of a reduction in mineral content. Demarcated opacities (hypomineralised enamel) are visible because of an increase in inorganic component such as amelogenin. Changes in the mineral content of enamel can be developmental (hypomineralisation) or acquired (demineralisation or remineralisation therapy) and all influence the reflective properties of this hard tissue. This causes variation in the RI of the enamel and ultimately alters the clinical appearance of the affected enamel (Ko et al., 2000, Kidd and Fejerskov, 2004, Hariri et al., 2013). For example, dissolution of the inorganic components of enamel, such as carbonate and magnesium during demineralisation, causes an increase in inter-rod spaces, which then facilitate diffusion of oral dietary-induced acids through the enamel microstructure, resulting in porous enamel. The porous structure (pores) has a lower mineral content than sound enamel. When the pores within the demineralised lesion are filled with fluid (e.g. saliva) the enamel’s RI will be altered to be closer to that of water (1.33) and the lesion will appear more opaque than the normal enamel (Hariri et al., 2013), reflecting light back and having a reduced translucency.

When a demineralised surface is dried, water around the enamel rods is replaced with air which possess a lower RI (1.00) than sound enamel, hence the lesion becomes even more apparent (Kim et al., 2011a). This is the rationale for drying a ‘white spot lesion’ to aid clinical detection and diagnosis (Subramaniam et al., 2014). A similar explanation can be applied to an enamel opacity caused by a developmental defect of enamel formation such as hypomineralisation. When the enamel development progresses normally, the organic components of the matrix are removed during the maturation stage as detailed above (Section 2.2.4). Any disruption during degradation of the organic components will cause voids within inter-rod spaces of hypomineralised enamel and this will increase the enamel porosity (Mahoney et al., 2004). An excess of water that is released during the maturation stage occupies the pores. Hypomineralised enamel therefore appears more opaque than the usually translucent enamel because light is scattered through its more porous structure. As observed in demineralised enamel, developmental opacities also become more apparent when the enamel is dried because drying intensifies the difference in the refractive index between affected and unaffected enamel (Mahoney et al., 2004).

2.3 Developmental defects of enamel

2.3.1 Underlying mechanisms

Three types of developmental defects of enamel (DDE) have been broadly distinguished based on their macroscopic enamel appearance, namely: hypoplasia, a demarcated opacity, and a diffuse opacity (Kaplova et al., 2012).

Hypoplasia is a quantitative (or morphological) defect, as it is characterised by a reduction in enamel thickness due to a disturbance during enamel matrix production (secretory stage) and disruption of crystal elongation (Giro, 1945, Nikiforuk and Fraser, 1981, Suckling and Pearce, 1984, Suckling et al., 1989). Hypoplastic enamel is discoloured, sensitive to normally innocuous oral thermal, chemical and mechanical stimuli, and prone to wear and tooth fracture due to the poorly developed and thin enamel. The clinical appearance of hypoplastic enamel varies from partial enamel loss presenting as pits and grooves to complete enamel loss (Suckling, 1980, William et al., 2006b). Hypoplastic enamel tends to have a well-defined boundary with the adjacent unaffected enamel (Kaplova et al., 2012), theoretically distinguishing it from post-eruptive breakdown, where the boundary with unaffected enamel is less distinct.

Demarcated opacities, on the other hand, have normal enamel thickness and morphology, but are structurally soft and have an altered translucency due to the presence of large organic material remnants between the hydroxyapatite crystals (Koch et al., 1987). These lesions have a clear border separating abnormal and normal enamel. Variations occur in the degree of enamel translucency and colour, which ranges from white to cream, yellow, and brown (Kaplova et al., 2012). It is a qualitative defect due to disturbance during the calcification and maturation stages of amelogenesis, also known as hypomineralisation.

Similar to demarcated opacities, diffuse opacities are also qualitative defects, which involve alterations in enamel translucency but retaining normal enamel thickness (William et al., 2006b, Kaplova et al., 2012). The enamel appears opaque with a linear, patchy or confluent distribution, commonly seen on the incisal or labial one-third of the crown. In contrast to demarcated opacities, a diffuse opacity has no clear boundary with the adjacent sound enamel. Histologically, diffuse opacities are subsurface hypomineralised defects with a

well-mineralised outer enamel surface. It is believed that these defects result from a long, continuous low-grade insult (Suckling, 1980, Wong, 2014). Fluorosis is an example of this type of defect (Kaplova et al., 2012).

2.3.2 General presenting features and causes

Developmental defects of enamel are common in both primary and permanent dentitions. It is accepted that ameloblasts are vulnerable to environmental disturbances throughout amelogenesis, particularly during the transitional and early maturation stage (Suga, 1989). Types of DDE can be broadly categorised as being generalised, involving all teeth in the dentition, or localised to an isolated tooth (or teeth).

Generalised enamel defects are attributed to a systemic cause and can be further classified as inherited (hereditary) or environmental (acquired). Inherited enamel defects include amelogenesis imperfecta and those occurring in conjunction with another inherited disorder or syndrome. In contrast, enamel defects on a single tooth are related to localised aetiological factors such as trauma, chronic infection, iatrogenic damage, or radiation therapy. The location of the defects indicates the approximate timing when the insult occurred (Seow, 2014).

A host of environmental factors and medical conditions have been associated with the presence of DDE. These include maternal infection during pregnancy, prolonged delivery, premature birth, isolated cleft lip and palate, nutritional deficiencies (e.g. vitamin D deficiency, coeliac disease), renal and liver diseases (e.g. biliary atresia, renal failure), infections (bacterial, viral or fungal), and exposure to chemicals and toxins (such as high dose fluoride) (Aguirre et al., 1997, Rugg-Gunn et al., 1998, Aine et al., 2000, Avşar and Kalayci, 2008, Seow, 2014).

2.3.3 Hereditary enamel defects

Amelogenesis Imperfecta

Amelogenesis Imperfecta (AI) is a hereditary condition that causes generalised enamel defects in both primary and permanent dentitions. This condition is associated with a single gene defect, with a variety of different inheritance

patterns such as X-linked, Autosomal Dominant (AD), or Autosomal Recessive (AR). In general, any mutation in ameloblast genes can cause a deficiency in secretion of the gene product, or malformation of the encoded proteins or proteinases, leading to its malfunction (Moradian-Oldak, 2013). Normal physiological processes may be disturbed, including: cell adhesion, mineral nucleation and crystal growth, mineral organisation, and proteolysis of the organic matrix (Moradian-Oldak, 2013).

Four main types of AI are generally recognised: hypoplastic (Type 1); hypomaturate (Type II); hypocalcified (Type III); and hypomaturate/hypoplastic with taurodontism (Type IV) which are distinguished according to their clinical presentation (Crawford et al., 2007, Salanitri and Seow, 2013, Lee et al., 2014, Wong, 2014, Seow, 2014). Recently, several genes associated with AI have been identified. These include AMELX (amelogenin, X-linked), ENAM (enamelin), MMP-20 (matrix metalloptidase 20), KLK-4 (kallikerin-related peptidase 4), FAM83H (family with sequence similarity 83, member H), WDR72 (WD repeat domain 72), SLC24A4 (solute carrier family 24 [sodium/potassium/calcium exchanger], member 4), ITGß6 (integrin beta 6), and LAMß3 (laminin beta 3) (Lee *et al.*, 2014). Mutation of different genes encoding for different types of enzymes will result in varying degrees of defect, for example a mutation of ENAM causes pitting and thin enamel (Seow, 2014).

The prevalence of AI reportedly ranges from between 1:800 to 1:16,000 depending on the populations studied (Seow, 2014, Wong, 2014). It may occur in isolation or in association with other syndromes/conditions such as epidermolysis bullosa, ectodermal dysplasia, Heimler syndrome, pseudohypoparathyroidism and tricho-dento-osseous syndrome (Crawford et al., 2007, Moradian-Oldak, 2013, Wong, 2014). In its mildest form, AI causes aesthetic problems mainly due to presence of discoloured enamel; while in the most severe presentation the enamel disintegrates, exposing the underlying dentine (Pousette Lundgren et al., 2015). This may lead to extreme dental sensitivity, increased caries risk and periodontal disease. Children with AI have soft enamel, which may break down with normal masticatory force and lead to tissue breakdown/loss. In some subtypes of AI there are other features such as an anterior open bite (Seow, 2014).

2.3.4 Environmental causes of developmental defects of enamel

Fluorosis

The therapeutic use of low dosage fluoride has been widely advocated and has a robust evidence-base for a reduction in dental caries worldwide (Mcknight et al., 1999, Martins et al., 2009). Fluoride has been used either in community water fluoridation, fluoridated toothpaste, professionally applied topical fluoride, and fluoride supplements. Fluoride is safe and crucial for the prevention of dental caries when used at its recommended dose. As mentioned earlier in section 2.2.5, excessive uptake of fluoride during the early maturation stage, however, may interfere with the degradation of enamel proteins (Mcknight et al., 1999, Wong, 2014) causing protein retention, delayed crystal growth and a porous immature enamel structure (Alaluusua, 2010, Robinson, 2014, Seow, 2014, Ji et al., 2018). Prolonged and excessive intake of fluoride via systemic ingestion or topical fluoride usage (above the recommended dose) during the child's first two to three years of life thus has the potential to cause dental fluorosis in the permanent dentition, but not in primary teeth as their mineralisation has already completed by this age. Interestingly, excessive uptake of fluoride by the pregnant mother does not seem to have much influence on the developing primary teeth because very little fluoride crosses the placental barrier.

Porous enamel is more susceptible to staining (Ritter, 2005). Therefore, dental fluorosis is characterised by generalised visual changes of enamel discolouration (white, yellow, brown) due to its subsurface porosity. The enamel appearance ranges from mild superficial white striations to stained pitting brown spots also known as mottled enamel (Levy, 2003, Ritter, 2005) and may cause aesthetic concerns (Mcknight et al., 1999). Pitting on the enamel surface may also cause plaque retention and consequently increases the caries risk in the affected child (Levy, 2003, Ritter, 2005). Clinically, dental fluorosis is commonly seen on the apical third of the crown and characterised by banding that follows the developmental lines of the enamel suggesting systemic disturbance during enamel formation (Levy, 2003). The global prevalence is reported between 2-12% (Mcknight et al., 1999, Ritter, 2005). Considering the high prevalence of dental fluorosis, and increasing public concern regarding its aesthetic problem, parental supervision is crucial especially during the first 2-3 years of the children's lives as they have tendency to swallow fluoridated toothpaste while

brushing their teeth.

2.3.5 Localised enamel defects

Enamel defects on a single primary or permanent tooth are most likely to be related to a localised aetiological factor such as chronic localised infection or trauma to the primary tooth during development of the permanent successor (Suckling et al., 1987, Jalevik and Noren, 2000, Valinoti et al., 2011, Pitiphat et al., 2014, Skaare et al., 2015).

2.3.5.1 Trauma

The most likely cause of localised enamel damage to a developing permanent tooth is following a luxation injury to the primary tooth. Direct impact from the root apex of a primary tooth during a luxation injury (such as intrusion and lateral luxation) may also result in localised enamel defects to the developing permanent successor tooth germs (Holan et al., 1992, Wong, 2014). It has also been reported, that local trauma associated with a laryngoscopy or endotracheal intubation during general anaesthesia may also increase risk of damage to the developing enamel of both primary and permanent tooth germs close to the intubated area (Broadbent et al., 2005, Salanitri and Seow, 2013).

2.3.5.2 Localised infection

Periapical/furcation infection of primary teeth has been associated with an increased prevalence of DDE on the succedaneous tooth (Lo et al., 2003, Broadbent et al., 2005). One of the most common local causes of infection is untreated dental caries in primary dentition as this may progress to pulpal necrosis and periapical pathology. Any focus of inflammation may interfere with the normal process of enamel matrix deposition or mineralisation and may result in demarcated opacities and/or hypoplastic defects (Broadbent et al., 2005, Wong, 2014). Such defects more commonly affect the buccal surface of the successor due to its close approximation with the apical of predecessor tooth.

2.3.6 Developmental defects of enamel in the primary dentition

Enamel defects are common in both primary and permanent dentitions, with a global prevalence between 4.6% and 78.9% (see Table 2.1). An epidemiological

study of DDE among 3-to-5-year-old children from South East Brazil found a prevalence of 29.9% with demarcated opacities being the most common defect observed, followed by diffuse opacities and hypoplasia (Correa-Faria et al., 2013).

Table 2.1 Prevalence of development defects of enamel (DDE) in primary dentition.

Study	Country of study	Sample size	Age	Prevalence	Index
Li et al. (1995)	China	1344 (676 boys, 668 girls)	3-5 years old	23.9%	Modified DDE
Rugg-Gun (1998)	Riyadh, Saudi Arabia	390 (all boys)	2, 4, 6 years old	43%	DDE
Agarwal et al. (2003)	India	280	0- 3 years old	30%	Modified DDE
Lunardelli et al. (2006)	Itajai, Southern Brazil	431	3- to- 5- years old	24%	Modified DDE
Chaves et al. (2007)	Brazil	228	1-3 years old	78.9%	DDE
Elfrink et al. (2008)	Netherlands	386 (174 girls, 212 boys)	5 years old	4.9%	EAPD 2003
Seow et al. (2011)	Australia	517	5-6 years old	25%	Modified DDE
Correa-Faria et al. (2013)	Brazil	381	3-5 years old	29.9%	DDE
Temilola et al. (2015)	Nigeria	327	3-5 years old	4.6%	EAPD 2003
Correa-Faria et al. (2016)	Brazil	646	2-6 years old	22.8%	DDE
Owen et al., (2018)	Melbourne, Australia	623	3-to-5 years	14.1%	Combined EAPD 2003 and mDDE (Ghanim et al., 2015)

The presence of enamel defects on primary teeth can be used as a indicator of potential enamel defects in the permanent dentition (Elfrink, 2012). However, when an insult or injury occurs during the overlapping period of development of both dentitions, an enamel defect may occur in both dentitions (Aine et al., 2000).

2.3.7 Developmental defects of enamel in the permanent dentition

First permanent molars and central incisors are the first permanent teeth to develop in the permanent dentition. Both first permanent molars and central incisors begin to develop during the 7th month of gestation (week 28) and their mineralisation commences at, or soon after, birth. Mineralisation of the first permanent molars is complete at the age of three years, and at five years for the incisors (Reid and Dean, 2006). Therefore, any systemic disturbances during the first five years of life may result in a DDE, especially on the first permanent molars and incisors. The 2013 Children's Dental Health Survey for England, Wales, and Northern Ireland recorded DDE on index teeth amongst 12-year-old children. This survey reported an overall prevalence of DDE in 28%, interestingly this was a 7% decrease from the prevalence reported in the previous 2003 survey (Murray et al., 2015, Pitts et al., 2015). It is acknowledged that by the age of 12-years, severely hypoplastic or hypomineralised first permanent molars of poor prognosis may have already been extracted, potentially leading to an under-reporting of DDE in this population. It has been suggested that a diagnosis for DDE, particularly MIH, is ideally undertaken at around 8 years of age when the first permanent molars and central incisors have erupted into the oral cavity (Weerheijm et al., 2003).

Globally, the overall prevalence of DDE in the permanent dentition has been reported at between 7.5% to 89.9% (Casanova-Rosado et al., 2011, Wong et al., 2014). This wide variation can be attributed to the use of different criteria and terminologies to describe enamel defects. In addition, some studies report DDE for clinical populations, where a higher DDE prevalence may be expected, compared to studies that have involved larger cross-sectional general populations.

2.3.8 Indices for developmental defects of enamel

Indices used in DDE studies can be categorised into specific dental fluorosis indices or more general descriptive indices. Fluorosis indices, such as Dean's index, Moller's index, Thylstrup and Fejerskov's index and the Tooth Surface Index of Fluorosis are specifically designed to measure the severity of dental fluorosis. Descriptive indices, for example the Developmental Defects of Enamel (DDE) Index, modified DDE Index and Enamel Defect Index (EDI), have been

used to measure defects other than fluorosis. A diagnosis is made based on the clinical presentation of the defects, without any reference to their aetiology. The Developmental Defects of Enamel (DDE) Index (FDI, 1977) is complicated and time-consuming because it involves recording not only types (opacity, hypoplasia, discoloration) and extent of defects, but also the number of tooth/teeth involved and location/surface affected by the defects. An amended version of this index was therefore introduced by Clarkson and O'Mullane (Clarkson and O'Mullane, 1989). The modified DDE Index involves recording the type (demarcated opacities, diffuse opacities and hypoplastic, and other defects) and extent of the defects, and classifying these defects as white or yellow (Clarkson and O'Mullane, 1989). This index appears to be easier and simpler to use and has been widely adopted in research and epidemiological studies relating to DDE (other than fluorosis). More recent approaches have been proposed including the Enamel Defects Index (EDI) (Elcock et al., 2006) and a specific measure of Molar Incisor Hypomineralisation/Hypomineralised Second Primary Molars (MIH/HSPM) (Ghanim et al., 2015). The EDI has been used in fewer studies but shows high levels of reproducibility and is reportedly less time-consuming than the modified DDE Index (Elcock et al., 2006). The MIH/HSPM index combined the EAPD 2003 diagnositc criteria for MIH and mDDE. However, it has yet to be validated in any epidemiological studies. The authors formulated two versions of the MIH/HPSM index for use in both epidemiological and clinical settings (Ghanim et al., 2015). The short charting form is designed for recording the clinical status and extent of MIH on index teeth (first permanent molars, permanent incisors and second primary molars) whilst the long form includes assessment of all teeth in the dentition. This index provides detailed information of MIH/HSPM and enables evaluation of incremental severity of MIH/HSPM. However, it is acknowledged complicated and time consuming thus requires training and calibration prior to implementation.

2.4. Molar Incisor Hypomineralisation

2.4.1 Definition and background

The term molar incisor hypomineralisation (MIH) was first introduced by Weerhijm in 2001 to describe 'hypomineralisation of believed systemic origin involving one to all first permanent molar, with or without involvement of incisors' (Weerheijm et al., 2001b). This defect is characterised by the presence of enamel

with normal thickness and morphology but which is structurally soft and with an altered translucency (Weerheijm et al., 2001b, Weerheijm, 2003). Previously, this particular defect was known as ‘idiopathic enamel hypomineralisation’, ‘cheese molars’ or ‘non-fluoride hypomineralisation’ (Koch et al., 1987, Weerheijm et al., 2001b). Since the recognition of this clinical entity, there has been a rapid expansion of interest in MIH, with an exponential increase in the number of publications and clinical guidelines for its management. Studies have mostly related to laboratory investigations of tooth structure, epidemiology and exploration of risk factors.

More recently, researchers have also shown an interest in investigating hypomineralisation involving second primary molars because the timing of their formation overlaps that of the first permanent molars and central incisors (Elfrink, 2012, ten Cate et al., 2012, Ghanim et al., 2013b). The prevalence of hypomineralisation on second primary molars (HSPM) has been reported as being between 0% to 21.8% (Elfrink et al., 2015). The clinical presentation of HSPM is similar to that of MIH, visually characterised by the presence of an enamel opacity, which has a clear margin, separating it from the adjacent unaffected enamel. There is wide variation in severity and opacities range from white to yellow and brown. According to Elfrink *et al*., white opacities have a similar mineral content to that of sound enamel, but yellow and brown opacities have a 20-22% lower mineral density than the unaffected enamel (Elfrink et al., 2013b). Very few studies have investigated the possible causes or risk factors for HSPM, although studies in Dutch populations suggest alcohol consumption during pregnancy or having fever during the child’s first year of life may be relevant (Ghanim et al., 2012, Elfrink et al., 2013a, Elfrink et al., 2014).

2.4.2 Clinical presentation

The enamel of MIH-affected teeth varies widely in colour, distribution pattern and severity between children (Weerheijm et al., 2001b, Weerheijm, 2003, Cho et al., 2008). The defect is asymmetrical in nature and the degree of opacity and severity even varies from one tooth to another in the same individual (Weerheijm, 2003). One first permanent molar can be severely affected, whereas the contralateral molar appears sound or has minor defects only (Weerhrijm and Mejare, 2003). This lends supports to the hypothesis that a systemic insult occurred during the development of these index teeth but that different groups of

ameloblasts are active at different times during this period (Allazzam et al., 2014).

There appears to be no discernable reduction in enamel thickness, but the affected enamel is soft and porous due to defective mineralisation (Fearne et al., 2004, Farah et al., 2010b). Therefore, any reduction seen in enamel thickness is likely to have resulted from post-eruptive breakdown (PEB) under normal masticatory forces, which can occur soon after tooth emergence. This may further exacerbate any tooth sensitivity due to dentine exposure and underlying pulpal inflammation (Rodd et al., 2007b). Post-eruptive breakdown may mimic the appearance of hypoplasia, but should be distinguishable by its irregular border with the sound enamel. In contrast, hypoplastic enamel has a smooth and well-defined margin, defining it from sound enamel (Fearne et al., 2004, Weerheijm, 2004, Farah et al., 2010b). Hypomineralised enamel defects may also be misdiagnosed as dental caries, although their location on teeth, plus their colour, shape and hardness are different from that of dental caries. Unlike dental caries, hypomineralised enamel is commonly seen on the coronal or incisal one third, the cervical/gingival areas where plaque usually accumulates are rarely involved (Seow, 1997, Weerheijm, 2004, Ghanim et al., 2015). In general, when incisors are involved, the defects are milder than those seen in the molars and PEB is rarely a feature (Koch et al., 1987, Weerheijm, 2003, Lygidakis et al., 2008).

2.4.3 Diagnostic criteria

In order to standardise the diagnosis of MIH in epidemiological surveys, thereby avoiding inclusion of other DDEs, Weerheijm and colleagues have outlined the diagnostic criteria for MIH, which are presented in Table 2.2 (Weerheijm et al., 2003).

Table 2.2 Diagnostic criteria for MIH proposed by Weerheijm et al., (2003).

Criteria	Definition
Presence of demarcated opacity	A demarcated defect involving an alteration in the translucency of the enamel, variable in degree. The defective enamel is of normal thickness with a smooth surface and can be white, yellow, or brown in colour
Post-eruptive enamel breakdown (PEB)	A defect that indicates deficiency of the surface after eruption of the tooth. Loss of initially formed surface enamel after tooth eruption. The loss is often associated with a pre-existing demarcated opacity
Atypical restoration	The size and shape of restorations are not conforming to the temporary caries picture. In most cases in molars there will be restorations extended to the buccal or palatal smooth surface. At the border of the restorations frequently an opacity can be noticed. In incisors a buccal restoration can be noticed not related to trauma
Extracted molar due to MIH	Absence of a first permanent molar should be related to the other teeth of the dentition. Suspected for extraction due to MIH are: opacities or atypical restorations in the other first permanent molars combined with absence of a first permanent molar. Also the absence of first permanent molars in a sound dentition in combination with demarcated opacities on the incisors is suspected for MIH. It is not likely that incisors will be extracted due to MIH
Unerupted first permanent molars or incisors	The first permanent molar or the incisor to be examined are not yet erupted

2.4.3.1 Severity of MIH and clinical implications

Assessment of the severity of the defects in children with MIH is important to predict the clinical course of any hypomineralised teeth and formulate a treatment plan. It is also important for clinicians to determine the extent to which the condition is having an impact on different aspects of the individual patient's life. Predicting the clinical course of hypomineralised first permanent molars can be challenging because some apparently mild defects require preventive intervention only while other teeth with a similar clinical presentation may suffer enamel breakdown and need comprehensive care (Chawla et al., 2008). Therefore, an index based on the clinical appearance of hypomineralisation of first permanent molars (FPMs) may assist clinicians in formulating a treatment plan most appropriate for the tooth (and individual) based on the expected clinical outcome (Chawla et al., 2008, Lygidakis et al., 2010). The severity of enamel

hypomineralisation has been previously classified on the basis of the clinical presentation. An alteration in enamel lucency and colour has been considered as the mildest form of this condition, while presence of atypical restorations, enamel disintegration (post-eruptive breakdown) and premature extraction of first permanent molars indicates the most severe presentation of MIH (Weerheijm et al., 2001b). Some studies have categorised these defects as mild or moderate/severe (Jasulaityte et al., 2007, Lygidakis et al., 2008, Chawla et al., 2008) while others further divided the defects into mild, moderate or severe (Leppäniemi et al., 2001, da Costa-Silva et al., 2010, Sonmez et al., 2013, Leal et al., 2017). Jalevik et al (2001) and Dietrich et al (2003) took into account treatment history or treatment need when classifying the severity of the defect into mild, moderate and severe (Jälevik et al., 2001, Dietrich et al., 2003).

The original EAPD criteria (2003) did not include scores for the severity of MIH (Weerheijm et al., 2003). This criteria has been subsequently amended and included in more recent EAPD guidelines (Lygidakis et al., 2010). The severity of hypomineralised enamel is now categorised as mild, moderate or severe. Mild cases are those with enamel discolouration only and occasional sensitivity to external stimuli such as cold/hot drinks. Severe cases are characterised by an alteration in enamel colour with enamel breakdown which may result in persistent or spontaneous hypersensitivity (Lygidakis et al., 2010). Teeth with severe MIH may cause aesthetic concern especially when permanent incisors are involved and there may be associated psychosocial impacts (Lygidakis et al., 2010). This EAPD consensus document also provides recommendations for clinicians treating young children with MIH.

Chawla et al. (2008) subsequently redefined this EAPD criteria and developed a numerical scale to represent the severity of MIH (Chawla et al., 2008). According to this index, each first permanent molar is assessed and scored according to four clinical measures: presence of hypomineralisation, extent of hypomineralisation, sensitivity and number of restorative treatments undertaken on the affected tooth (see Table 2.3). The scores from each clinical measure are summed to give a score for each first permanent molar. The final score for an individual is then calculated by adding all scores for each first permanent molar and then dividing this by the number of erupted first permanent molars, with potential scores thus ranging from 1.25 (least severe) to 7.00 (most severe). It is

proposed that this score could inform treatment approaches. For example, preventive treatment only would be indicated for an individual with low severity score while an individual with a high severity score may require an interdisciplinary approach. This index however did not take into account any hypomineralised incisors and has not been used in any MIH population-based studies so its validity and reliability has yet to be established.

Table 2.3 MIH Severity Index by Chawla et al., 2008.

Clinical measures	Severity Characteristics	Score
Presence of first permanent molar	Unerupted	0
	Erupted	1
Extent of hypomineralisation	None	0
	Mild (white-opaque)	1
	Moderate-severe (yellow/brown teeth and/or teeth with post-eruptive breakdown)	2
Sensitivity	None	0
	Sensitive	1
Number of restorative procedures (the number of times the molar had been restored)	None	0
	One	1
	Two	2
	Three or more	3

A more comprehensive severity index, known as the Molar Hypomineralisation Severity Index (MHSI) has been proposed by Oliver et al., (2014) (see Table 2.4). Oliver et al. (2014) was the first to combine the defect size of individual tooth and the entire dentition with a treatment recommendation (Oliver et al., 2014). A score for three clinical measures (colour, location and previous restorations placed/replaced) is undertaken on the basis of increasing severity while the weightings for the other four criteria (eruption, atypical restoration, PEB and sensitivity) are recorded simply as present or absent (Oliver et al., 2014). Each MIH-affected tooth (first permanent molar and permanent incisor) is scored individually by adding the scores of each parameter and a tooth-related score could range from 3 to 13. Each tooth can then be classified as mildly affected (scores 3-6), moderately affected (scores 7-9) or severely affected (scores 10-13). Clinicians can then relate these scores to the treatment recommendations proposed by the authors (Oliver et al., 2014) (see Appendix 1). A final score for the whole dentition is obtained by summing the scores for each first permanent

molar (scores for permanent incisors are not included for the dentition score). The final dentition score may range from 5 to 52. Based on the final score, the individual will be categorised as having mild (scores 5-20), moderate (scores 21-36) or severe (scores 37-52) MIH. It is suggested that clinicians can use the final dentition score as a guideline when treatment-planning for an individual with MIH (see Appendix 14). Applying the MHSI can be time-consuming, but this index reportedly facilitates decision-making when dealing with MIH cases. Although it has not been employed in any other MIH studies, data collected using this index may have merit when correlating the severity of the clinical condition with children's oral health-related quality of life.

Table 2.4 Characteristics of hypomineralised defects on permanent molars and permanent incisors and severity weightings by Oliver et al., 2014.

Characteristics of molar hypomineralisation defects	**Severity of Characteristics**	**Weighting Assigned**
Eruption status	Unerupted	0
	Erupted	1
Colour of most severe defect	None	0
	White/Cream	1
	Yellow	2
	Brown	3
Location of most severe defect	None	0
	Smooth surface	1
	Occlusal surface (FPMs)	2
	Incisal surface (PIs)	2
	Cuspal involvement (FPMs)	3
Restorations placed/replaced (prior to study entry)	None	0
	One	1
	Two or more	2
Atypical restorations (prior to study entry)	None	0
	Present	1
Post eruptive enamel breakdown (PEB)	None	0
	Present	1
Sensitive to temperature (child report)	None	0
	Sensitive	1
Sensitive to tooth brushing (child report)	None	0
	Sensitive	1

More recently, Ghanim et al., (2015) proposed a simplified index for use in MIH epidemiological studies, which combines the EAPD 2003 judgment criteria and the modified index of developmental defects of enamel (mDDE index) (Ghanim et al., 2015). To minimise the potential for a misdiagnosis of MIH, this index considers other DDE which may be mistaken for MIH such as a localised hypomineralised tooth, enamel hypoplasia and amelogenesis imperfecta. Each clinical status is coded as in Table 2.5.

Table 2.5 Clinical codes and its definitions of MIH index by Ghanim et al., 2015. Text highlighted in blue relates only to the long form version.

Code	Definition
0	No visible enamel defect: tooth/surface is apparently free of enamel lesions represented by diffuse opacities, hypoplasia, demarcated hypomineralisation and amelogenesis imperfecta.
1	**Enamel defect, non-MIH/HSPM:** Quantitative or qualitative defects that are not comply with the characteristic features mentioned in the MIH/HSPM definitions. These defects include the following;
11	**Diffuse opacities:** These defects can have a linear, patchy or patchy confluent distribution with indistinct borders with the surrounding normal enamel exists. Also includes opacities due to fluorosis.
12	**Hypoplasia:** Defect can present as pit, groove and areas of partial or total enamel missing with rounded
13	**Amelogenesis imperfecta:** Includes a range of enamel malformations, genomic in origin, and include variations in thickness (hypoplastic malformation), smoothness and hardness (hypocalcified and hypomatures malformation) or a combination of these.
14	**Hypomineralisation defect (not MIH/HSPM):** Includes MIH/HSPM-like demarcated defects diagnosed in primary or permanent teeth other than MIH/HSPM index teeth.
2	**Demarcated opacities:** A demarcated defect involving an alteration in the translucency of the enamel, variable in degree from white/creamy to yellow/brown in colour. The defective enamel is of normal thickness with a smooth surface and a clear defined boundary from adjacent, apparently sound, enamel.
21	**White or creamy opacities:** Demarcated opacity, white or creamy in colour.
22	**Yellow or brown opacities:** Demarcated opacity yellow or brown in colour.
3	**Post-eruptive enamel breakdown (PEB):** Is a defect that indicates loss of initially formed surface enamel subsequent to tooth eruption that it appears clinically as if the enamel has not formed at all. The loss is often associated with a pre-existing demarcated opacity. PEB exists on surfaces traditionally considered at low caries risk (i.e. cuspal ridges and smooth surfaces) and its areas are rough and have uneven margins.
4	**Atypical restorations:** The size and shape of restorations do not conform to the usual picture of plaque related caries. In most cases in posterior teeth there will be restorations extended to the buccal or palatal smooth surfaces. The restorations may have residual affected enamel visible at the margins. In anterior teeth the buccal restoration is not related to trauma. It is often seen in otherwise caries-free mouths.
5	**Atypical caries:** The size and form of the caries lesion do not match the present caries distribution in the patient's mouth. The unusual pattern of caries can be further confirmed as associated to MIH/HSPM if signs of MIH/HSPM are seen in other teeth in the same mouth.
6	**Atypical extraction (Missing due to MIH/HSPM):** Suspect when absence of a FPM or SPM in an otherwise sound dentition and associated with opacities, PEB, atypical restorations or atypical caries in at least one of the FPM or SPM. It is unlikely that PIs will be extracted due to MIH.
7	**Cannot be scored:** Index tooth with extensive coronal breakdown and where the potential cause of breakdown is impossible to determine.

The authors introduced two charting forms; a short form to be used in clinical practice while a long form can be employed in epidemiological surveys. This index is comprehensive but time consuming and requires training to be implemented. This index has been recently validated in two prevalence studies (Ghanim et al., 2018, Owen et al., 2018).

Another research team (the Würzburg group) have also introduced a treatment need index for MIH (MIH-TNI) (Steffen et al., 2017). Similar to the MHSI, the MIH-TNI includes sensitivity as well as the extent of the enamel destruction in the overall severity score (Steffen et al., 2017, Almuallem and Busuttil-Naudi, 2018). However, this scale only uses six index sites: maxillary right, maxillary anterior, maxillary left, mandibular left, mandibular anterior, and mandibular right. The coding for this index is shown in Table 2.6. This index has not been validated and was not available when the current study started in 2015. However, the authors suggested that this index could be used for epidemiological studies as well as for individual patients to aid assessment and treatment planning.

Table 2.6 The Wüzburg MIH concept: the MIH treatment need index (MIH-TNI) by Steffan et al., 2017.

Index	**Definition**
0	No MIH, clinically free of MIH
1	MIH without hypersensitivity, without defect
2	MIH without hypersensitivity, with defect
2a	<1/3 defect extension
2b	>1/3 <2/3 defect extension
2c	>2/3 defect extension or/and defect close to the pulp or extraction or atypical restoration
3	MIH with hypersensitivity, without defect
4	MIH with hypersensitivity, with defect
4a	<1/3 defect extension
4b	>1/3 <2/3 defect extension
4c	>2/3 defect extension or/and defect close to the pulp or extraction or atypical restoration

Despite the development of these multiple indices, some of which are intended for clinical use, decision-making for children with MIH is complex and presents considerable challenges for the dental team. Other factors, such as behavioural

aspects, malocclusion, and personal preferences all need to be taken into consideration, sometimes involving a multi-disciplinary approach. The sole reliance on MIH severity indices, in treatment decisions, would not therefore provide a holistic approach to care.

2.4.4 Prevalence

The reported prevalence of MIH is between 2.8 % to 40.2% depending on the country in which the study was carried out and the different population cohorts (Jalevik, 2010, Oliver et al., 2014, Silva et al., 2016). A recent meta-analysis suggested an estimated 13-14% of children have MIH worldwide (Zhao et al., 2018, Schwendicke et al., 2018). In Northern England, a region similar to that included in this research, it has been estimated that 15.9% of children were affected by this defect (Balmer et al., 2012). There is considerable variation in the reported prevalence of MIH in published studies, likely because of a lack of methodological standardisation in diagnostic criteria or thresholds, which precludes comparisons between studies.

It is therefore challenging to make valid comparisons between various epidemiological studies because of a lack of consensus with regards to research protocols, calibration methods, choice of index, number of participants, and population characteristics. Recently, Elfrink and colleagues (2015) have outlined standard protocols for carrying out MIH studies. They suggest the optimal age for examination of children is 8-years because by this time all first permanent molars and incisors should have erupted and minimum destruction of hypomineralised enamel will have occurred (Elfrink et al., 2015). However, some caution may need to be exercised in reaching a definitive diagnosis, before the eruption of the full permanent dentition. MIH diagnosis using EAPD judgement criteria (Weerheijm et al., 2003) and subsequent amendments (Jalevik, 2010) is recommended when conducting such studies. Scoring of the teeth needs to be performed by calibrated examiners, preferably calibrated using a standard set of photographs (Elfrink et al., 2015). To illustrate this wide global variation, Table 2.7 summarises the prevalence of MIH cited for different populations and the respective indices that were employed to diagnose this condition

Table 2.7 Prevalence of Molar Incisor Hypomineralisation in different populations.

Authors	Region/Country	Age (years)	Sample Size	Prevalence of MIH	Index used
Jalevik et al. (2001)	Sweden	7-8	516	18.4% (MIH); 33.3% DDE	DDE
Weerheijm et al. (2001)	Netherlands	11	497	9.7%	mDDE
Dietrich et al. (2003)	Dresden, Germany	10-17	2408	5.6%	mDDE
Muratbegovic et al. (2007)	Bosnia Herzegovina	12	560	12.3%	EAPD 2003
Arrow (2008)	Australia	7	511	22%	mDDE
Lygidakis et al, (2008)	Greece	5.5 – 12	3518	10.2%	EAPD 2003
Cho et al. (2008)	Hong Kong	12	2635	2.8%	EAPD 2003
Da Costa-Silva (2008)	Brazil	6-12	918	19.8%	EAPD 2003
Mahoney & Morrison (2009)	New Zealand	7 – 10	522	14.9%	mDDE
Soviero et al. (2009)	Brazil	7-13	249	40.2%	EAPD 2003
Allazzam et al. (2011)	Saudi Arabia	8-12	267	8.6%	EAPD 2003
Ahmadi (2012)	Iran	7-9	433	12.7%	DDE
Balmer et al., (2012)	Northern England	12	3233	15.9%	mDDE
Jankovic (2013)	Bosnia Herzegovina	8	141	18.4%	mDDE
Bhaskar and Hedge (2014)	India	8-13	1173	9.46%	EAPD 2003
Hussein et al., 2015	Malaysia	7-12	150	16.9%	EAPD 2003
Ng et al. (2015)	Singapore	7	1083	12.5%	EAPD 2003
Oyadele et al., (2015)	Ile, Ife Nigeria	8-16	469	17.7%	EAPD 2003
Schmalfuss et al.,(2015)	Northern Norway	16	794	13.9%	EAPD 2003
Temiola et al. (2015)	Nigeria	8 – 10	237	9.7%	EAPD 2003
Dantas-Neta et al. (2016)	Brazil	11-14	594	18.4%	EAPD 2003
Saitoh et al., (2018)	Japan	7-9	4496	19.8%	EAPD 2003

2.4.5 Aetiology of MIH

The aetiology of MIH is still not clearly identified, although several potential risk factors have been proposed. MIH has been associated with systemic causes occurring around the third trimester of pregnancy through to the first three years of a child's life when the first permanent molars and incisors are forming. To date, three systematic reviews have been undertaken to critically analyse and evaluate the strength of evidence for the possible aetiology of MIH (Crombie et al., 2009, Alaluusua, 2010, Silva et al., 2016). However, researchers are still unable to conclusively identify any one specific factor. Silva et al., (2016) have

highlighted three main limitations of previous aetiological studies: one inherent problem is that most studies fail to recognise any confounding factor(s), which may exaggerate or diminish the importance of the variables of interest. This can be overcome using statistical methods, such as multiple regression but most studies made no attempt to adjust for potential confounders (Silva et al., 2016). Secondly, most studies have been conducted retrospectively, which may introduce recall bias. Mothers are shown to be able to recall perinatal factors such as gestational age, birth-weight, and mode of delivery accurately (Alaluusua, 2010). However, they are less likely to be reliable when reporting some aspects of pre- and post-natal events such as maternal health during pregnancy, duration of breastfeeding, childhood illnesses, and medication taken during early childhood, factors which may have relevance for MIH risk (Silva et al., 2016). Finally, lack of detail and consistency with the exposures investigated limits comparisons between studies. Despite these reservations, there is considerable evidence for an association between early childhood illnesses/infections and MIH (Silva et al., 2016).

In more recent years, attention has turned to the genetic contribution to MIH and current opinion very much favours a multifactorial aetiology, with genetic modification of environmental risk factors. Jeremias and co-workers analysed salivary DNA from a cohort of Brazilian and Turkish children and found numerous genes (ENAM, AMBN, TFIP11, and TUFT1) to be either protective of, or highly associated with, a diagnosis of MIH. Interestingly, no association was found between AMELX (a gene implicated in amelogenesis imperfecta with a primary function of amelogenin deposition) and MIH (Jeremias et al., 2013b). Undoubtedly, the most robust evidence for a genetic contribution to MIH has been obtained from studying its distribution in monozygotic and dizygotic twins. It has been shown that not only are twins at greater risk of MIH than the normal population, but monozygotic twins are twice more likely to have this condition than dizygotic twins (Teixeira et al., 2017). In view of this emerging evidence, the aetiology of MIH must be considered multifactorial with likely polygenetic and environmental influences (Silva et al., 2016, Taylor, 2017).

As described earlier, ameloblast function is highly sensitive to changes in the surrounding environment, including pH and temperature, which may be induced by a systemic illness (Tung et al., 2006). Animal studies have shown that

elevated temperatures may interfere with the function of ameloblasts, adversely affecting mineralisation, whilst overall tooth morphology remains normal (Ryynanen et al., 2014, Tung et al., 2006). The actual mechanism for how such determinants interfere with ameloblast function is still unclear although laboratory studies have proposed several possibilities. For example, exposure to erupting-disrupting chemicals (EDCs) such as bisphenol A (BPA) may increase expression of enamel proteins, reduce expression of the KLK-4 enzyme and lead to an accumulation of albumin, which could impede crystal growth (Jedeon et al., 2013). In addition, high temperatures can be teratogenic and may alter expression of genes, cause various congenital defects including enamel defects, clefts and tooth malformation (Ryynanen et al., 2014). Hyperthermia also decreases expression of BMPs, causes delay in cytodifferentiation and initiation of amelogenesis (Ryynanen et al., 2014).

Localised inflammation and hypoxia may make the environment more acidic and cause metabolic disturbances which prevent crystal growth due to the build-up of hydrogen ions (Sui et al., 2003). *In vitro* studies have proposed that hypoxic conditions increase the secretion of the enamel extracellular matrix and enhance the expression of enzymes MMP-20, AMBN, ENAM and AMELX in ameloblast-derived cells (Sidaly et al., 2015). This will disrupt the critical balance between hydroxyapatite crystal growth and degradation of enamel matrix protein. An increase in enamel matrix production may limit MMP-20 and KLK-proteases function to degenerate protein, thereby resulting in inhibition of hydroxyapatite crystal growth (Sidaly et al., 2015).

2.4.5.1 Prenatal period

Studies have proposed maternal illnesses or infections during pregnancy such as hypocalcemia, Vitamin D deficiency, hypoparathyroidism, hypertension, gestational diabetes, pre-eclampsia, maternal smoking, and maternal medication as potential risk factors for MIH, although no robust evidence for causal effects exist (Muratbegovic et al., 2007, Fagrell et al., 2011, Ahmadi et al., 2012, Ghanim et al., 2013a, Silva et al., 2016). Maternal stress has also been associated with higher risk of MIH, as reported in an Iraqi study, but no other data has confirmed or refuted this finding (Ghanim et al., 2013a).

2.4.5.2 Perinatal period

There are conflicting data for any association between MIH and perinatal factors. Perinatal events at the time of delivery such as breech presentation, prolonged delivery, caesarean section are speculated to cause hypoxia during this critical period which may cause a resultant insult to enamel formation (Alaluusua, 2010, Wong, 2014, Wong et al., 2014). Some studies have reported that hypomineralised teeth are more prevalent in children who were born prematurely, had known episodes of hypoxia, were delivered via Caesarean section, had a prolonged delivery, had low birth weight, spent time in an incubator after birth and in twins (Lygidakis et al., 2008, Ghanim et al., 2013a, Jankovic et al., 2013, Pitiphat et al., 2014, Garot et al., 2016). These infants may suffer complications such as respiratory problems due to immature lung development, cardiovascular and renal abnormalities, which indirectly can also cause hypoxia. Thus, they also remain at risk of developing MIH due to compromised ameloblast function and inadequate absorption of calcium and phosphorus (Ahmadi et al., 2012, Wong, 2014).

In contrast, other investigators have not identified a correlation between enamel defects and complications during pregnancy and birth (Beentjes et al., 2002, Whatling and Fearne, 2008, Jankovic et al., 2013, Wong, 2014, Wong et al., 2014).

2.4.5.3 Postnatal period

Associations between post-natal factors and MIH have been widely investigated. Early childhood illnesses occurring during the first three to four years of children's lives have been associated with increased risk of having MIH. Common infections may include upper and lower respiratory tract infections, chicken pox, urinary tract infections, recurrent high fever, tonsillectomy, and asthma (Jalevik et al., 2001a, Beentjes et al., 2002, Tapias-Ledesma et al., 2003, Whatling and Fearne, 2008, Ghanim et al., 2013a, Sonmez et al., 2013, Silva et al., 2016). Seow suggested that during such infections, microorganisms may either affect the ameloblastic function or cause indirect alteration to cellular functions through their metabolic products or the inherent high fever experienced by the patients (Seow, 2014). Again, there is lack of consensus regarding the association of infections and MIH risk: some studies suggest that these infections do contribute to an increased prevalence of MIH in children (Beentjes et al., 2002, Ahmadi et

al., 2012, Allazzam et al., 2014), while others did not find such association (Muratbegovic et al., 2007, Crombie et al., 2009, Jankovic et al., 2013).

Studies have also reported a positive correlation between antibiotic consumption, especially amoxicillin, during this critical period, and MIH (Tapias-Ledesma et al., 2003, Whatling and Fearne, 2008, Crombie et al., 2009, Laisi et al., 2009, Souza et al., 2012). This finding, however, might be confounded by other factors because the use of antibiotics is accompanied by the presence of early childhood infection and fever. It is therefore difficult to determine whether MIH stems directly from the effect of amoxicillin on ameloblast function, is attributed to the infectious disease or fever that antibiotic was prescribed for, or indeed results from a synergistic effect of both factors (Willmott et al., 2008, Ahmadi et al., 2012, Jankovic et al., 2013).

Prolonged exposure to environmental organic pollutants, such as polychlorinated dibenzo-p-dioxins dibenzoflurans (PCDD) and polychlorinated dibenzo-p-dioxins flurans (PCDF), which may be present in human breast milk has also been suggested as a causative factor for the occurrence of MIH (Alaluusua et al., 1996). However, this finding has been contested by other authors (Beentjes et al., 2002, Muratbegovic et al., 2007, Laisi et al., 2008, Whatling and Fearne, 2008). Furthermore, some researchers found that children who have never been breast fed were more at risk of having enamel defects compared to those who were breastfed, although the difference was not statistically significant (Li et al., 1995, Lunardelli and Peres, 2006, Jankovic et al., 2013). One possible explanation is that children who were breast-fed were protected from early childhood infections because breast milk contains antibodies against these infections (Lunardelli and Peres, 2006).

2.4.6 Comparison of normal and hypomineralised enamel

Histological analysis of hypomineralised enamel has revealed that it has marked mechanical and chemical differences to ‘normal’ enamel. Fundamentally, it has disorganised enamel rods, loosely packed calcium hydroxyapatites, a less dense rod structure and marked inter-rod spaces occupied by protein and water (Xie et al., 2008, Chan et al., 2010). The presence of large amounts of protein within the inter-rod spaces reduces mineral uptake and prevents growth of calcium hydroxyapatite, with a resultant poorly mineralised and porous enamel structure

(Jalevik and Noren, 2000, Jalevik et al., 2005, Wong, 2014). Failure to remove organic material from between the calcium hydroxyapatite crystals in hypomineralised enamel suggests that the disturbance occurred during the maturation stage of amelogenesis (Farah et al., 2010b, Wong, 2014). For these reasons, hypomineralised enamel has markedly lower enamel hardness and elastic modulus, which compromises the overall mechanical properties of the affected enamel (Chan et al., 2010, Fagrell et al., 2010). Histopathological investigation of hypomineralised enamel has revealed that the defect starts at the DEJ and not on the outer enamel surface (Jalevik and Noren, 2000, Fearne et al., 2004, Denis et al., 2013). Furthermore, the defects occur mostly on the cuspal/incisal regions, while the cervical areas appear largely unaffected (Farah et al., 2010c). This is because the defect is confined to the inner enamel on the cervical area. As it extends occlusally, towards the outer enamel surface, the defect becomes more obvious and involves the entire thickness of the enamel on the occlusal or incisal region (Farah et al., 2010c).

On average, the mineral density of hypomineralised first permanent molars is reportedly about 19-20% lower than that of sound enamel (Jalevik and Noren, 2000, Fearne et al., 2004, Farah et al., 2010c). MIH-affected enamel has a lower mean Calcium:Phosphorus (Ca:P) ratio than sound enamel (1:4 and 1:8 respectively) because it contains a higher carbon content than sound enamel (Jalevik et al., 2001b, Fearne et al., 2004). MIH-affected enamel has also been found to have considerably higher inclusion of trace elements such as sodium, magnesium and potassium, while chlorine and strontium content is almost similar to that of sound enamel (Fearne et al., 2004). In contrast to sound enamel, the mineral concentration shows some reduction from the dentino-enamel junction to the subsurface MIH enamel, which supports the hypothesis that the second phase of maturation is also disturbed (Fearne et al., 2004).

As previously mentioned in Section 2.2.6, when there is a difference in refractive indices of tissue components, there will be a resultant deviation in reflection and scatter of light rays (Denis et al., 2013). High water and protein retention in poorly mineralised enamel increases enamel subsurface porosity below an apparently intact enamel surface layer. Excess water in hypomineralised enamel occupies the pores in the inter-rod spaces and alters the RI of enamel (1.62) to more resemble that of water (1.33). This makes the defective enamel appear more

opaque than the adjacent ‘normal’ and translucent enamel. At present, it is still not clear why there is such a widely observed spectrum of colours within the opacities of hypomineralised enamel, even within the same tooth. However, the severity of hypomineralisation has been associated with the colour of opacity. Darker opacities are found to be microscopically more porous, and to have lower mineral density and lower hardness value than white opacities, hence these are at a greater risk of undergoing post-eruptive breakdown (da Costa-Silva et al., 2011, Crombie et al., 2013, Jeremias et al., 2013a, Chay et al., 2014). Farah et al., (2010) reported that yellow and chalky enamel showed about an 8-fold higher protein content, while brown enamel had a 15 to 21-fold higher protein content than normal enamel (Farah et al., 2010b). Serum proteins such as albumin and antitrypsin may inhibit protein degradation by the enzyme KLK-4, thereby contributing to the elevated organic content in hypomineralised enamel (Farah et al., 2010b). High protein and carbon content in hypomineralised enamel means that normal acid etching results are not achieved, with resultant decreased bond strength between hypomineralised enamel and restorative materials such as composite resin or fissure sealants. These organic materials act as physical or chemical barriers preventing optimum penetration of bonding agents which may partly explain the high failure rate of adhesive restorations or sealants in MIH (Mejàre et al., 2005, Jalevik and Klingberg, 2012, Chay et al., 2014). It has also been suggested that a reduction of mineral content in hypomineralised molars, below a certain level can lead to the inability of enamel to withstand the occlusal forces needed to sustain bonded materials. Hence, there may be further disintegration of enamel underneath the restoration and this clinically may resemble the appearance of hypoplastic enamel (William et al., 2006a, Farah et al., 2010a).

It has been shown that there is a relationship between hardness values, mineral density and the colour of hypomineralised enamel with yellow/brown opacities being softer than white ones. Jalevik and Noren showed that yellow/brown opacities were more porous than lighter opacities (Jalevik and Noren, 2000). *In vitro* studies reported a reduction in mineral density of yellow or brown opacities in both second primary molars and permanent first molars by 20-22% and 19-20% respectively (Farah et al., 2010c, Elfrink et al., 2013b). White opacities show negligible differences in mineral density when compared with the unaffected enamel (Elfrink et al., 2013b). In addition, darker lesions (yellow/brown) are

shown to be more porous than lighter-coloured opacities (da Costa-Silva et al., 2011). Thus, the clinical presentation of enamel opacities may be used as an indicator of the severity of MIH defects (Farah et al., 2010a).

Yellow or brownish-yellow defects indicate a full thickness defect whilst creamy-yellow or whitish-creamy defects are located in the inner part of the enamel (Jalevik and Noren, 2000).

2.4.7 Management of incisor opacities

2.4.7.1 Overview

Having described the underlying biophysical characteristics of hypomineralised enamel, the following section will consider the clinical implications of such defects and the rationale for the various (cosmetic) treatment options. An understanding of the structure and mechanical properties of hypomineralised enamel and knowledge of materials to be used are fundamental when choosing the most appropriate intervention to manage the unaesthetic anterior enamel defects, such as those seen in MIH. The clinician's ability to reach the correct diagnosis and assess the severity of the opacity, alongside the patient's expectations of treatment, are crucial in determining the success of the intervention. It is acknowledged that there is a wealth of literature describing the management strategies for hypomineralised first permanent molars, within the context of MIH, but his thesis will focus on interventions for anterior permanent teeth.

Visible enamel opacities on incisors (and indeed canines) may cause cosmetic impairment and aesthetic concerns that must be managed appropriately to meet the patients' (and parents') expectations. The majority of patients seeking treatment for enamel opacities associated with MIH (and other conditions) are children and young people, therefore the aim of treatment must be to improve aesthetics without sacrificing an excessive amount of tooth structure at an early age (Kim et al., 2011a, Subramaniam et al., 2014). Several treatment approaches have been suggested to manage discoloured hypomineralised incisors. Remineralisation approaches using topical fluoride or casein phosphopeptide-amorphous calcium phosphate (CPP-ACP, also known as tooth mousse^{TM}) have been proposed and they may be effective especially if applied

immediately following tooth eruption. However, there may be some time before any aesthetic improvements are seen if, indeed, they are seen (Ng and Manton, 2007, Kim et al., 2011a, Reema et al., 2014). This approach is recommended for outer surface lesions only, as topical preparations, such as these, cannot penetrate into deeper lesions. It is recommended that tooth mousse is applied daily on the defective area by patients at home, therefore, the effectiveness of this method depends on patient compliance, and the efficiency is unpredictable (Kim et al., 2011a). Furthermore, the evidence-base for the use of casein preparations has not yet been established.

Minimally invasive interventions such as microabrasion, resin infiltration (for example Icon-Infiltrant™ DMG, Hamburg, Germany), tooth whitening, and conventional resin bonded composite can be performed to improve the aesthetics of hypomineralised enamel on anterior teeth. The use of microabrasion and resin infiltration minimises the need to use handpieces for removal of tooth tissue and are relatively painless procedures, hence local anaesthesia is usually not required. Therefore, they are more conservative to tooth tissue and more acceptable to paediatric dental patients. With the exception of tooth whitening, these interventions also do not rely on patient compliance at home, the outcomes are more predictable and do not require such frequent recalls as compared to remineralisation therapies. Microabrasion is indicated for surface opacities, whereas tooth whitening can treat opacities deeper within the tooth. Infiltration resins on the other hand aim to alter the enamel's refractive index by sealing/occluding the opacity. However, these interventions may not be effective for deeper lesions, hence the need for conventional composite resin restorations to mask the defects may still be indicated. Although these cosmetic interventions appear promising in their ability to camouflage enamel opacities, most published articles to date are clinical reports and *in vitro* studies. These interventions may be effective in improving the appearance of discoloured enamel in MIH patients, but the evidence for their effectiveness is still anecdotal and empirical. A more detailed description of these approaches will now be provided.

2.4.7.2 Microabrasion

Enamel microabrasion was first developed in 1986 to remove superficial intrinsic discolouration due to DDE, particularly those related to dental fluorosis (Croll and Helpin, 2000). It has also been applied to remove staining associated with

enamel decalcification post-orthodontic treatment (Murphy et al., 2007, Sundfeld et al., 2007). Microabrasion is conservative to tooth structure as it removes only 25 to 200μm enamel, yet improves aesthetics. This method can be combined with other techniques such as conventional composite restoration and tooth whitening to mask deeper enamel defects (Sundfeld et al., 2007, Sundfeld et al., 2014, AlShehri and Kwon, 2016). Interestingly, some authors have advised against this technique in patients with incompetent oral seals (Sundfeld et al., 2014, Pini et al., 2015). The rationale is that these patients' anterior teeth are constantly dehydrated because of exposure to air, therefore the opacity, which is commonly located on the incisal third of the tooth, may actually become more evident following microabrasion (Sundfeld et al., 2014, Pini et al., 2015). However, this procedure is not absolutely contra-indicated for children with inadequate lip coverage but patients need to be informed about the potential risks and benefits before proceeding with the treatment.

Microabrasion involves a combination of erosion and abrasion of the discoloured enamel using slurry of acid (either hydrochloric acid or phosphoric acid) and pumice together with mechanical rubbing using abrasive silicon carbide particles to produce the "abrosion effect" on the discoloured enamel (Waggoner et al., 1989, Sheoran et al., 2014, AlShehri and Kwon, 2016). The technique removes the porous and unaesthetic surface enamel layer, exposes sound enamel underneath and smooths the surface irregularity (Sheoran et al., 2014, Pini et al., 2015). The overall effect of this procedure is to create a smooth, rod-free layer and lustrous enamel surface, most likely due to compaction of minerals such as calcium and phosphate in the enamel crystals resulting from the simultaneous erosive and abrasive action of the microabrasion compound on the enamel (Sheoran et al., 2014, Sundfeld et al., 2014). The use of this technique has been shown to be effective clinically in removal of both opaque and brown defects (Sundfeld et al., 2014, Sheoran et al., 2014). Microabrasion gives an immediate reduction in the visibility of opacities and long lasting results, with minimal loss of the enamel layer, and gives a lustrous and shiny enamel surface which may improve the optical properties of the enamel, hence improving aesthetics (Sheoran et al., 2014, Sundfeld et al., 2014). Many clinicians would advocate the use of microabrasion as the first treatment choice for management of enamel opacities (Pini et al., 2015).

The effectiveness of both 18% hydrochloric acid (HCl) and 37% phosphoric acid (H_3PO_4) and pumice has been evaluated clinically as microabrasion medicaments (Sheoran et al., 2014, Sundfeld et al., 2014). Both acids have been shown to be effective in reducing opacities but aesthetic improvement has been observed significantly more quickly when using HCl and pumice compared to H_3PO_4 and pumice; suggesting the effectiveness of this compound might be superior than the latter (Sundfeld et al., 2014). It is important to note that, although this technique involves the removal of the enamel layer, the enamel lost is not clinically significant, since it removes only up to quarter (250μm) of the enamel thickness; so it is unlikely to cause dental sensitivity (Waggoner et al., 1989). However, post-treatment application of a fluoridated prophylaxis paste or casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) on the exposed enamel has been recommended to prevent sensitivity and aid remineralisation of the treated surface (Sheoran et al., 2014, Sundfeld et al., 2014, AlShehri and Kwon, 2016). *In vitro*, microabrasion followed by polishing with diamond paste fluoride prophylactic paste has been shown to result in higher hardness and better surface smoothness of the enamel (Fragoso et al., 2011).

Since 1986, microabrasion techniques and related materials have been continually improved to ensure safety and effectiveness. There are a few commercially available products for microabrasion in the market, for example, Prema compound (Premier Dental Company), Opalustre (Ultradent) and Pumice (Pumex). Opalustre (Ultradent) appears to be one of the most commonly used and effective products for microabrasion. This product contains 6.6% HCl combined with silicone carbide microparticles in a highly visible (purple) water-soluble paste. This technique requires careful isolation with rubber dam to protect the patient's soft tissues from acid burns, so it might be difficult to use if the teeth are not fully erupted. Opalustre kits contain the Opalustre material in a syringe, Oraseal and Opal prophy cups. It is recommended to apply 'Oraseal' prior to placement of the Opalustre paste to protect the gingiva against any acid leakage. Opalustre paste is then placed on the surface of the defective enamel through the syringe tip. Mechanical rubbing of the hypomineralised enamel surface is then carried out by using the Opal prophylaxis cup directly on the lesion for about one minute at speed of 1:10 revolutions per minute (RPM) using a slow-speed handpiece. Next, teeth are rinsed thoroughly and the clinician should re-evaluate tooth/opacity colour. The procedure can be repeated for up to ten cycles, if

required, until anticipated results are achieved. It is recommended that the treated enamel surface is polished with a polishing disc, followed by application of a fluoride gel to promote remineralisation (Pini et al., 2015). This procedure can also be combined with tooth whitening or conventional composite restoration, if optimum aesthetics are not achieved through microabrasion alone. Although widely considered a safe, and predictable technique, a recent case study did highlight the potential problem of post-treatment staining through consumption of tomato-based foods and patients should be advised accordingly (Rogers et al., 2016).

To date, few studies have tried to evaluate the outcomes of microabrasion from the patient's perspective. Wong and Winter (2002) treated 32 patients (14 male, 18 female) with different types of enamel opacity (single line, multi-line, patched and diffused) on both upper central incisors, using Prèma abrasive paste mixed with 18% HCl (Wong and Winter, 2002). The overall aim was to determine which type of opacity was most conducive to cosmetic improvement using a microabrasion approach. The age of the cohort was not reported, although this was a paediatric dentistry case-mix. The patients were treated by one of the authors (FW) and followed up for four years post-treatment (1991-1995). The key findings were that microabrasion was effective in improving single line and demarcated opacities and the outcomes were stable in the long term. The majority of the participants and their parents (65.6%) were reportedly satisfied with the immediate outcome following the treatment and felt it was still acceptable six months post-treatment, indicating a stable and long-lasting improvement (Wong and Winter, 2002). There was no difference in satisfaction according to gender, although female patients appeared less satisfied with long-term outcomes of the treatment. The main limitation of this study was that no quantitative instrument or approach was used to measure patient satisfaction and aesthetic improvement, thus findings were not measured objectively. Moreover, this study did not evaluate the psychosocial impact of treatment for DDE.

A more recent study undertaken at a UK dental hospital, involved children aged 7-16 years with visible enamel defects on permanent incisor treated with microabrasion only or followed by composite treatment (Rodd et al., 2011a). This study sought patients' views before and after treatment, using a 10cm visual analogue scale (VAS). This study reported that microabrasion with or without

composite restoration was effective in the management of enamel opacities and resulted in positive impacts on children's self-reported confidence and happiness (Rodd et al., 2011a). Difference in satisfaction between genders was also not significant, although females were significantly more worried about their appearance before treatment than boys (Rodd et al., 2011a). Although most children reported positive outcomes following treatment, some had high expectations for a 'perfect' tooth appearance following treatment, which may lead to disappointment when expectations were not met. To overcome this problem, the authors suggested the use of photographs to show patients the range of realistic outcomes that might be achieved following treatment (Rodd et al., 2011a). Prior to treatment, it is imperative that both clinicians and patient (and parents) manage expectations about what improvements might be possible, and the risks/benefits of different treatment regimens, including any long-term implications.

Appropriate case selection and meticulous technique are therefore crucial to ensure the success of this regimen. As microabrasion only removes superficial discolouration, multiple applications might be required to reduce the opacity associated with deeper lesions (Paris and Meyer-Lueckel, 2009, Kim et al., 2011a, AlShehri and Kwon, 2016).

2.4.7.3 Resin Infiltration

Resin infiltrants, such as ICON-Infiltrant™ (DMG, Hamburg, Germany), are low viscosity hydrophilic light curing resins, which were primarily developed for the treatment of early interproximal caries lesions. Their purported mode of action was by replacing lost tooth structure and delaying caries progression by sealing the porous enamel and blocking the diffusion pathways for acid penetration and ionic movement (Meyer-Lueckel and Paris, 2010, Chay et al., 2014). Thus, most of the studies to date relate to the technique of resin infiltration for caries management rather than for DDE. The technique is non-invasive, as it does not require drilling or sacrificing healthy tooth structure, and the material is capable of penetrating 5-25 μm of porous enamel, driven by capillary forces (Subramaniam et al., 2014). Resin infiltrations are also proven to strengthen the enamel structure mechanically by occluding porous enamel, thereby preventing further breakdown of the enamel surface (Paris et al., 2007b, Kim et al., 2011a). This

material also has been shown to be effective in masking the visibility of smooth surface decalcified ‘white spot lesions’ *in vitro* and clinically, with reportedly good outcomes in the management of ‘unsightly’ post-orthodontic decalcified lesions (Paris and Meyer-Lueckel, 2009, Kim et al., 2011a, Knosel et al., 2013, Lee et al., 2013, Paris et al., 2013). Resin infiltrations appear to have a refractive index (RI) of 1.52, close to that of enamel crystals (RI 1.62-1.65). The resin infiltration penetrates the hypomineralised enamel and fills the pores, thus altering the RI of the porous enamel and making it almost similar to the RI of sound enamel. Decreasing the difference in refractive index between the hypomineralised surface and hydroxyapatite crystals on unaffected enamel reduces light scattering (Denis et al., 2013). Therefore, the lesion loses its opaque appearance and blends reasonably well with the surrounding natural tooth structure, thus improving overall aesthetics (Paris et al., 2013, Subramaniam et al., 2014).

The clinical outcome, however, is dependent to a variety of clinical conditions such as lesion characteristics, complete or incomplete penetration of the material, polymerisation shrinkage, and resin colour (Paris et al., 2013). Active carious lesions have a thin and porous surface layer, which allows better penetration of resin infiltrations than do inactive or remineralised lesions (Arnold et al., 2014). Infiltration within the enamel surface layer is better than can be achieved in deeper lesions because the degree of porosity decreases from the outer enamel surface towards the dentinoenamel junction (Arnold et al., 2014). Thus, the use of resin infiltrations is limited to lesions within its infiltration capacity; deeper lesions may receive minimal therapeutic benefit from this technique (Lee et al., 2013, Arnold et al., 2014). Individual factors such as saliva properties, biofilm and intraoral pH may also influence the depth of penetration of the resin infiltrations (Subramaniam et al., 2014).

Following on from the success of resin infiltration in improving the appearance of post-orthodontic decalcified enamel lesions, there was interest in the theoretical application of the same approach to improve the appearance of hypomineralised enamel defects. Low viscosity resin infiltrations have now been shown *in vitro* and *in vivo* to be able to penetrate into demineralised enamel (Paris et al., 2007a, Paris et al., 2007b, Paris and Meyer-Lueckel, 2009, Senestraro et al., 2013, Subramaniam et al., 2014). It is acknowledged that hypomineralised enamel has poor bond strength and poor etch pattern due to its high inorganic content of

proteins. It has been suggested that pre-treatment of hypomineralised enamel with sodium hypochloride (NaOCl) could help to remove the excess protein and enhance etching and bonding of the hypomineralised enamel surface. However, this procedure has been shown to further weaken hypomineralised enamel because other structures such as collagen are also removed by the NaOCl, resulting in the reduction of mechanical properties of hypomineralised enamel. Recently, Chay *et al*., (2014) suggested that pre-treatment of hypomineralised enamel with NaOCl with or without resin infiltration placement, increased bond strength of composite resin to the defective enamel (Chay et al., 2014). Pre-treatment of hypomineralised enamel with resin infiltration may improve adhesion by increasing surface hydrophobicity and the area of the resin–enamel interface; therefore compensating for the poor etching patterns. The use of high concentration acid etching may, however, be contraindicated in hypomineralised enamel as this might exacerbate any sensitivity experienced by some of these children (Crombie et al., 2014). Furthermore, a recent *in vitro* study by Crombie *et al*., using extracted hypomineralised first permanent molars, reported that two minutes pre-treatment with 0.95% sodium NaOCl did not produce significantly improve results as compared to standard application procedures recommended by the manufacturer, probably because this procedure removed surface protein only. This study also showed that resin infiltrations are capable of penetrating and sealing microporosities in hypomineralised enamel and thereby increasing the microhardness of the defective areas (Crombie et al., 2014). Although the improved microhardness did not reach normal values and the pattern of penetration was inconsistent, pre-treatment of hypomineralised enamel with resin infiltrations may improve bonding between the resin-to-enamel surfaces. Further studies are required to confirm this finding. Pre-treatment with NaOCl and Icon did not improve bond between hypomineralised enamel and composite resin restorations (Kramer et al., 2018).

Resin infiltrations theoretically have the potential to improve aesthetic and mechanical properties of hypomineralised enamel. However, the outermost surface of hypomineralised enamel may not be as permeable as normal or demineralised enamel if there has been a previous use of remineralisation agents such as CPP-ACP and fluoride, which may have been prescribed to remineralise the tooth surface and reduce patient sensitivity. Hence, it may be more difficult for the resin infiltrations to penetrate into the defective lesion underneath

(Crombie et al., 2014). The resin infiltration system Icon™ (DMG, Hamburg) therefore benefits from the use of 15% HCL to eliminate the relatively intact surface layer and open up access to the body of the lesion (Denis et al., 2013).

Isolation using rubber dam is mandatory when performing this procedure because resin bonded materials are sensitive to water contamination and to ensure patient safety when using etching material (Subramaniam et al., 2014). Further *in vivo* investigations are needed to determine the effectiveness and efficiency of resin infiltrations in the aesthetic management of hypomineralised incisors and to confirm the practicality of using these materials in a clinical setting, particularly with young patients.

2.4.7.4 Tooth whitening

Tooth whitening is used to lighten and 'blend in' intrinsic enamel discolouration, such as a DDE, to better match the surrounding naturally translucent enamel and give a more uniform appearance. Tooth whitening involves the diffusion of whitening agents such as hydrogen peroxide or carbamide peroxide into enamel and dentine to interact with stained molecules, with the overall effect of lightening enamel colour. Tooth whitening also alters the tooth surface and changes its optical properties. It can be performed professionally 'in-office' by a dentist, or by using take-home products under the supervision of a dentist. They may also be available as self-administered 'over the counter' whitening products. The in-surgery tooth whitening procedure by a dental professional involves the use of highly concentrated materials of up to 40% hydrogen peroxide, and is frequently combined with light activating devices. However, post-treatment sensitivity has been widely reported by patients who have undergone this procedure (Kim et al., 2011a, Mastroberardino et al., 2012). The use of low concentration hydrogen peroxides, however, can change the calcium and phosphate mineral content of the bleached enamel. Reduction in the mineral content of bleached enamel can alter the enamel's RI, making the opacities become lighter and more apparent (Mastroberardino et al., 2012). Thus patients might notice that a tooth with a white opacity may seem more obvious after the tooth whitening procedure, because of temporary dehydration, but after a while the tooth will be rehydrated by the saliva and the opacity will be less visible (Sundfeld et al., 2014). Furthermore, when this material is applied on decalcified or hypocalcified enamel

(as in hypomineralised enamel), the microhardness of the enamel surface might be reduced and surface roughness increased due to further mineral loss from the procedure (Kim et al., 2011a, Mastroberardino et al., 2012, Lee et al., 2013). Kelleher and Roe however disputed this finding and stated that, if there were any changes in enamel microhardness following tooth whitening, the effect would be much less detrimental compared to invasive dental procedures such as enamel removal before veneer placement (Kelleher and Roe, 1999).

Despite claims that tooth whitening may contribute to heightened self-esteem, improved oral hygiene and increased patient involvement with dentistry, its uptake by patients was relatively slow in the 1980s because of fears over the safety of peroxide-containing cosmetic treatments (Westland et al., 2007). However, the development of tray-based bleaching systems in the late 1980s enabled dentists to achieve tooth whitening with minimal surgery time and greater patient tolerance (Westland et al., 2007). Professional tooth whitening is now ubiquitous in dental care and there is a large and growing market for home-based whitening systems. Home-based whitening systems typically contain low levels of bleaching agent (e.g. 3-6% hydrogen peroxide) that are self-applied to the gum via gum shields (trays), strips or paint-on products and require twice daily applications for about two weeks. The wide range of treatments available now necessitate that reliable and accurate methods be developed for the measurement of efficacy of whitening treatments (Westland et al., 2007).

Prior to 2012, the use of tooth whitening products that contained carbamide peroxide releasing more than 0.1% hydrogen peroxide, were banned in countries within the European Union. Carbamide peroxide contains urea and hydrogen peroxide. Commercial products, for prescription by dental professionals only, were classified as a cosmetic product by the UK Government Departments of Trade and Industry (DTI) in 1993 and were considered illegal. Although one of the market leaders (Oplascence^{TM}) was granted a CE mark as a medical device in 1995, the UK Government Agencies still considered this product as a cosmetic product (Kelleher and Roe, 1999).

However, the British Dental Association (BDA), other bodies and the manufacturers, continued to vigorously challenge this legal position. It was argued that humans are exposed to hydrogen peroxide not only from tooth

whitening, but also as part of daily activities such as movement and growth and conversion of food to energy, which causes disintegration of oxygen-free radicals such as hydrogen-peroxide (Kelleher and Roe, 1999).

Finally, in 2012, an EU Directive allowed an increase in permissible maximum concentration of hydrogen peroxide release to 6%. However, the use of such products in the under 18s remained an area of confusion and ambiguity. The GDC's position is that such products can be used in under 18s providing it is for the treatment or prevention of a disease or condition. Despite this guidance, many dental defense organisations decline to provide indemnity to its members who prescribe tooth whitening for patients under the age 18 years. In cases such as DDE, when tooth whitening needs to be provided for young children, a detailed discussion with patients/parents regarding the potential risks and benefits of the procedure, other treatment options, the legal status of tooth whitening and the possibility of delaying treatment until patient is above 18-years-old, must be documental carefully in the patient's notes. Dental practitioners are advised to consult their own dental defense organisations prior to embarking on this treatment regimen for their young patients.
(http://www.dentalprotection.org/uk/publications-resources/updates/position-statements-display-page/2014/12/08/tooth-whitening).

However, tooth whitening alone may not always adequate to camouflage or reduce the visibility of discrete enamel opacities on hypomineralised permanent incisors. Denise et al., (2013) suggested that resin infiltration can be combined with carbamide peroxide tooth whitening to achieve satisfactory aesthetic results (Denis et al., 2013). During tooth whitening, carbamide peroxide decomposes to hydrogen peroxide and urea. The hydrogen peroxide component releases oxygen and lightens the tooth colour while urea denatures the protein, which may enhance bonding between hypomineralised enamel and resin infiltration (Denis et al., 2013, Aschheim, 2015). A combination of treatment also gives favourable results among patients with diffuse opacities such as fluorosis. A study of adolescents and adults patients with fluorosis, aged 15- to 39-years-old who received microabrasion using a mixture of pumice with 27% phosphoric acid followed by home-used application of 10% carbamide peroxide tooth whitening gel were reportedly more satisfied with the results when compares with those who received microabrasion only (Castro et al., 2014).

2.4.7.5 Composite resin restoration

Conventional restorative treatment with composite resin materials may be indicated when other minimally invasive approaches, such as remineralisation, tooth whitening, microabrasion and infiltrants are unsuccessful in camouflaging the enamel opacity (Kim et al., 2011a, AlShehri and Kwon, 2016). This is often the case for deeper and more severe lesions. Modern composite resin restorative materials are however, translucent, allowing the discolouration of the underlying enamel opacity to still show through. Therefore, clinicians should consider the use of opaque or less translucent composite as a base layer to mask the underlying 'abnormal' enamel colour. The use of a directly placed composite resin 'veneer' is a relatively quick and easy option for masking enamel opacities in hypomineralised anterior teeth, but as mentioned previously, bonding to hypomineralised enamel may be defective and unpredictable. Thus, composite resin restorations may require re-treatment due to bond failure. A degree of tooth structure may therefore be removed each time the tooth needs re-treatment, resulting in undesirable loss of tooth tissue at an earlier age. To date, no studies have measured outcomes following composite resin placement for the aesthetic management of incisor opacities associated with MIH.

2.4.8 Patient-reported impacts of MIH

2.4.8.1. Pain

One of the main patient-reported complaints associated with poorly mineralised teeth is hypersensitivity. This occurs either due to enamel disintegration following normal masticatory force which exposes dentine underneath, or penetration of oral bacterial into the dentinal tubules which may trigger an inflammatory response in the tooth pulp (Weerheijm et al., 2001b, Jalevik and Klingberg, 2002, Rodd et al., 2007a, Rodd et al., 2007b, Lygidakis, 2010). Dental sensitivity can cause problems for both patients and dentists. The affected teeth can be very sensitive to cold food and beverages, cold or warm air, and mechanical stimuli such as tooth brushing. Tooth brushing exacerbates pain on the affected tooth, which may result in children avoiding toothbrushing, becoming dentally anxious, and further increasing the caries risk of affected teeth.

2.4.8.2. Burden of dental care

Obtaining adequate analgesia for restorative care may be challenging in children with hypersensitive MIH-affected teeth (Lygidakis et al., 2010, Lygidakis, 2010, Almuallem and Busuttil-Naudi, 2018). Inappropriate pain control may complicate dental procedures and may be one reason for high treatment failures in MIH cases. Another reason for dental restoration failure may stem from the difficulty in achieving bonding between the resin-bonded material and porous hypomineralised enamel. It has been speculated that higher protein content and poorly organised enamel rods in hypomineralised enamel alters the solubility of these crystallites to acid, making it resistant to acid etching (Jalevik et al., 2005). Children with MIH have been reported to undergo dental treatment ten times more often than unaffected children because restorations on these teeth were replaced so frequently (Jalevik and Klingberg, 2002, Kotsanos et al., 2005). Other authors have found that restorations and sealants in children with MIH are three times as likely to need retreatment as those interventions performed in children without MIH (Kotsanos et al., 2005, Americano et al., 2016). The need for more frequent treatment (and re-treatment) and the experience of pain during restorative interventions, may account for the higher levels of dental anxiety seen in MIH children (Jalevik and Klingberg, 2002, Allazzam et al., 2014). Kosma and colleagues, however, found that affected children who had never received any dental treatment also reported higher mean levels of dental fear than those who had received treatment (Kosma et al., 2016). They also found that older children and girls reported higher mean dental fear than younger children and boys (Kosma et al., 2016). Further study on the associations between MIH and dental fear is warranted.

Severely affected molars sometimes require extraction, often before 10-years of age (Crombie et al., 2009). This decision, however, is usually made in consultation with an orthodontist. Parents and children should be advised of, and supported in, the knowledge that management of hypomineralised teeth requires lifelong maintenance and a multidisciplinary approach, which has cost implications. Apart from financial considerations of dental treatment, there are also societal costs including children's absence from school, which may negatively impact their academic performance and parents' absence from work to attend multiple appointments (Willmott et al., 2008, Almuallem and Busuttil-

Naudi, 2018).

2.4.8.3. Caries experience

As mentioned previously, numerous studies have shown that the presence of MIH correlates positively with an increased prevalence of dental caries in the permanent dentition (Leppäniemi et al., 2001, Muratbegovic et al., 2007, da Costa-Silva et al., 2010, Garcia-Margarit et al., 2014, Kosma et al., 2016). Soft and porous enamel may predispose to plaque accumulation, making the tooth more susceptible to dental caries and enhancing caries progression (Weerheijm et al., 2001b, Weerheijm, 2003, Lygidakis et al., 2010, Kosma et al., 2016). Furthermore, porous hypomineralised enamel may favour the invasion of cariogenic bacteria (Leppäniemi et al., 2001). A recent systematic review stated that children with MIH were 2.1 to 4.6 times more likely to have caries in the permanent dentition than unaffected children (Americano et al., 2016). The association between hypomineralised second primary molars and dental caries in the primary dentition has also been reported (Elfrink et al., 2010).

A recent study conducted by Ulusoy et al (2016) which compared the oral health status of 81 Turkish children aged 8- to 11-years, with and without MIH, reported that children with MIH had a significantly higher DMFT values than the control groups (Ulusoy et al., 2016). A longitudinal study by Arrow (2016) reported that an increase in the number of teeth affected by enamel defects increased the odds of the tooth experiencing caries, and was marginally statistically significant (OR=1.93, P=0.042) (Arrow, 2016). However, teeth affected by diffuse enamel defects were protected from experiencing caries (OR=0.15, P=0.042) (Arrow, 2016). It was speculated that the presence of diffuse enamel defects may be an indicator of fluoride exposure (dental fluorosis) and thus reduced caries risk (Arrow, 2016).

2.4.8.4. Aesthetic concerns and oral health-related quality of life

According to the literature, about a third (30%) of children diagnosed with MIH present with one or more hypomineralised permanent incisors, in addition to hypomineralised molars (Weerheijm et al., 2001a, Ghanim et al., 2013b). A higher prevalence of MIH on permanent incisors, 41.8%, was reported among 16-year old children in Northern Norway (Schmalfuss et al., 2016). Any disruption

during mineralisation of permanent first molars and incisors may affect the permanent canines too because they were developing at around the same period. A few studies have reported canine involvement in MIH cases; the prevalence of affected permanent canines, in MIH children, appears to range from 19.2% to 27%.

Enamel opacities on the labial surface of anterior teeth are not normally sensitive or subject to post-eruptive breakdown, but the altered appearance may present considerable aesthetic concern for children and their parents (Muratbegovic et al., 2007, Laisi et al., 2009, Leal et al., 2016). Visible differences to normal dental appearance cannot be dismissed as merely an aesthetic problem as there may be negative impacts on the individual's self-worth, social interactions and overall quality of life. Children with enamel defects may experience low self-esteem and lack of confidence because they perceive 'marks' on their teeth as unattractive (Mcknight et al., 1999, Wong, 2014, Dantas-Neta et al., 2016). Children with DDE, due to a variety of different conditions, have been reportedly subject to unkind remarks, are reluctant to smile, and may be judged more negatively and bullied by others due to their dental appearance (Feng et al., 2001, Willmott et al., 2008, Rodd et al., 2011a, Craig et al., 2015).

Marshman and colleagues reported that 'marks' on teeth (DDE) may cause a range of impacts on young patients, depending on their age, gender, severity of the defects and their sense of self (i.e. how important appearance is to them) (Marshman et al., 2009). In this detailed qualitative enquiry, some young patients were reportedly not bothered by their visible opacities, while others felt upset and self-conscious about their appearance (Marshman et al., 2009). Some children indicated that things like personality and friendships were more important than dental appearance, even though they experienced negative comments about their teeth. It is also acknowledged that children may feel more or less self-conscious about their dental appearance at different times, with a move to a new school being a particularly difficult time for some of them, as they worry about how they will be viewed by new peers (Junior et al., 2009, Rodd et al., 2011b).

Much of the work to date on appearance-related concerns and DDE has been in relation to dental fluorosis, rather than MIH. Interestingly, with respect to dental fluorosis, children with discoloured enamel may have less concern if they live in an area where dental fluorosis is endemic and is the 'norm' (Sujak et al., 2004,

McGrady et al., 2012).

The impact of having a DDE, including MIH, has started to gain wider appreciation in recent years with the increasing knowledge and application of oral health-related quality of life (OHRQoL) measures (Marshman et al., 2009, Vargas-Ferreira and Ardenghi, 2011, Arrow, 2013). At the time of writing, eight studies, involving MIH participants, have used validated OHRQoL questionnaires (Vargas-Ferreira and Ardenghi, 2011, Arrow, 2013, Arrow, 2016, Dantas-Neta et al., 2016, Leal et al., 2017, Folayan et al., 2018, Velandia et al., 2018, Portella et al., 2019), while a further study has taken a combined quantitative and qualitative approach (Rodd et al., 2011a). Arrow (2013) found that a high caries experience, in conjunction with MIH, was associated with poorer OHRQoL, but the results did not reach significance. Furthermore, this study was conducted in children aged 6- to 8-years, which may have precluded the aesthetic impact of DDE as many children would not yet have had the eruption of all their permanent incisors (Arrow, 2013). In addition, this study used parents as a proxy, which may not accurately represent the children's view. A study of the impact of DDE in an older age group found that DDE had the greatest impact on the functional domain of OHRQoL, which is likely to relate to having sensitive first permanent molars (Vargas-Ferreira and Ardenghi, 2011).

A current gap in knowledge, however, relates to the longitudinal impact of developmental enamel defects (particularly MIH) on children's (OHRQoL) (Arrow, 2016). Most studies are cross-sectional and are based on global assessment of the presence of enamel defects. The associations between children's OHRQoL and the presence of dental enamel defects have been conflicting. Some studies reporting an adverse impact of the presence of enamel defects on quality of life (Marshman et al., 2009, Vargas-Ferreira and Ardenghi, 2011); while others reported no association between enamel defects and children's OHRQoL (Castro et al., 2011, Paula et al., 2012, Scarpelli et al., 2013, Correa-Faria et al., 2016). Furthermore, many studies to date have failed to consider potential confounders on the impact of DDE on children's OHRQoL, such as socio-economic status, self-esteem or other dental conditions (traumatic dental injury, malocclusion).

2.5 Health and oral health-related quality of life

Modern medicine and dentistry now recognises that health, including oral health is a wider construct than simply the absence of disease or a condition. This section will set the scene for the role of psychosocial influences in overall health, as this is fundamental to the underlying theory and rationale for this research.

2.5.1 Concept of health

The absence of disease or illness has been conventionally denoted as health, but the World Health Organisation (WHO) actually defines health as “a state of complete physical, mental, and social well-being and not merely the absence of disease and infirmity” (WHO, 2006). This broad definition emphasises that health is multidimensional. Being healthy does not simply imply that an individual is physically fit and free of disease, other dimensions (physical, mental, emotional, social, spiritual, and sexual) may influence an individual’s quality of life and therefore must be considered (de Chavez et al., 2005, Naidoo and Wills, 2009, Huber et al., 2011). This concept of health (together with related medical interventions) has gradually evolved from a biomedical construct to a biopsychosocial one, and most recently, to a model that considers quality of life.

2.5.1.1 The biomedical construct

The traditional model of health has viewed an individual as physically separated from their emotional and psychological processes. Thus it has focused on health as being ‘free of sickness’, without acknowledging the role of social and psychological domains which may contribute to development or maintenance of a disease or illness (Allen, 2003, Warwick-Booth et al., 2012). This model has therefore been unable to explain health issues without apparent physical symptoms, such as psychological and social problems and proposes that health can be restored simply by eliminating the cause of the disease (Wade and Halligan, 2004).

2.5.1.2 Biopsychosocial concept

The biopsychosocial model of health was first introduced by Engel around forty years ago and combines biological aspects of health with social and psychological interactions (Engel, 1997). It is widely acknowledged that physical

health is significantly affected by psychological and social factors which influence a patient's perceptions and actions to give an individual experience of feeling ill (Wade and Halligan, 2004). Biological factors comprise genetic factors and physiological conditions whereas psychological factors relate to behaviours, thoughts and feelings. Social factors relate to the fact that we are social beings who interact with others within groups, communities and societies (Engel, 1997).

2.5.1.3 Quality of life

Quality of life (QoL) is defined as an 'individual's perception of their position in life in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns' (WHOQOL, 1995). This paradigm takes into account factors such as social (e.g. gender and ethnicity), psychological, economic (socio-economic status, house location), and physical environment as determinants, which may all influence a person's health (Allen, 2003, Broder and Wilson-Genderson, 2007). This holistic health concept focuses on dimensions of functioning and overall well-being (Wilson and Cleary, 1995, Slade, 1997).

Current health research using the QoL model examines ways to accurately measure complex behaviours and feelings (Wilson and Cleary, 1995). This information may be beneficial for policy makers when developing health policy, and may enhance communication with patients and help to identify a range of problems that affect individuals (Broder and Wilson-Genderson, 2007, Walters, 2009). However, a recognised limitation of this way of thinking is that it does not provide information on how to prioritise the different determinants which lead to disease or illness (Ghaemi, 2009).

2.5.2 Oral health-related quality of life

2.5.2.1 Overview

Clinical indicators have been used extensively in oral health research to measure oral health status, but in recent years, many studies have incorporated an assessment of quality of life (QoL) to supplement the measurement of the clinical indicators, which exemplifies the move away from a purely biomedical model of health. Assessment of self-reported oral health-related quality of life (OHRQoL)

together with a clinical examination provides a better understanding of how diseases or disorders and related treatments may affect the individual (Piovesan et al., 2010). This information is important to understand the patient's perspectives and experience of oral health care, which can be beneficial to improving clinical outcomes, enhancing clinical research and prioritising dental care for target groups.

Slade (1997) first introduced oral health-related quality of life (OHRQoL) as a multidimensional concept, to measure the impact of oral diseases and disorders in relation to an individual's function and psychosocial health (Slade, 1997). Assessment of OHRQoL has important applications as an outcome measure in clinical trials through assessment of perceptions of health status and to describe the outcomes of oral health conditions and treatment at the individual and population level. It is assumed that the functional and psychosocial impacts documented as measures will affect the quality of life (Locker and Allen, 2007). It is useful to monitor the health status of populations, assess the general population's needs, identify target population's needs and prioritise oral health care services to target populations (McGrath et al., 2004, Marshman and Robinson, 2007, Vargas-Ferreira and Ardenghi, 2011). OHRQoL is used to describe the outcomes of oral health conditions and treatment provided for these conditions. It also facilitates communications with patients and helps identify patient's preferences in terms of types of treatment strategies (Locker and Allen, 2007, Vargas-Ferreira and Ardenghi, 2011). This model focuses on relationships between different domains, which may all influence health. A direct relationship between OHRQoL and the domains should be interpreted with caution, however, as these impacts could be mediated by other factors, such as social and environmental variables.

2.5.3 Instruments to measure children's OHRQoL

Over the past two to three decades, OHRQoL has become widely recognised as important in understanding children's experiences of various dental conditions and treatment interventions. To date, a number of instruments have been developed to measure children's OHRQoL, irrespective of the type of oral condition the individuals may have, and therefore they can be used for healthy as well as 'affected' populations (Walters, 2009). Children's OHRQoL instruments

must be tailored to their cognitive abilities and lifestyle, and thus it is not appropriate to simply 'adapt' adult measures. It is essential that an instrument is able to identify factors of relevance to younger populations such as self-image, social importance and school environment, which may all have an impact on children's well-being (McGrath et al., 2004, Genderson et al., 2013a). Currently, there are several validated instruments available to measure children's self-reported OHRQoL, the most common of which include: the Child Perceptions Questionnaire (CPQ); the Child Oral Impacts on Daily Performances (C-OIDP) and the Child Oral Health Impact Profile (COHIP). A recent systematic review critiqued these three measures, highlighting that they each have different strengths and limitations (Gilchrist et al., 2014).

The Child Perceptions Questionnaire (CPQ) is one of the most frequently used instruments. It is part of the Children Oral Health Quality of Life Questionnaire (COHQoL), which is a set of multidimensional scales intended to measure the negative effects of oral and oro-facial disorders (such as caries, malocclusion and craniofacial anomalies) on children's well-being. COHQoL is designed for children aged between 8- and 14-years and their families (Jokovic et al., 2006). It comprises the Child Perceptions Questionnaire (CPQ), Parental-Caregiver Perceptions Questionnaire (P-CPQ), and Family Impact Scale (FIS). There are several versions of CPQ available: two age-specific questionnaires ($CPQ_{8\text{-}10}$ and $CPQ_{11\text{-}14}$) and the corresponding short forms (Jokovic et al., 2002, Jokovic et al., 2004, Jokovic et al., 2006). These questionnaires have been validated in many different populations and have been translated into several different languages (Broder et al., 2012). It should be noted, however, that the original versions have yet to be tested longitudinally or in evaluative studies. They are also limited by the fact that they have not been validated for use in children under the age of 8-years (Broder et al., 2012, Genderson et al., 2013b). In addition, few studies have attempted to evaluate change in OHRQoL following treatment, thus information is lacking regarding clinically meaningful change in scores following any interventions (Gilchrist et al., 2014). The sensitivity and specificity of $CPQ_{11\text{-}14}$ and $CPQ_{11\text{–}14}$-ISF:16 has also been questioned, as highlighted in a study involving young orthodontic patients who felt that some of the questions were irrelevant or difficult to understand (Marshman et al., 2010).

Another widely used measure is one developed by Gherunpong and colleagues, who produced the Child Oral Impacts on Daily Performances (C-OIDP) by modifying the pre-existing adult version (Gherunpong et al., 2004a). This measure focuses on the negative impact of oral conditions on an individual's daily activities, and was initially designed for 11- to 12-year-old Thai children. It has subsequently been employed widely in other countries and languages (Gherunpong et al., 2004a, Yusuf et al., 2006). In their recent systematic review of children's OHRQoL measures, Gilchrist and co-authors suggested that C-OIDP, being the shortest validated instrument available (consisting of 8 items: eating, speaking, cleaning teeth, relaxing, emotion, smiling, studying, and social contact), could prove useful for epidemiological studies (Gilchrist et al., 2014).

The Children Oral Health Impact Profile (C-OHIP) is another generic OHRQoL instrument designed to measure the impact of a wide range of oral conditions such as caries, malocclusion and craniofacial disorders on children aged 7- to 17- years. This is currently the only instrument to measure both positive and negative impacts of oral conditions on children (Sischo and Broder, 2011). The instrument measures not only the absence of a disease/disorder, but also the positive outcomes following treatment, which has important clinical significance (Broder et al., 2012). The original questionnaire contained 34 items across five domains (oral health, functional well-being, social-emotional well-being, school environment and self-mage). However, a shorter version with 19 items has been developed and validated recently (Broder et al., 2012). This instrument has been employed in different populations and has been translated into several languages, although data on the validity of the translated versions is still not available. The present study will employ the short version of COHIP and will be discussed in greater details in Chapter Four.

2.6 Theoretical model for the proposed research

2.6.1 Overview

A theoretical framework or model of health is a 'conceptual framework' or 'map' that can be used to illustrate the relationships between different variables, which may influence an individual's general health perceptions and eventually health-related quality of life. An appropriate framework is valuable in understanding and

interpreting complex research data. A theoretical framework consists of a number of variables or domains where the theory is applied, and a set of relationships between the variables and specific predictions of the outcomes are hypothesised. A good framework will be able to provide a clear explanation of how and why specific relationships lead to specific outcomes or events and can highlight those determinants that have impacts on the outcomes, which in the context of the present study are OHRQoL and self-perceived oral health.

One of the most common models used in health research and quality of life is the Wilson and Cleary theoretical model of health. This well accepted approach classifies possible patient outcomes according to the health concepts they represent and proposes an association between predictors and the different health concepts (Wilson and Cleary, 1995). This model has been widely used to illustrate the relationships between different dimensions of health, including biological/clinical measures, individual characteristics, socio-environmental determinants and HRQoL (see Figure 2.1). The original Wilson and Cleary Theoretical Framework comprises five dimensions: biological and physiological, symptoms status, functioning, general health perceptions, and overall quality of life (Wilson and Cleary, 1995, Benson et al., 2015). To the author's knowledge, no study has yet been undertaken to conceptualise the relationships between different predictors, dimensions of health and OHRQoL in children with MIH. The choice of dimensions or variables and the hypothesised interconnection between these predictors and the dimensions of health for the proposed study will be discussed in Chapter Four (Section 4.8.3).

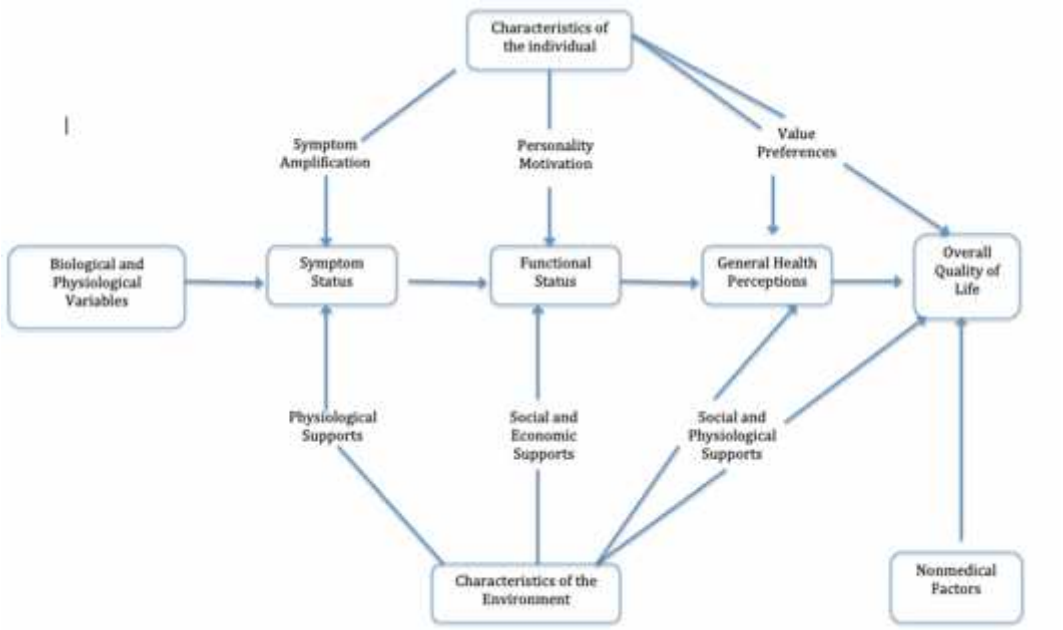

Figure 2.1 Wilson and Cleary Model (1995).

The current study applied the Wilson and Cleary's model of health (Wilson and Cleary, 1995) to examine the association between different variables related to OHRQoL and overall QoL of children with MIH. According to Wilson and Cleary's theoretical framework (1995), the proposed model has five domains: a biological component, symptom status, functional status, general health perceptions and overall QoL. The proposed model examines how individual characteristics (e.g. age, gender, social status), biological and physiological functions (e.g. severity of MIH, dental caries, and malocclusion), psychological characteristics (e.g. self-esteem) and clinical intervention are linked to OHRQoL and the children's overall quality of life (QoL) after aesthetic treatment for enamel opacities on permanent anterior teeth associated with MIH. The occurrence of oral clinical conditions (MIH, dental caries and malocclusion), and their severity must be assessed as important variables that determine health outcomes experienced by children (Wilson and Cleary, 1995, Barbosa et al., 2009). All these factors are described in greater details in the subsequent subsections.

Based on the contemporary literature and clinical observation, this study hypothesised the following relationships between the variables within the proposed theoretical model:

- Dental measures, including dental caries, malocclusion and number of teeth needing aesthetic treatment, socio-economic status, gender, age and self-concept would predict overall oral health and oral health-related quality of life before (T_0) and six-months after (T_2) the aesthetic dental treatment.
- Overall oral health and oral health-related quality of life at baseline would mediate the relationship of dental measures, socioeconomic status, gender, age and self-concept with overall oral health and oral health-related quality of life six months after MIH treatment.

Further analysis of this model using structural equation modeling (SEM) will highlight the complex relationships between clinical, demographic, psychosocial (including self-esteem) and patient-reported outcomes on OHRQoL and QoL.

Oral health is an important component of children's general health. It is anticipated that the adapted model will be able to enhance the understanding of the complex inter-relationships between measures potentially associated with OHRQoL among young people with MIH who seek aesthetic interventions to improve their dental appearance. This model can be employed to identify the true impact of this condition on children's quality of lives. Furthermore, this theoretical model can be utilised to better inform patients with MIH, parents and clinicians in future decision-making for management of affected permanent anterior teeth.

2.6.3 Individual factors

The following subsections will briefly describe and provide a rationale for inclusion of the proposed patient and clinical variables within the model and the context of a clinical intervention for the management of children with MIH and visible opacities of aesthetic concern. Specific details relating to methodology will be provided in the subsequent chapter.

2.6.3.1 Demographic data

Participants' personal information such as age in years, race/ethnicity, postal address and gender will be collected. These data will be used for descriptive

analysis of the study population as well as being included in the overall complex statistical analysis of the model.

- Socioeconomic status

Studies on the impact of oral diseases such as dental caries, dental trauma, malocclusion and developmental defects of enamel must take into consideration the individual's socioeconomic conditions. Dental caries, for example, is more prevalent in children from deprived areas and is strongly associated with presence of enamel defects in primary dentition. Children from lower socioeconomic backgrounds have reported poorer overall OHRQoL than children from higher socio-economic groups (Oliveira et al., 2006, Piovesan et al., 2010, Martins-Júnior et al., 2012, Dantas-Neta et al., 2016). Therefore, these relationships must be explored when assessing the impact of MIH on children's OHRQoL and QoL.

- Gender

Even though gender predilection was not observed when predicting the psychosocial impact of dental aesthetics in previous studies (Junior et al., 2009, Rodd et al., 2011a), it is generally considered an important predictor of OHRQoL and QoL. For example, a study conducted in New Zealand in children with caries, found that girls reported higher impacts of oral health-related quality of life (especially on emotional well-being) than males, although the difference did not quite reach significant difference (Foster Page et al., 2005). A recently published MIH study also found that female teenagers reported higher scores for oral symptoms and functional limitations than males, indicating a higher impact from MIH on these children's OHRQoL (Dantas-Neta et al., 2016). Younger girls aged 8- to 10-years-old are also reported to have higher impacts across all $CPQ_{8\text{-}10}$ domains than boys (Barbosa et al., 2009). This study suggests that children's perspectives towards OHRQoL may be affected by gender and age-related experience, although there are limited data to validate these findings. One possible explanation is females are generally more judgmental about aesthetics and their appearance and have greater awareness and expectations towards health than males (Junior et al., 2009). The possibility also exists that girls comprehend and complete QoL questionnaires in a different manner to their male peers, being more able to emotionally associate with the proposed items. A longitudinal study in Western Australia assessed the impact of having enamel

defects on children's OHRQoL and reported that girls were more likely to report poorer rates of oral health impact than boys (Arrow, 2016). The reasons for gender differences during adolescence to OHRQoL have been little explored, but may be related more to differences in self-esteem and self-perceptions of body image between boys and girls rather than clinical or sociodemographic differences (Arrow, 2016).

- Age

Generally, oral diseases tend to be cumulative and may become worse as children get older, which may in turn result in greater impact of the disease on children's OHRQoL (Correa-Faria et al., 2016). Younger children may have more limited cognitive ability and communication skills when comparing their self-image with their peers or reporting the impact of the diseases on their QoL. They may also view 'attractiveness' differently to older children (Junior et al., 2009, Correa-Faria et al., 2016). Therefore, age is an important indicator to consider when evaluating the impact of MIH on children's OHRQoL and overall QoL.

2.6.3.2 Self-concept

The "self" is a complicated concept comprising self-concept, self-esteem, self-knowledge and social self. Self-esteem is described as a "feeling of appreciation" and is an essential emotion for people to adapt better to society and live their lives while self-concept is the person's perceptions of himself/herself. This perception may not always match the reality but it is an important individual factor to consider when evaluating predictors for children's OHRQoL. The environment significantly influences development of self-concept especially in children (Harter, 1993). Children with high self-concept are more satisfied with their lives while having low self-esteem might lead to emotional and social problems such as depression and difficulty to adapt within society (Harter, 1993). One instrument that has been widely used to measure self-concept in children is the Self-Perception Profile for Children (SPPC). This instrument was developed for children to self-evaluate and define themselves across multiple domains (Harter, 1985, Harter, 2012). The self-complete measure has been widely validated for use in children aged 8- to-13-years. Details relating to completion and scoring of this measure will be provided in Chapter Four.

2.6.3.3 Health care satisfaction

The relationship between health care satisfaction experience of health care (including previous dental experience) and children's HRQoL has not been widely investigated. Previous dental experience has been linked with dental fear and identified as an important predictor of health related quality of life (Merdad and El-Housseiny, 2017). It was therefore considered important to evaluate if this variable fitted in the overall model. Within the UK National Health Service, the Friends and Family Test (FFT) for children and young people is the most widely accepted measure of health care experience (PickerEurope, 2015). This simple instrument was developed with children and young people and rigorously validated by the Picker Institute Europe in 2015 for use in the NHS by young patients. It includes one global question as well as the opportunity for free text feedback. It measures how likely the participant would be to recommend their medical (or dental) care to their family and friends, if they need similar treatment. A detailed explanation of the scoring system is provided in the Methods and Materials chapter.

2.6.4 Biological and clinical variables

It is important to consider potential confounders, such as the co-existence of other oral diseases or conditions on OHRQoL when exploring the impact of a specific condition, such as in the case of MIH. This study therefore will consider caries experience and orthodontic appearance as potential confounders, as has been described in previous studies on MIH and OHRQoL (Dantas-Neta et al., 2016, Leal et al., 2017).

2.6.4.1 Dental caries experience

As described earlier (see section 2.4.8), the presence of MIH has been positively associated with a higher prevalence of dental caries in the permanent dentition (Leppäniemi et al., 2001, Muratbegovic et al., 2007, da Costa-Silva et al., 2010, Garcia-Margarit et al., 2014, Ulusoy et al., 2016, Kühnisch et al., 2018). Dental caries itself may cause pain, loss of function and aesthetic problems when involving the anterior teeth. There may also be social impacts such as missing

school (Piovesan et al., 2010, Martins-Júnior et al., 2012, Correa-Faria et al., 2016). Indeed there is a wide literature to support the adverse effect of dental caries on children's OHRQoL (Piovesan et al., 2010). It is therefore essential to include caries experience as a potential confounder in the proposed model.

2.6.4.2 Malocclusion

Malocclusion is a term to broadly describe deviations of teeth from a "normal" relationship or alignment. A malocclusion may not only present functional limitations for an individual but may also present considerable psychosocial impacts.

A number of studies in adolescents have identified malocclusion as having a negative impact on emotional well-being and social domains (Foster Page et al., 2005, O'Brien et al., 2006). Interestingly, younger children (8- to 10-year-olds) have reported that malocclusion had a negative impact both physically (difficulty in eating due to tooth malalignment and difficulty in speaking due to a diastema) and psychosocially (bothered/ashamed with the appearance of their teeth) but social domains were not affected (Martins-Junior et al., 2012). These younger children were not reluctant to smile even though their teeth were considered to be malaligned (Martins-Júnior et al., 2012). This finding shows that different age groups may value OHRQoL differently. Adolescents are more conscious about their appearance while function may be of more concern to younger children. Therefore, it is important to consider age as a confounding factor when assessing the impact of malocclusion on children's OHRQoL. Results from these studies should also be interpreted cautiously because of the different criteria used to record a diagnosis of malocclusion. Some studies recorded malocclusion as presence or absence only (Aldrigui et al., 2011), while other studies investigated the impact of different types of malocclusion on children's OHRQoL (Kramer et al., 2013, Correa-Faria et al., 2016). Notwithstanding, there is a clear justification to include orthodontic status as a potential confounder within the proposed study.

In terms of actually quantifying or measuring malocclusion, the most commonly used measure is the Index of Treatment Need (IOTN) (Kok et al., 2004, Borzabadi-Farahani, 2011, Benson et al., 2015, Jaeken et al., 2018). This is a judgment criteria widely used by clinicians to assess the prevalence of orthodontic treatment need and prioritise free or subsidised orthodontic treatment

to those who are considered most in need (Brook and Shaw, 1989, Shaw et al., 1995). It consists of the Dental Health Component (DHC) and Aesthetic Component (AC) (Brook and Shaw, 1989, Shaw et al., 1995). The Dental Health Component (DHC) uses an acronym MOCDO, which represents the key malocclusion features: missing teeth, overjet, crossbite, displacement of contact points, and overbite. A patient will be graded as 1, 2, 3, 4, or 5 on the DHC, with grade 1 meaning little treatment need and grade 5 representing the greatest treatment need. The AC is a scale from 1-10, which is intended to correlate with the degree of dental 'attractiveness' and is based on 10 colour photographs of anterior teeth showing different levels of dental attractiveness. Clinicians grade the patient's teeth by comparing the patient's teeth with the photographs. Grades 1-4 of AC indicate no orthodontic treatment required, grades 5-7 represent borderline need and grades 8-10 reflect definite need for orthodontic treatment (Brook and Shaw, 1989, Hunt et al., 2002). The AC is a useful tool when assessing aesthetic impact of malocclusion on children's OHRQoL and will provide an objective variable for inclusion in the proposed model. Further details about its application will be provided in Chapter Four.

2.6.4.3. MIH severity

As described earlier, there is growing evidence to suggest that MIH has a negative impact on the OHRQoL of children, as perceived by both children and their families (Leal et al., 2016, Dantas-Neta et al., 2016, Velandia et al., 2018, Portella et al., 2019). However, none of these previous studies have attempted to correlate the severity of MIH on OHRQoL. Clearly, children with MIH may have a variable number of teeth affected, as well as differing degrees of severity. The proposed investigation will therefore include a clinical measure of MIH severity, using the Molar Incisor Severity Index, which will be described in detail in the Materials and Methods Chapter.

2.6.5 Measurement of OHRQoL

For the purposes of this research, the short form of the Child Oral Health Impact Profile (C-OHIP-SF19) was considered the most appropriate measure of OHRQoL. Since its development, C-OHIP-SF19 has been widely used for measurement of children's OHRQoL in relation to a variety of oral conditions. It has been validated for use in different populations and translated into several

different languages Furthermore, C-OHIP-SF19 is considered suitable for longitudinal and long-term prospective studies, for example to evaluate treatment outcome over a certain time. In addition, this instrument allows assessment of changes in children's OHRQoL following treatment, which is of clinical advantage. Change in children's OHRQoL following treatment can be measured by using the Global Assessment Scale. Clinical changes are rated as follows: minimal change (score -1 to -3 or 1 to 3), moderate change (score -4 to -5 or 4 to 5) and large change (score -6 to -7 or 6 to 7). Higher scores indicate substantial changes following treatment either indicating worse (negative rating) or better (positive rating) OHRQoL (Genderson et al., 2013a).

2.6.5.1 Symptoms status domain

The symptom status domain in the proposed theoretical framework will be measured using items one to five in the oral health domain of the of the short form 19-items C-OHIP-SF19 (Broder et al., 2012). Children will be asked if they have experienced the problem regarding their teeth, mouth or face, as described by each item in the past three months. The children will rate how they really feel about each problem on a 5-point Likert scale ranging from 0 ('almost all the time') to 4 ('never'). The total score for the oral health domain may range from 0 to 20, with higher higher C-OHIP-SF19 score implying more positive OHRQoL.

2.6.5.2 Functioning status domain

The functioning status domain of the applied Wilson and Cleary model will be represented by four items from the functional well-being subscale of the short form 19-items C-OHIP-SF19 (Broder et al., 2012). Children will be asked if they have experienced the problem described by each item over the past three months. The children will rate how often they have experienced a problem on a 5-point Likert scale ranging from 0 ('almost all the time') to 4 ('never). The total score for functional well-being domain ranges from 0 to 16. A higher C-OHIP-SF19 score for this domain reflects better OHRQoL.

2.6.5.3 Overall OHRQoL

In order to obtain an overall OHRQoL score, the C-OHIP-SF19 questionnaire also includes a global question, which will be incorporated within the model.

"Overall, how healthy do you think your teeth are?"

2.6.7 Overall quality of life

In the present study, the model requires a patient-reported rating of overall QoL, which will be measured using a single global question. Global questions may be employed to assess changes over time, which is important when an evaluation of treatment effect is being undertaken (Rowan, 1994). It is important that measures can detect clinically important changes. Patients will be asked to answer a question to assess any change in their oral health status since the specified point in time, for example one month after treatment or six months post-treatment. Change in oral health status is then evaluated by calculating the difference between scores at different points in time. The difference between scores gives the global score for change in health status (Rowan, 1994). A high global score indicates better overall quality of life over time.

Chapter 3
Aims and objectives

3.1 Rationale for study

As described in the preceding literature review, MIH is a very common condition seen in children and presents a number of problems for affected individuals, not least the psychosocial impacts relating to visible enamel opacities on permanent incisors. A variety of clinical interventions have been proposed for the management of enamel opacities, both in MIH and other DDE, but surprisingly little evaluation of patient-reported outcomes has been undertaken. There is, therefore, considerable scope to undertake a more holistic and patient-centred line of enquiry to further understanding of the impact of MIH, and its related treatment, in young people with visible incisor opacities. Findings from this study will have clear relevance for clinicians, in terms of helping them better advise their patients of likely outcomes following interventions, and thereby improving decision-making. In addition, evidence for improved OHRQoL in this patient group will help to justify the need for such treatments to commissioners and providers of dental care for children. The proposed study is therefore considered novel and in an area of acknowledged need.

3.2 Aim

This broad aim of this study is to explore the relationships between socio-demographics, clinical status and oral health-related quality of life (OHRQoL) in children with MIH who received aesthetic treatment for their incisor opacities.

3.3 Objectives

The specific research objectives are to:

1. describe the sociodemographic characteristics and clinical status of children with MIH who are referred to a hospital service for the management of incisor opacities of cosmetic concern

2. determine whether routine clinical interventions (microabrasion, resin infiltration (Icon™,DMG, Hamburg, Germany), partial composite veneer and/or tooth whitening) to improve the aesthetic appearance of permanent anterior teeth affected by MIH have any influence on children's OHRQoL and HRQoL
3. test Wilson and Cleary's theoretical model in young patients with MIH
4. evaluate the relationships between demographic, dental (clinical), psychosocial factors (including self-concept) and OHRQoL following these clinical interventions
5. identify pathways predicting associations between demographic, dental clinical and psychosocial factors, environmental and OHRQoL

Chapter 4
Materials and methods

4.1 Ethical approval and research governance

This study was granted ethical approval by the National Research Ethics Committee in April 2017 (ref: 17/WA/0096). A copy of the Health Research Authority (HRA) and ethical approval letters can be seen in Appendix 1 and 2. A participant log and site file was kept by the chief investigator (N.H.) in accordance with research governance and Good Clinical Practice guidelines (GCP, 2016, HRA, 2017).

All members of the clinical research team completed a face-to-face course for Good Clinical Practice, to satisfy the requirements for taking consent from research participants (GCP, 2016, HRA, 2017).

The chief investigator (N.H.) worked under direct supervision of a consultant in paediatric dentistry at all times. Furthermore, she was supported by a senior dental nurse or a research nurse during her clinical treatment sessions.

4.1.1 Patient and public involvement

Feedback was sought from children at the initial stages of the study. Four children (a boy and girl aged 7-10 years; a boy and girl aged 11-16 years) were invited to comment on the format and content of the questionnaire booklets, information sheets and assent forms. Minor revisions were undertaken in response to their comments.

4.2 Study population

Children, aged 7-16 years, who requested treatment for visible enamel opacities involving one or more of their permanent incisors were invited to participate in this study. These children were initially referred to the Paediatric Dentistry Department, Charles Clifford Dental Hospital, Sheffield, for specialist

management of their MIH. Children who met the inclusion criteria were invited to participate in this study. Inclusion criteria were as follows:

- Children diagnosed with MIH by a consultant paediatric dentist (H.R.), according to well established clinical criteria (Weerheijm et al., 2003)
- Children with MIH and who have a visible enamel opacity involving at least one fully erupted upper permanent incisor
- Children who requested improvement in their incisor aesthetics (with the agreement of their parents/carers)
- Children were happy and able to accept dental treatment without the need for inhalation sedation
- Children aged between 7- and 16-years

Exclusion criteria were applied as below:

Dental

- Children who presented with an acute dental symptom and required urgent treatment
- Children who were planned to undergo active treatment for their hypomineralised molars during the study period (children who underwent restorations or extractions of their molars during the period of study will be excluded from data analysis)
- Children with an enamel defect other than MIH
- Children with any other dental or facial anomaly other than MIH (e.g. hypodontia, cleft lip and palate)
- Children with compromised incisor aesthetics due to a traumatic dental injury, tooth surface loss or caries
- Children who are planned to commence orthodontic treatment during the study period

Social

- Children with severe learning disabilities who are unable to understand and undertake the research even with support from the research team
- Children or parents who do not speak English

4.3 Measures

This following section will describe the various validated self-complete measures that were included within the participant questionnaire booklet as well as socio-demographic and clinical variables collected from the participants. Data from these measures will be analysed within the adopted Wilson and Cleary theoretical framework as shown in the Figure 4.10. The questionnaire booklet was completed at three time points during the study: at baseline pre-treatment T_0; one-month following treatment T_1, and six-months following treatment T_2. In total, participants responded to 45 items. These were kept to a minimum to reduce the burden to the participant and to ensure that the questionnaire could be reasonably completed in approximately 15-20 minutes. Two age-specific versions were developed: one questionnaire booklet was produced for 7- to 10-year olds and a second version for 11- to 16-year-olds. These are provided in full in appendices 10 to 15**.**

4.3.1 Assessment of oral health-related quality of life

The impact of having MIH on the children's oral health-related quality of life (OHRQoL) was measured using the Child Oral Health Impact Profile Short Form 19 questionnaire (C-OHIP-SF19) as described previously (Sischo and Broder, 2011, Broder et al., 2012). The C-OHIP is a generic instrument, comprising 34 items, and which measures both positive and negative impacts of oral conditions in children on their overall lives. It has been used extensively in children's oral health research (Broder and Wilson-Genderson, 2007, Gilchrist et al., 2014). Measurement of positive impacts of an oral condition allows assessment of changes in children's OHRQoL following treatment, which is of clinical advantage. Therefore, C-OHIP is considered suitable for longitudinal and long-term prospective studies, for example to evaluate treatment outcome over a certain time. Although it is a reliable measure, the lengthy questionnaire may not be appropriate for use with younger children, who may have a shorter attention span and less cognitive ability. Therefore, a short form of C-OHIP-SF19 was developed for ease of use and practicality when conducting research with young populations.

C-OHIP-SF19 was initially developed for 8- to 15-years-olds but recent publications showed that it is suitable for children aged from 7- to 17-years, offering a wider age range than the CPQ (which exists as two versions CPQ_{8-10}

and CPQ_{11-14}) and C-OIDP (aimed at 11-12 years-olds) (Broder et al., 2012, Li et al., 2014). This questionnaire has been used in different populations and translated in different languages (Li et al., 2014, Sierwald et al., 2016, Kragt et al., 2016, Agnew et al., 2017, Arheiam et al., 2017).

For the purpose of this study, the short form of C-OHIP (C-OHIP-SF19) was considered the most appropriate measure of OHRQoL. All items in the questionnaires were designed in such a way to prompt self-reports from the child. In keeping with the original version, all participants are instructed as follows:

'*Please read each statement carefully and choose the answer that best describes you in the past 3 months regarding your teeth, mouth or face. We want to know how you really feel'*.

The short form has 19 items corresponding to three domains: oral health (five items), functional wellbeing (four items) and socio-emotional wellbeing (10 items); and a global item concerning children's self-perceptions of their own overall oral health (see Section 4.3.1.1). The oral health domain is comprised of specific oral symptoms that are not necessarily related to one another (e.g., pain, spots on teeth). Children are asked if they have experienced the problem regarding their teeth, mouth or face, as described by each item in the past three months. The children will rate how they really feel about each problem on a 5-point Likert scale ranging from 0 ('almost all the time') to 4 ('never'). The total score for the oral health domain may range from 0 to 20, with higher C-OHIP-SF19 score implying more positive OHRQoL.

The functional well-being domain includes four items related to the child's ability to carry out specific everyday tasks or activities (e.g. speaking clearly, chewing). Children were asked if they have experienced the problem described by each item over the past three months. The children will rate how often they have experienced a problem on a 5-point Likert scale ranging from 0 ('almost all the time') to 4 ('never). The total score for functional well-being domain ranges from 0 to 16. A higher C-OHIP-SF19 score for this domain reflects better OHRQoL.

The socio-emotional well-being domain (combines social-emotional wellbeing, school environment and self-image domains) includes items pertaining to peer

interactions, mood states, school environment, and positive feelings about the self. There were ten items in this domain with two of the questions were positively worded. Children will be asked how frequent they have experienced the feelings or problems on a 5-point Likert scale. Responses for positive items ranging from 'never'= 0 to 4 (almost all the time) while responses for the negatively worded items are reversed. The total score for socio-emotional well-being domain ranges from 0 to 40 with a higher score indicates better OHRQoL for this domain.

Two of the C-OHIP-SF19 questions were positively worded. Participants were asked to report on the frequency of events over the past three months on a 5-point Likert scale. Responses for positive items will be recorded as 'never'=0, 'almost never'=1, 'sometimes'=2, 'fairly often'=3, and 'almost all the time'=4. Scoring for the negatively worded items is reversed. Total scores for each domain are calculated by summing the responses of all items specific to the domain. The total C-OHIP-SF19 score is computed by summing the total domain scores of all three domains. The total score can range from 0 (worst OHRQoL) to 76 (best OHRQoL) (Broder et al., 2012, Genderson et al., 2013a).

Domain scores are calculated by summing the responses of the items specific to the subscale. The overall OHRQoL score is computed by summing the subscale scores. Treatment expectation scores and the overall oral health response are not included in the overall C-OHIP scale, but these items are relevant when C-OHIP is used as part of a treatment assessment, as in the present study. Scores may range from 0 to 76 for the overall scale. If more than two-thirds of the items in a domain are missing, the domain and the overall score are set to missing data. If fewer items are missing for a domain, the average of available items is used and the sum of the domain is calculated (Broder and Wilson-Genderson, 2007).

4.3.1.1 Assessment of self-rated overall oral health

In order to obtain an overall OHRQoL score, the C-OHIP-SF19 questionnaire also includes a global question:

"Overall, how healthy do you think your teeth are?"

Participants are invited to respond to this question using a 5-point Likert scale: 0 (poor), 1 (fair), 2 (average), 3 (good) or 4 (excellent). A higher score indicates that participants perceive their overall oral health status to be better. This item is evaluated as a separate item and not included in the overall C-OHIP-SF19 scores. A final score for change in self-rated overall oral health can be obtained by comparing the score between baseline and follow-up visits.

4.3.2 Assessment of self-concept

The "self" is a complicated concept comprising self-concept, self-esteem, self-knowledge and social self. Self-esteem is the "feeling of appreciation" and is an essential emotion for people to adapt better to society and live their lives while self-concept is the person's perceptions of their own competency in different self-concept subscales. Although this perception may not always match the reality, self-concept is an important determinant to consider when evaluating children's OHRQoL. One instrument that has been widely used to measure self-concept in children is the Self-Perception Profile for Children (SPPC). This instrument was developed for children to self-evaluate and define themselves across multiple domains (Harter, 1985, Harter, 2012). The self-complete measure has been widely validated for use in children age 8- to-13-years old in different populations (Pereda and Forns, 2004, Broc, 2014, Gacek et al., 2014).

The original SPPC scale has five subscales: Scholastic Competence, Social Acceptance, Athletic Competence, Physical Appearance, and Behavioural Conduct, together with a Global Self-worth subscale (Harter, 1985, Harter, 2012). Each subscale contains six items and each item consists of two opposite statements. Children were asked to choose which statement best reflects himself/herself. Once they have chosen which statement (on the left or right) is most like them, they have to decide whether the statement is "really true for me" or "sort of true for me". Each item is scored on a four-point scale from 1 to 4, where a score of 1 indicates the lowest perceived competence or adequacy, and a score of 4 reflects the most positive judgment of oneself (Harter, 1985, Muris et al., 2003, Harter, 2012). A total mean score for each domain is computed by summing all scores and then taking an average for each subscale, resulting in an individual mean for the subscale (Muris et al., 2003, Pereda and Forns, 2004). The Global Self-worth subscale is rated by its own items and scored separately.

The mean scores for each domain can range from 1 to 4. If a child scored 1 to all six questions in the domain, the average mean score for the child is 1. There is no short form for this instrument, but Harter 'allows' researchers to choose any subscale pertinent to their study. However, she stipulates that all six items within a subscale must be included in the questionnaire (Harter, 2012).

For the proposed study, two relevant subscales, Social Acceptance and Physical Appearance as well as Global Self-worth were selected. These were selected to reduce the burden on participants of completing a lengthy questionnaire, as well as being most relevant to the context of the study. The Social Acceptance subscale explores how well the children perceive themselves and the degree to which they feel accepted by peers or feel popular. The Physical Appearance domain-specific subscale measures how much the child likes their own physical characteristics such as height, weight, hair, and face, as well as the way he or she looks overall (Harter, 1985, Pereda and Forns, 2004, Harter, 2012, Gacek et al., 2014). The global self-worth subscale constitutes a global judgment of personal self-worth and how much the child likes himself or herself as a person (Pereda and Forns, 2004, Harter, 2012, Gacek et al., 2014). Participants were asked to decide (using a tick box response format) how closely they aligned themselves to the given statement ('*sort of true for me'* or '*really true for me'*). An example of which is given below (Figure 4.1). A higher total average mean SPPC score in each subscale represents greater Social Acceptance, Physical Appearance or greater Global Self-worth respectively.

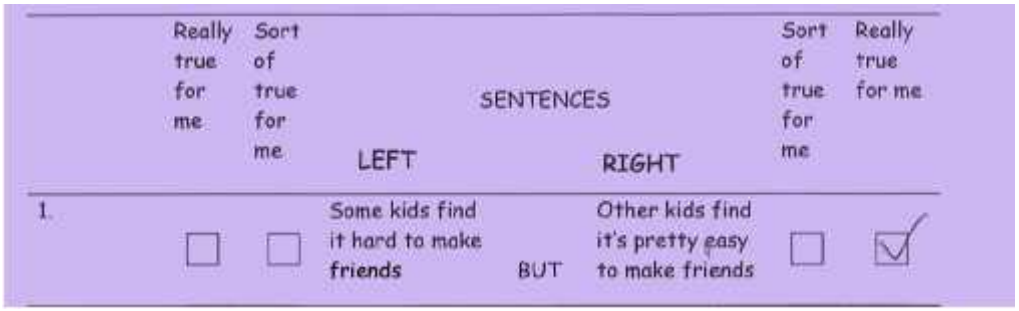

Figure 4.1 An example of participant's response to one of the Self-Perception Profile for Children questions.

4.3.3 Assessment of self-perception of enamel defects

In order to capture each participant's views on the appearance of their permanent incisors, both before and after treatment, four specific questions were asked.

These key questions had been previously developed by children themselves and used in research in the department for children undergoing similar treatment (Rodd et al., 2011a) and are listed below:

- *How worried are you about the marks on your front teeth?*
- *How embarrassed are you about the marks on your front teeth?*
- *How 'chalky' or discoloured do you think your front teeth are?*
- *How happy are you with your front teeth?*

These questions related to children's self-assessment of being worried and embarrassed about their teeth, as well as their view on whether the treatment had improved the colour of their teeth and made them feel happier or not. A 10cm visual analogue scale (VAS) was used to evaluate each participant's response, before and after treatment. A score of 10 represented the most positive response while a zero the most negative. The chief investigator (N.H.) used a 10cm ruler to measure the participants' responses and entered these data in the final electronic dataset.

4.3.4 Assessment of self-rated overall health-related quality of life

One global question was used to gather data on children's views of their own overall health status as stated below (Rowan, 1994):

> *"Overall, would you say your general health is?"*

The response format to this item was a 5-point scale from 1 (poor), 2 (fair), 3 (good), very good (4) and 5 (excellent).

A second global question was used at T_1 and T_2 to assess the extent to which patients perceived that their overall health may or may not have changed since their dental treatment (Rowan, 1994).

> *"Overall, how has your general health changed since our last meeting 1 month/ 6 months ago?*

The response format to this item was a 5-point scale from: 1 (much worse), 2 (worse), 3 (same), 4 (better) to 5 (much better).

4.3.5 Health care satisfaction

The Friends and Family Test (FFT) for children and young people was used to measure each participant's experiences of their dental care within the hospital service (Picker Europe, 2015). This instrument was developed in 2015 by the Picker Institute Europe, in conjunction with St Barts Hospital for use in the UK National Health Service (NHS) by young patients. The measure was subject to rigorous development with children themselves. It incorporates one global question and children are also invited to comment on what was good or bad about their experience using the free text box (PickerEurope, 2015) (See website: http://www.pickereurope.org/case-studies/recommending-friends-family-test-fft-children-young-people/).

Participants were asked to rate their experience on 5-point scale as shown in figure 4.2. In the current study, FFT scores will be presented as a percentage of participants who:

i) would recommend the dental hospital to friends and family if they needed similar treatment (score 5= "agree a lot" and score 4= "agree a bit")
ii) would not recommend (score 3= "I disagree a bit" and score 2= "I disagree a lot")
iii) could not decide (score 1= "I can't decide/don't know")

The final result for the FFT test will show the percentage of participants who would recommend, would not recommend and were uncertain of their response at baseline, one-month and six-month follow-up. The following calculation for the overall study population will be applied, as described by the Picker Institute.

The percentage FFT score is determined as follows:

Recommend (%) =

$$\frac{\text{Number of participants who chose "agree a lot" and "agree a bit"}}{\text{Total number of participants}} \times 100$$

Not recommend (%) =

$$\frac{\text{Number of participants who chose "I disagree a bit" and "I disagree a lot"}}{\text{Total number of participants}} \times 100$$

The percentage of participants thus recommending the service can range from 0 to 100 (where 100% equates to all participants being likely recommend). Similarly, in terms of not recommending the service, the minimum score of 0 would indicate that all participants are likely to recommend and the maximum score of 100 is when all participants are not likely to recommend. The "I can't decide/Don't know" score is not included in the final calculation of FFT score, but will be considered as an overall response base size (PickerEurope, 2014). The final score of FFT can be obtained by calculating the difference between the percentage of participants who are likely to recommend those who are not likely to recommend the dental hospital to their family and friends when they need similar treatment. The free text was entered into the final dataset but not subject to formal qualitative analysis. However, direct quotes will be employed in the results section to support the quantitative data. Figure 4.2 shows an example of participant's response to the Friends and Family Test (FFT).

Figure 4.2 An example of one of the participant's response to the Friends and Family Test question.

4.4 Clinical data collection

A clinical data sheet (see Appendix 16) was used to record key information from the patient's clinical records and clinical examination. The clinical data sheet was piloted on five patients and revised as necessary prior to study commencement. The participants' general demographic information such as gender, age, ethnic group and postcode, and clinical variables such as severity of MIH, IOTN AC, and caries status were recorded and used in subsequent analysis. These data are detailed below.

4.4.1 Patient-related data

I. Age (recorded in years and months, and confirmed from their clinical notes and in person)

II. Gender (male or female)

III. Postcode (as a proxy for socio-economic status)

Children's postal addresses will be extrapolated from their clinical records and used to derive a measure of social deprivation. An Index of Multiple Deprivation (IMD) score was determined for each patient using the following website https://tools.npeu.ox.ac.uk/imd/ (NPEU, 2013, Hall-Scullin et al., 2017). The IMD is an official measure of relative deprivation for small geographical areas in England. This index is derived from information relating to seven domains including: income, employment, health deprivation and disability, education, skills and training deprivation, crime, and living environment. It can be used to rank an individual's postal address as falling into one of five areas (quintiles) from IMD quintile 1 (the least deprived area) to IMD quintile 5 (the most deprived area). For ease of statistical analysis, three social deprivation status groups were established: high (children from the upper and upper middle quintile), middle (children from the middle quintile) and low (children from the lower middle and lower quintile).

IV. Ethnicity was self-reported by the parent on the child's medical history sheet according to these categories:

i. White English/Welsh/Scottish/Northern Irish/British

ii. Any other White

iii. Any ethnic minority group

4.4.2 Dental examination

All participants underwent an initial routine clinical examination at their first attendance to the hospital with a variety of junior or senior paediatric dentistry staff. Radiographs were taken, if appropriate at this first assessment visit, for the purposes of diagnosis and treatment planning. All children were seen by a consultant in paediatric dentistry to confirm the treatment plan as part of their routine care. Children, who agreed to participate in the research project, underwent a further clinical examination conducted by the chief investigator (N.H.) or a paediatric dentistry specialist registrar (J.L.) who was part of the research team. This standard oral examination was conducted in a dental chair with an overhead dental light and a dental mirror only. Teeth were lightly dried with gauze prior to inspection. The following clinical variables were recorded: caries experience (dmft/DMFT); orthodontic status/treatment need (IOTN AC) and severity of molar incisor hypomineralisation (MHSI). The assessment and categorisation of these clinical variables is described below.

4.4.2.1 Dental caries

The participant's caries experience (dmft/DMFT) index was recorded as the total number of decayed (d/D), missing (m/M) and filled (f/F) primary and/or permanent teeth (t/T) because of dental caries. This was determined from the clinical and/or radiographic examination conducted by the paediatric dental consultant at the child's initial assessment visit and was not determined by N.H. These data were therefore obtained from participants' clinical notes. The individual's DMFT scores for this group of participants can range from 0-28 (permanent teeth) while dmft scores could range from 0-20 (primary teeth). The calculation for DMFT/dmft excluded unerupted teeth, congenitally missing teeth or supernumerary teeth, and teeth extracted for reasons other than dental caries. Total dmft and DMFT scores will be calculated and employed in the final statistical analysis.

4.4.2.2 Orthodontic status

The child's orthodontic status, or degree of any malocclusion was recorded according to the well-established Aesthetic Component (AC) of the Index of Treatment Need (IOTN) (Burden et al., 2001, Grzywacz, 2003, Jaeken et al., 2018). For scoring the AC, a dental attractiveness scale was used, which

consists of 10 photographs with “descending attractiveness” as shown in Figure 4.3. Evaluations were made by the examiners, N.H. or J.L. by matching the dental ‘attractiveness’ of the patient to one of the photographs that best matched the patient’s dental appearance (Jaeken et al., 2018). Orthodontic treatment need was then categorised into one of three subgroups: where 1 relates to no or little treatment need, and 3 represents the greatest need for orthodontic treatment (Richmond et al., 1994, Richmond et al., 1995), as described below:

1=No /slight need for treatment (AC scores 1-4)

2=Moderate/borderline need for treatment (AC scores 5-7)

3=Substantial need for treatment (AC scores 8-10)

Prior to the application of this measure for research participants, rigorous training and calibration was conducted as described in section 4.4.3.2. .

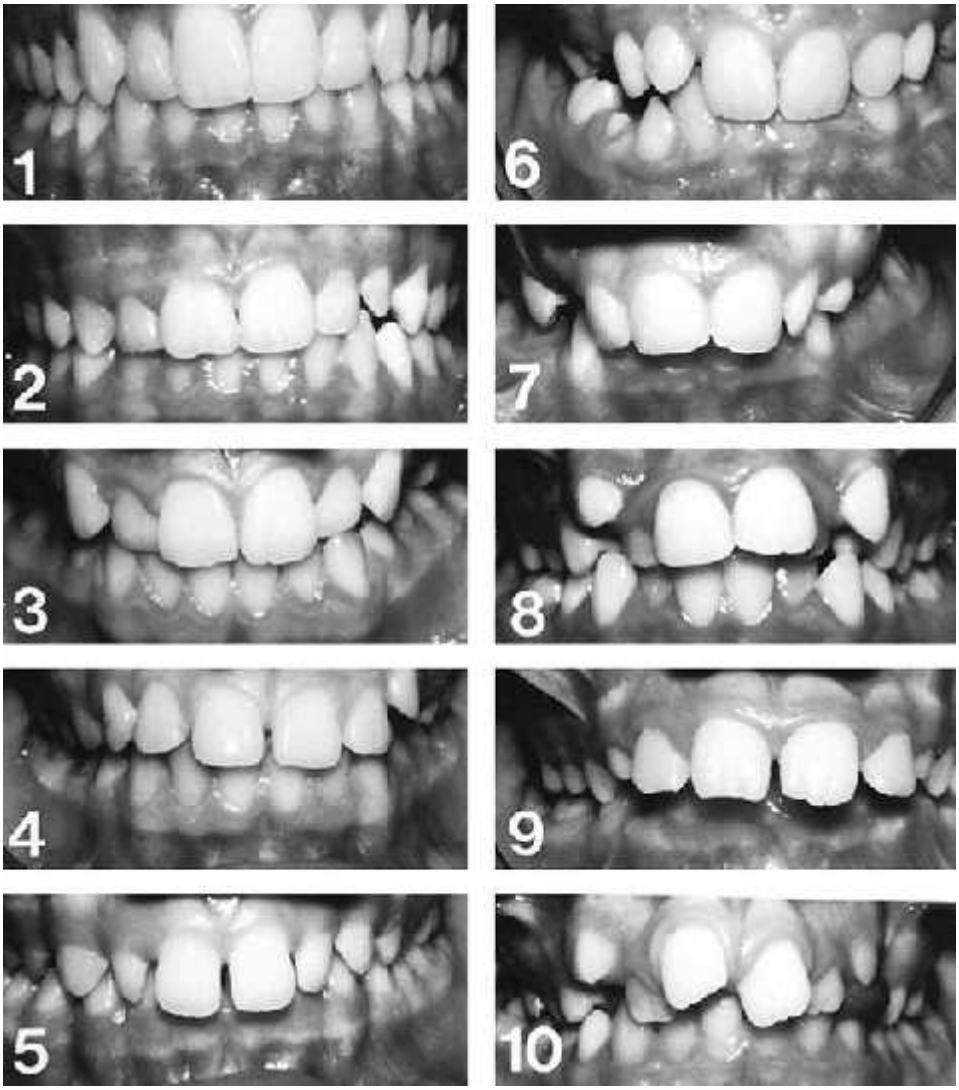

Figure 4.3 Aesthetic Component (AC) of Index of Orthodontic Treatment Need (IOTN) taken from Borzabadi-Farahai (2011).

4.4.2.3 Molar Hypomineralisation Severity Index (MHSI)

The severity of MIH was evaluated and recorded using the Molar Incisor Hypomineralisation Severity Index (MHSI) (Oliver et al., 2014). This measure was developed to guide clinicians in managing teeth and dentitions diagnosed with MIH. Although this severity index has not, to our knowledge been yet used in any other studies, it is more comprehensive than any of the other available MIH severity indices (Leppäniemi et al., 2001, Weerheijm, 2003, Jasulaityte et al., 2007, Lygidakis et al., 2008). This severity index is the first of its kind to include both the enamel defect's clinical characteristics (location and colour) and

sensitivity in its classification. A careful clinical examination is undertaken of each first permanent molar and permanent incisor to ascribe a score relating to each of the following parameters: eruption status, colour of most severe defect, location of most severe defect, number of restorations placed/replaced on first permanent molars and incisors, presence of atypical restorations, presence of post-eruptive breakdown (PEB) and any child-reported sensitivity (anterior or posterior region) (Oliver et al., 2014). The descriptive criteria and scores (weighting) are detailed in Table 4.1 below:

Table 4.1 Criteria and scoring used to determine Molar Incisor Hypomineralisation Severity Index (MHSI) by Oliver et al., 2014.

Characteristics of molar hypomineralisation defects	Severity of characteristics	Weighting Assigned
Eruption status	Unerupted	0
	Erupted	1
Colour of most severe defect	None	0
	White/Cream	1
	Yellow	2
	Brown	3
Location of most severe defect	None	0
	Smooth surface	1
	Occlusal surface (FPMs)	2
	Incisal surface (PIs)	2
	Cuspal involvement (FPMs)	3
Restorations placed/replaced (prior to study entry)	None	0
	One	1
	Two or more	2
Atypical restorations (prior to study entry)	None	0
	Present	1
Post eruptive enamel breakdown (PEB)	None	0
	Present	1
Sensitive to temperature (child report)	None	0
	Sensitive	1
Sensitive to tooth brushing (child report)	None	0
	Sensitive	1
Stainless steel crown (SSC)	None	0
	Yes	10
Extraction due to MIH	None	0
	Yes	12

FPMs=first permanent molars
PIs= permanent Incisors

Following training and calibration in the use of this index by the research team (see section 4.4.3.1 for details) a few minor modifications were made to the original index to improve inter- and intra-examiner agreement, as described below:

- Colour of the most severe defect

The colour of the most severe defect (on an individual tooth) was re-categorised from no colour change (code=0), white/cream (code=1), yellow (code=2) and brown (code=3) to: no colour change (code=0) white (code=1), cream/yellow (code=2), and orange/brown (code=3). This was felt to be more representative of the clinical presentation of opacities seen in the patient group and allowed better inter-examiner agreement for coloured opacities which could not readily be distinguished as cream or yellow.

- Restorations placed/replaced (prior to study entry)

This item was omitted from the index, as it was not possible to accurately determine the restorative history of an individual tooth. Children who participated in this study had received their routine dental care, including any previous treatment for their hypomineralised molars, with their own dentists (GDPs) and were being referred to the dental hospital for aesthetic management of their permanent anterior teeth only. Thus, data about the number of restoration placed and/or replaced on hypomineralised molars were not available from the referring dentists. Furthermore, children and their parents/carers were not able to recall with any certainty how many times a restoration had been placed on an individual tooth, There would also be expected cases of children with a severely hypomineralised tooth that had not previously been restored by the referring dentist, thus the total severity score may have been 'artificially' reduced due to the absence of a restoration which was, in fact, clinically indicated.

- Sensitivity to temperature and tooth brushing (child report)

Clinical experience also suggested that some children were not able to reliably differentiate, for individual teeth and stimuli (thermal, chemical, mechanical), whether this tooth was 'sensitive' or not. In order to simplify the response, the sensitivity criteria (both temperature and tooth brushing) were combined as one criteria only. When eliciting this sensitivity history from children, the investigators were careful to use child-friendly descriptors such as 'jumpy' or 'tingly' as appropriate to the child's understanding. Scoring was therefore amended as shown in Table 4.2.

Table 4.2 Scoring for sensitivity on anterior and posterior teeth.

Sensitivity on front teeth	None	0
	Sensitive	1
Sensitivity on back teeth	None	0
	Sensitive	1

However, this criteria relating to tooth sensitivity was not included in the overall calculation for MHSI score. The modified MHSI used in this study is therefore shown in Table 4.3 below.

Table 4.3 Modified Molar Hypomineralisation Severity Index (MHSI) adopted for the present study.

Characteristics of molar hypomineralisation defect	**Severity of characteristics**	**Weighting Assigned**
Eruption status	Unerupted	0
	Erupted	1
Colour of most severe defect	None	0
	White	1
	Cream/Yellow	2
	Orange/Brown	3
Location of most severe defect	None	0
	Smooth surface	1
	Occlusal surface (FPMs)	2
	Incisal surface (edge) (PIs)	2
	Cuspal involvement (FPMs)	3
Atypical restorations (prior to study entry)	None	0
	Present	1
Post eruptive enamel breakdown (PEB)	None	0
	Present	1
Stainless steel crown (SSC)	None	0
	Yes	7
Extraction due to MIH	None	0
	Yes	8
Unable to score		99

Tooth MHSI scores [MHSI(t)] could range from 3 to 8. For example, a score of 3 reflected the least severe presentation which could equate to one MIH-affected FPM with a white opacity on intact smooth surface without an atypical restoration. In computing MHSI(t), extracted FPMs and FPMs with prior SSCs were excluded

(as defect scoring was not possible). In accordance with the original MHSI index by Oliver et, 2014, the dentition's MHSI scores [MHSI(d)] were summed weightings for all FPMs only (permanent incisors were not included) and ranged from 3 to 32. For example, the most severe score of 32 would equate to four extracted FPMs due to MIH.

4.4.3 Training and calibration

4.4.3.1 Molar Incisor Hypomineralisation Severity Index (MHSI)

There were two examiners involved in obtaining these data for participants in the study, N.H. and J.L. Inter-examiner and intra-examiner training and calibration were undertaken using a series of anonymised printed clinical images provided by the supervisor (H.R.). This material comprised intra-oral A4 colour printed clinical images of 20 paediatric patients with MIH seen by H.R. She then pre-selected ten hypomineralised first permanent molars and ten hypomineralised incisors with a variety of clinical presentations for scoring. An initial training session was held to discuss and agree on the characteristics being scored according to the MHSI scores. H.R. acted as the 'gold standard' against which the two examiners were calibrated. Following training, each examiner examined the clinical images individually and gave scores for each of the 20 selected hypomineralised teeth. A week later, the examiners repeated the scoring using the same images and method.

Intra- and inter-examiner agreements were calculated and are presented in Table 4.4. Kappa (κ) scores and intraclass correlation coefficient scores (ICC) for intra- and inter-examiner agreement for all characteristics examined were good and fell within a range of 0.83 -1.00. However, Kappa scores for "location of most severe defect" were slightly lower, ranging from 0.49-0.56. The Intraclass Correlation Coefficient (ICC) for all characteristics for intra-and inter-examiner reliability showed high scores between 0.94-0.99, demonstrating excellent agreement in applying these scores.

Table 4.4 Inter-and intra- reliability scores for Molar Hypomineralisation Severity Index (with the consultant, H.R. as the gold standard).

	Kappa Coefficients				ICC*
Examiners	Colour of most severe defect	Location of most severe defect	Atypical restorations	Post-eruptive breakdown	MIH severity score
HR Intra	0.845	0.923	1.000	1.000	0.995
NH Intra	0.919	1.000	1.000	0.800	0.993
JL Intra	0.829	0.846	1.000	0.900	0.987
HR1*NH1	0.842	0.485	1.000	0.706	0.983
HR1*JL1	0.677	0.427	1.000	0.900	0.978
HR2*NH2	0.763	0.493	1.000	0.900	0.975
HR2*JL2	0.836	0.556	1.000	1.000	0.979
HR1*NH1*JL1	-	-	-	-	0.989
HR2*NH2*JL2	-	-	-	-	0.986

*ICC=Intraclass Correlation Coefficient

4.4.3.2 Aesthetic component (AC) index of orthodontic treatment need (IOTN)

The training and calibration procedures for adoption of the Aesthetic Component (AC) of Index of Orthodontic Treatment Need (IOTN) were informed by two consultant orthodontic colleagues (N.P. and S.B.) who had undertaken this training nationally. They provided the standard material for the purposes of training and calibration, together with the 'gold standard' scores to benchmark against. This exercise was undertaken by both examiners, N.H. and J.L. and the research supervisor (H.R.). All examiners scored the 20 study models provided which showed a range of malocclusions. They graded them from 1 to 10, according to the ten-point AC system, with reference to the photographs shown earlier (Figure 4.3). The 10 scores were then subgrouped into three categories, as proposed by Richmond (Richmond et al., 1995), to reflect the overall treatment need as follows:

Score 1 No/slight need for treatment (AC grades 1-4)
Score 2 Moderate/borderline need (AC grades 5-7)
Score 3 Substantial need for orthodontic treatment (AC grades 8-10)

Each examiner then repeated the scoring exercise a week later. Intra- and inter-

examiner agreement between the examiners, N.H. and J.L. against the gold standard, H.R. was measured using Kappa (κ) and intraclass correlation coefficient scores (ICC). The inter- and intra-agreement scores are presented in Table 4.5. Inter-and intra-agreement reliability showed good agreement for the Treatment Need assessment (Kappa [κ] scores between 0.62-0.92) and very good agreement for ascribing the Aesthetic Component score (Kappa [κ] scores between 0.91-0.98;Altman, 1991).

Table 4.5 Inter-and intra-examiner reliabilty scores for Aesthetic Component (AC) and the Treatment Need of IOTN (with the consultant, H.R. as the gold standard).

	Kappa Coefficients	95% Confidence Interval		*ICC	95% Confidence Interval	
Examiners	Treatment Need group	Lower bound	Upper bound	Aesthetic Component (AC) score	Lower bound	Upper bound
HR Intra	0.924	0.779	1.069	0.978	0.944	0.991
NH Intra	0.925	0.782	1.068	0.979	0.946	0.992
JL Intra	0.623	0.337	0.909	0.943	0.857	0.978
HR1*NH1	0.701	0.443	0.960	0.929	0.821	0.972
HR1*JL1	0.699	0.436	0.961	0.950	0.874	0.980
HR2*NH2	0.698	0.431	0.965	0.956	0.888	0.982
HR2*JL2	0.776	0.547	1.005	0.912	0.777	0.965
HR1*NH1*JL1	-	-	-	0.957	0.910	0.982
HR2*NH2*JL2	-	-	-	0.953	0.901	0.980

*ICC=intraclass correlation coefficient

4.5 Sample size

The primary outcome measure in this study will be the numerical score derived from the child-completed oral health-related quality of life (OHRQoL) questionnaire. The study employed the Child Oral Health Impact Profile Short Form 19 questionnaire (C-OHIP-SF19) as described earlier in section 4.3.2, which has a score range of 0-76. A sample size calculation was therefore carried out with a view to testing for any statistically significant difference between mean C-OHIP-SF19 scores pre- and post-treatment intervention. As this questionnaire has not been applied in a similar clinical context and population previously, data have been derived from a published study which used this measure to assess the

impact of dental caries and need for orthodontic treatment among 644 7-to-13 year old children (Li et al., 2014). Assuming a mean change in C-OHIP-SF19 score (pre- and post-treatment) of 2.5 and a standard deviation of 8.0 in the mean score, it was calculated that a sample size of 85 children would result in a study with 81% power and a 5% level of significance.

Assuming a dropout rate of 20% between baseline and follow-up data collection and applying the following formula: N1=n/(1-d); n (participant required)=85 and d (dropout rate)=0.2, the intention was to recruit a total of 106 patients to the study.

4.6 Recruitment

Participants were recruited from the Paediatric Dentistry Department, Charles Clifford Dental Hospital, Sheffield, UK. These children had a diagnosis of MIH as determined by any of the unit's consultant paediatric dentists, before seeing the chief investigator (N.H.) or J.L. (research team member) for treatment to improve their incisor aesthetics. MIH was diagnosed using the criteria proposed by the European Academic of Paediatric Dentistry (EAPD) (Weerheijm et al., 2003) and the diagnosis was confirmed by the lead consultant (H.R.) prior to research participation. The patients may have already undergone treatment for one or more of their hypomineralised first permanent molars, either at the Charles Clifford Dental Hospital or with their own dental practitioner (e.g. extractions or restorations, and this clinical detail was recorded in the patients' clinical notes). In cases where treatment was also deemed necessary for FPMs (e.g. interim or permanent restorations), this was provided prior to any aesthetic intervention and completion of the baseline questionnaire. For some children, extractions were considered necessary, and these were planned, wherever possible for before or after the study period, so as not to affect any change in OHRQoL scores. In cases where extractions were ultimately planned (at an appropriate stage of dental development), children were still provided with temporary restorations (using resin modified glass ionomer), minimising the possibility that they could be experiencing discomfort from these teeth during the period of research.

All staff in the paediatric dentistry clinic was informed about the nature of the project, prior to its commencement and their support was confirmed. Potential participants, who met the inclusion criteria, were briefly told about the study by

the direct care team member and, if interested, were directed to a member of the research team. During the period of participant recruitment, N.H. was present on the clinic every day. She explained the purpose of the study verbally in simple terms, and provided the child and parent/carer with written information leaflets explaining the study in more detail, giving the individuals time to read and reflect on the study prior to giving consent (see Appendices 4, 5 and 6). Children were offered an appointment to re-attend for the necessary treatment of their permanent anterior tooth/teeth with N.H. or J.L.

At this subsequent appointment, children and parents/carers were asked if they would like to participate in the research or had any questions about it. If they were happy to take part, assent/consent forms were issued and completed and the child continued on the research pathway (see appendices 6-8). If the child or parent did not wish to participate, then N.H. or a direct care team member still provided their treatment as part of their ‘normal’ care. Recruitment, subsequent treatment and review visits took place between June 2017 and October 2018. Figure 4.4 illustrates the patient journey through the research project.

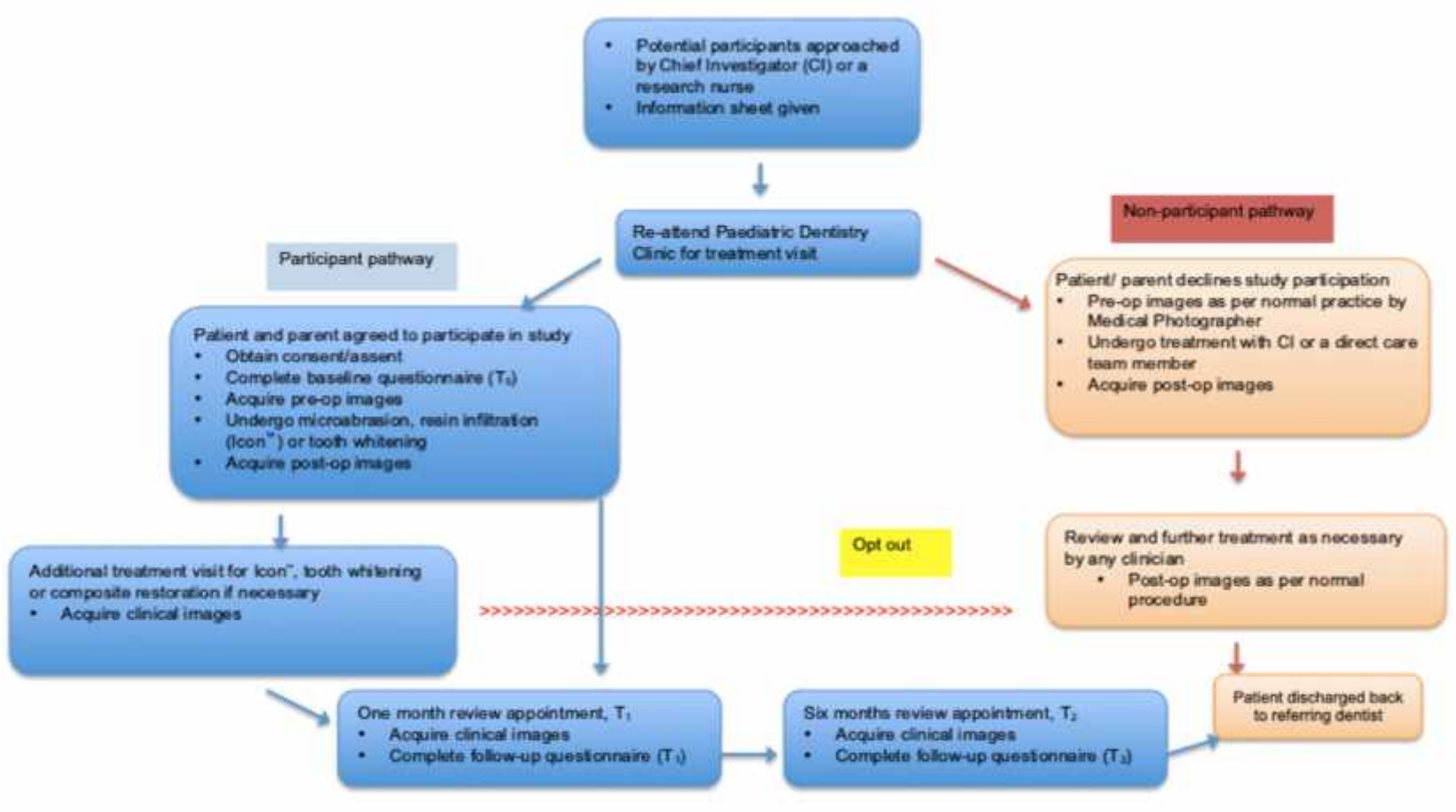

Figure 4.4 Flowchart shows the participants pathways through the study.

4.6.1 Dental visits

4.6.1.1 Baseline dental visit (T_0)

At their baseline visit (T_0), following written assent and consent, child participants were asked to complete a questionnaire booklet, comprising 45 items as described before in section 4.3 (see Appendices 9 and 10) prior to commencing any treatment. The chief investigator (N.H.) or a research nurse provided support if any child needed help to complete their questionnaire. All children approached and invited to participate in this study were assigned a unique identification number that was used for questionnaire booklets, clinical data sheets and clinical images, so that all participants were anonymous and not identifiable. The ID number contains three digits, which starts from 001 for the first child approached to 111 (the last child invited into the study). Only the research team was aware of the participant's identity and participants were informed of this in writing.

Clinical images of maxillary and mandibular permanent anterior teeth were then taken with a digital SLR camera (Nikon D3400). Images were taken to show the anterior teeth in occlusion as well as a close-up view of the tooth/teeth to be treated. These images consititued part of the patient's routine dental records, as well as being required for research purposes. They provided a permanent record of the colour and size of the enamel opacity/opacities prior to any intervention.

All participants received a variety of minimally invasive interventions to improve the appearance of their enamel opacities. The treatment decision was made pragmatically by H.R. depending on the clinical presentation of the opacity, and according to the child/parent wishes. Treatment options could include: microabrasion, resin infiltration (Icon™), tooth whitening or composite resin restoration as appropriate (see section 4.6.3. for details). An appointment was then made for participants to attend a one-month review (T_1) and six-month review (T_2).

4.6.1.2 Interim treatment visit

Following the first intervention, children, parents/carers, clinician and lead consultant (H.R.) appraised the clinical outcome. The clinical research team members were careful not to impose their views but to seek those of the

child/parent as to how much improvement had been achieved, although they did explain the possible options, risks and benefits of further treatment as appropriate. If the child and their parents indicated that they would like more treatment to try to further conceal the enamel opacity, then an interim visit was scheduled. At this additional visit/s, treatment options could include: repeated microabrasion and/or repeated resin infiltration (ICON™, DMG, Hamburg, Germany), tooth whitening (but not if ICON had already been undertaken); composite resin restoration (Filtek™, 3M ESPE, Bracknell, UK) placed over the enamel opacity to further mask any residual discolouration. Clinical images were taken prior to and after the intervention but the child was not required to complete any questionnaires at this time point.

4.6.1.3 One-month review appointment (T_1)

All participants were then reviewed one-month following their microabrasion, or additional microabrasion, ICON™ and/or composite resin restoration (T_1). This visit was in-line with routine care adopted within the unit, to ensure that the patients were happy with the improved aesthetics, there had been no relapse in colour improvement or restoration failure, and the tooth was symptom free. Clinical imaging was repeated at this visit and participants were asked to complete the follow-up questionnaire (see Appendices 12 and 13). Further treatment was provided as necessary depending on the presenting complaint.

4.6.1.4 Six-month review appointment (T_2)

All participants were invited to attend a final six-month review appointment (T_2) prior to their discharge from the hospital service. At this visit, a full dental assessment was undertaken and any further treatment performed as necessary (e.g. polishing of composite resin restoration or infiltrated enamel surface. Participants and their parent/carer were invited to give feedback on the treatment they had received for their permanent anterior teeth. Clinical imaging was repeated, and patients were asked to complete the final review questionnaire (see Appendices 14 and 15). Patients were then discharged back to the care of their general dental practitioner. A discharge summary was completed, to inform the referring dentist of the treatment that had been provided, as well as details about the child's participation in a research study.

4.6.1.5 Missed appointments

In accordance with standard local protocol, the parents of participants who were not brought for their dental visit were first contacted by phone to see if they would like another appointment. If they requested this, a further appointment was sent out to them at the earliest opportunity. If the child had completed their treatment but did not wish to attend their six-month review (due to other commitments), the family were asked if they be willing to complete the final questionnaire, with their agreement this was sent out to them in the post with a pre-paid envelope for its return. If the questionnaire was not completed within two weeks, a further questionnaire was sent out.

4.6.2 Clinical imaging

An anterior (labial) view of the six upper and lower permanent anterior teeth (incisors and canines, if erupted) was taken prior to any intervention. The same view was taken immediately after treatment and at subsequent review visits (one month and six months post-treatment). The clinical images were taken with the teeth in occlusion and a close-up view of the anterior maxillary mandibular teeth needing treatment. For the close-up view images, children were asked to bite on a wooden stick, with calibration colour discs (red, green, blue black and white) which were also coded with their study ID number (Figure 4.5) (Smith et al., 2008). This approach was taken to ensure that the correct images were matched to each participant, and to ensure that any colour deviations between pre- and post treatment images could be corrected digitally if necessary. All calibration colour discs (red, green, blue, black and white) were bought from the same stationery shop (Ivy Stationery Ltd, Peterborough, UK) and were 8 mm in diameter (Figure 4.5). For image analysis purposes, the ranges of pixel values of red, blue, green, black and white discs were determined by N.H. and her supervisor, C.E. before they were used in the clinic. The mean pixel values for these calibration discs should not change in ideal conditions and give the same reading when measured using image analysis software. Therefore, this method ensures that changes seen in pixel values are due to change in enamel colour after treatment, not random or systematic errors (Smith et al., 2008). It should be noted that the initial ethics application sought approval for detailed computer analysis of the images themselves, pre- and post-treatment. However, this was

beyond the scope of the current research but the stored images will form an important archive for future planned research as described in the discussion chapter (section 6.7).

Clinical images were taken using a digital SLR camera (Nikon D3400, Nikon UK Ltd, Kingston upon Thames, UK) with Tamron 90mm macro lens (TAMRON Europe GmbH, Berkshire, UK) and Sigma EM 140DG macro ring flash (Sigma Imaging (UK) Ltd, Welwyn Garden City, UK). The camera was set to manual and these clinical images were taken using standardised settings (ISO 100, 1/160 speed and F/22 aperture), distance (about 20 cm between operator and the patient), and natural and room illumination conditions. Clinical images were captured on 64 GB SanDisk® Ultra SDHC™ UHS-I card (Western Digital Technologies, Inc., Milpitas, California) as Joint Photographic Experts Group (JPEG) images. These images were anonymised before being transferred and stored onto a password-protected university computer using an USB 3.0 universal reader (Delkin Europe Ltd.,Walsall, UK). All images were anonymised and stored according to the participants ID. Support and training for taking clinical images was provided by one of the supervisors (C.E.), online dental photography course from Massive Open Online Course (MOOC) as well as the Sheffield Teaching Hospital Medical Photography team.

Figure 4.5 Anterior view of hypomineralised maxillary permanent anterior teeth with calibration discs attached on a patient-coded wooded stick.

These clinical images were subsequently also added to the dental hospital intra-net, after discussion with the hospital management team and clinical photography department. It was essential that any clinician could access these images in the

future as they formed part of the patient's clinical records, as well as contributing to a specific research project.

4.6.3 Clinical interventions

The choice of treatment was largely informed by the clinical presentation (colour, severity, post-eruptive tissue loss) of the enamel opacity on each permanent incisor and/or canine. Commonly, hypomineralised incisors presented with well-defined demarcated white, yellow or brown opacities on the incisal third of labial surfaces. Some opacities could be associated with enamel loss following post-eruptive breakdown or even accompanying areas of hypoplasia. Due to the diversity of lesion presentation, treatment regimens were tailored for individual patients on discussion with the lead consultant (H.R.), together with the child and their parent/carers. However, the most common approach was to undertake an initial two to three cycles of microabrasion (Opalustre™, Optident Ltd, Ilkley, UK), immediately followed by resin infiltration (ICON™, DMG, Hamburg, Germany). However, some children had microabrasion alone, and others had ICON alone. For children with multiple affected teeth, a tooth whitening gel (Opalescence™ 16% carbamide peroxide, Optident Ltd, Ilkley, UK) was advocated for up to four hours a day in custom made trays, for 2-4 weeks prior to any further treatment. Children (with parental input) who were not satisfied with the aesthetic outcome at their one-month review were given the option of repeating the resin infiltration procedure or having a direct composite resin restoration (Filtek™, 3M ESPE, Bracknell, UK) to further mask the enamel opacity. All children were treated using rubber dam and appropriate protection of soft tissues. They were advised not to have any highly coloured food or drinks for four days following their treatment and were given written post-treatment instructions. The clinical procedures adopted for each intervention are described in more detail below.

4.6.3.1 Microabrasion

Prior to any intervention, teeth surfaces to be treated were cleaned with pumice to remove any oral debris. The microabrasion treatment was undertaken according to a well-established clinical protocol that is in routine use within the department (Benbachir et al., 2007, Sunfeld et al., 2014, Pini et al., 2015). The tooth/teeth to be treated were isolated with rubber dam and a commercial paste

of 6.6% hydrochloric acid and silica carbide particles was applied to the area of discolouration (Opalustre™ Optident Ltd., Ilkley, UK). The paste was rubbed into the opacity using a dental stick and light forces. Each cycle was conducted for 60 seconds before washing and drying the tooth. The cycle was repeated for a maximum of five times, with close inspection for any change in colour, whilst also ensuring that there was no visible tooth surface loss. Topical fluoride varnish was applied on the treated tooth surface to facilitate remineralisation for two minutes prior to a final polish using a fine Sof-lex™ finishing and polishing disc (3M ESPE, Bracknell, UK) or polishing cup (Dentsply Sirona, Surrey, UK). Clinical imaging was repeated immediately after treatment. The resultant change in appearance was appraised by the patient, parent/carer and clinician (N.H. or J.L. in conjunction with H.R.). In some cases, where there was little/no appreciable improvement in appearance, particularly in cases of discrete white opacities, further treatment options were discussed with the child (with parental input). These options could include: repeat microabrasion; masking the opacity with resin infiltration; a composite resin restoration or tooth whitening, taking into consideration the pros and cons of any further intervention.

Participants were advised to refrain from having any highly coloured food or drinks for four days following microabrasion to avoid potential staining from these food or drinks (Rogers et al., 2016).

Figure 4.6 (a-d) shown on the next page illustrates the step-by-step procedures undertaken for microabrasion for patients involved in the study.

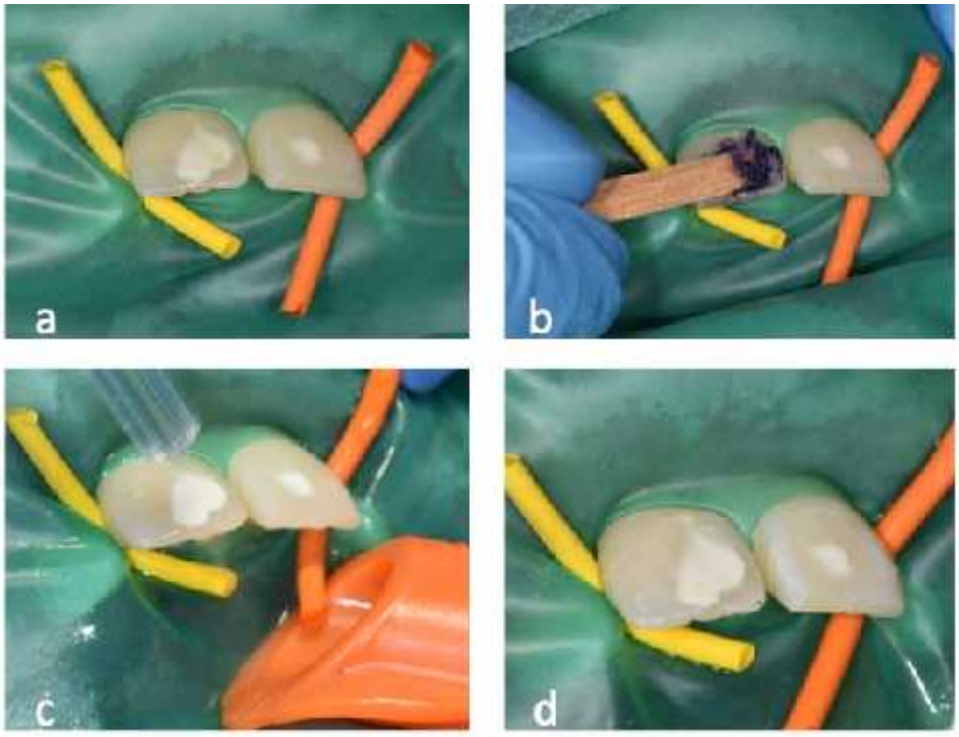

Figure 4.6 a) Rubber dam application to protect soft tissue; b) Application of Opalustre™ (slurry 6.6% hydrochloric acid paste) using a dental stick for 60 seconds; c) Washing and drying for 30 seconds; d) Appearance of the treated tooth immediately post-microabrasion.

4.6.3.2 Resin infiltration Icon™, DMG

The method of application for resin infiltration (Icon™ DMG, Hamburg, Germany) has been well researched and documented (Paris et al., 2007a, Paris and Meyer-Lueckel, 2009, Kim et al., 2011b, Hammad et al., 2012, Knosel et al., 2013, Paris et al., 2013). Rubber dam was applied prior to resin application to protect the soft tissues. If necessary, the tooth surfaces were cleaned with a rubber cup and pumice. This was followed by the application of 15% hydrochloric acid gel (Icon™- Etch, DMG, Hamburg, Germany) for 2 minutes to erode the surface layer and expose the underlying hypomineralised lesion. The manufacturer recommends to occasionally stir the gel with a microbrush during application to enhance erosion of the enamel surface layer (Paris and Meyer-Lueckel, 2009). Then, the etchant gel was removed by washing thoroughly for 30 seconds using the triple air syringe. Subsequently, ethanol (Icon™-Dry, DMG, Hamburg, Germany) was placed on the tooth surface using the applicator provided for 30

seconds, followed by oil-free air-drying. This step was important because ethanol removes water and desiccates the hypomineralised area as a preparation for resin infiltration. The opacity visibility was appraised carefully after the application of ethanol, as it should be masked to some degree due to the relatively high refractive index (1.36) of the ethanol. Thus some indication was gained of how successful the subsequent resin infiltration application would be, or not (Attal et al., 2014). The operator (N.H. or J.L.) would evaluate any reduction in opacity visibility following ethanol application and decide whether this step needed to be repeated or not. This phase can be repeated three times as per the manufacturer's recommendation. Resin infiltration (Icon™, DMG, Hamburg, Germany) was finally applied to the lesion surface in a circular motion, using the applicator provided, and allowed to penetrate for 3 minutes. The direct overhead dental light was removed prior to resin application to avoid any premature curing of the resin infiltration. Excessive material on the labial and proximal tooth surfaces was cleaned with dental floss prior to curing with a light cure. The resin was light-cured for 40 seconds. Using a new applicator tip each time, the resin application step can be repeated twice for 1 minute each application and light cured for 40 seconds. Finally, the treated surface was polished using polishing discs (Sof-lex disc, 3M ESPE, Bracknell, UK). Figure 4.7 (a-j) demonstrates the step-by-step procedures for the application of the resin infiltrant.

Participants were advised not to have any highly coloured food or drinks for four days following Icon™ treatment to avoid potential staining from consumption of these food or drinks.

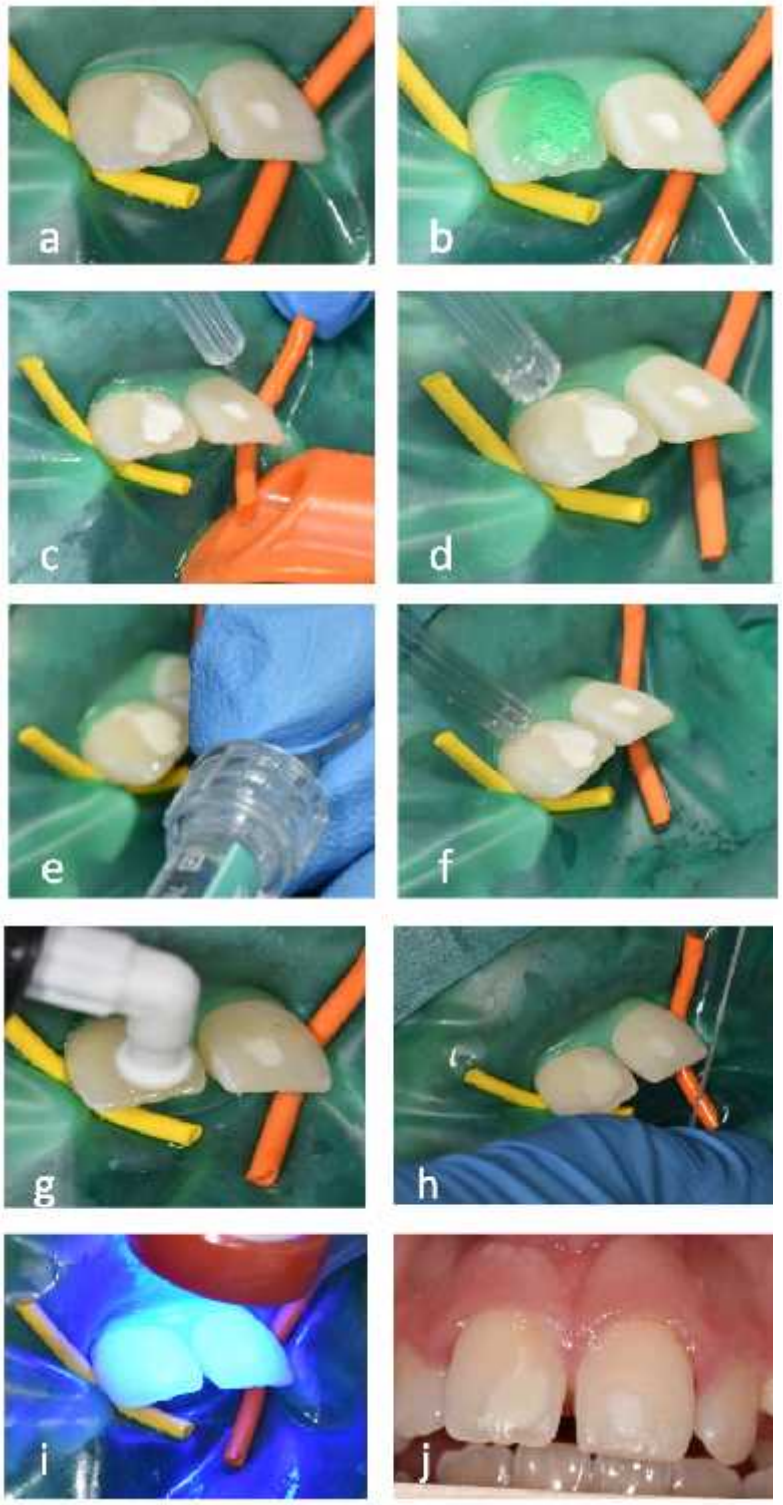

Figure 4.7 Stages employed for resin infiltrant. a) Rubber dam application; b) Icon™-Etch application; c) Washing; d) Drying; e) Application of Icon™-Dry (ethanol); f) Drying; g) Application of resin infiltration (Icon™-Infiltrant); h) Flossing between teeth; i) Light-curing; j) Immediate post-operative appearance.

4.6.3.3 Composite resin restoration

Another treatment option was the application of a composite resin restoration to further camouflage the visible hypomineralised enamel. The process for partial composite resin restoration followed conventional resin restoration protocol, but without tooth preparation. Therefore, no tooth structure was removed prior to composite resin placement. First, a shade guide was used to assist in shade selection, to select the shade which best matched the non-affected enamel. Furthermore, an opaque dentine (body) composite resin was selected to reduce the 'shine through' of any underlying opacity (Esthet. X™,Dentsply Sirona, Surrey, UK). Participants and their parent/caregiver were involved in the selection of the composite shade, which took place in both optimal natural light and dental light settings. Then, the teeth were cleaned using a rubber cup and pumice, if necessary. A rubber dam was applied to protect the soft tissues and achieve optimum moisture control. The lesion surface including part of the non-affected enamel was then etched using the acid etching, 37% phosphoric acid (3M ESPE, Bracknell, UK) for 15 seconds. After this, the etchant gel was washed and dried. The primer was then applied for 10 seconds and was gently dried and light cured for a further 10 seconds. Finally, composite resin was placed over the lesion and part of the non-affected enamel to further camouflage the hypomineralised enamel and was light-cured for 40 seconds. The direct overhead dental light was removed prior to resin application to avoid any premature curing of the composite resin. The restoration was finally polished using polishing discs (Sof-lex disc, 3M ESPE, Bracknell, UK).

4.6.3.4 Tooth whitening

In cases where the hypomineralised enamel involved an extensive area of the tooth surface or affected multiple teeth, tooth whitening was considered as a first line treatment, with the aim of reducing the contrast between white enamel opacities and the surrounding unaffected enamel surface (Castro et al., 2014). The product used in this study was Opalescence™ containing 16% carbamide peroxide, and breaking down to release 5.8% hydrogen peroxide. Discussion about the advantages and possible complications of tooth whitening was undertaken with the child and legal guardian, and a written patient information leaflet was provided prior to any whitening. Written consent was sought prior to

commencing treatment, in line with guidelines stipulated by the General Dental Council, UK, for the use of whitening products for children under 18 years of age (GDC, 2016). An alginate impression was taken to construct a custom-made tray using soft ethylene-vinyl acetate for home application of the whitening gel. Participants were advised to apply one drop of whitening gel into the corresponding sites in the tray for teeth needing treatment and to keep the gel in the fridge in the interim. Patients were asked to use the tray for 3- to 4-hours a day for a period of 2-3 weeks. They were advised to stop using the product if they experienced any sensitivity, and/or to apply desensitising toothpaste in the tray on alternate days if necessary. Participants were also advised to consume a 'non coloured diet' during and the period of bleaching treatment as highly coloured food or drinks may compromise the effectiveness and stability of the tooth whitening process (Matis et al., 2015). They were reviewed after treatment was completed to evaluate the clinical outcome and patient's satisfaction. Figures 4.8 and 4.9 demonstrate the product used for tooth whitening and the tray constructed from an alginate impression.

Figure 4.8 Opalescence™ (16% carbamide peroxide) tooth whitening gel.

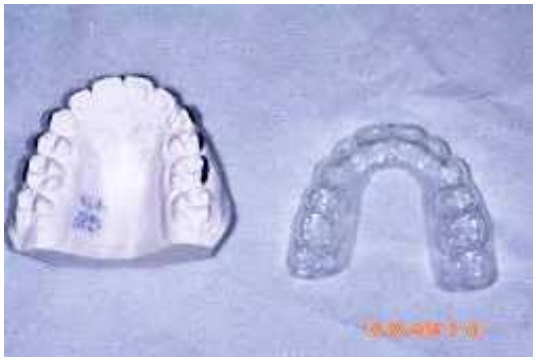

Figure 4.9 Upper whitening tray fabricated by the hospital dental technicians.

4.7 Outcomes measures

4.7.1 Primary outcome

The primary outcome measure was the change of child-reported OHRQoL, where an improved OHRQoL following MIH treatment was recorded as overall change (increase) in total COHIP-S19 score. The relationships between the predictors of children's OHRQoL and HRQoL following microabrasion with/without Icon™,DMG, composite restoration or tooth whitening will be explored using the theoretical framework proposed by Wilson and Cleary. This theoretical model will be tested to evaluate how clinical, demographic, social deprivation and psychological factors influence the children's OHRQoL and overall HRQoL following interventions to improve incisor aesthetics in MIH cases.

4.7.2 Secondary outcomes

In addition, the following secondary outcomes were determined following the intervention for MIH

- Change in self-concept (SPPC)
- Patient satisfaction and experiences in relation to their treatment
- Change in patient self-evaluation of how worried, embarrassed or happy they were in relation to their incisor aesthetics
- Change in overall quality of life, recorded as a global item

4.8 Statistical analysis

4.8.1 Descriptive analysis

All data collected were transferred into an electronic database, Statistical Package for the Social Sciences, (SPSS) v24.0 (IBM Corp., Chicago, IL, USA) by N.H. Descriptive analyses for means (standard deviations, range), and proportions of variables such as age, gender, ethnicity, deprivation (quintile) score and MHSI were undertaken. All statistical analysis results were considered significant at $p<0.05$. For any missing data in the OHRQoL or self-concept questionnaires, the median score for each item was used to impute missing data (only in cases where there was less than 50% of data missing from the scale).

Distributions of normality of the C-OHIP-SF19, Visual Analog Scale score (VAS), and SPPC scores were assessed using the Shapiro-Wilk test ($\alpha<0.05$). Any significant changes in children's OHRQoL between baseline, one-month and six-months follow-up were analysed using the Wilcoxon Signed Rank test or paired-t-test, depending on the normality distribution of the total C-OHIP-SF19 and all its domain's mean scores (Li et al., 2014, Kragt et al., 2016). Any difference in C-OHIP-SF19 scores according to gender and age group were determined using an Independent-sample t-test or Independent sample Mann-Whitney U test, depending on the normality distribution of the data. The same test was used for SPPPC and VAS score, depending on the distribution of normality. The scale reliability for C-OHIP-SF19, SPPC and VAS was estimated using Cronbach's Alpha coefficient, with a higher score indicating greater internal consistency of all items in the scale. The numerical values for Cronbach's Alpha coefficient, *r*, ranges from -1.0 to +1.0 with the closer the values to +1.0, the greater the reliability was (Altman, 1991). This analysis showed very good to excellent internal consistency of these scales used in this study. For example, the Cronbach's Alpha coefficient for C-OHIP-SF19 pre-treatment was 0.759, 0.810 at one-month follow-up and 0.834 at the six-month review visit. The Cronbach's Alpha coefficient of these indices at each visit was presented in the table 4.6.

Table 4.6 Cronbach's Alpha scores for reliability and accuracy check of C-OHIP-SF19, SPPC and VAS at baseline, one-month and six-month follow-up visits.

Scales	Baseline, T_0	1-month follow-up, T_1	6-month follow-up, T_2
C-OHIP-SF19	0.759	0.810	0.834
SPPC	0.900	0.928	0.938
VAS	0.825	0.893	0.889

N.H. repeated data entry for a randomly selected 50% (n=43) of participants who had completed the study three months after all data has been collected to check for the accuracy of data entry. The Intraclass Correlation Coefficient (ICC) and the upper and lower bound of 95% Confidence Interval (CI) scores for selected variables used in this study were presented in Table 4.7. The results showed that the ICC scores for each variable were between 0.995 to 1.000, indicating substantial reliability and high accuracy between the actual and the repeated SPSS data entry.

Table 4.7 Intraclass Correlation Coefficient (ICC) and 95% Confidence Interval (CI) of selected variables between the total sample (n=86) and repeated data entry (n=43) at baseline, one-month and six-month follow-up visits.

Variables	Baseline, T_0 ICC (95% CI)	1-month follow-up, T_1 ICC (95% CI)	6-month follow-up, T_2 ICC (95% CI)
Total C-OHIP-SF19	1.000 (1.000-1.000)	0.997 (0.995-0.999)	0.999 (0.998-0.999)
Average Social SPPC	0.999 (0.999-1.000)	1.000 (0.999-1.000)	0.998 (0.997-0.999)
Average Physical SPPC	0.995 (0.990-0.997)	1.000 (1.000-1.000)	0.995 (0.991-0.997)
Average Global Self-worth SPPC	0.998 (0.996-0.999)	0.999 (0.998-1.000)	0.998 (0.996-0.999)
VAS 1	1.000 (1.000-1.000)	1.000 (1.000-1.000)	1.000 (1.000-1.000)
VAS 2	1.000 (1.000-1.000)	1.000 (1.000-1.000)	0.999 (0.998-1.000)
VAS 3	1.000 (1.000-1.000)	1.000 (1.000-1.000)	0.999 (0.998-1.000)
VAS 4	1.000 (1.000-1.000)	1.000 (1.000-1.000)	0.998 (0.997-0.999)
Age	0.998 (0.996-0.999)		
dmft score	1.000 (1.000-1.000		

Further structural equation modeling confirmatory factor analysis and growth curve models were undertaken to test the total effects, direct and indirect effects of the theoretical model, as described below.

4.8.2 Structural equation modeling

Structural equation modeling (SEM) is a multivariate statistical analysis to analyse structural relationships between observed and latent variables using AMOS (Analysis of Moment Structures) software version 24 (IBM Corp., Chicago, IL, USA). N.H attended a practical course for SEM using AMOS software organised by Essex Business School. She also attended a lecture on an introduction to SEM AMOS by her supervisor, M.V. Structural Equation Modelling (SEM) involves Confirmatory Factor Analysis (CFA) of hypothesised latent variables followed by testing of the full model with all observed and latent

variables to explore the link between them. The non-significant links and variables from the full model will then be removed to produce the final parsimonious model.

Confirmatory Factor Analysis (CFA) using maximum likelihood estimation (ML) was conducted to test the hypothesised measurement model through assessing associations between the self-concept assessed at initial visit (baseline, T_0) latent variable, and its observed indicators (Social Acceptance, Physical Acceptance, and Global self-worth subscales assessed at baseline). This was followed by SEM to explore the direct and indirect relationships between observed and latent variables. Direct effects (representing the direct path from one variable to another) and indirect effect (where the link was mediated by other variables) were estimated using SPSS AMOS v24 AMOS (Analysis of Moment indirect effects represent the sum of one or more specific paths). A bias-corrected bootstrap confidence interval (CI) was used to assess mediation by analysing statistical significance of indirect effects. In addition, maximum likelihood estimation and bootstrapping were also estimated using AMOS. Nine hundred bootstrap samples were resampled from the original data set to derive less biased standard errors and 95% CI bootstrap percentiles. The Chi-squared (χ^2) test statistic was used to assess adequacy of overall model fit. Root mean square error of approximation (RMSEA) with 90% CI, standardised root mean square residual (SRMR), goodness of fit index (GFI), and comparative fit index (CFI) were also used. The threshold for a good model fit was χ^2/degrees of freedom (df) ranges between 1 to 3, SRMR less than 0.08, RMSEA not larger than 0.06, and GFI and CFI values larger than 0.90 (Hu and Bentler, 1999, Arbuckle, 2016). All links with p value <0.20 were removed and the model was re-estimated to create a parsimonious model.

It was predicted that number of permanent anterior teeth with enamel opacities needing aesthetic treatment, need for orthodontic treatment (AC), age, gender, social deprivation status and self-concept (SPPC) at baseline T_0 are directly linked to the overall oral health perception and socio-emotional wellbeing domain of C-OHIP-SF19 at baseline and at the six-month follow-up visit.

A bias-corrected bootstrap confidence interval (CI) was then employed to assess mediation by analysing the statistical significance of indirect effects. In addition,

maximum likelihood estimation and bootstrapping were also estimated using AMOS. Nine hundred bootstrap samples were resampled from the original data set to derive less biased standard errors and 95% CI bootstrap percentiles. The Chi-squared (χ^2) test statistic was used to assess adequacy of overall model fit. Root mean squared error of approximation (RMSEA) with 90% CI, standardised root mean square residual (SRMR), goodness of fit index (GFI), and comparative fit index (CFI) were also used. The threshold for a good model fit was χ^2/degrees of freedom (df) ranges between 1 to 3, SRMR less than 0.08, RMSEA not larger than 0.06, and GFI and CFI values larger than 0.90 (Hu and Bentler, 1999).

Next, a full model was tested if the model proved an adequate fit to the present data. This analysis simultaneously tested the interrelationships specified within the a priori augmented univariate latent growth model. The Chi-square test, together with goodness of fit indices as described earlier, were used to estimate the adequacy of hypothesised model to the present data. Then, non-significant links with *p*-value larger than 0.020 were removed and the full model was re-estimated to produce a statistically parsimonious model. The full model was compared with the parsimonious model using chi-square test. Maximum likelihood estimation and bootstrapping were estimated using AMOS 24.0. Nine hundred bootstrap samples were resampled from the original data set to derive less-biased standard errors and 95% CI bootstrap percentiles. Model fit was assessed using the recommended key indicators of goodness-of-fit values as mentioned earlier.

4.8.3 Proposed model

As mentioned in chapter 3, this study aimed to explore the association between different variables and oral health related quality of life. The current study applied the Wilson and Cleary's theoretical framework of health (Wilson and Cleary, 1995). The conceptual model was adopted to support the selection of variables and to guide the analysis (Figure 4.10). This model represents the biopsychosocial model of health. It encompasses the biological components (Aesthetic Component of IOTN, dmft/DMFT, and number of teeth needing aesthetic dental treatment); followed by socio-emotional and overall oral health measured at baseline and ends with socio-emotional wellbeing and overall oral health at the final review visit (T_2). Each of the levels are related and influenced

by characteristics of the individual (e.g. age and gender) and environment (social deprivation status).

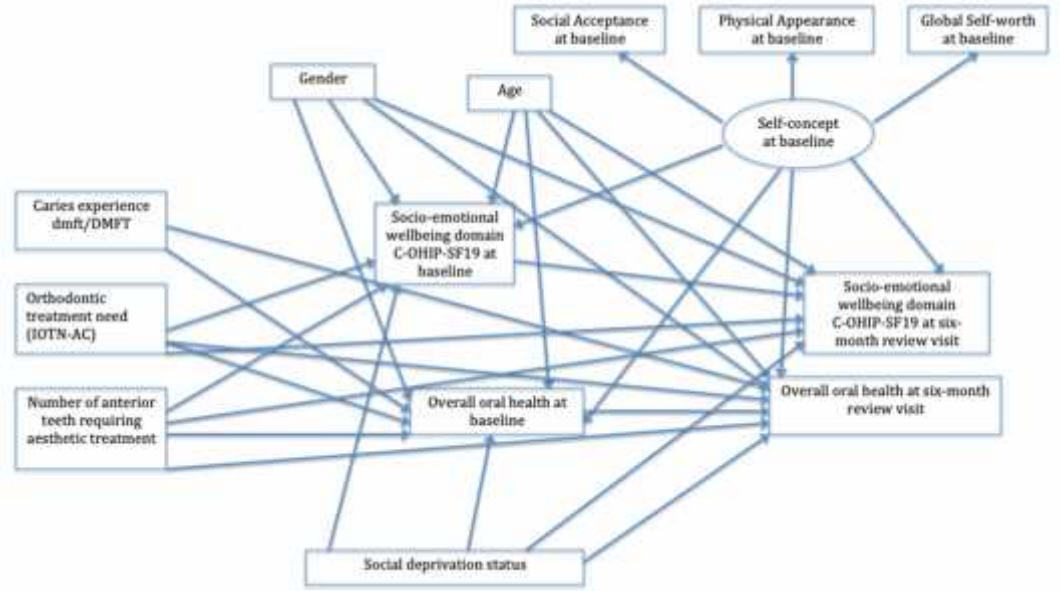

Figure 4.10 Proposed full model of Structural Equation Modeling adapted from the Wilson and Cleary theoretical model (1995).

4.3.8.1 Summary of included variables

Observed variables

Clinical variables

- Caries experience: total caries experience combining dmft/DMFT for primary and permanent dentitions
- Orthodontic treatment need: IOTN Aesthetic Component (AC) assessed by clinician (N.H. or J.L.)
- Number of permanent anterior teeth affected by MIH needing aesthetic treatment

Characteristics of individual

- Gender
- Age (in year)

Characteristics of the environment

- Social deprivation status measured using IMD scores

Outcome variables

- Socio-emotional wellbeing domain: socio-emotional wellbeing domain of C-OHIP-SF19 assessed at baseline (T_1) and six month follow-up dental visit (T_2)
- OHRQoL: Final question of C-OHIP-SF19 concerning overall oral health status perceived by the participants evaluated at baseline (T_1) and six-month follow-up dental visit (T_2)

Latent variables

Self-concept measured using three subscales of Self-Perception Profile of Children (SPPC) at baseline. The two domain-specific subscales are Physical Appearance, Social Acceptance, and Global Self-worth subscale.

Based on the existing literature, it was hypothesised that the requirement for orthodontic treatment (high AC-IOTN scores) and an increased number of teeth with opacities, may have a direct effect on self-rated overall oral health and socio-emotional wellbeing domain of C-OHIP-SF19 before treatment (baseline,T_0) and at the six-month follow-up dental visit (T_2). It was also hypothesised that participants' individual characteristics (age, gender, self-concept) may be directly linked to both overall oral health and socioemotional wellbeing domain at baseline and six-month follow-up visit. Children with high caries risk (total dmftDMFT) may have a direct relationship with overall oral health at initial and the final follow-up dental visits (T_0 and T_2). The outcome measures are socio-emotional wellbeing domain of C-OHIP-SF19 and overall oral health perception at baseline (T_0) and six-month follow-up visit (T_2). Children's perceptions of their overall oral health and socio-emotional wellbeing at baseline will have impact on their perceptions on their overall oral health and socio-emotional wellbeing at the final dental follow-up visit (T_2).

It was also hypothesised that self-concept at baseline was a latent variable, which predicts the link between observed variables and the outcome measures. Self-concept may have a direct relationship with the children's perception of their overall oral health at baseline and six-month follow-up visit and also their self-rated socio-emotional wellbeing both prior to any dental treatment (T_0) and six-month post-treatment visit (T_2). Oral health is an important component of

children’s general health. It is anticipated that the adapted model will be able to enhance understanding of the complex inter-relationships between measures potentially associated with oral-health related quality of life among the young people with MIH seeking aesthetic interventions to improve their dental appearance. This model can be employed to identify the true impact of this condition on the quality of children’s lives.

Chapter 5
Results

5.1 Introduction

The first section in this chapter presents the characteristics of participants involved in this study. The second section provides the descriptive statistics and analysis for all study variables. The final section describes findings from the Structural Equation Modeling (SEM), which includes the Confirmatory Factor Analysis of the latent variables, measurement model, full and parsimonious model.

5.2 Participants' characteristics

A total of 111 children, aged 7-16 years, who met the inclusion criteria were invited to participate in this study. These children were referred to the Charles Clifford Dental Hospital, Sheffield, by their own dentist for management of enamel opacities on their anterior teeth due to development defects of enamel. Of the 111 patients initially approached, 103 (92.8% response rate) children and their parents agreed and consented to take part in this study. One child was excluded at baseline visit, T_0, because they were very anxious and declined any treatment. Another child was excluded because of the inability to isolate the tooth to be treated satisfactorily. N.H. treated the majority of children but 20 received initial treatment and their one-month follow-up visit with another paediatric dentist (J.L.) who was part of the research team. All participants were then reviewed at six months by N.H.

In total, ten children were not brought to their one-month review appointments, giving a 9.71% dropout rate. A further seven participants (7.53%) were not brought to their final review dental visit (T_2). Thus, completion rates were 90.3% (n=93) at one-month post-treatment and 83.5% (n=86) at the six-month follow-up visit. Of the 93 children who were reviewed at one-month, one child did not attend the visit but completed and returned the postal questionnaire. For the final

review visit, 80 children attended and completed the questionnaires in person, while the other six children returned their completed questionnaire via the mail. Figure 5.1 summarises the number of children who attended each dental visit.

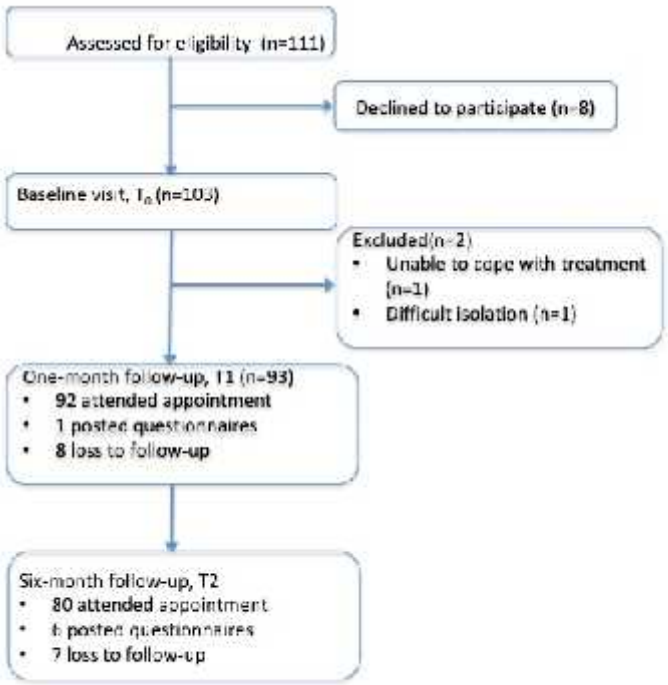

Figure 5.1 Flowchart to show the number of participants attended each dental visit.

At baseline, ninety participants (87.4%) were diagnosed with MIH but the remaining 13 children (12.6%) presented with more generalised white diffuse opacities thought more likely to be due to a hypomature form of amelogenesis imperfecta (AI). These children with suspected AI only had enamel opacities, which compromised the aesthetic appearance of their teeth and did not have signs of enamel loss or compromised posterior teeth. Therefore, it was decided to include these children in this study. Table 5.1 shows the prevalence of children with MIH and suspected AI in the studied sample at baseline, one-month after treatment and six-month follow-up.

Table 5.1 Prevalence of Molar Incisor Hypomineralisation (MIH) and Amelogenesis Imperfecta (AI) in the study sample at baseline, one-month and six-month follow-up visits.

Diagnosis	Baseline, T_0 (n,%)	1-month follow-up, T_1 (n,%)	6-month follow-up, T_2 (n,%)
Molar Incisor Hypomineralisation (MIH)	90 (87.4)	81 (87.1)	75 (87.2)
Amelogenesis Imperfecta (AI)	13 (12.6)	12 (12.9)	11 (12.8)
Total	103 (100)	93 (100)	86 (100)

5.2.1 Characteristics of participants

Full details about the participants and the treatment/s they received at all three time points are provided in Table 5.2.

At the baseline visit, 60% of the participants were females (n=62). The majority of participants (n=94, 91.3%) were identified as White English, Welsh, Scottish, Northern Irish or British and further 8.7% (n=9) were from an ethnic minority group.

The mean age of the participants was 11.02 years (range=7-16; SD=2.59). Almost half of the participants (n=46, 44.7%) lived in the least deprived areas of the country (1st and 2nd quintiles of Index of Multiple Deprivation). The average number of treated teeth was three for each participant. At baseline, the majority of participants (n=64, 62.1%) received a combination of microabrasion followed by resin infiltration ICON™.

Ninety-three participants attended their one-month dental review visit and 86 children attended the six-month follow-up visit and completed the study. The definitive results (SEM) presented in this chapter refer to the 86 participants who completed this study. There were 35 males (40.7%) and 51 (69.3%) females in the final study group, and they had a mean age of 11-years. Around half of the participants (n=47, 54.7%) were in the 7-10 year old group and the remaining 39

children (45.3%) were in the 11-16 year old group. The majority of children who completed the study (n=79, 91.9%) identified themselves as White English, Welsh, Scottish, Northern Irish or British ethnic background and 41% (n=35) lived in the areas of greatest deprivation (4th and 5th IMD quintiles).

Table 5.2. Study participants' sociodemographic and clinical characteristics at baseline, one-month and six-month follow-up visits.

		Baseline, T_0		1-month follow-up, T_1		6-month follow-up, T_2	
		Mean (SD, range)	n (%)	Mean (SD, range)	n (%)	Mean (SD, range)	n (%)
Age (years)	All participants	11.02 (2.59, 7-16)		10.95 (2.54, 7-16		10.93 (2.49, 7-16)	
	7-10		55(53.4)		50(53.8)		47(54.7)
	11-16		48(46.6)		43(46.2)		39(45.3)
Gender	Male		41(39.8)		38(40.9)	34 (45.3)	35(40.7)
	Female		62(60.2)		55(59.1)	41(54.7)	51(59.3)
Ethnic background	White British/Northern European		94(91.3)		85(91.4)		79(91.9)
	Any other group		9(8.7)		8 (8.6)		7(8.1)
Social deprivation score	High (1st & 2nd quintiles -least deprived)		46(44.7)		42(45.2)		41(47.7)
	Middle (3rd quintile)		17(16.5)		14 (15.1)		10(11.6)
	Low (4th and 5th quintiles)		40(38.8)		37 (29.8)		35(40.7)
Number of treated teeth		3.09 (2.65, 1-12)		3.13 (2.65, 1-12)		3.20 (2.73, 1-12)	
Treatment regimen	Microabrasion alone		9(8.74)		6 (6.45)		4(4.65)
	ICON™ alone		6 (5.83)		4 (4.30)		4(4.65)
	Tooth whitening alone		4 (3.88)		4 (4.30)		4(4.65)
	Composite restoration alone		2 (1.94)		2 (2.15)		2(2.32)
	Microabrasion followed by ICON™		64 (62.14)		59(63.44)		54 (62.79)
	Microabrasion followed by tooth whitening		8 (7.77)		8 (8.60)		8(9.3)
	Microbrasion followed by ICON™ and resin composite restoration		3 (2.91)		3 (3.22)		3(3.49)
	Tooth whitening followed by microabrasion and/or ICON™		7(6.80)		7(7.53)		7(8.14)

The following clinical images show some example of cases treated using different regimens at baseline (T_0), one-month (T_1) and six-month (T_2) dental review visits. Figure 5.2 shows enamel opacities on upper central incisors of an 8-year-old girl treated with a combination of microabrasion and resin infiltration (Icon™, DMG). The visibility of the opacities shows a marked reduction following treatment and the improvement was maintained (stable) at the six-month review visit. Although the opacities were still visible at the final dental visit (T_2), the patient was happy and did not request any further treatment.

Figure 5.2 Opacities treated with microabrasion and resin infiltration (Icon™ DMG).

The clinical images seen in Figure 5.3 are of cream-coloured opacities on the upper left central incisor of a 16-year-old boy. The opacities were treated with microabrasion and resin infiltration Icon™. At the one-month review visit, he requested further treatment to 'mask' the opacities on that tooth. Composite resin restoration was provided and the restoration was still intact at the final dental review visit (T_2).

Figure 5.3 Opacity treated with microabrasion, resin infiltration (Icon™ DMG) and finally composite resin restoration.

Figure 5.4 shows clinical images of a 14-year-old girl who presented with multiple creamy-yellow opacities involving all six of her upper anterior teeth. Following discussion with the lead consultant (H.R), the child and her parent, tooth whitening using Opalescence™ (16% carbamide peroxide) was prescibed for home use for 2-3 weeks. She was reviewed at one-month post-treatment and the

opacities were seen to have lightened but were still visible. The teeth were further treated with microabrasion and resin infiltration Icon™. The girl was extremely happy with the clinical outcome and no further treatment was requested at the final review visit, T_2.

Figure 5.4 Opacities managed with tooth whitening, then microabrasion and resin infiltration (Icon™ DMG).

5.3 Descriptive analysis of patient-reported outcomes

As mentioned in Chapter Four, all participants completed a questionnaire prior to any intervention at baseline (T_0). They were invited to complete the same questionnaire at one-month (T_1) and six-month (T_2) follow-up visits. There were no missing data, as N.H and J.L. checked that all questionnaires were completed in full at each dental visit. The following results relate to the 86 participants who received a variety of minimally invasive dental treatment to conceal the visibility of enamel opacities on their permanent anterior teeth and attended the one-month and six-month follow-up dental visits.

5.3.1 Oral Health-Related Quality of Life

Summary data for the completed C-OHIP-SF19 questionnaires for the 86 participants at each dental visit (baseline T_0, one-month follow-up, and six-month follow-up) are presented in Table 5.3. Use of the Shapiro-Wilk test showed that the data (C-OHIP-SF19 scores) were not normally distributed. Therefore, non-parametric tests, including Friedman's Two Way Analysis (represents by *p-value) and the Wilkinson Signed Rank Test (represents by **p-value) were used to compare the median C-OHIP-SF19 total score as well as the median C-OHIP-SF19 score for each of the three different domains (oral health, functional wellbeing, and socio-emotional wellbeing) at each dental visit (T_0, T_1 and T_2). Floor and ceiling effects were generally not observed since no children gave the lowest possible score (zero) at T_0, T_1, T_2. One child did reach the highest

possible score (76) prior to treatment (T_0) but no children reported the maximum score at their review visits. Further analyses comparing the median C-OHIP-SF19 total scores and median C-OHIP-SF19 domain scores according to gender and between the two age groups were undertaken using the Independent Sample Mann-Whitney U test. The significant level was set at *p*-value<0.05 in all analyses.

There was a statistically significant difference in the C-OHIP-SF19 total scores between baseline (before treatment) and at six-months post-treatment (*p*<0.001, Friedman's Two Way test) for the whole sample. The mean C-OHIP-SF19 total score was 47.41 (SD=9.34; range 0-76) prior to any treatment (T_0) and increased to 58.53 (SD= 9.39; range 0-76) at the one-month follow-up (T_1). This increase was statistically significant. The C-OHIP-SF19 total score was seen to further increase between T_1 and the final review, T_2 to 59.82 (SD= 9.69; range 0-76), however T_1 and T_2 scores were not found to be statistically different (*p*=0.079, Wilcoxon Signed Rank test). These findings suggest that children perceived a marked improvement in their OHRQoL when questioned one-month post-treatment. However, there were no meaningful changes in OHRQoL between the one-month follow-up and the final dental visit.

Similarly, the C-OHIP-SF19 domain scores also increased significantly between baseline and one-month post-treatment. The C-OHIP-S19 domain scores was seen to further increase increased between T_1 and the final dental visit (T_2) but this change was not statistically significant. The greatest improvement (increase in score) was observed for socio-emotional wellbeing domain scores between T_0 and T_1 (p<0.001, Wilcoxon Signed Rank test), as well as between T_0 and T_2 (*p*<0.001, Wilcoxon Signed Rank test). Tables 5.4 and 5.5 provide the raw data and demonstrate that there was statistically significant score changes for all C-OHIP-SF19 domains at T_0, T_1 and T_2 (p<0.001, Friedman's Two way test; represents by **p*-value) with the exception of the functional wellbeing domain among male participants. The scores for the functional wellbeing domain among male participants was 13.20 (SD=3.06, range=0-16) prior to treatment (T_0) and these scores increased significantly at T_1 (p=0.033, Wilcoxon Signed Rank test) but reduced marginally at T_2 (p=0.746, Wilcoxon Signed Rank test; represents by ***p*-value). Among the teenage group (11-16 years age), the scores for the functional wellbeing domain were significantly different between baseline (T_0),

one-month follow-up (T_1) and six-month follow-up (T_2) (p=0.036, Friedman's Two Way test). Similarly, these scores differed statistically between T_0 and T_1 and between T_0 and T_2 as shown on Table 5.4. The score at the final review, T_2, reduced but the difference was not statistically significant (p=0.761, Wilcoxon Signed Rank test). The socio-emotional wellbeing domain for younger age group (7-10 years) also showed similar findings where the T_1 scores were statistically different between baseline, T_0, one-month (T_1) and six-month follow-up (T_2) respectively, (p<0.001, Friedman's Two Way test). The decline in the scores from T_1 and T_2 was not statistically significant (p=0.455, Wilcoxon Signed Rank test). Statistically significant results (p<0.01) are highlighted in grey (Tables 5.4 and 5.5).

Table 5.3 Child Oral Health Impact Profile Short Form 19 (C-OHIP-SF19) mean scores (SD) at baseline, one-and six-month follow-up visits for all participants (n=86) and according to gender (males, n=35; females, n=51).

C-OHIP-SF19	Participants (n)	Baseline (T_0) Mean (SD,range)	1-month (T_1) Mean (SD,range)	6-months (T_2) Mean (SD,range)	*p*-value*	T_0 x T_1 Mean change(SD)	*p*-value**	T_0 x T_2 Mean change(SD)	*p*-value**	T_1 x T_2 Mean change(SD)	*p*-value**
Overall score	All	47.41 (9.34, 0-76)	58.53 (9.39,0-76)	59.81 (9.69,0-76)	*p*<0.001	11.13 (10.36)	*p*<0.001	12.41 (10.23)	*p*<0.001	1.28 (7.69)	*p*=0.079
	Male	48.71 (9.07, 0-76)	58.57 (8.77, 0-76)	59.60 (9.47, 0-76)	*p*<0.001	9.86 (9.34)	*p*<0.001	10.88 (9.46)	*p*<0.001	1.03 (6.06)	*p*=0.223
	Female	46.51 (9.50, 0-76)	58.51 (9.87, 0-76)	59.96 (9.91, 0-76)	*p*<0.001	12.00 (10.98)	*p*<0.001	13.45 (10.69)	*p*<0.001	1.45 (8.69)	*p*=0.146
Oral health domain	All	11.30 (2.82, 0-20)	14.19 (3.45, 0-20)	14.74 (3.28, 0-20)	*p*<0.001	2.88 (3.29)	*p*<0.001	3.44 (3.49)	*p*<0.001	0.56 (3.21)	*p*=0.072
	Male	11.46 (2.68,0-20)	13.74 (3.41,0-20)	14.51 (3.53,0-20)	*p*<0.001	2.28 (3.58)	*p*<0.001	3.06 (3.83)	*p*<0.001	0.77 (3.04)	*p*=0.120
	Female	11.19 (2.92,0-20)	14.49 (3.48,0-20)	14.90 (3.11,0-20)	*p*<0.001	3.29 (3.05)	*p*<0.001	3.71 (3.26)	*p*<0.001	0.41 (3.34)	*p*=0.280
Functional wellbeing domain	All	13.30 (2.59, 0-16)	14.24 (1.91, 0-16)	14.30 (1.92,0-16)	*p*<0.001	0.94 (2.27)	*p*<0.001	1.00 (2.28)	*p*<0.001	0.06 (1.83)	*p*=0.790
	Male	13.20 (3.06,0-16)	14.14 (1.99,0-16)	14.03 (2.25,0-16)	*p*=0.224	0.94 (2.36)	*p*=0.033	0.83 (2.57)	*p*=0.170	-0.11 (2.15)	*p*=0.746
	Female	13.37 (2.23,0-16)	14.31 (1.87,0-16)	14.49 (1.64,0-16)	*p*<0.001	0.94 (2.23)	*p*=0.007	1.12 (2.08)	*p*<0.001	0.18 (1.58)	*p*=0.480
Socio-emotional wellbeing domain	All	22.80 (7.81,0-40)	30.10 (6.25, 0-40)	30.77 (6.45, 0-40)	*p*<0.001	7.30 (7.94)	*p*<0.001	7.96 (7.45)	*p*<0.001	0.66 (5.62)	*p*=0.140
	Male	24.06 (6.88,0-40)	30.69 (5.61,0-40)	31.06 (5.47,0-40)	*p*<0.001	6.63 (6.92)	*p*<0.001	7.00 (6.61)	*p*<0.001	0.37 (4.11)	*p*=0.386
	Female	21.94 (8.35,0-40)	29.71 (6.68,0-40)	30.57 (7.09,0-40)	*p*<0.001	7.76 (8.61)	*p*<0.001	8.63 (7.97)	*p*<0.001	0.86 (6.48)	*p*=0.220

**p*-value refers to Friedman's Two Way test

***p*-value refers to Wilcoxon Signed Rank test

(Note: mean values are presented for ease of interpretation, but median scores were used in the statistical analyses)

Table 5.4 Child Oral Health Impact Profile Short Form 19 (C-OHIP-SF19) mean scores (SD) at baseline, one- and six-month follow-up visits according to age groups (7-10 years old, n=47; 11-16 years old, n=39).

C-OHIP-SF19	Age groups	Baseline (T_0) Mean (SD,range)	1-month (T_1) Mean (SD,range)	6-months (T_2) Mean (SD,range)	*p*-value*	T_0 xT_1 Mean change (SD)	*p*-value**	T_0 xT_2 Mean change (SD)	*p*-value**	T_1 xT_2 Mean change (SD	*p*-value**
Overall score	7-10	47.32 (9.01,0-76)	60.17 (9.12,0-76)	59.96 (9.83,0-76)	*p*<0.001	12.85 (10.81)	*p*<0.001	12.64 (1.62)	*p*<0.001	0.21 (8.56)	*p*=0.983
	11-16	47.51 (9.83,0-76)	56.56 (9.57,0-76)	59.64 (9.63,0-76)	*p*<0.001	9.05 (9.51)	*p*<0.001	12.12 (9.23)	*p*<0.001	3.08 (6.14)	*p*=0.005
Oral health domain	7-10	10.59 (2.88.0-20)	14.13 (3.41,0-20)	14.42 (3.54, 0-20)	*p*<0.001	3.53 (3.67)	*p*<0.001	3.83 (3.79)	*p*<0.001	0.29 (3.37)	*p=0.457*
	11-16	12.15 (2.52,0-20)	14.26 (3.53,0-20)	15.13 (2.92, 0-20)	*p*<0.001	2.10 (2.59)	*p*<0.001	2.97 (3.09)	*p*<0.001	0.87 (3.01)	*p=0.057*
Functional wellbeing domain	7-10	13.21 (2.19,0-16)	14.02 (1.88,0-16)	14.25 (1.66,0-16)	*p*=0.011	0.81 (2.18)	*p*=0.018	1.04 (2.40)	*p*=0.011	0.23 (1.98)	*p=0.485*
	11-16	13.41 (3.02,0-16)	14.51 (1.93,0-16)	14.36 (1.93,0-16)	*p*=0.036	1.10 (2.39)	*p*=0.012	0.95 (2.15)	*p*=0.012	-0.15 (1.63)	*p=0.761*
Socio-emotional wellbeing domain	7-10	23.51 (7.92,0-40)	32.02 (5.58,0-40)	31.28 (6.62,0-40)	*p*<0.001	8.51 (8.29)	*p*<0.001	7.77 (7.88)	*p*<0.001	-0.75 (6.27)	*p*=0.455
	11-16	21.95 (7.69,0-40)	27.79 (7.79,0-40)	30.15 (6.270-40)	*p*<0.001	5.85 (1.17)	*p*<0.001	8.20 (6.98)	*p*<0.001	2.36 (4.20)	*p*=0.002

**p*-value refers to Friedman's Two Way test
***p*-value refers to Wilcoxon Signed Rank test
(Note: mean values are presented for ease of interpretation, but median scores were used in the statistical analyses)

5.3.1.1 Gender-related differences in OHRQoL

The total score of C-OHIP-SF19 and the domain scores were also compared according to gender groups. The scores were not normally distributed, therefore these analyses were conducted using Independent-sample Mann-Whitney U test. There were no significant differences in the total C-OHIP-SF19 scores and all the domain scores according to gender at any of the time periods (p>0.005).

5.3.1.2 Age-related differences in OHRQoL

In addition, the total C-OHIP-SF19 scores and the domain scores were compared between the younger age group (7-10 years) and the adolescent age group (11-16 years). Prior to treatment, the oral health domain scores were significantly higher (p<0.004) for the adolescents that for the 7-10 year-old group. Put another way, prior to the intervention, younger children reported being more (negatively) affected in terms of the oral health domain than older children. The younger cohort also reported greater improvement in the socio-emotional wellbeing domain between baseline and one-month follow-up (T_1) as observed by a marked increase in the socio-emotional wellbeing scores (p<0.002). The scores increased further at the final review visit (T_2) but the change between T_1 and T_2 was not statistically significant (p<0.309) (Table 5.5). Statistically significant associations are highlighted in grey in Table 5.5.

Table 5.5 Comparison of Child Oral Health Impact Profile Short Form 19 (C-OHIP-SF19) mean scores (SD) between gender and age groups at baseline, one-and six-month follow-up visits (males, n=35; females, n=51); (7-10 years, n=47; 11-16 years old, n=39)

C-OHIP-SF19	Gender and Age Groups	Baseline (T_0) Mean (SD, range)	*p-value**	1-month (T_1) Mean (SD, range)	*p-value**	6-months (T_2) Mean (SD, range)	*p-value**
Overall score	Female	46.51 (9.50,0-76)	*p*=0.221	58.51 (9.87,0-76)	*p*=0.916	59.96 (9.91, 0-76)	*p*=0.778
	Male	48.71 (9.07,0-76)		58.57 (8.77,0-76)		59.60 (9.47, 0-76)	
	7-16	47.32 (9.01,0-76)	*p*=0.621	60.17 (9.12,0-76)	*p*=0.083	59.96 (9.83,0-76)	*p*=0.818
	11-16	47.51 (9.83,0-76)		56.56 (9.57,0-76)		59.64 (9.63,0-76)	
Oral health domain	Female	11.19 (2.92,0-20)	*p*=0.693	14.49 (3.48,0-20)	*p*=0.314	14.90 (3.11,0-20)	*p*=0.548
	Male	11.46 (2.68,0-20)		13.74 (3.41,0-20)		14.51 (3.53,0-20)	
	7-16	10.59 (2.88,0-20)	*p*=0.004	14.13 (3.41,0-20)	*p*=0.787	14.42 (3.54,0-20)	*p*=0.378
	11-16	12.15 (2.52,0-20)		14.26 (3.53,0-20)		15.13 (2.92,0-20)	
Functional wellbeing domain	Female	13.37 (2.23,0-16)	*p*=0.831	14.31 (1.87,0-16)	*p*=0.635	14.49 (1.64,0-16)	*p*=0.521
	Male	13.20 (3.06,0-16)		14.14 (1.99,0-16)		14.03 (2.25,0-16)	
	7-16	13.21 (2.19,0-16)	*p*=0.289	14.02 (1.88,0-16)	*p*=0.126	14.25 (1.66,0-16)	*p*=0.350
	11-16	13.41 (3.02,0-16)		14.51 (1.93,0-16)		14.36 (1.93,0-16)	
Socio-emotional wellbeing domain	Female	21.94 (8.35,0-40)	*p*=0.293	29.71 (6.68,0-40)	*p*=0.650	30.57 (7.09,0-40)	*p*=0.919
	Male	24.06 (6.88,0-40)		30.69 (5.61,0-40)		31.06 (5.47,0-40)	
	7-16	23.51 (7.92,0-40)	*p*=0.482	32.02 (5.58,0-40)	*p*=0.002	31.28 (6.62,0-40)	*p=0.309*
	11-16	21.95 (7.69, 0-40)		27.79 (7.79,0-40)		30.15 (6.27,0-40)	

**p*-value* refers to Independent Sample Mann-Whitney U test

5.3.1.3 Condition-related differences in OHRQoL

For completeness, analysis was also conducted to determine if there were any differences in the C-OHIP-SF19 total scores between children with MIH and AI. As can be seen from Figure 5.5, there were no statistical differences in C-OHIP-SF19 total scores and all its domain scores between MIH-affected and AI groups at baseline, one-month follow-up and six-month follow-up visits (p>0.05, Independent sample Mann-Whitney U test). Figure 5.5 illustrates the comparison in C-OHIP-SF19 overall and its domain scores between children with MIH and AI at each dental visit. Children in both groups perceived positive improvement in overall and all C-OHIP-SF19 domain scores following treatment but the improvement did not significantly differ between groups.

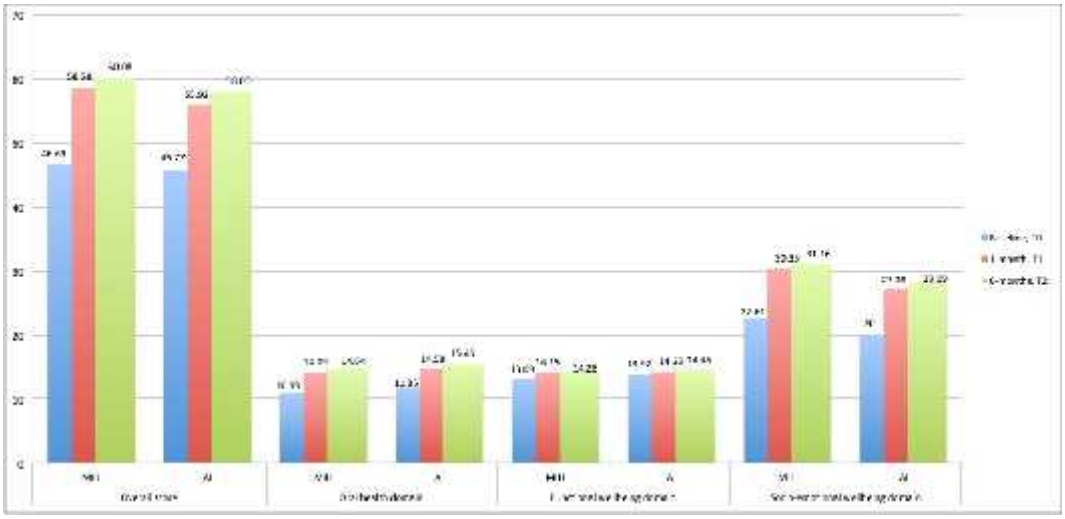

Figure 5.5 Comparison of Child Oral Health Impact Profile Short Form 19 (C-OHIP-SF19) mean scores for MIH (n=75) and AI (n=11) overall, and mean domain scores at baseline, one-month and six-month follow-up visits. There were no significant differences between between groups (Independent Sample Mann-Whitney U test).

5.3.2 Self-concept

The SPCC questionnaire was employed to measure the impact on children's self-concept as a result of having enamel opacities on their permanent anterior teeth. As previously mentioned in 4.3.4, two domain-specific subscales, Social Acceptance and Physical Appearance together with Global Self-worth subscale were selected for this current study.

The SPPC scores were not found to be normally distributed according to the Shapiro-Wilk test. Thus, Friedman's Two Way Analysis of Variance by Rank test (represents by **p*-value) was used to compare the median scores for Social Acceptance, Physical Appearance domain-specific subscales and Global Self-worth subscale of SPPC at each visit. In addition, the Wilcoxon Signed Rank test (represents by ***p*-value) was used to compare scores changes for each subscale between two dental visits; for example, differences between baseline and one-month follow-up (T_0 x T_1). These results are presented and significant associations are highlighted in grey in Table 5.6. The most substantial findings to emerge from these data were that all participants, regardless of their gender and age group, self-rated a statistically significant difference (improvement) in the Physical Appearance subscale before treatment (T_0), one-month following treatment (T_1) and six-months post-treatment (T_2). This positive change was seen for both genders and both age groups. However, there were no significant changes for Social Acceptance subscale of Global Self-worth at any time point, or in any subgroup.

Table 5.6 Self-Perception Profile for Children (SPPC) subscales mean average scores (SD) at baseline, one- and six-month follow-up visits for all participants (n=86); males (n=35) and females (n=51) participants and age groups (7-10 years old, n=47; 11-16 years old, n=39).

SPPC subscale	Participants	Baseline (T_0) Mean (SD,range)	1-month (T_1) Mean (SD,range)	6-months (T_2) Mean (SD,range)	*p*-value*	T_0 x T_1 Mean change (SD)	*p*-value**	T_0 x T_2 Mean change (SD)	*p*-value**	T_1 x T_2 Mean change (SD)	*p*-value**
Social Acceptance	All	3.08(0.67,1-4)	3.12 (0.66,1-4)	3.13(0.68,1-4)	*p*=0.613	0.04 (0.41)	*p*=0.429	0.04 (0.54)	*p*=0.628	0.01(0.50)	*p*=0.912
	Male	3.01(0.67,1-4)	3.15(0.64,1-4)	3.15(0.71,1-4)	*p*=0.305	0.14(0.39)	*p*=0.053	0.14(0.56)	*p*=0.110	0.00(0.52)	*p*=0.771
	Female	3.13(0.68,1-4)	3.10(0.67,1-4)	3.11(0.66,1-4)	*p*=0.888	-0.03(0.40)	*p*=0.516	-0.02(0.53)	*p*=0.548	0.01(0.49)	*p*=0.924
	7-10	3.17(0.62,1-4)	3.27 (0.58,1-4)	3.24(0.66,1-4)	*p*=0.205	0.09(0.44)	*p*=0.153	0.07(0.57)	*p*=0.328	-0.03(0.59)	*p*=0.833
	11-16	2.97(0.72,1-4)	2.94(0.71,1-4)	2.99(0.69,1-4)	*p*=0.447	-0.03(0.36)	*p*=0.357	0.02(0.52)	*p*=0.624	0.05(0.38)	*p*=0.654
Physical Appearance	All	2.85(0.08,1-4)	2.97(0.66,1-4)	3.11(0.62,1-4)	*p*<0.001	0.12 (0.58)	*p*=0.049	0.26(0.66)	*p*<0.001	0.14(0.48)	*p*=0.002
	Male	2.87(0.62,1-4)	3.01(0.63,1-4)	3 .16(0.63,1-4)	*p*=0.011	0.13 (0.58)	*p*=0.197	0.28(0.65)	*p*=0.014	0.15(0.37)	*p*=0.015
	Female	2.82(0.79,1-4)	2.94 (0.69,1-4)	3.07(0.62,1-4)	*p*=0.020	0.12(0.59)	*p*=0.136	0.25(0.67)	*p*=0.017	0.13(0.54)	*p*=0.045
	7-10	2.99(0.62,1-4)	3.17 (0.59,1-4)	3.29(0.55,1-4)	*p*=0.005	0.18(0.59)	*p*=0.061	0.30(0.69)	*p*=0.006	0.12(0.48)	*p*=0.037
	11-16	2.67(0.81,1-4)	2.73(0.67,1-4)	2.88(0.63,1-4)	*p*=0.043	0.06(0.56)	*p*=0.419	0.22(0.62)	*p*=0.054	0.16(0.48)	*p*=0.027
Global Self-worth	All	3.14(0.55,1-4)	3.22 (0.55,1-4)	3.24 (0.57,1-4)	*p*=0.442	0.07(0.46)	*p*=0.184	0.10(0.48)	*p*=0.114	0.03 (0.39)	*p*=0.732
	Male	3.05(0.57,1-4)	3.18 (0.58,1-4)	3.19 (0.58,1-4)	*p*=0.198	0.13(0.51)	*p*=0.172	0.14(0.48)	*p*=0.129	0.01(0.39)	*p*=0.977
	Female	3.21(0.53,1-4)	3.25(0.54,1-4)	3.28(0.57,1-4)	*p*=0.982	0.04(0.42)	*p*=0.560	0.07(0.48)	*p*=0.579	0.03(0.39)	*p*=0.632
	7-10	3.32(0.49,1-4)	3.380.51,1-4)	3.41(0.50,1-4)	*p*=0.351	0.05(0.46)	*p*=0.497	0.09(0.47)	*p*=0.380	0.04(0.41)	*p*=0.580
	11-16	2.93(0.55,1-4)	3.03(0.55,1-4)	3.04(0.59,1-4)	*p*=0.728	0.10(0.46)	*p*=0.217	0.11(0.49)	*p*=0.239	0.01(0.38)	*p*=0.954

**p*-value refers to Friedman's Two Way test; ***p*-value refers to Wilcoxon Signed Rank test

5.3.2.1 Gender and age-related differences in self-concept

Reported changes in the SPPC subscales scores according to gender and age groups were compared using the Independent Sample Mann-Whitney U test (see Table 5.7). Children in the younger age group (7-10 years) evaluated themselves more positively in regards to how they perceived themselves socially, how they accepted their physical features and how they valued themselves as a person than the older children. There was a statistically significant difference in the mean Social Acceptance subscale score between age groups at one-month post-treatment visit (T_1) ($p=0.005$) with younger children rating themselves more positively. Similarly, younger children rated themselves significantly more positively that adolescents for the Physical Appearance subscale at T_1 and T_2.

In terms of Global Self-worth, participants in the younger age group consistently rated themselves significantly more positively than older children at all three time points. There were no significant differences in mean SPPC subscale scores between gender groups at any time point

Table 5.7 Comparison of Self-Perception Profile for Children (SPPC) subscales mean average score (SD) according to gender (males, n=35 and females, n=51) and age groups (7-10 years old, n=47; 11-16 years old, n=39).

SPPC subscale	Participants	Baseline (T_0) Mean (SD, range)	*p*-value*	1-month (T_1) Mean (SD, range)	*p*-value*	6-months (T_2) Mean (SD, range)	*p*-value*
Social Acceptance	Male	3.01 (0.67,1-4)	*p*=0.505	3.15 (0.64,1-4)	*p*=0.760	3.15 (0.71,1-4)	*p*=0.630
	Female	3.13 (0.68,1-4)		3.10 (0.67,1-4)		3.11 (0.66,1-4)	
	7-10	3.17 (0.62,1-4)	*p*=0.226	3.27 (0.58,1-4)	*p*=0.050	3.24 (0.66,1-4)	*p*=0.095
	11-16	2.97 (0.72,1-4)		2.94 (0.71,1-4)		2.99 (0.69,1-4)	
Physical Appearance	Male	2.87 (0.62,1-4)	*p*=0.989	3.01 (0.63,1-4)	*p*=0.808	3 .16 (0.63,1-4)	*p*=0.584
	Female	2.82 (0.79,1-4)		2.94 (0.69,1-4)		3.07 (0.62,1-4)	
	7-10	2.99 (0.62,1-4)	*p*=0.076	3.17 (0.59,1-4)	*p*=0.004	3.29 (0.55,1-4)	*p*=0.003
	11-16	2.67 (0.81,1-4)		2.73 (0.67,1-4)		2.88 (0.63,1-4)	
Global Self-worth	Male	3.05 (0.57,1-4)	*p*=0.283	3.18 (0.58,1-4)	*p*=0.733	3.19 (0.58,1-4)	*p*=0.450
	Female	3.21 (0.53,1-4)		3.25 (0.54,1-4)		3.28 (0.57,1-4)	
	7-10	3.32 (0.49,1-4)	*p*<0.001	3.38 (0.51,1-4)	*p*=0.010	3.41 (0.50,1-4)	*p*=0.004
	11-16	2.93 (0.55,1-4)		3.03 (0.55,1-4)		3.04 (0.59,1-4)	

**p*-value refers to Independent Sample Mann-Whitney U test

5.3.2.2 Condition-related differences in self-concept

The scores for all SPPC subscales according to the enamel defect diagnosis were also compared. Although only 11 participants were thought to have AI, the mean average score for the Social Acceptance subscale was significantly lower in these children at all dental visits (T_0, T_1 and T_2) compared to participants with MIH (see Figure 5.6). Similar findings were also observed for the Physical Appearance subscale scores at T_0 and T_2 (*p*=0.024 and *p*=0.020 respectively, Independent Sample Mann-Whitney U test). Children

with AI rated Global Self-worth at T_2 significantly lower than those with MIH (p=0.034, Independent Sample Mann-Whitney U test). These findings suggest that the impact of AI on children's self-concept was greater than is the case for children with MIH (Figure 5.6).

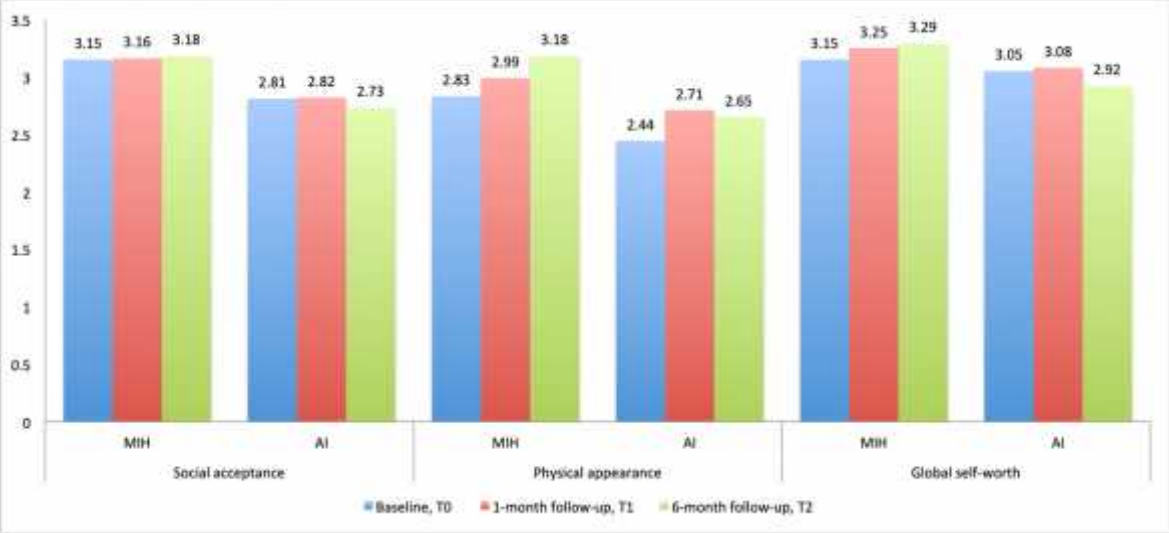

Figure 5.6 Comparison of Self-Perception Profile for Children (SPPC) subscales mean average scores (SD) for MIH (n-75) and AI (n=11) groups at baseline, one-month and six-month follow-up visits. There were no significant differences between groups (Independent Sample Mann-Whitney U test).

5.3.3 Self-perception of enamel defects

A Visual Analogue Scale (VAS) was used to assess children's views on how chalky/discoloured they felt their front teeth looked as well as their perceptions of being worried, embarrassed and happy about their teeth. The distribution of VAS scores was analysed for normality using the Shapiro-Wilk test and the data were found not to be normally distributed. An Independent Samples Mann-Whitney U test was therefore used to assess whether there were significant differences in mean VAS scores at baseline and both follow-up dental visits according to gender and age groups. The significance level was set at p<0.05 for all analyses.

Prior to any treatment, children reported high levels of worry about their teeth with a mean VAS score of 4.08 (SD=2.54, range=0-10). They expressed similar levels of embarrassment at T_0 with mean score of 3.87 (SD=3.09, range 0-10) and a strong belief that their teeth looked 'chalky'/discoloured (mean VAS=3.56 SD=2.15, range=0-10). They also self-rated themselves as being unhappy because of their teeth with mean VAS of 3.04 (SD=2.41, range=0-10).

One-month post treatment, children were generally much positive about their dental appearance as evidenced by the increase in VAS scores. They assessed their teeth as looking much less chalky/discoloured (mean VAS=5.96, SD=2.64, range=0-10) and they feel much happier about their teeth as indicated by marked increased in mean VAS score by 3.50 (SD=3.04) from baseline to 6.55 (SD=2.86,range=0-10) at T_1. Children also reported that they were less worried (mean VAS=6.99, SD=2.55, range=0-10) and less embarrassed about their teeth (mean VAS=7.18, SD=2.94, range=0-10). Participants continued to be positive about their teeth and their feelings at the final dental review visit. Mean VAS scores for all four items relating to how worried, how embarrassed, how 'chalky'/discoloured they felt their teeth looked and how happy they were with their teeth were significantly different (improved) at one-month and six-months after treatment. Table 5.8 presents the results from these analyses. Statistically significant relationships were highlighted in grey to enhance readability of the results. **p*-value refers to refers to Friedman's Two Way test while ***p*-value indicates the Wilcoxon Signed Rank test.

Table 5.8 Visual Analogue Scale (VAS) mean scores (SD) at baseline, one- and six-month follow-up visits for all participants (n=86) and according to gender (males, n=35; females, n=51) and age groups (7-10 years old, n=47; 11-16 years old, n=39)

VAS	Participants (n)	Baseline (T_0) Mean (SD,range)	1-month (T_1) Mean (SD,range)	6-months (T_2) Mean (SD,range)	*p*-value*	T_0 xT_1 Mean change (SD)	*p*-value**	T_0 xT_2 Mean change (SD)	*p*-value**	T_1 xT_2 Mean change (SD)	*p*-value**
Worried 0=very worried	All	4.08(2.54,0-10)	6.99(2.55,0-10)	7.94(2.11,0-10)	*p*<0.001	2.92(3.29)	*p*<0.001	3.86(0.30)	*p*<0.001	0.95(2.81)	*p*=0.002
	Male	4.64(2.63,0-10)	7.18(2.57,0-10)	8.03(2.11,0-10)	*p*<0.001	2.54(2.42)	*p*<0.001	3.38(2.46)	*p*<0.001	0.84(3.02)	*p*=0.111
	Female	3.70(2.42,0-10)	6.87(2.57,0-10)	7.89(2.13,0-10)	*p*<0.001	3.17(3.77)	*p*<0.001	4.19(3.03)	*p*<0.001	1.02(2.69)	*p*=0.005
	7-10	4.31(2.61,0-10)	7.22(2.40,0-10)	7.75(2.23,0-10)	*p*<0.001	2.91(3.41)	*p*<0.001	3.44(2.89)	*p*<0.001	0.53(2.72)	*p*=0.148
	11-16	3.80(2.45,0-10)	6.73(2.74,0-10)	8.18(1.94,0-10)	*p*<0.001	2.93(3.17)	*p*<0.001	4.37(2.70)	*p*<0.001	1.45(2.88)	*p*=0.003
Embarrassed 0=very embarrassed	All	3.87(3.09,0-10)	7.18(2.94,0-10)	7.90(2.52,0-10)	*p*<0.001	3.31(3.85)	*p*<0.001	4.03(3.53)	*p*<0.001	0.72(3.42)	*p*=0.038
	Male	4.98(2.95,0-10)	7.29(3.01,0-10)	8.14(2.18,0-10)	*p*<0.001	2.31(2.86)	*p*<0.001	3.16(3.58)	*p*<0.001	0.85(3.48)	*p*=0.141
	Female	3.10(2.99,0-10)	7.10(2.92,0-10)	7.73(2.74,0-10)	*p*<0.001	4.00(4.30)	*p*<0.001	4.63(3.40)	*p*<0.001	0.64(3.42)	*p*=0.133
	7-10	3.85(3.31,0-10)	7.66(2.87,0-10)	7.76(2.74,0-10)	*p*<0.001	3.80(4.15)	*p*<0.001	3.91(3.50)	*p*<0.001	0.11(3.44)	*p*=0.502
	11-16	3.88(2.87,0-10)	6.60(2.95,0-10)	8.07(2.25,0-10)	*p*<0.001	2.72(3.42)	*p*<0.001	4.18(3.61)	*p*<0.001	1.47(3.30)	*p*=0.014
Discoloured 0=very discoloured	All	3.56(2.15,0-10)	5.96(2.64,0-10)	6.96(2.34,0-10)	*p*<0.001	2.39(2.84)	*p*<0.001	3.39(2.88)	*p*<0.001	1.00(3.05)	*p*=0.004
	Male	4.04(2.13,0-10)	5.56(2.66,0-10)	6.96(2.23,0-10)	*p*<0.001	1.52(2.87)	*p*<0.001	2.92(2.77)	*p*<0.001	1.40(3.18)	*p*=0.018
	Female	3.24(2.13,0-10)	6.23(2.61,0-10)	6.96(2.43,0-10)	*p*<0.001	2.99(2.69)	*p*<0.001	3.72(2.94)	*p*<0.001	0.73(2.96)	*p*=0.072
	7-10	3.53(2.34,0-10)	6.41(2.61,0-10)	6.80(2.44,0-10)	*p*<0.001	2.88(2.85)	*p*<0.001	3.27(2.86)	*p*<0.001	0.39(2.95)	*p*=0.398
	11-16	3.61(1.92,0-10)	5.41(2.59,0-10)	7.15(2.22,0-10)	*p*<0.001	1.80(2.75)	*p*<0.001	3.54(2.93)	*p*<0.001	1.74(3.03)	*p*=0.002
Happy 0=very unhappy	All	3.04(2.41,0-10)	6.55(2.68,0-10)	7.47(2.58,0-10)	*p*<0.001	3.50(3.04)	*p*<0.001	4.43(3.09)	*p*<0.001	0.92(2.91)	*p*<0.001
	Male	3.62(2.41,0-10)	6.50(2.63,0-10)	7.65(2.23,0-10)	*p*<0.001	2.88(2.65)	*p*<0.001	4.03(3.18)	*p*<0.001	1.15(2.83)	*p*=0.015
	Female	2.65(2.35,0-10)	6.58(2.75,0-10)	7.35(2.81,0-10)	*p*<0.001	3.93(3.24)	*p*<0.001	4.70(2.92)	*p*<0.001	0.76(2.98)	*p*=0.031
	7-10	2.92(2.69,0-10)	7.00(2.66,0-10)	7.45(2.60,0-10)	*p*<0.001	4.08(3.43)	*p*<0.001	4.52(3.08)	*p*<0.001	0.44(2.81)	*p*=0.152
	11-16	3.19(2.05,0-10)	6.00(2.64,0-10)	7.50(2.58,0-10)	*p*<0.001	2.81(2.34)	*p*<0.001	4.31(3.00)	*p*<0.001	1.50(2.96)	*p*=0.003

**p*-value refers to Friedman's Two Way test; ***p*-value refers to Wilcoxon Signed Rank test

5.3.3.1 Self-perception of enamel defects according to gender and age

Table 5.9 compares the VAS scores according to gender and age groups. A key finding was that, prior to treatment, females were significantly more embarrassed about their teeth than males (p=0.003, Independent Sample Mann-Whitney U test) but there were no differences in reported worry following interventions. Further analysis to compare VAS scores between age groups revealed no significant differences for any of the items at any time period (p>0.005, Independent Sample Mann-Whitney U test). Significant relationships were highlighted in gray.

Table 5.9 Comparison of Visual Analogue Scale (VAS) mean scores (SD) between gender (males, n=35; females, n=51) and age groups (7-10 years old, n=47; 11-16 years old, n=39.

Visual Analogue Scale	Participants	Baseline (T_0) Mean (SD, range)	p-value	1-month (T_1) Mean (SD, range)	p-value	6-months (T_2) Mean (SD, range)	p-value
Worried 0=very worried	Male	4.64 (2.63,0-10)	p=0.056	7.18 (2.57,0-10)	p=0.582	8.03 (2.11,0-10)	p=0.643
	Female	3.70 (2.42,0-10)		6.87 (2.57,0-10)		7.89 (2.13,0-10)	
	7-10	4.31 (2.61,0-10)	p=0.360	7.22 (2.40,0-10)	p=0.458	7.75 (2.23,0-10)	p=0.396
	11-16	3.80 (2.45,0-10)		6.73 (2.74,0-10)		8.18 (1.94,0-10)	
Embarrassed 0=very embarrassed	Male	4.98 (2.95,0-10)	p=0.003	7.29 (3.01,0-10)	p=0.863	8.14 (2.18,0-10)	p=0.870
	Female	3.10 (2.99,0-10)		7.10 (2.92,0-10)		7.73 (2.74,0-10)	
	7-10	3.85 (3.31,0-10)	p=0.791	7.66 (2.87,0-10)	p=0.064	7.76 (2.74,0-10)	*p=0.729*
	11-16	3.88 (2.87,0-10)		6.60 (2.95,0-10)		8.07 (2.25,0-10)	
Discoloured 0=very discoloured	Male	4.04 (2.13,0-10)	p=0.044	5.56 (2.66,0-10)	p=0.223	6.96 (2.23,0-10)	p=0.853
	Female	3.24 (2.13,0-10)		6.23 (2.61,0-10)		6.96 (2.43,0-10)	
	7-10	3.53 (2.34,0-10)	p=0.801	6.41 (2.61,0-10)	p=0.083	6.80 (2.44,0-10)	p=0.549
	11-16	3.61 (1.92,0-10)		5.41 (2.59,0-10)		7.15 (2.22,0-10)	
Happy 0=very unhappy	Male	3.62 (2.41,0-10)	p=0.056	6.50 (2.63,0-10)	p=0.731	7.65 (2.23,0-10)	p=0.916
	Female	2.65 (2.35,0-10)		6.58 (2.75,0-10)		7.35 (2.81,0-10)	
	7-10	2.92 (2.69,0-10)	p=0.219	7.00 (2.66,0-10)	p=0.073	7.45 (2.60,0-10)	p=0.834

p-value refers to Independent Sample Mann-Whitney U test

5.3.3.2 Self-perception of enamel defects according to condition

Children with mild AI consistently scored lower VAS scores for all four questions than children with MIH at baseline, one-month and six-month follow-up visits. However, the differences in VAS scores for all four questions between MIH and AI groups were not statistically significant (p>0.005, Independent Sample Mann-Whitney U test). These data are presented in Figure 5.7.

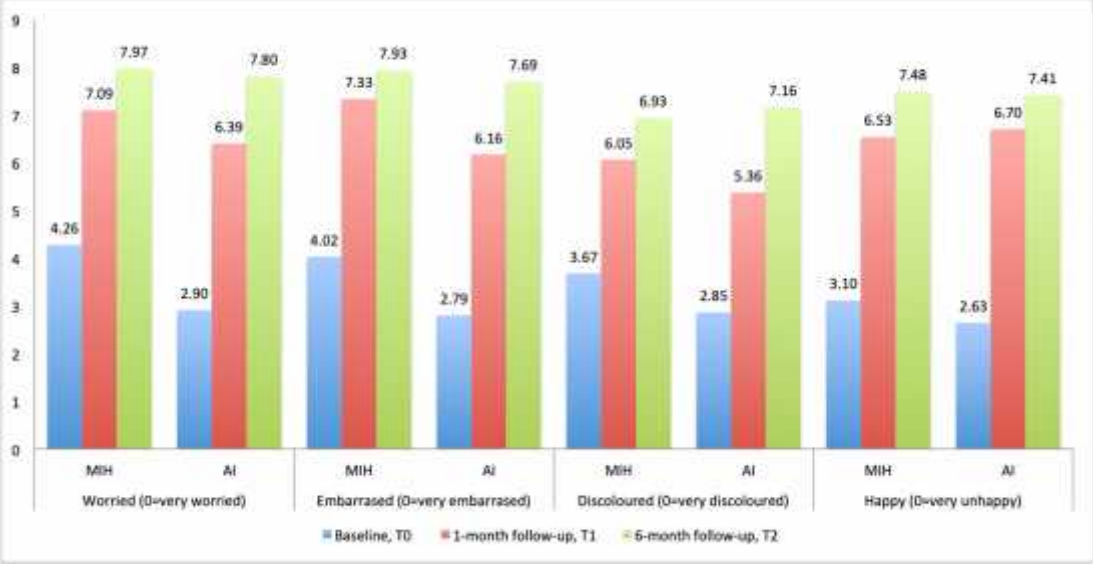

Figure 5.7 Comparison of Visual Analogue Scale (VAS) mean scores (SD) between MIH (n=75) and AI (n=11) groups at baseline, one-and six-month follow-up visits. There were no significant differences between groups (Independent Sample Mann-Whitney U test).

5.3.4 Children's self-perception of their overall oral health and general health

Children's self-perception of their overall oral health was assessed using a global question from the C-OHIP-SF19 while their perceived general overall health was assessed using a general health perception question. Responses were on a 5-point Likert scale ranging from poor to excellent. Responses to both questions were then categorised into three groups: 1=poor/fair; 2=good; and 3=very good/excellent for analysis purposes.

Prior to treatment, 37 participants (43.02%) rated their overall oral health as ‘poor/fair’. Of these, 13 children (15.12%) still considered their overall oral health status as ‘poor/fair’ one-month post treatment while the other 24 children perceived that their oral health had improved to a rating of ‘good’ or ‘very good/excellent’. Three children (3.49%) who rated their overall oral health as ‘good’ at baseline rated their overall oral health as ‘poor/fair’ at T_1 and one child (5.9%) who was very satisfied with their overall oral health at baseline rated his/her overall oral health as ’poor/fair’ one-month after treatment. The number of participants who rated their overall oral health as ‘very good/excellent’ at one-month follow-up visit was twice as high as those who rated it as ‘very good/excellent’ prior to any treatment, which was a statistically significant difference (p<0.001, Mc-Nemar-Bowker Chi-Square test).

At the beginning of the study, seven children (8.14%) rated their general health as ‘poor/fair’ and two of them still perceived their general health as ‘poor/fair” one-month post treatment. Five of these children rated their general health status more positively (good) following treatment. Among those children who regarded their general health as ‘good’, four considered their general health improved to ‘very good/excellent’ and one child reported that his/her general health status declined to ‘poor/fair’ following treatment. The remaining 11 participants reported that their general health status remained the same after treatment. Over half of the children (n=56, 65.1%) were very satisfied with their general health one-month after treatment. Children’s perception of their general oral health before and after treatment did not differ statistically (p = 0.175, Mc-Nemar-Bowker Chi-Square test). Table 5.10 summarises the change in children’s perceived overall oral health and general health before any treatment and one-month post-treatment. Statistically significant result was highlighted in grey.

Table 5.10 Change in children's overall (global) oral health and general health at baseline and one-month follow-up visit for all participants (n=86).

Overall C-OHIP Baseline (T_0)	1-month (T_1)			*p*-value
	Poor/Fair (n,%)	Good (n,%)	Very Good/Excellent (n,%)	
Poor/Fair	13(15.12)	15(17.44)	9(10.47)	*p*< 0.001
Good	3(3.49)	10(11.63)	15(17.44)	
Very Good/Excellent	1(1.16)	3(3.49)	17(19.77)	
Overall QoL Baseline (T_0)	Poor/Fair (n,%)	Good (n,%)	Very Good/Excellent (n,%)	
Poor/Fair	2 (2.33)	5 (5.81)	0 (0.00)	*p* = 0.175
Good	1 (1.16)	11(12.79)	4 (4.65)	
Very Good/Excellent	0 (0.00)	7 (8.14)	56(65.12)	

p-value refers to Mc-Nemar-Bowker Chi-Square test

Table 5.11 presents data to observe any changes in children's perceived overall oral health and general health before (T_0), one-month (T_1) after treatment and at the final review visit (T_2). Significant associations were highlighted in grey. There was a significant change in children's perception of their overall oral health from baseline to six-months post-treatment with a greater proportion rating their oral health as good/excellent (*p*<0.001, Mc-Nemar-Bowker Chi-Square). However, there was no significant difference in perceived overall oral health between one-month and six-months follow-up using the global response score (*p*=0.263, Mc-Nemar-Bowker Chi-Square).

Children's perception towards their general oral health and overall wellbeing was also compared between baseline and six-month post treatment. Children's self-rated general health status before and one-month after treatment did not differ statistically (*p*=0.378, Mc-Nemar-Bowker Chi-Square).

Children's overall health status one-month and six-months after treatment was also compared (see Table 5.11). Again, there was no significant difference in children's perceived overall health status between these two review visits (*p*=0.344, Mc-Nemar-Bowker Chi-Square). More than two-thirds of the children (n=60, 69.77%) rated their general health as 'very good/excellent' at both dental review visits.

Further analysis using structural equation modeling will explore how patient and clinical variables may predict the change in children's perceived oral health and general oral health status, and will be discussed later in this Chapter.

Table 5.11 Change in children's overall (global) oral health and general health at baseline, one-month and six-month follow-up visits for all participants (n=86).

	6-month (T_2)			*p*-value
	Poor/Fair (n,%)	Good (n,%)	Very Good/Excellent (n,%)	
Overall C-OHIP-SF19 Baseline (T_0)				
Poor/Fair	8(9.30)	15(17.44)	14(16.28)	*p*< 0.001
Good	3(3.49)	12(13.95)	13(15.12)	
Very Good/Excellent	0(0.00)	2(2.33)	19(22.09)	
Overall C-OHIP-SF19 One-month (T_1)				
Poor/Fair	4(4.65)	8(9.3)	5(5.81)	*p*=0.263
Good	3(3.49)	18(20.93)	7(8.14)	
Very Good/Excellent	4(4.65)	3(3.49)	34(39.53)	
Overall QoL Baseline (T_0)	Poor/Fair (n,%)	Good (n,%)	Very Good/Excellent (n,%)	
Poor/Fair	0(0.00)	6(6.98)	1(1.16)	*p*=0.378
Good	2(2.33)	9(10.47)	5(5.81)	
Very Good/Excellent	0(0.00)	6(6.98)	57(66.28)	
Overall QoL One-month (T_1)				
Poor/Fair	1(1.16)	2(2.33)	0(0.00)	*p*=0.344
Good	1(1.16)	18(20.93)	4(4.65)	
Very Good/Excellent	0(0.00)	1(1.16)	59(68.6)	

p-value refers to Mc-Nemar-Bowker Chi-Square test

5.3.5 Health care satisfaction

Participants' satisfaction towards the health care that was provided at the dental hospital was measured using the Friends and Family Test (FFT) and responses are summarised in Table 5.12. This tool provides an opportunity for participants to give their overall feedback about the dental hospital and the treatment they received and how likely they would suggest the dental hospital to their family and friends. As

described in section 4.3.5, FFT scores were presented as the percentage of participants who would recommend and would not recommend the dental hospital to their friends and family if they required similar treatment.

The overall response to FFT was extremely positive: none of the children responded that they would not recommend the dental treatment or the dental hospital to their friends and relatives at any of the visits. Prior to any treatment, two participants (2.33%) responded 'I can't decide/I don't know) to the FFT question. However, following treatment (at both review visits), all participants (n=86) selected "I agree a bit" or "I agree a lot" which indicated that they valued the service provided at the dental hospital. Almost 92% children (n=79) strongly agreed that they would recommend the dental hospital and similar treatment to their friends and family at their final review visit (T_2).

Table 5.12 Summary of participants' responses to the Friends and Family Test at baseline, one-and six-month follow-up visits for all participants (n=86)

Response to FFT (*I would say this is a good dental hospital for friends or family if they needed similar treatment or care*)	Baseline, T_0 (n,%)	1-month follow-up, T_1 (n,%)	6-month follow-up, T_2 (n,%)
I agree a lot	77 (89.53)	74 (86.05)	79 (91.86)
I agree a bit	7 (8.14)	12 (13.95)	7 (8.14)
I disagree a bit	0 (0.00)	0 (0.00)	0 (0.00)
I disagree a lot	0 (0.00)	0 (0.00)	0 (0.00)
I can't decide/ I don't know	2 (2.33)	0 (0.00)	0 (0.00)

5.4 Structural Equation Modeling

5.4.1 Confirmatory Factor Analysis

CFA was conducted in order to test self-concept as a hypothesised latent variable at baseline. Figure 5.8 illustrates this analysis. The item loadings, confirming

children's self-concept (SPPC) at baseline, were the "Social Acceptance subscale at baseline" (ß=0.440,p<0.01); the "Physical Appearance subscale at baseline" (ß=0.501,p<0.01); and the "Global self-worth subscale at baseline" (ß=0.497,p<0.01). The item "Global self-worth subscale" had the highest R^2 for self-concept (SPPC) at baseline (R^2=0.773).

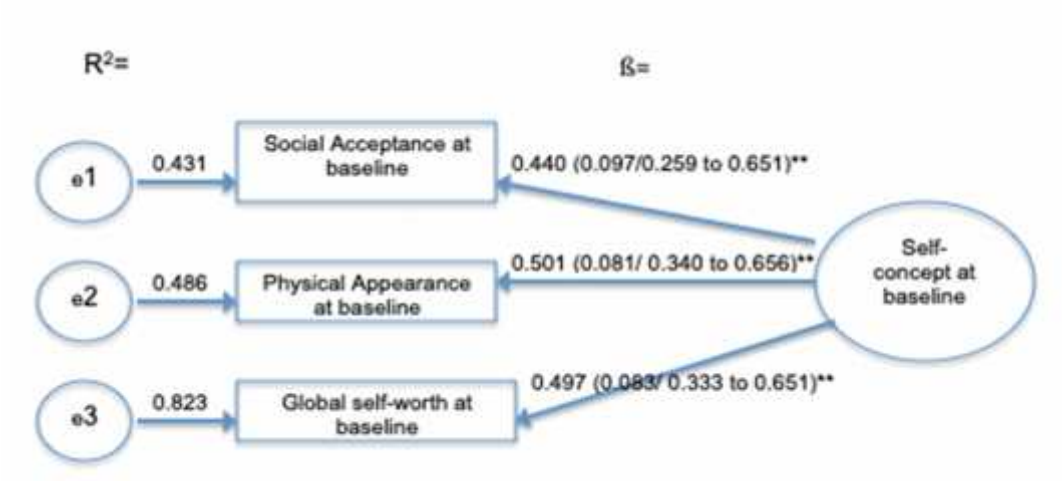

Figure 5.8 Confirmatory Factor Analysis (CFA) of a three-item self-concept latent variable at baseline obtained through bootstrap item loadings (standard error/bias-corrected 95% CI). **Significant standardised coefficient (p<0.01).

5.4.2 Parsimonious model (SEM)

The full model was estimated and met all five criteria recommended by Hu and Bentler (Hu and Bentler, 1999) and Arbuckle (Arbuckle, 2016), confirming that the model adequately fits to the data. All pre-established fit indices: X^2/df<3.0; GFI>0.90;CFI>0.90; and RMSEA <0.06 were adequate for the full model and parsimonious model, except RMSEA for the full model.

The variables age and socio-economic which had a status path with a p-value >0.20 were removed. The model was then re-estimated to obtain a statistically parsimonious model. Figure 5.9 overleaf illustrates the direct and indirect paths in the parsimonious model. Goodness-of-fit is presented in Table 5.13 below. The

parsimonious model showed adequate fit to the data, meeting all five a priori criteria.

Table 5.13 Fit indices for the full and parsimonious models used in this study

Model	X^2/df ratio	GFI	CFI	RMSEA
Full	1.423	0.911	0.921	0.071
Parsimonious	1.072	0.913	0.985	0.029

The X^2 difference between the full model and parsimonious model was 9.411(df=41) and was not statistically significant (p=0.978). This suggests that removal of age and socio-economic status and the non-significant paths were not relevant to the model. Figure 5.9 presents the final statistically parsimonious model of the present study. Direct effects for the final statistically parsimonious model are indicated by solid lines and indirect effect are indicated by dashed lines. Indicators and observed variables are given in rectangles. Latent variables are given in circles.

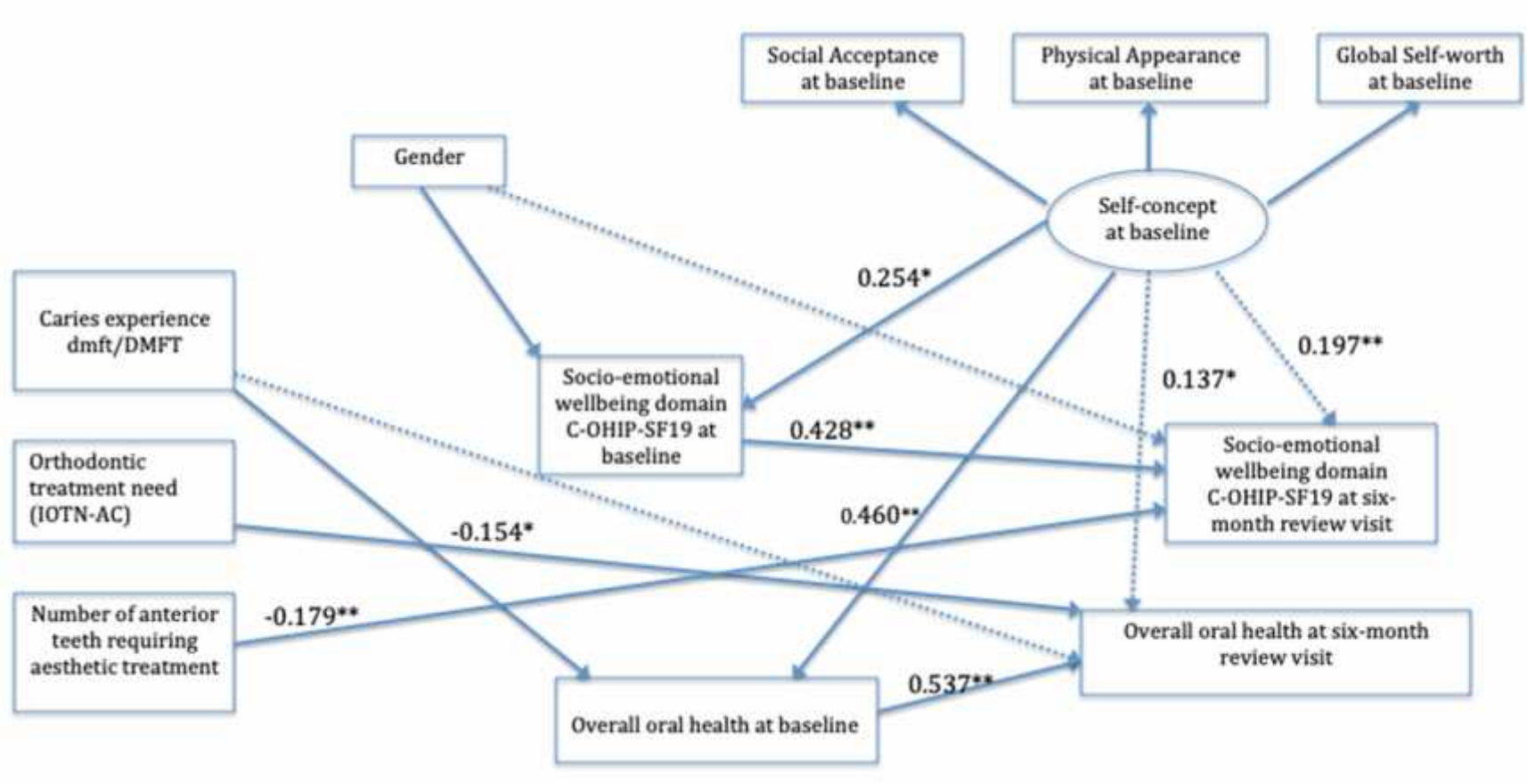

Figure 5.9 The parsimonious model

Direct effects are indicated by solid lines and indirect effects are indicated by dashed lines. Indicators and observed variables are shown in rectangles. Latent variables are represented in circles.

*p-value<0.05 **p-value<0.01

Table 5.14 summarises the significant direct and indirect paths between variables in the parsimonious model. Significant associations were highlighted in grey. The following assertions can be made from the direct path relationships:

A higher number of teeth needing aesthetic treatment at baseline was linked to lower socio-emotional wellbeing scores at the six-month follow-up dental visit (ß-0.179, $p<0.01$).
Greater need for orthodontic treatment at baseline was linked to worse overall oral health at the six-month follow-up visit (ß=-0.154, $p<0.05$).
Socio-emotional wellbeing at baseline predicted socio-emotional wellbeing at the six-month follow-up visit (ß=0.428, $p<0.01$).
Overall oral health at baseline was linked directly to higher overall oral health at the final review visit (ß=0.537, $p<0.01$).
Higher self-concept prior to any treatment (baseline) was significantly linked to higher overall oral health and socio-emotional wellbeing at baseline (ß= 0.460, $p<0.01$ and ß=0.254, $p<0.05$).
Self-concept at baseline indirectly predicted socio-emotional wellbeing at six-month follow-up visit via socio-emotional wellbeing at baseline (ß=0.197, $p<0.01$). Overall (global) oral health at the six-month follow-up visit was indirectly predicted by self-concept at baseline through overall oral health at baseline (ß=0.137, $p<0.05$).

Table 5.14 Direct and indirect effects of the parsimonious theoretical model

Parameter	ß	Bootstrap SE	Bias-Corrected 95% CI
Direct effects			
Number of teeth need treatment - Socio-emotional wellbeing domain C-OHIPSF19 at T_2	-0.179	0.073	-0.324 to -0.044**
Orthodontic treatment need - overall oral health at T_2	-0.154	0.075	-0.309 to -0.017*
Gender – socio-emotional wellbeing domain C-OHIPSF19 at T_0	-0.149	0.098	-0.357 to 0.028
dmftDMFT – overall oral health at T_0	-0.112	0.092	-0.299 to 0.078
Self-concept at T_0 - Socio-emotional wellbeing domain C-OHIPSF19 at T_0	0.460	0.135	0.155 to 0.669**
Self-concept at T_0 –overall oral health at T_0	0.254	0.111	0.016 to 0.454*
Socio-emotional wellbeing domain C-OHIPSF19 at T_0 - Socio-emotional wellbeing domain C-OHIPSF19 at T_2	0.428	0.083	0.251 to 0.575**
Overall oral health at T_0 –overall oral health at T_2	0.537	0.075	0.382 to 0.677**
Indirect effects			
Gender - Socio-emotional wellbeing domain C-OHIPSF19 at T_2	-0.064	0.042	-0.169 to 0.006
dmftDMFT - overall oral health at T_2	-0.060	0.050	-0.159 to 0.036
Self-concept at T_0 - Socio-emotional wellbeing domain C-OHIPSF19 at T_2	0.197	0.071	0.074 to 0.341**
Self-concept at T_0 –overall oral health at T_2	0.137	0.066	0.017 to 0.265*

*p-value<0.05
**p-value<0.01

Chapter 6
Discussion

6.1 Introduction

Over the past two decades there has been a growing understanding of the impact that various dental conditions may have on children and their families. Data on these impacts have been gained primarily through the completion of validated OHRQoL measures. However, it is only relatively recently that interest has turned specifically to the impact and burden of MIH, with increasing worldwide awareness and public health concern.

The presence of MIH, with involvement of permanent first molars, is associated with oral sensitivity, a higher risk of dental caries, resultant increased treatment burden and even tooth loss. Numerous studies have highlighted the oral symptoms and functional limitations associated with this condition in terms of poorer OHRQoL (Oyedele et al., 2015, Dantas-Neta et al., 2016, Leal et al., 2017, Velandia et al., 2018). However, children may also present with visible opacities, sometimes involving multiple anterior teeth, which may adversely affect their general wellbeing and sense of self (Leal et al., 2017). In view of the current paucity of research addressing the psychosocial impacts of enamel opacities on children with MIH, and the absence of any intervention studies, this study was undertaken to address an acknowledged area of need. Furthermore, the study had a longitudinal design, following children for 6-months after their intervention, which also brought a novel aspect to the existing literature. Another area of interest, explored by this study, was how variables, such as gender, self-concept and social deprivation status, could all inter-relate in affecting children's self-rated OHRQoL.

The key findings were that mean total C-OHIP-SF19 and all its domain scores were increased significantly following treatment, indicating an improvement in children's OHRQoL in terms of functional and emotional status. Furthermore, children reported significant improvement in the perception of their own physical appearance.

Children's self-concept, prior to receiving any treatment, was the main determinant factor of how the aesthetic dental treatment impacted on their self-rated outcome measures, within the theoretic model used (Wilson and Cleary, 1995). Clinical variables such as the number of teeth requiring aesthetic treatment and the need for orthodontic treatment were also found to influence children's psychosocial well-being and overall perceptions on their own oral health at follow up visits.

This discussion chapter will now consider aspects of the study design and the main findings in more detail. The first part will consider ethical issues and recruitment, before reflecting on the socio-demographic and clinical profile of the participants. Consideration will then be given to the key findings, and how they compare with or refute findings from other bodies of work. The clinical implications of the findings will also be discussed, from both the patients' and clinicians' perspective. Strengths and acknowledged limitations of the research will be presented, before finally making recommendations for future research priorities.

6.2 Ethical and governance considerations

Data collection and treatment for patients in this study was carried out between June 2017 and October 2018. No ethical concerns arose during the study period, and there were no patient complaints or clinical incidents. The study was able to recruit participants in a timely manner, satisfying the initial power calculation, and was completed within the allocated timeframe. The conduct of this clinical study was reviewed monthly and reports were submitted through the University of Sheffield on-line doctoral portal. The C.I (N.H.) was responsible for maintaining the project site file, with support from a designated hospital research nurse. The success of studies of this nature is greatly dependent on the goodwill and contribution of the whole clinical team, in identifying suitable participants, as well as the input of research nurses and research administrators to satisfy the complex ethical and governance requirements.

At the end of the study, a report was submitted to the Research Ethics Committee and a lay summary of the key findings was sent to all participants (see Appendix 17), which is considered good practice. It was encouraging to receive an unsolicited communication from the mother of one participant, stating

her thanks for the report, and expressing the family's interest in hearing about any further research projects. It is apparent that children and their family value being fully engaged in oral health research, rather than taking a passive role.

The study was fully supported by a clinical PhD scholarship from the Government of Malaysia, which covered the costs of all clinical materials and nursing support. However, it should be noted, that DMG™ Hamburg, Germany supplied the resin infiltration, Icon™ for use on study participants (and indeed other patients within the unit), following a request made by the clinical supervisor (H.R.). This did not present any conflict of interest as there was no incentive provided for using Icon™ and the company has no ownership of the results.

A governance issue which presented shortly after completion of this study relates to the use of tooth whitening for the under 18s. The host unit has currently ceased the use of carbamide peroxide products for young patients, due to statements issued by some U.K. Dental Defense Organisations not to support members in any legal cases relating to tooth whitening in the under 18s. This remains an area of ongoing concern and debate amongst paediatric dentists in the U.K.

6.3 Participants

6.3.1 Response rates and diversity

The first point to highlight about the participants in this study was the high response and completion rates (92.8 and 83.5% respectively). The fact that children had to re-attend for a review at 6-months makes the high completion rate all the more noteworthy. Other clinical studies, involving children with caries, recently conducted in the host unit have achieved response rates of between 40 and 80%, depending on the patient group involved (Gilchrist et al., 2018, Subka et al., 2019). There have been no similar clinical studies involving children with enamel defects with which to make meaningful comparisons. To date, studies relating to OHRQoL in children with MIH have largely involved non-clinical (school) populations in Brazil, where response rates are understandably higher (Oyedele et al., 2015, Dantas-Neta et al., 2016, Leal et al., 2017, Velandia et al., 2018). Clearly, children and their families in the present study were highly

motivated as they were keen to pursue aesthetic treatment, thus tended not to miss their appointments. Furthermore, as they were research participants, appointments were expedited after their assessment visit and were scheduled at the families' convenience. All the MIH treatment was provided by the same two clinicians (N.H. and J.L.) and dental nurse, allowing continuity of care and building a rapport, which could have also contributed to the excellent completion rates. For a small number of children who were unable to attend their final review (due to school or other commitments) a questionnaire was posted out, again contributing to higher final completion rates. It is also surmised that children who did not attend for their 6-month review were likely to be satisfied with the clinical outcome, and therefore did not seek further treatment.

A second point to debate is the higher proportion of females (59.3%) than males who participated in the study. However, there was no difference in gender according initial recruitment and retention to the study. Furthermore, there is no suggestion that MIH is actually more common in females, as confirmed by a recent large epidemiological study conducted in the North of England (Balmer et al., 2012). Thus, it can only be deduced that girls (and/or their parents/carers) experience greater concern about the visibility of enamel opacities and are more proactive in seeking earlier referral for specialist treatment. This hypothesis is supported by orthodontic-related studies that have explored children's satisfaction with their dental appearance and OHRQoL (Spalj et al., 2010, Benson et al., 2015). Spalj and co-workers (2010) found no significant difference in how children rated their dental attractiveness and OHRQoL scores according to gender, although it was noted that a higher proportion of female participants sought orthodontic treatment (Spalj et al., 2010).

Overall, there can be reasonable confidence that the findings from this study are widely generalisable, due to representation from children from lower social deprivation backgrounds and ethnic minority populations. Due to the very small number of children who declined to participate or failed to complete treatment, it was not felt necessary to compare their deprivation status with those who did participate, to identify any differences between the two groups. It was encouraging to see good representation from children from the more disadvantaged sectors of society (the bottom two quintiles for deprivation) suggesting that this group is able to access specialist care and is not being disadvantaged. Interestingly, Balmer and colleagues (2012) found MIH was more

common in children from higher socio-economic groups. Similar with the current study, social deprivation status (represented by the IMD scores) was used as proxy for socioeconomic status. It is generally acknowledged that recruitment of study participants from ethnic minority groups may be more challenging due to cultural and language barriers, thus it was good to see recruitment of non-White British children to the present study. However, the proportion of participants from an ethnic minority group (8.1%) was slightly lower than the U.K's ethnic minority population as a whole (14%) (GOV.UK, 2011). There have been no previously published data on the prevalence of MIH according to ethnicity in the UK, and this may be an interesting line of enquiry.

6.3.2 Clinical status

In addition to the presence and severity of MIH, dental caries experience and orthodontic status (appearance) were also assessed for each participant and were included in the model; being two common conditions known to impact on children's OHRQoL (Wong et al., 2006, Barbosa and Gaviao, 2008, Sischo and Broder, 2011, Li et al., 2014, Arheiam et al., 2017). It was therefore important to account for any confounding effect of these factors. However, children with visible anterior dental caries, tooth tissue loss, restorations or previous dental traumatic injury were excluded from the study, as these would have created too many variables, making the sample size unrealistic within the time frame of the study.

6.3.2.1 Dental caries experience

Most of the children participating in the present study were in their mixed dentition, therefore, their dental caries experience was determined by combining the number of decayed/missing/filled primary and permanent teeth (total dmft/DMFT score) for the purposes of the statistical model. Interestingly, the current study, did not find a significant correlation between dental caries experience and children's OHRQoL, which is in contrast to some previous studies (Ratnayake and Ekanayake, 2005, Krisdapong et al., 2012, Alsumait et al., 2015). Children included in this study had a mean dmft of 0.79, which is similar to the U.K. average, but their mean DMFT of 1.89 was greater than that reported for British 12-year-olds (NHSDigital, 2015). In view of their co-existing MIH, the higher DMFT was entirely expected. This patient group has compromised first permanent molars, requiring restorative care or even extraction. However, one of the inclusion criteria

for this study was that children had 'stable' first permanent molars; meaning that they had received definitive treatment or the teeth were at least temporised with resin modified glass ionomer restorations, to avoid the possibility of any symptoms. The application of this inclusion criterion may therefore explain why dmft/DMFT (as an indicator of caries experience) appeared to have no impact on OHRQoL in this group of children. Furthermore, dental caries experience did not mediate any associations between other variables and oral health status. Another important point to bear in mind is that children were reminded by the investigator to think about their response in relation to their front teeth, and not their back teeth, when completing the C-OHIP-SF19 questionnaire.

6.3.2.2 Orthodontic status

In the current study, children's need for orthodontic treatment was assessed using the Aesthetic Component of IOTN, as this was felt to account for any visible differences in the appearance of anterior teeth, which could potentially impact on children's OHRQoL and self-concept. Within the model, analysis confirmed that a greater need for orthodontic treatment was significantly linked to poorer socio-emotional wellbeing and OHRQoL as reported by children. Furthermore, even after treatment to reduce the visibility of enamel defects, children with poor alignment of their anterior teeth still perceived their OHRQoL as being poor. This is not an unexpected finding and highlights the importance of a holistic approach when managing children's expectations about dental appearance.

Indeed, a number of previous studies have shown malocclusion to be an important predicator of children's OHRQoL (Gherunpong et al., 2004b, Kok et al., 2004, Foster Page et al., 2005). Tooth alignment and position greatly influences children's perception of how attractive their smile is, and their willingness to show their teeth in everyday social interactions. Foster Page et al., (2005) found that children with a greater need of orthodontic treatment reported more severe impact on emotional and social well-being domain scores than those with moderate or low need of treatment. Within the host unit of this study, there appear to be an increasing number of orthodontic referrals of older children, who have completed orthodontic treatment, but still have unmet concerns about their enamel opacities. It is not known, however, whether once children have undergone

tooth alignment, they then become more aware of any pre-existing opacities, seeking that 'perfect' smile.

6.3.2.3 Severity of MIH

It was felt important to assess the severity of the participant's MIH, not just to correlate it with OHRQoL, but to also to provide descriptive data about the condition in this particular hospital population. This was achieved using the Molar Hypomineralisation Severity Index (MHSI), developed by Oliver and colleagues (Oliver et al., 2014). This index was primarily developed to classify the severity of MIH in order to inform an appropriate management strategy at both the tooth and patient level. Oliver et al., (2014) categorised the severity of MIH for a child's dentition as a whole within three groups: mild (scores 5-20); moderate (scores 21-36) and severe (scores 37-52). Participants in the current study had moderate MIH because the mean MHSI (dentition) score was 21. Oliver and colleagues (2014) did not mention the mean MHSI (dentition) scores of the participants in their study, thus it was not possible to compare the severity of MIH scores with the current study. However, Oliver et al., did state that 54% of their study participants were in the moderate group (Oliver et al., 2014). The MHSI proved complicated to use hence an amendment was made as described in the results chapter. Furthermore, a limitation of this index was that it did not provide a severity score for incisors, only molars. However, at the start of the study, the index was felt to be the most appropriate of those available (Chawla et al., 2008). Interestingly, there have been a number of recent publications describing the development and evaluation of several new MIH-specific indices including the MIH-severity scoring system (MIH-SSS); MIH/HSPM index and the MIH treatment need index (MIH TNI) (Ghanim et al., 2015, Steffen et al., 2017, Ghanim et al., 2019, Cabral et al., 2019). Each of these indices has strengths and limitations, but may have proved simpler to use, and were subject to a more robust validation process, than the MHSI index used in the present study.

As no other investigations have correlated MHSI scores with children's self-reported OHRQoL, it is not possible to make comparisons with findings from the present study. An initial assumption may have been that children with a higher MHSI score (more severe MIH) would have poorer OHRQoL. However, the present study did not find any significant

association between the severity of MIH and children's OHRQoL. This is may again be accounted for, in part, by the inclusion criteria that children had 'stable' first permanent molars, ensuring they were asymptomatic and not causing functional problems, thus masking the 'true' effect of MIH severity on OHRQoL. The fact that the index did not give a severity score for incisors (i.e. was not a sensitive enough measure) may also have been a factor for failing to identify any correlations. A third possibility also has to be considered; that is there is no direct correlation between the severity of MIH (in terms of incisor aesthetics) and OHRQoL. It is recognised that the severity of a health condition itself, does not necessarily correlate directly with the severity of any impacts, as other factors may mediate the effects. For example, Marshman and co-workers (2009) conducted a qualitative study with a group of children with enamel defects and found that children's sense of self, not the severity or visibility of the defects, was a contributory factor in how much the enamel defects impacted on them (Marshman et al., 2009). Furthermore, a previous quantitative study, using structural equation analysis, did not find any association between the severity of a child's dento-alveolar injury and the child's self-reported OHRQoL (Poritt et al., 2015). Considering this evidence, it is speculated that the severity of a child's enamel opacity (in terms of number of teeth affected, colour and size) may not directly correlate with their OHRQoL, other factors may play a role. However, further research would be needed to explore this hypothesis, using a validated measure to quantity the severity of hypomineralised incisor aesthetics.

6.4 Clinical decisions and outcomes

6.4.1 A pragmatic approach to decision-making

Decision-making for the aesthetic management of developmental enamel opacities, in the investigator's experience, remains largely down to clinical acumen with each patient being treated on a case-by-case basis. There is a paucity of evidence to dictate which approach should be taken for opacities associated with MIH. It is acknowledged that, treatment decisions for participants in this study, was undertaken pragmatically with modifications dependent on the success achieved by each regimen. However, with increasing numbers of patients treated, it was possible to develop a more standard approach, and better advise children and families on expected outcomes. In general,

microabrasion was the first line of treatment, with the exception of children who had multiple lesions involving incisors and canines, where tooth whitening was more likely to be adopted. Following the use of microabrasion, if the result was not considered optimal, resin infiltration would then usually be undertaken. Composite resin restorations were applied if the opacities remained highly visible, and/or there was any tooth surface loss. A recent systematic review for the management of dental hypomineralisation, as a whole, also highlighted the lack clear-cut protocols for ensuring the reduction in visibility of anterior enamel opacities (da Cunha Coelho et al., 2019). Although the pragmatic approach adopted in the present study could be open to criticism, it could also be argued that the primary objective was simply to measure change in children's OHRQoL, using an 'every day' approach to decision-making. Nonetheless, it is clear that further work, in the form of a randomised controlled trial, would be necessary to provide definitive evidence for the most effective regimen.

One area that continues to generate considerable debate is how the characteristics of the opacity (colour, whether it is diffuse or demarcated) may influence the likely success of various interventions (Wong and Winter, 2002). The depth of the lesion is purported to correlate with appearance, and this in turn may dictate the success of penetration of resin infiltration. In theory, low viscosity Icon™ can infiltrate enamel porosities within hypomineralised enamel, changing the refractive index to closer to that of normal enamel, thus making the opacities less visible (Paris and Meyer-Lueckel, 2009, Tirlet et al., 2013). Assessment using polarised light microscopy on extracted hypomineralised molars suggested that lighter opacities are located in the innermost layer of enamel (Denis et al., 2013). Thus, resin infiltration may not actually be able to penetrate to this depth. Applying this basic science knowledge, together with the observation that Icon™ was not always successful for more diffuse creamy white opacities, a 'default' approach was adopted after a few cases: the relatively intact surface layer of enamel was first gently removed/disrupted with a few cycles of microabrasion (Opalustre™) to facilitate the subsequent penetration of resin infiltration (Icon™). This approach appeared to improve the outcome for creamy/white more diffuse lesions. The literature relating to the use of resin infiltration for developmental enamel defects is still emerging, with most papers being simple case studies and lacking a robust evidence base (Denis et al., 2013, Tirlet et al., 2013, Attal et al., 2014, de Souza et al., 2014, Torres and Borges, 2015, Bhandari et al., 2018).

6.4.2 Future diagnostic aids

The ability to accurately determine the depth of enamel hypomineralisation, in the clinical setting, would theoretically be of great benefit in selecting the most appropriate treatment option. One possibility, in the future, would be to use optical coherence tomography (OCT). This imaging tool uses scattered light from a near-infrared (NIR) laser to produce a 2-D grayscale image, from the scattering and absorption properties of the structures under investigation. It is able to scan to a depth of around 2mm. A fascinating in vitro study, conducted at the Eastman Dental Hospital, London, used OCT to explore the characteristics of different coloured opacities and areas of post eruptive breakdown in extracted hypomineralised and intact permanent molars (Al-Azri et al., 2016). The resultant images were convincing in revealing areas of abnormal enamel, beneath the surface opacity, but the authors stated that the data were complex to interpret, and further work was necessary before the technology could be applied clinically.

6.4.3 Clinical outcomes

It is important to reiterate that it was not the aim of the study to compare the success of different interventions, in improving opacity aesthetics, but rather to determine the impact of interventions on the psychosocial status of young patients and to explore what factors might predict this change. However, some reflection on the clinical outcomes achieved is warranted.

6.4.3.1 Patient perspectives

Firstly, in terms of patient appraisals of the outcome achieved, it is important to note that around a third of children requested further treatment at their one-month review, suggesting that they (and/or their parent/carers) were not fully satisfied with the aesthetic improvement. At the final follow-up visit, just eight children requested more treatment to further reduce the visibility of the opacity/ies. Treatment provided at these visits included a simple polish, composite resin restoration or a repeat cycle of resin infiltration. This is in agreement with a previous study which showed that, although participants perceived improvement after management of incisor enamel defects, they still had high expectations which were not always be met (Rodd et al., 2011a). Thus, it is important for clinicians to

assess the children's and their parent's expectations and discuss the potential limitations of the treatment to be provided prior to any treatment. Many children and parents asked to see photos of what results could be expected, and this should be an area for future development to improve patient experiences and managing expectations. Clinicians should also feel comfortable in telling children and parents that, sometimes, total removal of the opacity is not actually possible. However, there is no doubt that patients and parents were generally very pleased with the aesthetic outcome. They also rated the service highly, and greatly appreciated the efforts taken by the clinical team in trying to reduce the visibility of the opacities, whilst conserving tooth tissue.

6.4.3.2 Clinician perspectives

Further research is currently in progress to develop a simple grading system for the improvement in aesthetics, achieved for participants in the present study, using the archive of pre- and post-treatment images. An abstract has been submitted to the 2019 British Society of Paediatric Dentistry Annual Scientific Meeting (see Appendix 18). Preliminary analysis suggests that an excellent or good result, from a clinician's perspective, was achieved in 80% cases, and no further intervention could be justified for these patients.

One observation to make, however, relates to the stability of aesthetic improvement following the use of Icon™. The majority of participants who received Icon™ treatment either alone or in combination with microabrasion were satisfied with the outcome. Furthermore, the improvement was still satisfactory at the six-month follow-up visit. However, three participants complained of yellow discolouration affecting the treated tooth at their final dental review visit. This yellowish appearance, was acknowledged by the investigator, and was removed following a fine polish using Sof-Lex discs. This is in agreement with observations made by other researchers that resin infiltrant (Icon™) may become discoloured over time (Denis et al., 2013, Attal et al., 2014). This may be attributed to inadequate 'curing' of the material the time of placement, and patients should be advised that future polishing might be required to maintain satisfactory results. In contrast, Knosel and colleagues reported stable results over six months following resin infiltration for white spot (early caries) lesions (Knosel et al., 2013).

A further point to discuss, in terms of clinical outcomes, relates to the failure of composite resin bonding. Of a total of five children who received a composite resin restoration, two patients were found to have lost their filling at the 6-month follow up. Interestingly, both cases related to a restoration failure on a maxillary canine. It is widely recognised that bond strengths are compromised in areas of enamel hypomineralisation (William et al., 2006a). An *in vitro* study on extracted hypomineralised molars showed that the microshear bond strength of composite resin restoration to hypomineralised enamel was significantly lower than to the unaffected enamel (William et al., 2006a). A number of recommendations have been made to try to overcome this problem, including pre-treatment with resin infiltration to enhance bonding between hypomineralised enamel and the composite resin restoration. However, findings from in vitro studies are conflicting; some support the use of Icon™ (Paris and Meyer-Lueckel, 2009, Paris et al., 2013, Borges et al., 2017) while others did not observe any improvement in adhesion (Kramer et al., 2018). From a practical point, it is suggested that the margins of any composite resin restoration should be extended, if possible, onto sound (normal coloured) enamel, and this was the case in the present study. Indeed as there were no bond failures of incisor restorations it is speculated that the fractures could have been due to excessive masticatory forces involving the canine tips, rather than purely because of poor bond strength.

6.5 Patient-reported outcome measures

On reflection, the decision to employ C-OHIP-SF19 as the primary outcome measure was well informed. At the time of the study onset there were no other validated measures that appeared to offer any advantages over C-OHIP-SF19 (Gilchrist et al., 2014). It proved easy for children to understand and complete and, importantly, proved sensitive enough to measure change in OHRQoL following an intervention. There were also few (or no) floor and ceiling effects identified. The rationale for using this measure was that it incorporated both negative and positive health impacts, and included an item which could be specifically applied to enamel opacities (it asks about spots/marks on teeth) (Genderson et al., 2013a). However, the response format is not considered ideal; children are asked how often in the last three months they have been affected by (for example) marks or spots on their teeth. From the child's perspective, they are more likely to respond in terms of the severity of any impact (how much) rather than frequency of the

impact (how often) (Rogers et al., 2019b). Furthermore, data from a previous intervention study, albeit conducted in China with young orthodontic patients, allowed the calculation of a sample size for the present study (Li et al., 2014).

During the protocol development for the present study, serious consideration was also given to the use of a child-report questionnaire on incisor aesthetics that was originally developed to measure psychosocial impacts relating to dental fluorosis; the Child and Parent Questionnaire about Tooth Appearance (Martinez-Mier et al., 2004). This 12-item instrument was developed with children and parents in the USA and Mexico, and reportedly has acceptable psychometric properties. It has been translated into Spanish and Portuguese and is designed for use for children (and their parents) from the age of 7-years. Importantly, the response format for some of the questions is in terms of severity, for example: During the past two months, how much has the way your teeth look kept you from smiling freely? (A lot; Some; A little; Not at all). Leal and colleagues (2017) used this questionnaire to assess the impact of dental appearance (incisor aesthetics) in Brazilian children with and without MIH (Leal et al., 2017). Interestingly, children without MIH were as likely to be upset by the colour of their teeth as were children with MIH, and there was little agreement between children and their parents in terms of reported impacts. Although this Child and Parent Questionnaire about Tooth Appearance have merit and definite relevance to the present study aims, it was not felt to be the best choice. Firstly, it has not been validated for use in an English-speaking European population, and would need further testing in terms of language and content before use in the UK. Secondly, with the exception of the Leal study (published after the start of the current study), it had not been employed in any previous studies, thus there were no data from which to base a power calculation for the present study. Finally, as the focus is entirely on aesthetics, any impacts relating to function would not have been captured.

In contrast to the C-OHIP-SF19, some children found the SPPC questionnaire very difficult to understand. It was necessary for the research team to help children with this measure, and to ensure they completed it correctly. However, the instrument has been widely validated and used throughout the world and is highly regarded.

6.6 Reflections on key findings

Overall, it was felt that the study did satisfy the initial aims and objectives. Furthermore, it is the first longitudinal clinical study to demonstrate how routine clinical interventions to conceal the visibility of enamel opacities on permanent anterior teeth associated with MIH improved children's oral health-related quality of life. Data collected from this study fitted within the Wilson and Cleary theoretical model which established the employability of this model for young patients with MIH. The associations between different predictors (such as clinical status, socio-demographic and self-concept) and children's OHRQoL were also successfully illustrated using this theoretical model. These main findings will now be considered in more detail.

6.6.1 Reliability of C-OHIP-SF19

The first thing to comment on is the fact that substantial internal consistency reliability for all items in the C-OHIP-SF19 was achieved, with Cronbach's Alpha values ranging from 0.76 to 0.83 at baseline, one-month and six-month follow-up visits. The study therefore provides verification for the suitable psychometric properties of C-OHIP-SF19 when used with children with MIH. This questionnaire has previously been used for children with dental caries, cleft lip/palate and children seeking orthodontic treatment in various populations (Broder et al., 2012, Li et al., 2014, Thiruvenkadam et al., 2015, Kragt et al., 2016, Sierwald et al., 2016, Agnew et al., 2017, Arheiam et al., 2017). Although this is the first study to report its use in children with an enamel defect, the results showed that this measure is sensitive enough to measure change following an intervention. However, it should also be recognised that the intervention was extremely effective in improving dental aesthetics. Thus, the measure may have not been able to identify significant change in OHRQoL if the clinical outcome had not been so marked.

6.6.2 Effect of gender

The present study did not find an influence of gender on children's OHRQoL. On first inspection this seems to conflict with previous studies which found that girls with MIH and AI report poorer OHRQoL than their male counterparts (Parekh et al., 2014, Dantas-Neta

et al., 2016). There have also been studies involving children with other dental conditions, where again females tend to report poorer OHRQoL, including children with cleft lip and palate (Broder et al., 2014) and those who have sustained dento-alveolar trauma (Poritt et al., 2015). It would appear that girls do not just report poorer outcomes in relation to dental aesthetics (i.e. impacts on social and psychological well-being) but girls with dental caries may also experience worse functional impacts than boys (Arheiam et al., 2017). To explain the apparent difference, it has to be borne in mind that the present study was a self-selecting sample. All children were referred to a secondary care service, because of aesthetic-related concerns about their enamel opacities. Thus, any gender differences would have already been accounted for, by the fact that there were a slightly higher proportion of girls than boys in the group of potential participants. Interestingly, Agnew's study with children with an orofacial cleft in Australia reported that there was no influence of gender on children's OHRQoL (Agnew et al., 2017). These observations suggest that both boys and girls perceived similar impacts of dental attractiveness and aesthetic appearance on their OHRQoL.

A common finding in previous SPPC research is that gender does influence self-evaluation across the domains. Harter (1985) and Gacek and colleagues (2014) reported that boys rated themselves more positively than girls in athletic competence, physical appearance and global self-worth subscales (Harter, 1985, Gacek et al., 2014). Again, the present study did not observe any significant differences in the two subscales according to gender. It may be that, in the past, girls may have viewed themselves more critically, and been unhappier about how they looked, but cultural norms have changed, and this is no longer the case.

6.6.3 Effect of age

A key point to highlight about the age of the participants, is that over half were in the 7-10 age-group, thus were not yet at secondary school. Furthermore, there were no significant age-related differences in C-OHIP-SF19 scores, with the exception of the oral health domain, where younger children reported poorer outcomes at baseline. On first inspection, this finding is surprising, given that previous work has reported heightened appearance-related concerns in slightly older children, especially just before the transition to secondary school (Rodd et al., 2011b, Rodd et al., 2012). Furthermore, the findings are

in contrast with a Brazilian study, involving over 700 8-year-old children with MIH, which found that these younger children did not appear to experience any negative OHRQoL impacts in relation to their incisor opacities (Portella et al., 2019). The authors attributed this to the fact that the children were not yet concerned about their dental appearance, particularly as they were in the early mixed dentition phase, with teeth still erupting. This may well be true, but there are children, as young as 7-years, who report negative impacts from their incisor opacities, as evidenced by children who were included in this study. The study conducted by Agnew et al (2017) also found that older children (with a cleft lip/palate) reported poorer socio-emotional wellbeing and lower overall COHIP-SF19 scores compared to younger children (Agnew et al., 2017). One explanation for the lack of age-related differences in the present study, compared to previous studies, may be due to the fact that these children live in a more developed country than Brazil, with different social and health contexts. Furthermore, the presence of enamel opacities on permanent anterior teeth cannot be considered as severe an impact as having a facial difference such as an orofacial cleft hence the impact of age was not substantial in the current study group.

When it comes to age-related differences in self-concept, SPPC data also suggest that younger children evaluate themselves more highly than older children (Harter, 1985, Gacek et al., 2014). Data from the present study is therefore in agreement with previous work, with children becoming more self- critical about their physical features and social abilities as they reach adolescence.

6.6.4 Perceptions of self

Gacek et al., (2014), in their study of Polish children, also reported that how children rated themselves in the SPPC physical appearance subscale was the strongest predictor of global self-worth. Put another way, when children are happy with the way they look they are more likely to evaluate themselves positively as a person and be content with their lives (Gacek et al., 2014). The current study was not able to determine which SPPC subscale predicted the global self-worth domain of SPPC because only two domain-specific subscales were used (Social Acceptance and Physical Appearance). However, within the limited scope of the study, the Physical Appearance subscale scores showed significant differences between pre-, one-month and six-month post treatment scores,

suggesting that participants perceived that they were generally better looking following treatment.

Clearly, there are parallels to be drawn in the present study. If children with visible enamel defects do not perceive themselves as being physically attractive, this in turn may negatively affect their global self-worth. It is important therefore that dentists are sensitive to this relationship and provide appropriate aesthetic dental care for these patients, thereby reducing the potential for psychosocial consequences.

6.6.5 Other patient-reported outcomes

Four single items (worry, embarrassment, happiness and perception of tooth discolouration) were used, with a visual analogue scale response format, to capture further patient-reported outcomes following intervention. These were selected on the basis of a previous study with children with visible opacities (Rodd et al., 2011a). One point worth noting is that there continued to be a significant improvement in scores between the one-month and six-month review. In terms of being less 'worried' about their teeth, this positive change may reflect the fact that MIH had been explained fully to children and they realised that similar enamel opacities were common in other children too (they were sometimes introduced to other study participants). On first presentation, children and their families did not know what the marks on the teeth were due to, and believed that they were because they had not looked after them or had had a deficient diet. They were also worried that the tooth condition would worsen over time. Thus, information and reassurance about the aetiology of MIH (or AI) clearly reduced their level of worry, highlighting the value of effective communication by the clinicians. Another interesting point is that children perceived that their teeth were less discoloured at six-months than at the one-month review. This may be due to greater acceptance of the tooth colour by the children over time, or due to an actual measurable improvement in tooth aesthetics. The need to objectively assess the stability of clinical outcomes (as described in section 6.8.4 below) is therefore warranted in future research.

6.7 Strengths of the study

It is felt that the study had a number of positive attributes, not least the fact that it is the first to explore the effect of 'aesthetic' dental treatment on children's OHRQoL, it incorporated a longitudinal design and was underpinned by an established theoretical model. The main strengths of the study will now be described in greater detail.

6.7.1 Patient-centred approach

The current study adopted the ethos of carrying out research with children rather than on them. In keeping with the recommendations made by Marshman and colleagues in their systematic review, children were viewed as active participants (Marshman et al., 2015). Children were involved from the outset of the study, and helped with the format and design of information sheets and questionnaire booklets. Measures that children completed (C-OHIP-SF19 and FFT) had also been originally developed with children themselves, rather than being adult-generated questionnaires. It was also very important to listen to the child's opinions when discussing treatment options. There were instances when parents were keen for further treatment and the child was not. This scenario is generic to paediatric health care as a whole. However, the investigator was careful to elicit the child's views and opinions, and this was found to be valued in the free text of the FFT. Initially, two children (2.33%) could not decide if they would recommend the same treatment (and hospital) to their family and friends should they have the same condition, but at one-month and 6-month review visits all children were happy to recommend the treatment (and hospital) to their family and friends. This suggests that they were satisfied with the treatment and care they received. Within the free text of the FFT, the participants wrote that the staff were friendly and welcoming. They also appreciated being involved in decision-making:

"The staff was very friendly and welcoming. They also made everything I needed to know very clear to me" (Boy aged 15)

"It was good how they gave me choices and I felt really comfortable" (Girl aged 11)

One participant wrote a thank you card to express her appreciation towards the dental care provided (Appendix 19).

6.7.2 Use of a theoretical model

One criticism that has been raised about paediatric oral research as a whole is that studies are not always driven by a sound theoretical model (Knapp et al., 2017, Rogers et al., 2019a). This study was driven by the well-established Wilson and Cleary model for HRQoL (Wilson and Cleary, 1995). Furthermore, the variables selected for inclusion in the model (e.g. gender, socioeconomic status) were selected on the basis of previous studies that highlighted their role in determining OHRQoL.

The Wilson and Cleary model (1995) has been widely used in dentistry (Baker et al., 2010, Gururatana et al., 2014, Benson et al., 2015, Gupta et al., 2015, Vettore et al., 2019) but it has not been previously applied for children with MIH. Therefore, this is the first study to test the adaptability of this model to conceptualise the associations between various variables to predict any improvement in patient-reported outcome measures following interventions to improve aesthetic appearance of permanent anterior teeth for young patients with MIH.

Although the final sample size (n=86) was considered small for structural equation modeling analysis, the data fitted within the simplified Wilson and Cleary theoretical model. Kline (2011) has suggested that 10 participants are needed for each parameter investigated (Kline, 2011). In view of this limitation, only the socio-emotional wellbeing domain of C-OHIP-SF19 was included in the model because this variable was considered most relevant to the study aim. Preliminary analysis was also undertaken to test whether a change in self-concept over time predicted change in overall oral health, but the data were not found to fit the model and therefore excluded from the final analysis. Due to the relatively small number of participants, other outcome measures such as health satisfaction and general health perceptions were not analysed in the current study. Previous studies have shown that self-esteem is an important predictor of children's OHRQoL (Benson et al., 2015, Kragt et al., 2017). Findings from the present study would concur, as it was established that self-concept (which is a part of 'the self') is an important predictor of overall oral health status and socio-emotional wellbeing among young children with MIH who have cosmetic concerns.

Data collected from this longitudinal clinical study can also be employed to measure the average rate of change in overall oral health status from the initial time point (baseline) and each review visits (individual growth model). This could be used to estimate if there was any significant difference in the rate of change between participants over time using growth curve analysis in AMOS software. However, this analysis is beyond the scope of the current study.

A further positive aspect to mention is the use of structural equation modeling (SEM). This is a powerful statistical method that allows the multiple analyses of different predictors and outcomes and it is considered the ideal approach for studies using theoretical frameworks and longitudinal data. However, some researchers are concerned that SEM requires a large sample size to perform the analysis and test a theoretical model. This may have discouraged them from using SEM to analyse their data. Another limitation of using SEM is that, similar with other model testing, SEM analysis involves omitting variables during model approximation to get a good model fit. It is interesting to note that omitted variables are rarely acknowledged by researchers, even though omission of important variables may result in biased parameter estimates and inaccurate estimates of standard errors. Thus it is important for researchers to appreciate that a good model fit does not guarantee the inclusion of all relevant variables in a model (Tomarken and Waller, 2005). Therefore, researchers must have background knowledge on the area being tested and include variables based on the previous studies conducted in the same field.

6.7.3 Longitudinal design

The current study evaluated the longitudinal impact of dental treatment on children's OHRQoL, as participants were reviewed six-months after their treatment. Within a teaching hospital setting, such as this, it would not be usual practice to review patients in the longer term following simple aesthetic interventions; they would have been discharged back to their dentist. Secondary care settings do not have the capacity to routinely review fit and healthy patients after a course of treatment. Therefore, the research allowed both the unique opportunity to review the stability of the clinical outcomes, but also provided more than just a 'snapshot' assessment of children's OHRQoL. This allowed the identification of clinical or patient-related variables that could predict any longer term

change to children's OHRQoL, following the intervention. It should be borne in mind that OHRQoL can vary according each child's stage of overall development as well as the influence of external factors, such as changing schools or other important life events (Rodd et al., 2012). Interestingly, OHRQoL generally remained stable for participants in the six-month period between their first intervention and their final review. However, a longer follow-up period would be of value throughout adolescence, to see if the positive effects of the aesthetic dental treatment persisted.

6.8 Limitations

6.8.1 Lack of a control group

The current study identified a significant improvement in children's self-report OHRQoL following treatment, as indicated by a substantial increase in the total C-OHIP-SF19 score and domain scores. However, a justifiable criticism of the study design is the lack of a control group. It may be argued that children's OHRQoL could have changed (improved) over time without any intervention, and thus the findings cannot be attributed exclusively to the effects of the aesthetic dental treatment provided. However, it would be unethical to withhold treatment for children with MIH who had psychosocial concerns about their incisor opacities. The possibility of simply delaying treatment for some children for six-months, so that they could essentially act as a control group (by completing the measures at baseline and after six-months in the absence of any intervention) was also considered. However, this was not felt to be an option within the hospital service due to barriers relating to care pathways and enforced 18 weeks targets for patient waiting times from referral to first treatment.

6.8.2 Inclusion of non MIH patients

Inclusion criteria, set at the beginning of the study, aimed to only recruit children with a definitive diagnosis of MIH. However, despite staff training, a small number of patients (n=11) who had more generalised opacities, suggestive of a diagnosis of hypomature amelogenesis imperfecta, were booked onto the investigator's treatment clinics. The

intention was that the lead consultant and clinical supervisor (H.R) would act as the 'gatekeeper' to confirm eligibility of all potential participants. In practice, the enthusiasm of the clinical team, receptionists, as well as reduced capacity on other treatment clinics, meant that some children, who requested aesthetic treatment for anterior enamel opacities were informed about the study and booked onto the investigator's clinics, without meeting the criteria of having MIH. This presented an initial dilemma; whether to rebook these patients with another clinician, or to go ahead and treat them as study participants. It was felt that if all other criteria were satisfied, and the children had mild opacities (i.e. no hypoplasia and sensitivity) they could be included in the study. No children with 'severe' enamel defects or children who were experiencing impacts from their posterior teeth were included. As the interventions were the same for these children, and change in OHRQoL scores was determined for individuals, the inclusion of these children was not felt to compromise the study aim and objectives. Furthermore, there were no significant differences in C-OHIP-SF19 and Visual Analogue Scale scores between the two groups at any time points during the study, and with the need to fulfill the final sample size, the AI children were included in both descriptive and structural equation modeling analyses. However, it should be noted that the AI patients did perceive themselves more negatively than the MIH patients, in relation to the SPPC domain-specific subscales and Global self-worth. It is not clear why SPPC scores were 'poorer', as this was not the case for OHRQoL. Children with AI obviously had more generalised opacities (affecting all their teeth) compared to children with MIH, but further enquiry, possibly using a qualitative approach, would be needed to explore why AI patients feel differently about themselves.

6.8.3 Use of social deprivation status as proxy of socio-economic status

Social deprivation is one of the proxies available to measure an individual's position on a socio-economic scale. Social deprivation focuses on the material hardship or insufficient financial resources that limits an individual ability to participate in social, cultural and political activities. In the present study, socio-economic status is quantified using social deprivation status as a proxy. The rationale for using the index of multiple deprivation (IMD) scores to estimate the social deprivation status of participants in this study is because it is a practical way that considers socio-economic indicators such as income,

employment, crime rates and health status. The scores can be obtained easily using the IMD calculator that can be accessed by public. This method is less intimidating as parents do not have to report their occupation, income or education qualification to the researchers. However, it is recognised that IMD scores represent the social deprivation status of the small geographical area rather than the individual living in that small area. It presumes that people who live in the same area have relatively similar household characteristics and have similar socio-economic status. Future studies exploring the associations between predictors and children's oral health outcomes may consider other indicators or measures of socio-economic status, such as household income, parental education or occupation, that define the individual's socio-economic status, rather than the geographical area in which they reside.

6.8.4 Limited insights into patient perspectives

As alluded to above, the use of a purely quantitative approach to capture children's perspectives of having visible incisor opacities, as well as the impact of treatment, has obvious limitations. Whilst quantitative data has merit, in terms of providing a well-accepted evidence-base and allowing comparison with findings from other studies, it fails to generate any new or deeper insights into children's thoughts, feelings and behaviours. The data showed that there was a significant improvement in OHRQoL, following an intervention, but could not identify how this was perceived by children in their own daily lives and activities. Anecdotally, many children (and their parents) told the investigator how their treatment had made a difference to them, in terms of being happier and more confident at school, but these narratives deserve further exploration using qualitative approaches. Indeed, there seems to be a complete lack of qualitative enquiry with children with MIH, either in relation to aesthetic concerns, or functional ones. Ideally, future studies of this nature, should try to incorporate a mixed method approach, in order to fully understand the impact of enamel opacities on children's lives. It is also important to recognise that not all children with visible enamel opacities will experience negative impacts and thus may have no wish for treatment. There may also be other barriers to children seeking treatment, such as dental anxiety. Thus, the present study is limited in its scope, by only including children who viewed their teeth as unattractive, wished for corrective treatment and were able to access this.

6.8.5 Absence of clinical outcome data

As mentioned earlier, clinical outcome measures were not obtained for this study. An initial objective, as stated in the original study protocol and ethics application, was to measure change in opacity size and colour using standard pre- and post-treatment colour photographs of each child. The intention was to use image analysis software to obtain an objective measure of change in opacity visibility and to include this in the statistical model as a potential variable. One may assume that a 'better' aesthetic result (reduced visibility of the opacity/ies) would correlate directly with better OHRQoL at the six-month review. Standard photographs were taken of every participant, at every visit, and are currently being stored securely as part of the patients' clinical records. However, after considerable research of the supporting literature and use of the available image pro-plus software, it became clear that this was a project in itself, and was too ambitious within the time frame of the PhD study. It was therefore not possible to include a clinical outcome measure within the statistical model. However, the archive will be used in the future to achieve this aim, and secondary analysis can be performed.

6.9 Implications for clinical practice

There can be no doubt that some children suffer profound negative psychosocial impacts from having visible enamel opacities that may have lifelong consequences. It therefore seems entirely justified that all children, with concerns, should be offered simple interventions that may have a measurable improvement on their wellbeing. Unfortunately, children are unlikely to be offered this treatment within NHS general dental practice in the UK. This may be because of a lack of competence or confidence by non-specialist dentists, or it may be because of inadequate remuneration for these procedures. Certainly, the current cost of around £100 for the resin infiltration is prohibitive, and the manufacturers need to be made aware of this barrier to its wider use. The use of tooth whitening is also unlikely to be offered in primary care settings, due to concerns about its legality in the under 18s. These issues mean that children are travelling considerable distances for treatment in dental hospitals, placing a burden on their families and incurring

societal costs. A study in the host unit found that children with enamel opacities of cosmetic concern were travelling an average of 114km return trip to the dental hospital (Large et al., 2019). Furthermore, in only 1 out of 50 cases reviewed, had the referring dentist attempted any intervention (microabrasion). One option to address this problem could be to develop a culture of remote diagnosis and treatment planning. The use of 'teledentistry' has been found to be very effective in areas such as dento-alveolar trauma and screening of oral pathologies, and could well be applied to the management of children with more minor enamel defects (Estai et al., 2018). There also seems to be a need for regular postgraduate courses and training, in view of the high prevalence of incisor hypomineralisation in British children (Balmer et al., 2015).

6.10 Further research priorities

Molar incisor hypomineralisation is a common global condition, presenting in childhood, which seems to be generating considerable interest amongst researchers, clinicians and patients. The present study has gone some way in showing that simple minimally invasive dental treatment can improve children's self-report OHRQoL, as evidenced by comparing pre- and post-treatment quantitative data using validated questionnaires. However, questions remain about patient and parent experiences and expectations, as well as the predictability and evaluation of clinical outcomes achieved. The present research has generated ideas and data that will be used to continue this research further as outlined below.

6.10.1 Short term priorities

1. The first priority will be to utilise the clinical photography archive relating to the participants in order to develop a standard approach to measure the characteristics of the opacities (e,g, in terms of colour, lucency, demarcation, site and size). A protocol will then be applied to measure change in the 'visibility' of the opacities following intervention. These data will then be incorporated within the statistical model to see if the success of the clinical outcome (as determined by clinicians) predicted change in OHRQoL. It is anticipated analysis of the clinical outcome measure will also provide a

more objective insight into which treatment regimen worked best for which type of opacity.

2. In terms of ongoing child-engagement in oral health research, it would be desirable to ask children to 'grade' the clinical outcomes achieved from the photos. This could be achieved using some of the original study participants as well as including children who do not have opacities. Both qualitative and quantitative methods could be employed; using an on-line survey or focus group settings so that children's expectations of treatment outcomes could be explored more fully. A number of children from the original study were asked if they would like to help with this type of research in future and they (and their parents) gave their consent to be approached for this purpose.

3. Although not research *per se*, a third aim would be to develop some patient- and parent-friendly resources to help decision-making for future patients. Children and parents frequently ask to see examples of the results that can and cannot be achieved. It is felt that showing families a range of outcomes, and explaining the nature of the enamel defect and proposed treatment approach would help to better manage expectations and improve patient experiences overall.

6.10.2 Longer term goals

Driven by the present research, a more ambitious project is proposed which would necessitate further protocol development, ethics applications, multi-professional collaborations and acquisition of funding. Due to the unpredictability of the interventions in some cases, it would be advantageous to know how 'deep' the enamel opacity extends within the enamel structure and how porous or even hypermineralised the outermost surface layer is. This may help the clinician when providing a more informed decision about the likely success of the various treatment options, for example the potential ease of resin infiltration. Preliminary *in vivo* investigations were undertaken by the supervisory team using an OCT device (VivoSight OCT scanner, Michelson Diagnostics), which is in routine use at the dermatology clinic of the Royal Hallamshire Hospital, Sheffield. Scans were taken of the anterior teeth of volunteer staff and students (including the investigator herself) who had visible enamel opacity. This produced some interesting preliminary findings, but further refinements in the technique would be warranted prior to a full ethics

application to continue this work. The overall aim would be to determine the diagnostic value of this imaging technology, pre- and post- minimally invasive treatment, for children with enamel opacities.

Chapter 7

Conclusions

This research has contributed to current knowledge by showing how various clinical and personal factors inter-relate to predict children's OHRQoL, before and after minimally invasive treatment to reduce the visibility of their enamel opacities. This chapter will now summarise the findings and recommendations drawn from this body of work.

7.1 Summary of key findings

- Children with MIH, referred to specialist services due to concerns about the appearance of their incisor opacities, were found to be willing and engaged research participants, with excellent response and completion rates and representation from ethnic minority and socially deprived groups.
- There was a very high level of satisfaction from this patient group with the service provided.
- Minimally invasive dental treatment, which aimed to reduce the visibility of anterior enamel opacities, was found to have a significantly positive effect on children's self-reported OHRQoL, as measured by C-OHIP-SF19.
- There were no significant differences in pre- or post-treatment self-report OHRQoL between boys and girls, explained by the fact that this was a self-selecting group who had already requested referral to a secondary service for treatment.
- Self-concept, the need for orthodontic treatment and number of teeth needing aesthetic treatment were all important determinants of OHRQoL and socioemotional wellbeing, before and after treatment.

7.2 Recommendations

- All children, who are experiencing negative psychosocial impacts due to the visibility of their incisor opacities, should be able to access and benefit from minimally invasive dental interventions to improve their dental aesthetics and overall wellbeing.

- As few general dental practitioners currently appear to provide treatment for children with developmental enamel defects such as MIH (Large et al., 2019), children and their families may have to wait to be referred and travel long distances to access to specialist services. Further enquiry is therefore needed to explore what barriers exist to providing this (essentially simple) treatment in primary care settings. Further training and support for primary care providers would seem to be warranted in this field.

- Commissioners of dental services and policy makers should be provided with robust evidence, such as from in the present study, to highlight the negative psychosocial impacts of MIH (and other dental conditions) on children's OHRQoL, and the effectiveness of dental treatment in addressing these impacts.

- Further basic science and clinical research is indicated to determine the clinical outcomes (success) of the various regimens used to reduce the visibility of enamel opacities. However, utmost consideration should be given to preserving tooth tissue in this young patient group, whilst still providing the best possible aesthetic solution for their presenting complaint.

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References

AGNEW, C. M., FOSTER PAGE, L. & HIBBERT, S. 2017. Validity and reliability of the COHIP-SF in Australian children with orofacial cleft. *Int J Paediatr Dent,* 27**,** 574-582.

AGUIRRE, J. M., RODRÍGUEZ, R., ORIBE, D. & VITORIA, J. C. 1997. Dental enamel defects in celiac patients. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology,* 84**,** 646-650.

AHMADI, R., RAMAZANI, N. & NOURINASAB, R. 2012. Molar Incisor Hypomineralization: A Study of Prevalence and Etiology in a Group of Iranian Children. *Iran J Pediatr,* 22**,** 245-251.

AINE, L., BACKSTRÖM, M. C., MÄKI, R. & KUUSELA, A. L. 2000. Enamel defects in primary and permanent teeth of children born prematurely. *Journal of oral pathology & medicine,* 29**,** 403-409.

AL-AZRI, K., MELITA, L. N., STRANGE, A. P., FESTY, F., AL-JAWAD, M., COOK, R., PAREKH, S. & BOZEC, L. 2016. Optical coherence tomography use in the diagnosis of enamel defects. *J Biomed Opt,* 21**,** 36004.

ALALUUSUA, S. 2010. Aetiology of Molar-Incisor Hypomineralisation: A systematic review. *European Archives of Paediatric Dentistry,* 11**,** 53-58.

ALALUUSUA, S., LUKINMAA, P. L., KOSKIMIES, M., PIRINEN, S., HÖLTTÄ, P., KALLIO, M., HOLTTINEN, T. & SALMENPERÄ, L. 1996. Developmental dental defects associated with long breast feeding. *European Journal of Oral Sciences,* 104**,** 493-497.

ALDRIGUI, J. M., ABANTO, J., CARVALHO, T. S., MENDES, F. M., WANDERLEY, M. T., BÖNECKER, M. & RAGGIO, D. P. 2011. Impact of traumatic dental injuries and malocclusions on quality of life of young children. *Health and Quality of Life Outcomes,* 9**,** 1-7.

ALLAZZAM, S. M., ALAKI, S. M. & EL MELIGY, O. A. S. 2014. Molar Incisor Hypomineralization, Prevalence, and Etiology. *International Journal of Dentistry,* 2014**,** 1-8.

ALLEN, P. F. 2003. Assessment of oral health related quality of life. *Health and Quality of Life Outcomes,* 1**,** 40-47.

ALMUALLEM, Z. & BUSUTTIL-NAUDI, A. 2018. Molar incisor hypomineralisation (MIH) - an overview. *Br Dent J*.

ALSHEHRI, A. & KWON, S. R. 2016. Etiology and Management of white spot lesions. *The Journal of Multidisciplinary Care Decisions in Dentistry,* 1.

ALSUMAIT, A., ELSALHY, M., RAINE, K. & COR, K. 2015. Impact of dental health on children's oral health-related quality of life: a cross-sectional study. *Health and Quality of Life Outcomes,* 13**,** 98-107.

ALTMAN, D. G. 1991. *Practical Statistics for Medical research,* London, Chapman and Hall.

AMERICANO, G. C. A., JACOBSEN, P. E., SOVIERO, V. M. & HAUBEK, D. 2016. A systematic review on the association between molar incisor hypomineralization and dental caries. *International Journal of Paediatric Dentistry* 1-11.

AOBA, T. 1996. Recent observation of enamel crystal observation during mammalian amelogenesis. *The Anatomical Record,* 245**,** 208-218.

ARBUCKLE, J. L. 2016. IBM ® SPSS ® Amos TM 24 User's Guide.

ARHEIAM, A. A., BAKER, S. R., BALLO, L., ELAREIBI, I., FAKRON, S. & HARRIS, R. V. 2017. The development and psychometric properties of the Arabic version of the child oral health impact profile-short form (COHIP- SF 19). *Health Qual Life Outcomes,* 15**,** 218.

ARNOLD, W. H., BACHSTAEDTER, L., BENZ, K. & NAUMOVA, E. A. 2014. Resin Infiltration into Differentially Extended Experimental Carious Lesions. *The Open Dentistry Journal,* 8**,** 251-256.

ARROW, P. 2013. Child oral health-related quality of life (COHQoL), enamel defects of the first permanent molars and caries experience among children in Western Australia. *Community Dental Health,* 30**,** 183-188.

ARROW, P. 2016. Dental enamel defects, caries experience and oral health-related quality of life: a cohort study. *Aust Dent J*.

ASCHHEIM, K. W. 2015. *Esthetic Dentistry (Third Edition) A Clinical Approach to Techniques and Materials*, Mosby.

ATTAL, J.-P., ATLAN, A., DENIS, M., VENNAT, E. & TIRLET, G. 2014. White spots on enamel: Treatment protocol by superficial or deep infiltration (part 2). *International Orthodontics,* 12**,** 1-31.

AVŞAR, A. & KALAYCI, A. G. 2008. The presence and distribution of dental enamel defects and caries in children with celiac disease. *Turkish journal of pediatrics,* 50**,** 45-50.

BAKER, S. R., MAT, A. & ROBINSON, P. G. 2010. What Psychosocial Factors Influence Adolescents' Oral Health? *J Dent Res* 89**,** 1230-1235.

BALMER, R., TOUMBA, J., GODSON, J. & DUGGAL, M. 2012. The prevalence of molar incisor hypomineralisation in Northern England and its relationship to socioeconomic status and water fluoridation. *Int J Paediatr Dent,* 22**,** 250-7.

BALMER, R., TOUMBA, K. J., MUNYOMBWE, T., GODSON, J. & DUGGAL, M. S. 2015. The prevalence of incisor hypomineralisation and its relationship with the prevalence of molar incisor hypomineralisation. *Eur Arch Paediatr Dent,* 16**,** 265-9.

BARBOSA, T. S. & GAVIAO, M. B. 2008. Oral health-related quality of life in children: part II. Effects of clinical oral health status. A systematic review. *Int J Dent Hyg,* 6**,** 100-7.

BARBOSA, T. S., TURELI, M. C. M. & GAVIAO, M. B. D. 2009. Validity and reliability of the Child Perceptions Questionnaires applied in Brazilian children. *BMC Oral Health* 9**,** 1-8.

BARTLETT, J. D. 2013. Dental Enamel Development: Proteinases and Their Enamel Matrix Substrates. *ISRN Dentistry,* 2013**,** 1-24.

BATH-BALOGH, M. & FEHRENBACH, M. J. 2006. Chapter 12 Enamel. *Dental Embryology, Histology, and anatomy.* The United States of America: Elsevier Saunders.
BEENTJES, V. E. V. M., WEERHEIJM, K. L. & GROEN, H. J. 2002. Factors involved in the aetiology of molar-incisor hypomineralisation (MIH). *European Journal of Paediatric Dentistry,* 1**,** 9-13.
BENBACHIR, N., ARDU, S. & KREJCI, I. 2007. Indications and limits of the microabrasion technique. *Quintessence International,* 38**,** 811-815.
BENSON, P. E., DA'AS, T., JOHAL, A., MANDALL, N. A., WILLIAMS, A. C., BAKER, S. R. & MARSHMAN, Z. 2015. Relationships between dental appearance, self-esteem, socio-economic status, and oral health-related quality of life in UK schoolchildren: A 3-year cohort study. *Eur J Orthod. ,* 37**,** 481-490.
BHANDARI, R., THAKUR, S., SINGHAL, P., CHAUHAN, D., JAYAM, C. & JAIN, T. 2018. Concealment effect of resin infiltration on incisor of Grade I molar incisor hypomineralization patients: An in vivo study. *J Conserv Dent,* 21**,** 450-454.
BORGES, A. B., CANEPPELE, T. M. F., MASTERSON, D. & MAIA, L. C. 2017. Is resin infiltration an effective esthetic treatment for enamel development defects and white spot lesions? A systematic review.
BORZABADI-FARAHANI, A. 2011. An insight into four orthodontic treatment need indices. *Prog Orthod,* 12**,** 132-42.
BROADBENT, J. M., THOMSON, W. M. & WILLIAMS, S. M. 2005. Does caries in primary teeth predict enamel defects in permanent teeth? A longitudinal study. *Journal of dental research,* 84**,** 260-264.
BROC, M. A. 2014. Harter's Self-Perception Profile for Children: an adaptation and validation of the Spanish version. *Psychol Rep,* 115**,** 444-66.
BRODER, H. L. & WILSON-GENDERSON, M. 2007. Reliability and convergent and discriminant validity of the Child Oral Health Impact Profile (COHIP Child's version). *Community Dentistry and Oral Epidemiology,* 35**,** 20-31.
BRODER, H. L., WILSON-GENDERSON, M. & SISCHO, L. 2012. Reliability and validity testing for the Child Oral Health Impact Profile-Reduced (COHIP-SF 19). *J Public Health Dent. ,* 72**,** 302-312.
BRODER, H. L., WILSON-GENDERSON, M., SISCHO, L. & NORMAN, R. G. 2014. Examining factors associated with oral health-related quality of life for youth with cleft. *Plast Reconstr Surg,* 133**,** 828e-834e.
BROOK, P. H. & SHAW, W. C. 1989. The development of an index of orthodontic treatment priority. *Eur J Orthod,* 11**,** 309-20.
BROOKES, S. J., ROBINSON, C., KIRKHAM, J. & BONASS, W. A. 1995. Biochemistry and molecular biology of amelogenin proteins of developing dental enamel. *Archives of Oral Biology,* 40**,** 1-14.
BURDEN, D. J., PINE, C. M. & BURNSIDE, G. 2001. Modified IOTN: an orthodontic treatment need index for use in oral health surveys. *Community Dent Oral Epidemiol,* 29**,** 220-5.
CABRAL, R. N., NYVAD, B., SOVIERO, V., FREITAS, E. & LEAL, S. C. 2019. Reliability and validity of a new classification of MIH based on severity. *Clin Oral Investig*.

CASANOVA-ROSADO, A. J., MEDINA-SOLIS, C. E., CASANOVA-ROSADO, J. F., VALLEJOS-SANCHEZ, A. A., MARTINEZ-MIER, E. A., LOYOLA-RODRIGUEZ, J. P., ISLAS-MARQUEZ, A. J. & MAUPOME, G. 2011. Association between developmental enamel defects in the primary and permanent dentitions. *Eur J Paediatr Dent,* 12**,** 155-8.

CASTRO, K. S., FERREIRA, A. C., DUARTE, R. M., SAMPAIO, F. C. & MEIRELES, S. S. 2014. Acceptability, efficacy and safety of two treatment protocols for dental fluorosis: a randomized clinical trial. *J Dent,* 42**,** 938-44.

CASTRO, R. A. L., PORTELA, M. C., LEAO, A. T. & DE VASCONCELLOS, M. T. 2011. Oral health-related quality of life of 11- and 12-year-old public school children in Rio de Janeiro. *Community Dent Oral Epidemiol,* 39**,** 336-44.

CHAN, Y. L., NGAN, A. H. W. & KING, N. M. 2010. Degraded prism sheaths in the transition region of hypomineralized teeth. *Journal of Dentistry,* 38**,** 237-244.

CHAWLA, N., MESSER, L. B. & SILVA, M. 2008. Clinical Studies on Molar-Incisor-Hypomineralisation Part 2: Development of a Severity Index. *Eur Arch Paediatr Dent,* 9**,** 191-199.

CHAY, P. L., MANTON, D. J. & PALAMARA, J. E. A. 2014. The effect of resin infiltration and oxidative pre-treatment on microshear bond strength of resin composite to hypomineralised enamel. *International Journal of Paediatric Dentistry,* 24**,** 252-267.

CHO, S.-Y., KI, Y. & CHU, V. 2008. Molar incisor hypomineralization in Hong Kong Chinese children. *International Journal of Paediatric Dentistry,* 18**,** 348-352.

CLARKSON, J. & O'MULLANE, D. 1989. A Modified DDE Index for Use in Epidemiological Studies of Enamel Defects. *Journal of Dental Research,* 68**,** 445-450.

CORREA-FARIA, P., MARTINS-JUNIOR, P. A., VIEIRA-ANDRADE, R. G., OLIVEIRA-FERREIRA, F., MARQUES, L. S. & RAMOS-JORGE, M. L. 2013. Developmental defects of enamel in primary teeth: prevalence and associated factors. *International Journal of Paediatric Dentistry,* 23**,** 173-179.

CORREA-FARIA, P., PAIXAO-GONCALVES, S., PAIVA, S. M., MARTINS-JUNIOR, P. A., VIEIRA-ANDRADE, R. G., MARQUES, L. S. & RAMOS-JORGE, M. L. 2016. Dental caries, but not malocclusion or developmental defects, negatively impacts preschoolers' quality of life. *Int J Paediatr Dent,* 26**,** 211-9.

CRAIG, S. A., BAKER, S. R. & RODD, H. D. 2015. How do children view other children who have visible enamel defects? *International Journal of Paediatric Dentistry,* 25**,** 399-408.

CRAWFORD, P. J. M., ALDRED, M. & BLOCH-ZUPAN, A. 2007. Amelogenesis Imperfecta. *Orphanet Journal of Rare Diseases,* 2**,** 17-28.

CROLL, T. & HELPIN, M. L. 2000. Enamel microabrasion: a new approach. *J Esthet Dent* 12**,** 64-71.

CROMBIE, F., MANTON, D. & KILPATRICK, N. 2009. Aetiology of molar–incisor hypomineralization: a critical review. *International Journal of Paediatric Dentistry* 19**,** 73-83.

CROMBIE, F., MANTON, D., PALAMARA, J. & REYNOLDS, E. 2014. Resin infiltration of developmentally hypomineralised enamel. *International Journal of Paediatric Dentistry* 24**,** 51-55.
CROMBIE, F. A., MANTON, D. J., PALAMARA, J. E. A., ZALIZNIAK, I., COCHRANE, N. J. & C., R. E. 2013. Characterisation of developmentally hypomineralised human enamel. *Journal of Dentistry,* 41**,** 611-618.
DA COSTA-SILVA, C. M., AMBROSANO, G. M. B., JEREMIAS, F., DE SOUZA, J. F. & MIALHE, F. L. 2011. Increase in severity of molar–incisor hypomineralization and its relationship with the colour of enamel opacity: a prospective cohort study. *International Journal of Paediatric Dentistry,* 21**,** 333-341.
DA COSTA-SILVA, C. M., JEREMIAS, F., DE SOUZA, J. F., CORDEIRO, R. D. C. L., SANTOS-PINTO, L. & ZUANON, A. C. C. 2010. Molar incisor hypomineralization: prevalence, severity and clinical consequences in Brazilian children. *International Journal of Paediatric Dentistry,* 20**,** 426-434.
DA CUNHA COELHO, A. S. E., MATA, P. C. M., LINO, C. A., MACHO, V. M. P., AREIAS, C., NORTON, A. & AUGUSTO, A. 2019. Dental hypomineralization treatment: A systematic review. *J Esthet Restor Dent,* 31**,** 26-39.
DANTAS-NETA, N. B., MOURA, L. F., CRUZ, P. F., MOURA, M. S., PAIVA, S. M., MARTINS, C. C. & LIMA, M. D. 2016. Impact of molar-incisor hypomineralization on oral health-related quality of life in schoolchildren. *Braz Oral Res,* 30**,** e117.
DE CHAVEZ, A. C., BACKETT-MILBURN, K., PARRY, O. & PLATT, S. 2005. Understanding and researching wellbeing Its usage in different disciplines and potential for health research and health promotion. *Health Education Journal* 64**,** 70-78.
DE SOUZA, J. F., FRAGELLI, C. M. B., RESTREPO, M., MUSHASHE, A. M., LOSSO, E. M. & DA CUNHA, L. F. 2014. Aesthetic management of molar-incisor hypomineralization. *RSBO,* 11**,** 204-208.
DENIS, M., ATLAN, A., VENNAT, E., TIRLET, G. & ATTAL, J. P. 2013. White defects on enamel: diagnosis and anatomopathology: two essential factors for proper treatment (part 1). *Int Orthod,* 11**,** 139-65.
DIETRICH, G., SPERLING, S. & HETZER, G. 2003. Molar incisor hypomineralisation in a group of children and adolescents living in Dresden (Germany). *European Journal of Paediatric Dentistry,* 4**,** 133-137.
ELCOCK, C., LATH, D. L., LUTY, J. D., GALLAGHER, M. G., ABDELLATIF, A., BACKMAN, B. & BROOK, A. H. 2006. The new Enamel Defects Index: testing and expansion. *Eur J Oral Sci* 114**,** 35-38.
ELFRINK, M. E. C. 2012. *Deciduous Molar Hypomineralisation, its nature and nurture.* PhD, University
of Amsterdam and VU University Amsterdam, the Netherlands.
ELFRINK, M. E. C., GHANIM, A., MANTON, D. J. & WEERHEIJM, K. L. 2015. Standardised studies on Molar Incisor Hypomineralisation (MIH) and Hypomineralised Second Primary Molars (HSPM): a need. *Eur Arch Paediatr Dent,* 16**,** 247-225.
ELFRINK, M. E. C., MOLL, H. A., KIEFTE-DE JONG, J. C., EL MARROUN, H., JADDOE, V. W. V., HOFMAN, A., STRICKER, B. H., TEN CATE, J. M. & VEERKAMP, J. S. J.

2013a. Is Maternal Use of Medicines during Pregnancy Associated with Deciduous Molar Hypomineralisation in the Offspring? A Prospective, Population-Based Study. *Drug Saf* 36**,** 627-233.
ELFRINK, M. E. C., MOLL, H. A., KIEFTE-DE JONG, J. C., JADDOE, V. W. V., HOFMAN, A., TEN CATE, J. M. & VEERKAMP, J. S. J. 2014. Pre- and Postnatal Determinants of Deciduous Molar Hypomineralisation in 6-Year-Old Children. The Generation R Study. *PLOS ONE* 9**,** 1-8.
ELFRINK, M. E. C., SCHULLER, A. A., VEERKAMP, J. S. J., POORTERMAN, J. H. G., MOLL, H. A. & TEN CATE, B. J. M. 2010. Factors increasing the caries risk of second primary molars in 5-year-old Dutch children. *International Journal of Paediatric Dentistry,* 20**,** 151-157.
ELFRINK, M. E. C., TEN CATE, J. M., VAN RUIJVEN, L. J. & VEERKAMP, J. S. J. 2013b. Mineral content in teeth with Deciduous Molar Hypomineralisation (DMH). *Journal of Dentistry,* 41**,** 974-978.
ELHENNAWY, K., MANTON, D. J., CROMBIE, F., ZASLANSKY, P., RADLANSKI, R. J., JOST-BRINKMANN, P. G. & SCHWENDICKE, F. 2017. Structural, mechanical and chemical evaluation of molar-incisor hypomineralization-affected enamel: A systematic review. *Arch Oral Biol,* 83**,** 272-281.
ENGEL, G. L. 1997. From Biomedical to Biopsychosocial Being Scientific *in the Human Domain Psychosomatics* 38**,** 521-528.
ESTAI, M., KANAGASINGAM, Y., TENNANT, M. & BUNT, S. 2018. A systematic review of the research evidence for the benefits of teledentistry. *J Telemed Telecare,* 24**,** 147-156.
FAGRELL, T. G., DIETZ, W., JALEVIK, B. & NOREN, J. G. 2010. Chemical, mechanical and morphological properties of hypomineralized enamel of permanent first molars. *Acta Odontologica Scandinavica,* 68**,** 215-222.
FAGRELL, T. G., LUDVIGSSON, J., ULLBRO, C., LUNDIN, S.-A. & KOCH, G. 2011. Aetiology of severe demarcated enamel opacities an evaluation based on prospective medical and social data from 17000 children. *Swed Dent J* 35**,** 57-67.
FARAH, R., DRUMMOND, B., SWAIN, M. & WILLIAMS, S. 2010a. Linking the clinical presentation of molar-incisor hypomineralisation to its mineral density. *International Journal of Paediatric Dentistry* 20**,** 353-360.
FARAH, R., MONK, B., SWAIN, M. & DRUMMOND, B. 2010b. Protein content of molar–incisor hypomineralisation enamel. *Journal of Dentistry,* 38**,** 591-596.
FARAH, R., SWAIN, M., DRUMMOND, B., COOK, R. & ATIEH, M. 2010c. Mineral density of hypomineralised enamel *Journal of Dentistry,* 38**,** 50-58.
FEARNE, J., ANDERSON, P. & DAVIS, G. R. 2004. 3D X-ray microscopic study of the extent of variations in enamel density in first permanent molars with idiopathic enamel hypomineralisation. *British Dental Journal,* 196**,** 634-638.
FENG, X. P., NEWTON, J. T. & ROBINSON, P. G. 2001. The impact of dental appearance on perceptions of personal characteristics among Chinese people in the United Kingdom. *Int Dent J* 51**,** 282-286.
FOLAYAN, M. O., CHUKWUMAH, N. M., POPOOLA, B. O., TEMILOLA, D. O., ONYEJAKA, N. K., OYEDELE, T. A. & LAWAL, F. B. 2018. Developmental defects of the

enamel and its impact on the oral health quality of life of children resident in Southwest Nigeria. *BMC Oral Health,* 18**,** 160.
FOSTER PAGE, L. A., THOMSON, W. M., JOKOVIC, A. & LOCKER, D. 2005. Validation of the Child Perceptions Questionnaire (CPQ11-14). *Journal of Dental Research,* 84**,** 649-652.
FRAGOSO, L. S. M., LIMA, D. A. N. L., DE ALEXANDRE, R. S., BERTOLDO, C. E. S., AGUIAR, F. H. B. & LOVADINO, J. R. 2011. Evaluation of physical properties of enamel after microabrasion, polishing, and storage in artificial saliva. *Biomed. Mater,* 6**,** 1-6.
GACEK, M., PILECKA, W. & FUSIŃSKA-KORPIK, A. 2014. Psychometric Properties of Self-Perception Profile for Children in a Polish sample. *Polish Journal of Psychology,* 12**,** 85-104.
GARCIA-MARGARIT, M., CATALA-PIZARRO, M., MONTIEL-COMPANY, J. M. & ALMERICH-SILLA, J. M. 2014. Epidemiologic study of molar-incisor hypomineralization in 8-year-old Spanish children. *International Journal of Paediatric Dentistry* 24**,** 14-22.
GAROT, E., MANTON, D. & ROUAS, P. 2016. Peripartum events and molar-incisor hypomineralisation (MIH) amongst young patients in southwest France. *Eur Arch Paediatr Dent,* 17**,** 245-250.
GCP, N. 2016. Good Clinical Practice (GCP) Reference Guide. August 2016 ed. NIHR Clinical Research Network Coordinating Centre, 21 Queen Street, Leeds LS1 2TW: ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Secretariat, c/o IFPMA, 15 chemin Louis-Dunant, PO Box 195, 1211 Geneva 20, Switzerland.
GDC. 2016. *Position Statement on Tooth Whitening* [Online]. [Accessed 15/10/18 2018].
GENDERSON, M. W., SISCHO, L., MARKOWITZ, K., FINE, D. & BRODER, H. L. 2013a. An Overview of Children's Oral Health-Related Quality of Life Assessment: From Scale Development to Measuring Outcomes. *Caries Res* 47**,** 13-21.
GENDERSON, M. W., ·, SISCHO, L., ·, MARKOWITZ, K., ·, FINE, D., · & BRODER, H. L. 2013b. An Overview of Children's Oral Health-Related Quality of Life Assessment: From Scale Development to Measuring Outcomes. *Caries Res* 47**,** 13-21.
GHAEMI, S. N. 2009. The rise and fall of the biopsychosocial model *The British Journal of Psychiatry (2009)*
195, 3–4., 195**,** 3-4.
GHANIM, A., ELFRINK, M., WEERHEIJM, K., MARINO, R. & MANTON, D. 2015. A practical method for use in epidemiological studies on enamel hypomineralisation. *Eur Arch Paediatr Dent,* 16**,** 235-246.
GHANIM, A., MANTON, D., BAILEY, D., MARINO, R. & MORGAN, M. 2013a. Risk factors in the occurrence of molar–incisor hypomineralization amongst a group of Iraqi children. *International Journal of Paediatric Dentistry* 23**,** 197-206.

GHANIM, A., MANTON, D., MARINO, R., MORGAN, M. & BAILEY, D. 2013b. Prevalence of demarcated hypomineralisation defects in second primary molars in Iraqi children. *International Journal of Paediatric Dentistry,* 23**,** 48-55.
GHANIM, A., MARINO, R. & MANTON, D. J. 2018. Validity and reproducibility testing of the Molar Incisor Hypomineralisation (MIH) Index. *Int J Paediatr Dent*.
GHANIM, A., MARINO, R. & MANTON, D. J. 2019. Validity and reproducibility testing of the Molar Incisor Hypomineralisation (MIH) Index. *Int J Paediatr Dent*.
GHANIM, A. M., MORGAN, M. V., MARINO, R. J., BAILEY, D. L. & MANTON, D. J. 2012. Risk factors of hypomineralised second primary molars in a group of Iraqi schoolchildren. *European Archives of Paediatric Dentistry,* 13**,** 111-118.
GHERUNPONG, S., TSAKOS, G. & SHEIHAM, A. 2004a. Developing and evaluating an oral health-related quality of life index for children; The CHILD-OIDP. *Community Dental Health,* 21**,** 161-169.
GHERUNPONG, S., TSAKOS, G. & SHEIHAM, A. 2004b. The prevalence and severity of oral impacts on daily performances in Thai primary school children. *Health Qual Life Outcomes,* 2**,** 57.
GILCHRIST, F., RODD, H., DEERY, C. & MARSHMAN, Z. 2014. Assessment of the quality of measures of child oral health-related quality of life. *BMC Oral Health,* 14**,** 1-17.
GILCHRIST, F., RODD, H. D., DEERY, C. & MARSHMAN, Z. 2018. Development and evaluation of CARIES-QC: a caries-specific measure of quality of life for children. *BMC Oral Health,* 18**,** 202.
GIRO, C. 1945. Enamel Hypoplasia and Its Probable Relation to Oral Disease. *American Journal of Orthodontics and Oral Surgery,* 31**,** 327-332.
GOV.UK 2011. Ethnicity Facts and Figures. England and Wales.
GRZYWACZ, I. 2003. The value of the aesthetic component of the Index of Orthodontic Treatment Need in the assessment of subjective orthodontic treatment need. *The European Journal of Orthodontics,* 25**,** 57-63.
GUPTA, E., ROBINSON, P. G., MARYA, C. M. & BAKER, S. R. 2015. Oral Health Inequalities: Relationships between Environmental and Individual Factors. *Journal of Dental Research,* 94**,** 1362-1368.
GURURATANA, O., BAKER, S. R. & ROBINSON, P. G. 2014. Determinants of children's oral-health-related quality of life over time. *Community Dent Oral Epidemiol* 42**,** 206-215.
HALL-SCULLIN, E., WHITEHEAD, H., MILSOM, K., TICKLE, M., SU, T. L. & WALSH, T. 2017. Longitudinal Study of Caries Development from Childhood to Adolescence. *J Dent Res,* 96**,** 762-767.
HAMMAD, S. M., EL BANNA, M., EL ZAYAT, I. & MOHSEN, M. A. 2012. Effect of resin infiltration on white spot lesions after debonding orthodontic brackets. *Am J Dent,* 25**,** 3-8.
HARIRI, I., SADR, A., NAKASHIMA, S., SHIMADA, Y., TAGAMI, J. & SUMI, Y. 2013. Estimation of the enamel and dentin mineral content from the refractive index. *Caries Research,* 47**,** 18-26.
HARTER, S. 1985. *Manual for the Self-Perception Profile for Children,* Denver: University of Denver.

HARTER, S. 1993. *Self- esteem: the puzzle of low self-regard*, New York: Plenum.
HARTER, S. 2012. *Self-Perception Profile for Children:Manual and Questionnaires (Grades 3-8)(Revision of the Self Perception Profile for Children, 1985),* Department of Psychology, Arts, Humanities, and Social Studies, University of Denver.
HOLAN, G., TOPF, J. & FUKS, A. B. 1992. Effect of root canal infection and treatment of traumatized primary incisors on their permanent successors. *Endodontics & Dental Traumatology,* 8**,** 12-15.
HRA, N. 2017. *UK Policy Framework for Health and Social Care Research UK Policy Framework for Health and Social Care Research* [Online]. NHS Health Research Authority. Available: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/ [Accessed 15/10/18 2018].
HU, J. C.-C., CHUN, Y.-H. P., AL HAZZAZZI, T. & SIMMER, J. P. 2007. Enamel Formation and Amelogenesis Imperfecta. *Cells Tissues Organs,* 186**,** 78-85.
HU, L.-T. & BENTLER, P. M. 1999. Cutoff criteria for fit indexes in covariance structure analysis : Conventional criteria versus new alternatives. *Structural Equation Modeling,* 6**,** 1-55.
HUBER, M., KNOTTNERUS, J. A., GREEN, L., VAN DER HORST, H., JADAD, A. R., KROMHOUT, D., LEONARD, B., LORIG, K., LOUREIRO, M. I., VAN DER MEER, J. W. M., SCHNABEL, P., SMITH, R., VAN WEEL , C. & SMID, H. 2011. How should we define health? *British Medical Journal,* 343**,** 1-13.
HUNT, O., HEPPER, P., JOHNSTON, C., STEVENSON, M. & BURDEN, D. 2002. The Aesthetic Component of the Index of Orthodontic Treatment Need validated against lay opinion. *The European Journal of Orthodontics,* 24**,** 53-59.
JAEKEN, K., CADENAS DE LLANO-PERULA, M., LEMIERE, J., VERDONCK, A., FIEUWS, S. & WILLEMS, G. 2018. Reported changes in oral health-related quality of life in children and adolescents before, during, and after orthodontic treatment: a longitudinal study. *Eur J Orthod*.
JALEVIK, B. 2010. Prevalence and diagnosis of molar-incisor-hypomineralisation : a systematic review. *European Archives of Paediatric Dentistry,* 11**,** 59-64.
JALEVIK, B., DIETZ, W. & NOREN, J. G. 2005. Scanning electron micrograph analysis of hypomineralized enamel in permanent first molars. *International Journal of Paediatric Dentistry,* 15**,** 233-240.
JALEVIK, B. & KLINGBERG, G. 2012. Treatment outcomes and dental anxiety in 18-year-olds with MIH, comparisons with healthy controls – a longitudinal study. *International Journal of Paediatric Dentistry* 22**,** 85-91.
JALEVIK, B. & KLINGBERG, G. A. 2002. Dental treatment, dental fear and behaviour management problems in children with severe enamel hypomineralization of their permanent first molars. *International Journal of Paediatric Dentistry,* 12**,** 24-32.
JALEVIK, B. & NOREN, J. G. 2000. Enamel hypomineralization of permanent first molars: a morphological study and survey of possible aetiological factors. *International Journal of Paediatric Dentistry,* 10**,** 278-289.

JALEVIK, B., NOREN, J. G., KLINGBERG, G. & BARREGARD, L. 2001a. Etiologic factors influencing the prevalence of demarcated opacities in permanent first molars in a group of Swedish children. *Eur J Oral Sci* 109**,** 230-234.
JALEVIK, B., ODELIUS, H., DIETZ, W. & NORÉN, J. G. 2001b. Secondary ion mass spectrometry and X-ray microanalysis of hypomineralized enamel in human permanent first molars. *Archives of Oral Biology,* 46**,** 239-247.
JANKOVIC, S., IVANOVIC, M., DAVIDOVIC, B. & LECIC, J. 2013. Aetiological Factors of Molar Incisor Hypomineralization. *Serbian Dental Journal,* 60**,** 69-75.
JASULAITYTE, L., VEERKAMP, J. S. & WEERHEIJM, K. L. 2007. Molar incisor hypomineralisation : a review and prevalence data from the study of primary school children in Kaunas/Lithguania. *European Archives of Paediatric Dentistry,* 8**,** 87-94.
JEDEON, K., DE LA DURE-MOLLA, M., BROOKES, S. J., LOIODICE, S., MARCIANO, C., KIRKHAM, J., CANIVENC-LAVIER, M.-C., BOUDALIA, S., BERGÈS, R., HARADA, H., BERDAL, A. & BABAJKO, S. 2013. Enamel Defects Reflect Perinatal Exposure to Bisphenol A. *The American Journal of Pathology,* 183**,** 108-118.
JEREMIAS, F., KORUYUCU, M., KUCHLER, E. C., BAYRAM, M., TUNA, E. B., DEELEY, K., PIERRIA, R. A., SOUZA, J. F., FRAGELLI, C. M. B., PASCHOAL, M. A. B., GENCAY, K., SEYMEN, F., CAMINAGA, R. M. S., DOS SANTOS-PINTO, L. & VIEIRA, A. R. 2013a. Characterisation of developmentally hypomineralised human enamel. *Archives of Oral Biology,* 58**,** 1434-1442.
JEREMIAS, F., KORUYUCU, M., KUCHLER, E. R., BAYRAM, M., TUNA, E. B., DEELEY, K., PIERRI, R. A., SOUZA, J. F., FRAGELLI, M. B. C., PASCHOAL, A. B. M., GENCAY, K., SEYMEN, F., CAMINAGA, R. M. S., DOS SANTOS-PINTO, L. & VIEIRA, A. R. 2013b. Genes expressed in dental enamel development are associated with molar-incisor hypomineralization. *Archives of Oral Biology,* 58**,** 1434-1442.
JI, M., XIAO, L., XU, L., HUANG, S. & ZHANG, D. 2018. How pH is regulated during amelogenesis in dental fluorosis. *Exp Ther Med,* 16**,** 3759-3765.
JOKOVIC, A., LOCKER, D. & GUYATT, G. 2006. Short forms of the Child Perceptions Questionnaire for 11–14-year-old children (CPQ11–14): Development and initial evaluation. *Health and Quality of Life Outcomes,* 4**,** 1-9.
JOKOVIC, A., LOCKER, D., STEPHENS, M., KENNY, D., TOMPSON, B. & GUYATT, G. 2002. Validity and Reliability of a Questionnaire for Measuring Child Oral-health-related Quality of Life. *J Dent Res,* 81**,** 459-463.
JOKOVIC, A., LOCKER, D., TOMPSON, B. & GUYATT, G. 2004. Questionnaire for Measuring Oral Health-related Quality of Life in Eight- to Ten-year-old Children *Pediatr Dent,* 26**,** 512-518.
JUNIOR, D. F. D. P., SANTOS, N. C. M., DA SILVA, E. T., NUNES, M. D. F. & LELES, C. R. 2009. Psychosocial Impact of Dental Esthetics on Quality of Life in Adolescents Association with Malocclusion, Self-Image, and Oral Health–Related Issues. *Angle Orthodontist,* 79**,** 1188-1193.
JÄLEVIK, B., KLINGBERG, G., BARREGÅRD, L. & NORÉN, J. G. 2001. The prevalence of demarcated opacities in permanent first molars in a group of Swedish children. *Acta odontologica Scandinavica,* 59**,** 255-260.

KAPLOVA, E., TOMANKOVA, K., KOLAROVA, H. & KREJCI, P. 2012. Study of developmental enamel defects of permanent teeth by atomic force microscopy. *Current Microscopy Contributions to Advances in Science and Technology*, 555-560.
KELLEHER, M. G. D. & ROE, F. J. C. 1999. The safety-in-use of 10% carbamide peroxide (Opalescence) for bleaching teeth under the supervision of a dentist. *British Dental Journal,* 187, 190-194.
KIDD, E. A. M. & FEJERSKOV, O. 2004. What Constitutes Dental Caries? Histopathology of Carious Enamel and Dentin Related to the Action of Cariogenic Biofilms. *J Dent Res* 83, C35-C38.
KIM, S., KIM, E.-Y., JEONG, T.-S. & KIM, J.-W. 2011a. The evaluation of resin infiltration for masking labial enamel white spot lesions. *International Journal of Paediatric Dentistry* 21, 241-248.
KIM, S., KIM, E. Y., JEONG, T. S. & KIM, J. W. 2011b. The evaluation of resin infiltration for masking labial enamel white spot lesions. *Int J Paediatr Dent,* 21, 241-8.
KLINE, R. B. 2011. *Principle and Practice of Structural Equation Modeling,* New York, The Guilford Press.
KNAPP, R., GILCHRIST, F., RODD, H. D. & MARSHMAN, Z. 2017. Change in children's oral health-related quality of life following dental treatment under general anaesthesia for the management of dental caries: a systematic review. *Int J Paediatr Dent,* 27, 302-312.
KNOSEL, M., ECKSTEIN, A. & HELMS, H.-J. 2013. Durability of esthetic improvement following Icon resin infiltration of multibracket-induced white spot lesions compared with no therapy over 6 months: A single-center, split-mouth, randomized clinical trial. *Am J Orthod Dentofacial Orthop* 144, 86-96.
KO, C. C., TANTBIROJN, D., WANG, T. & DOUGLAS, W. H. 2000. Optical Scattering Power for Characterization of Mineral Loss. *Journal of Dental Research,* 79, 1584-1589.
KOCH, G., HALLONSTEN, A.-L., LUDVIGSSON, N. & HANSSON, B. O. 1987. Epidemiologic study of idiopathic enamel hypomineralization in permanent teeth of Swedish children. *Community Dentistry and Oral Epidemiology,* 15, 279-285.
KOK, Y. V., MAGESON, P., HARRADINE, N. W. T. & SPROD, A. J. 2004. Comparing a quality of life measure and the Aesthetic Component of the Index of Orthodontic Treatment Need (IOTN) in assessing orthodontic treatment need and concern. *Journal of Orthodontics,* 31, 312-318.
KOSMA, I., KEVREKIDOU, A., BOKA, V., ARAPOSTATHIS, K. & KOTSANOS, N. 2016. Molar incisor hypomineralisation (MIH): correlation with dental caries and dental fear. *Eur Arch Paediatr Dent* 17, 123-129.
KOTSANOS, N., KAKLAMANOS, E. G. & ARAPOSTATHIS, K. 2005. Treatment management of first permanent molars in children with Molar-Incisor Hypomineralisation *European Journal of Paediatric Dentistry,* 4, 179-184.
KRAGT, L., TIEMEIER, H., WOLVIUS, E. B. & ONGKOSUWITO, E. M. 2016. Measuring oral health-related quality of life in orthodontic patients with a short version

of the Child Oral Health Impact Profile (COHIP). *Journal of Public Health Dentistry,* 76**,** 105-112.
KRAGT, L., WOLVIUS, E. B., RAAT, H., JADDOE, V. W. V. & ONGKOSUWITO, E. M. 2017. Social inequalities in children's oral health-related quality of life: the Generation R Study. *Qual Life Res,* 26**,** 3429-3437.
KRAMER, N., BUI KHAC, N. N., LUCKER, S., STACHNISS, V. & FRANKENBERGER, R. 2018. Bonding strategies for MIH-affected enamel and dentin. *Dent Mater,* 34**,** 331-340.
KRAMER, P. F., FELDENS, C. A., FERREIRA, S. H., BERVIAN, J., RODRIGUES, P. H. & PERES, M. A. 2013. Exploring the impact of oral diseases and disorders on quality of life of preschool children. *Community Dent Oral Epidemiol,* 41**,** 327-35.
KRISDAPONG, S., PRASERTSOM, P., RATTANARANGSIMA, K. & SHEIHAM, A. 2012. Relationships between oral diseases and impacts on Thai schoolchildren's quality of life: evidence from a Thai national oral health survey of 12- and 15-year-olds. *Community Dent Oral Epidemiol,* 40**,** 550-9.
KÜHNISCH, J., KABARY, L., MALYK, Y., ROTHMAIER, K., METZ, I., HICKEL, R., HEINRICH, J., MANTON, D. & STANDL, M. 2018. Relationship between caries experience and demarcated hypomineralised lesions (including MIH) in the permanent dentition of 15-year-olds. *Clin Oral Investig,* 22**,** 2013-2019.
LAISI, S., ESS, A., SAHLBERG, C., ARVIO, P., LUKINMAA, P.-L. & ALALUUSUA, S. 2009. Amoxicillin May Cause Molar Incisor Hypomineralization. *J Dent Res,* 88**,** 132-136.
LAISI, S., KIVIRANTA, H., LUKINMAA, P.-L., VARTIAINEN, T. & ALALUUSUA, S. 2008. Molar-Incisor-Hypomineralisation and Dioxins: New Findings. *European Archives of Paediatric Dentistry* 9**,** 224-227.
LARGE, J. F., HASMUN, N., LAWSON, J. A., ELCOCK, C., VETTORE, M. V. & RODD, H. D. 2019. What children say and clinicians hear: accounts relating to incisor hypomineralisation of cosmetic concern. *Eur Arch Paediatr Dent*.
LEAL, S. C., OLIVEIRA, T. R. & RIBEIRO, A. P. 2016. Do parents and children perceive molar-incisor hypomineralization as an oral health problem? *Int J Paediatr Dent***,** 1-8.
LEAL, S. C., OLIVEIRA, T. R. M. & RIBEIRO, A. P. D. 2017. Do parents and children perceive molar-incisor hypomineralization as an oral health problem? *Int J Paediatr Dent,* 27**,** 372-379.
LEE, H.-S., KIM, S.-H., KIM, S.-O., LEE, J.-H., CHOI, H.-J., JUNG, H.-S. & SONG, J. S. 2014. A new type of dental anomaly: molar-incisor malformation (MIM). *Oral and Maxillofacial Pathology* 118**,** 101.
LEE, J.-H., KIM, D.-G., PARK, C.-J. & CHO, L.-R. 2013. Minimally invasive treatment for aesthetic enhancement of white spot lesion in adjacent tooth. *J Adv Prosthodont* 5**,** 359-363.
LEPPANIEMI, A., LUKINMAA, P.-L. & ALALUUSUA, S. 2001. Nonfluoride Hypomineralizations in the Permanent First Molars and Their Impact on the Treatment Need. *Caries Res* 35**,** 36-40.

LEVY, S. M. 2003. An Update on Fluorides and Fluorosis. *J Can Dent Assoc,* 69**,** 286-291.
LI, C., XIA, B., WANG, Y., GUAN, X., YUAN, J. & GE, L. 2014. Translation and psychometric properties of the Chinese (Mandarin) version of the Child Oral Health Impact Profile-Short Form 19 (COHIP-SF 19) for school-age children. *Health and Quality of Life Outcomes* 12**,** 1-8.
LI, Y., NAVIA, J. M. & BIAN, J.-Y. 1995. Prevalence and distribution of developmental enamel defects in primary dentition of Chinese children 3–5 years old. *Community Dentistry and Oral Epidemiology,* 23**,** 72-79.
LO, E. C. M., ZHENG, C. G. & KING, N. M. 2003. Relationship between the Presence of Demarcated Opacities and Hypoplasia in Permanent Teeth and Caries in Their Primary Predecessors. *Caries research,* 37**,** 456-461.
LOCKER, D. & ALLEN, F. 2007. What do measures of 'oral health-related quality of life' measure? *Community Dent Oral Epidemiol* 35**,** 401-411.
LUNARDELLI, S. E. & PERES, M. A. 2006. Breast-feeding and Other Mother-Child Factors Associated With Developmental Enamel Defects in the Primary Teeth of Brazilian Children. *Journal of dentistry for children (Chicago, Ill.),* 73**,** 70-78.
LYGIDAKIS, N. A. 2010. Treatment modalities in children with teeth affected by molar-incisor enamel hypomineralisation (MIH): A systematic review. *European Archives of Paediatric Dentistry,* 11**,** 65-74.
LYGIDAKIS, N. A., DIMOU, G. & BRISENIOU, E. 2008. Molar-Incisor-Hypomineralisation (MIH). Retrospective clinical study in Greek children.I. Prevalence and defect characteristics. *European Archives of Paediatric Dentistry* 9**,** 200-206.
LYGIDAKIS, N. A., WONG, F., JALEVIK, B., VIERROU, A.-M., ALALUUSUA, S. & ESPELID, I. 2010. Best Clinical Practice Guidance for clinicians dealing with children presenting with Molar-Incisor Hypomineralisation (MIH) An EAPD Policy Document. *European Archives of Paediatric Dentistry* 11**,** 75-81.
MAHONEY, E. K., ROHANIZADEH, R., ISMAIL, F. S. M., KILPATRICK, N. M. & SWAIN, M. V. 2004. Mechanical properties and microstructure of hypomineralised enamel of permanent teeth. *Biomaterials* 25**,** 5091-5100.
MARSHMAN, Z., GIBSON, B. & ROBINSON, P. G. 2009. The impact of developmental defects of enamel on young people in the UK. *Community Dent Oral Epidemiol,* 37**,** 45-57.
MARSHMAN, Z., GIBSON, B. J. & BENSON, P. E. 2010. Is the short-form child perceptions questionnaire meaningful and relevant to children with malocclusion in the UK? *Journal of Orthodontics,* 37**,** 29-36.
MARSHMAN, Z., GUPTA, E., BAKER, S. R., ROBINSON, P. G., OWENS, J., RODD, H. D., BENSON, P. E. & GIBSON, B. 2015. Seen and heard: towards child participation in dental research. *International Journal of Paediatric Dentistry* 25**,** 375-382.
MARSHMAN, Z. & ROBINSON, P. G. 2007. Child and Adolescent Oral Health-Related Quality of Life. *Semin Orthod,* 13**,** 88-95.
MARTINEZ-MIER, E. A., SOTO-ROJAS, A. E., MAUPOME, G. & STOOKEY, G. K. 2004. Development of questionnaire to measure perception of, and concerns derived from, dental fluorosis. *Community Dental Health,* 21**,** 299-305.

MARTINS, C. C., LIMA-ARSATI, Y. B. & PAIVA, S. M. 2009. Mothers' perception of dental aesthetics in their children. A study in two fluoridated communities. *Revista odonto ciência,* 24**,** 236-239.
MARTINS-JUNIOR, P. A., MARQUES, L. S. & RAMOS-JORGE, M. L. 2012. Malocclusion: social, functional and emotional influence on children. *J Clin Pediatr Dent,* 37**,** 103-8.
MARTINS-JÚNIOR, P. A., MARQUES, M., RAMOS-JORGE, L. S. & OLIVEIRA, M. L. 2012. Untreated dental caries: impact on the quality of life of children of low socioeconomic status. *Pediatric Dentistry,* 34**,** E49-E52.
MASTROBERARDINO, S., CAMPUS, G., STROHMENGER, L., VILLA, A. & CAGETTI, M. G. 2012. An Innovative Approach to Treat Incisors Hypomineralization (MIH): A Combined Use of Casein Phosphopeptide-Amorphous Calcium Phosphate and Hydrogen Peroxide—A Case Report. *Case Reports in Dentistry,* 2012**,** 1-5.
MATIS, B. A., WANG, G., MATIS, J. I., COOK, N. B. & ECKERT, G. J. 2015. White diet: is it necessary during tooth whitening? *Oper Dent,* 40**,** 235-40.
MCGRADY, M. G., ELLWOOD, R. P., GOODWIN, M. & BOOTHMAN, N. 2012. Adolescents' perceptions of the aesthetic impact of dental fluorosis vs. other dental conditions in areas with and without water fluoridation. *BMC oral health,* 12**,** 4.
MCGRATH, C., BRODER, H. & WILSON-GENDERSON, M. 2004. Assessing the impact of oral health on the life quality of children: implications for research and practice. *Community Dent Oral Epidemiol,* 32**,** 81-85.
MCKNIGHT, C. B., LEVY, S. M., COOPER, S. E., JAKOBSEN, J. R. & WARREN, J. J. 1999. A Pilot Study of Dental Students' Esthetic Perceptions of Computer-generated Mild Dental Fluorosis Compared to Other Conditions. *Journal of Public Health Dentistry,* 59**,** 18-23.
MEJÀRE, I., BERGMAN, E. & GINDERFJORD, M. 2005. Hypomineralized molars and incisors of unknown origin: treatment outcome at age 18 years. *International Journal of Paediatric Dentistry* 15**,** 20-28.
MERDAD, L. & EL-HOUSSEINY, A. A. 2017. Do children's previous dental experience and fear affect their perceived oral health-related quality of life (OHRQoL)? *BMC Oral Health,* 17**,** 47.
MEYER-LUECKEL, H. & PARIS, S. 2010. Infiltration of Natural Caries Lesions with Experimental Resins Differing in Penetration Coefficients and Ethanol Addition. *Caries Res,* 44**,** 408-414.
MORADIAN-OLDAK, J. 2013. Protein- mediated enamel mineralization. *Front Biosci,* 17**,** 1996-2023.
MURATBEGOVIC, A., MARKOVIC, N. & SELIMOVIC, M. G. 2007. Molar incisor hypomineralisation in Bosnia and Herzegovina: prevalence, aetiology and clinical consequences in medium caries activity population. *European Archives of Paediatric Dentistry,* 8**,** 189-194.
MURIS, P., MEESTERS, C. & FIJEN, P. 2003. The Self-Perception Profile for Children: further evidence for its factor structure, reliability, and validity. *Personality and Individual Differences* 35**,** 1791-1802.

MURPHY, T. C., WILLMOT, D. R. & RODD, H. D. 2007. Management of post orthodontic demineralized white lesions with micro abrasion: A quantitative assessment. *Am J Orthod Dentofacial Orthop,* 131**,** 27-33.
MURRAY, J. J., VERNAZZA, C. R. & HOLMES, R. D. 2015. Forty years of national surveys: An overview of children's dental health from 1973-2013. *British Dental Journal* 219**,** 281-285.
NAIDOO, J. & WILLS, J. 2009. Concepts of Health. *Foundation for health promotion.* Edinburgh; New York: Baillière Tindall/Elsevier.
NG, F. & MANTON, D. J. 2007. Aesthetic management of severely fluorosed incisors in an adolescent female. *Australian Dental Journal* 52**,** 243-248.
NHSDIGITAL 2015. Children's Dental Health Survey 2013. *In:* UK, N. D. (ed.).
NIKIFORUK, G. & FRASER, D. 1981. The etiology of enamel hypoplasia: a unifying concept. *The Journal of Paediatric,* 98**,** 888-893.
NPEU. 2013. *IMD postcode search tool* [Online]. University of Oxford. Available: https://tools.npeu.ox.ac.uk/imd/ [Accessed 20/06/17 2017].
OLIVEIRA, A. F., CHAVES, A. M. & ROSENBLATT, A. 2006. The influence of enamel defects on the development of early childhood caries in a population with low socioeconomic status: a longitudinal study. *Caries Res,* 40**,** 296-302.
OLIVER, O., MESSER, L. B., MANTON, D. J., KAN, K., NG, F., OLSEN, C., SHEAHAN, J., SILVA, M. & CHAWLA, N. 2014. Distribution and severity of molar hypomineralisation: trial of a new severity index. *International Journal of Paediatric Dentistry,* 24**,** 131-151.
OWEN, M. L., GHANIM, A., ELSBY, D. & MANTON, D. J. 2018. Hypomineralized second primary molars: prevalence, defect characteristics and relationship with dental caries in Melbourne preschool children. *Aust Dent J,* 63**,** 72-80.
OYEDELE, T. A., FOLAYAN, M. O., ADEKOYA-SOFOWORA, C. A. & OZIEGBE, E. O. 2015. Co-morbidities associated with molar-incisor hypomineralisation in 8 to 16 year old pupils in Ile-Ife, Nigeria. *BMC Oral Health* 15**,** 1-5.
O'BRIEN, K., WRIGHT, J. L., CONBOY, F., MACFARLANE, T. & MANDALL, N. 2006. The child perception questionnaire is valid for malocclusions in the United Kingdom. *American Journal of Orthodontics and Dentofacial Orthopedics* 129**,** 536-.
PAREKH, S., ALMEHATEB, M. & CUNNINGHAM, S. J. 2014. How do children with amelogenesis imperfecta feel about their teeth? *International Journal of Paediatric Dentistry* 24**,** 326-335.
PARIS, S. & MEYER-LUECKEL, H. 2009. Masking of labial enamel white spot lesions by resin infiltration- a clinical report. *Quintessence International,* 40**,** 713-718.
PARIS, S., MEYER-LUECKEL, H., COLFEN, H. & KIELBASSA, A. M. 2007a. Resin-infiltration of artificial enamel caries lesion with experimental light curing resins *Dent Mater J,* 26**,** 582-588.
PARIS, S., MEYER-LUECKEL, H. & KIELBASSA, A. M. 2007b. Resin Infiltration of Natural Caries Lesions *J Dent Res,* 86**,** 662-666.
PARIS, S., SCHWENDICKE, F., KELTSCH, J., DORFER, C. & MEYER-LUECKEL, H. 2013. Masking of white spot lesions by resin infiltration in vitro. *Journal of Dentistry* 41s**,** e28-e34.

PAULA, J. S., LEITE, I. C., ALMEIDA, A. B., AMBROSANO, G. M., PEREIRA, A. C. & MIALHE, F. L. 2012. The influence of oral health conditions, socioeconomic status and home environment factors on schoolchildren's self-perception of quality of life. *Health Qual Life Outcomes,* 10**,** 6.

PEREDA, N. & FORNS, M. 2004. Psychometric Properties of the Spanish version of the self-perception profile for children. *Perception and Motor Skills,* 98**,** 685-699.

PICKEREUROPE. 2014. The Friends and Family Test - A guide to understanding your FFT score. Available: http://www.pickereurope.org/wp-content/uploads/2014/12/Guide-to-understanding-your-FFT-score-AR-AC-181214-v1.pdf [Accessed 30th November 2016].

PICKEREUROPE. 2015. *Recommending a Friends and Family Test (FFT) for Children and Young People by Picker Institute Europe and Barts Health NHS Trust* [Online]. Available: http://www.pickereurope.org/case-studies/recommending-friends-family-test-fft-children-young-people/ [Accessed 14th October 2016 2016].

PINI, N. I. P., SUNDFELD-NETO, D., AGUIAR, F. H. B., SUNDFELD, R. H., MARTINS, L. R. M., LOVADINO, J. R. & LIMA, D. A. N. L. 2015. Enamel microabrasion: An overview of clinical and scientific considerations. *World J Clin Cases,* 3**,** 34-41.

PIOVESAN, C., ANTUNES, J. L., GUEDES, R. S. & ARDENGHI, T. M. 2010. Impact of socioeconomic and clinical factors on child oral health-related quality of life (COHRQoL). *Qual Life Res,* 19**,** 1359-66.

PITIPHAT, W., LUANGCHAICHAWENG, S., PUNGCHANCHAIKUL, P., ANGWARAVONG, O. & CHANSAMAK, N. 2014. Factors associated with molar incisor hypomineralization in Thai children. *Eur J Oral Sci* 122**,** 265-270.

PITTS, N., CHADWICK, B. & ANDERSON, T. 2015. Children's Dental Health Survey 2013 Report 2: Dental Disease and Damage in Children England, Wales and Northern Ireland.

PORITT, J. M., RODD, H. D. & BAKER, S. R. 2015. Childhood Dental Injuries: A resiliency model of adaptation. *International Journal of Paediatric Dentistry,* 25**,** 267-281.

PORTELLA, P. D., MENONCIN, B. L. V., DE SOUZA, J. F., DE MENEZES, J., FRAIZ, F. C. & ASSUNCAO, L. 2019. Impact of molar incisor hypomineralization on quality of life in children with early mixed dentition: A hierarchical approach. *Int J Paediatr Dent*.

POUSETTE LUNDGREN, G., KARSTEN, A. & DAHLLOF, G. 2015. Oral health-related quality of life before and after crown therapy in young patients with amelogenesis imperfecta. *Health Qual Life Outcomes,* 13**,** 197.

RATNAYAKE, N. & EKANAYAKE, L. 2005. Prevalence and impact of oral pain in 8-year-old children in Sri Lanka. *Int J Paediatr Dent,* 15**,** 105-12.

REEMA, S. D., LAHIRI, P. K. & ROY, S. S. 2014. Review of Casein Phosphopeptides-Amorphous Calcium Phosphate. *The Chinese Journal of Dental Research,* 17**,** 7-14.

REID, D. J. & DEAN, M. C. 2006. Variation in modern human enamel formation times *Journal of Human Evolution,* 50**,** 329-346.

REITH, E. J. 1970. The Stages of Amelogenesis as Observed in Molar Teeth of Young Rats. *Journal of Ultrastructure Research,* 30**,** 111-151.
RICHMOND, S., BUCHANAN, I. B., BURDEN, D. J., O'BRIEN, K. D., ANDREWS, M., ROBERTS, C. T. & TURBILL, E. A. 1995. Calibration of dentists in the use of occlusal indices. *Community Dent Oral Epidemiol,* 23**,** 173-6.
RICHMOND, S., O'BRIEN, K. D., ROBERTS, C. T. & ANDREWS, M. 1994. Dentists variation in the determination of orthodontic treatment need. *Br J Orthod,* 21**,** 65-8.
RITTER, A. V. 2005. Dental Fluorosis. *Journal of Esthetic and Restorative Dentistry,* 17**,** 326-327.
ROBINSON, C. 2014. Enamel maturation: a brief background with implications for some enamel dysplasias. *Frontiers in physiology,* 5**,** 1-6.
ROBINSON, C., BROOKES, S. J., SHORE, R. C. & KIRKHAM, J. 1998. The developing enamel matrix: nature and function. *European Journal Of Oral Science,* 106**,** 282-291.
ROBINSON, C., KIRKHAM, J., BROOKES, S. J., BONASS, W. A. & SHORE, R. C. 1995. The chemistry of enamel development. *The International Journal of Developmental Biology,* 39**,** 145-152.
RODD, H. D., ABDUL-KARIM, A., YESUDIAN, G., O'MAHONY, J. & MARSHMAN, Z. 2011a. Seeking children's perspectives in the management of visible enamel defects. *International Journal of Paediatric Dentistry* 21**,** 89-95.
RODD, H. D., BOISSONADE, F. M. & DAY, P. F. 2007a. Pulpal status of hypomineralized permanent molars. *Pediatr Dent,* 29**,** 514-20.
RODD, H. D., MARSHMAN, Z., PORRITT, J., BRADBURY, J. & BAKER, S. R. 2011b. Oral health-related quality of life of children in relation to dental appearance and educational transition. *British Dental Journal* 211**,** 1-6.
RODD, H. D., MARSHMAN, Z., PORRITT, J., BRADBURY, J. & BAKER, S. R. 2012. Psychosocial predictors of children's oral health-related quality of life during transition to secondary school. *Qual Life Res,* 21**,** 707-716.
RODD, H. D., MORGAN, C. R., DAY, P. F. & BOISSONADE, F. M. 2007b. Pulpal expression of TRPV1 in molar incisor hypomineralisation. *Eur Arch Paediatr Dent,* 8**,** 184-8.
ROGERS, H. J., RODD, H. D., VERMAIRE, J. H., STEVENS, K., KNAPP, R., EL YOUSFI, S. & MARSHMAN, Z. 2019a. A systematic review of the quality and scope of economic evaluations in child oral health research. *BMC Oral Health,* 19**,** 132.
ROGERS, H. J., VERMAIRE, J. H., GILCHRIST, F. & SCHULLER, A. A. 2019b. The Relationship between Caries-Specific Quality of Life and Generic Wellbeing in a Dutch Pediatric Population. *Dent J (Basel),* 7.
ROGERS, H. J., YESUDIAN, G. & RODD, H. D. 2016. Unusual extrinsic staining following microabrasion in a girl with amelogenesis imperfecta. *Eur Arch Paediatr Dent,* 17**,** 271-5.
RONNHOLM, E. 1962. The Amelogenesis of Human Teeth as Revealed by Electron Microscopy II. The Development of the Enamel Crystallites. *Journal of Ultrastructure Research,* 6**,** 249-303.

ROWAN, K. 1994. Global questions and scores. *In:* JENKINSON, C. (ed.) *Measuring health and medical outcomes.* London: UCL Press.
RUGG-GUNN, A. J., AL-MOHAMMADI, S. M. & BUTLER, T. J. 1998. Malnutrition and developmental defects of enamal in 2- to 6-year-old Saudi boys. *Caries research,* 32**,** 181-192.
RYYNANEN, H., SAHLBERG, C., LUKINMAA, P.-L. & ALALUUSUA, S. 2014. The effect of high temperature on the development of mouse dental enamel in vitro. *Archives of Oral Biology,* 59**,** 400-406.
SALANITRI, S. & SEOW, W. K. 2013. Developmental enamel defects in the primary dentition: aetiology and clinical management. *Australian Dental Journal* 58**,** 133-140.
SCARPELLI, A. C., PAIVA, S. M., VIEGAS, C. M., CARVALHO, A. C., FERREIRA, F. M. & PORDEUS, I. A. 2013. Oral health-related quality of life among Brazilian preschool children. *Community Dent Oral Epidemiol,* 41**,** 336-44.
SCHMALFUSS, A., STENHAGEN, K. R., TVEIT, A. B., CROSSNER, C. G. & ESPELID, I. 2016. Canines are affected in 16-year-olds with molar-incisor hypomineralisation (MIH): an epidemiological study based on the Tromso study: "Fit Futures". *Eur Arch Paediatr Dent,* 17**,** 107-13.
SCHWENDICKE, F., ELHENNAWY, K., REDA, S., BEKES, K., MANTON, D. J. & KROIS, J. 2018. Global burden of molar incisor hypomineralization. *J Dent,* 68**,** 10-18.
SENESTRARO, S. V., CROWE, J. J., WANG, M., VO, A., HUANG, G., FERRACANE, J. & COVELL JR., D. A. 2013. Minimally invasive resin infiltration of arrested white-spot lesions. A randomized clinical trial. *The Journal of the American Dental Association,* 144**,** 997-1005.
SEOW, W. K. 1997. Clinical diagnosis of enamel defects: pitfalls and practical guidelines. *Int Dent J,* 47**,** 173-82.
SEOW, W. K. 2014. Developmental defects of enamel and dentine: challenges for basic science research and clinical management. *Australian Dental Journal* 59**,** 143-154.
SHAW, W. C., RICHMOND, S. & O'BRIEN, K. D. 1995. The use of occlusal indices: a European perspective. *Am J Orthod Dentofacial Orthop,* 107**,** 1-10.
SHEORAN, N., GARG, S., DAMLE, S. G., DHINDSA, A., OPAL, S. & GUPTA, S. 2014. Esthetic Management of Developmental Enamel Opacities in Young Permanent Maxillary Incisors with Two Microabrasion Techniques—A Split Mouth Study. *J Esthet Restor Dent* 26**,** 345-352.
SIDALY, R., LANDIN, M. A., SUO, Z., SNEAD, M. L., LYNGSTADAAS, S. P. & RESELAND, J. E. 2015. Hypoxia increases the expression of enamel genes and cytokines in an ameloblast-derived cell line. *Eur J Oral Sci,* 123**,** 335-340.
SIERWALD, I., JOHN, M. T., SAGHERI, D., NEUSCHULZ, J., SCHULER, E., SPLIETH, C., JOST-BRINKMANN, P.-G. & REISSMANN, D. R. 2016. The German 19-item version of the Child Oral Health Impact Profile: translation and psychometric properties. *Clin Oral Invest,* 20**,** 301-313.
SILVA, M. J., SCURRAH, K. J., CRAIG, J. M., MANTON, D. J. & KILPATRICK, N. 2016. Etiology of molar incisor hypomineralization – A systematic review. *Community Dent Oral Epidemiol***,** 1-12.

SIMMER, J. P. & FINCHAM, A. G. 1995. Molecular mechanisms of dental enamel development. *Crit Rev Oral Biol Med,* 6**,** 84-108.
SIMMER, J. P. & HU, J. C.-C. 2001. Dental Enamel Formation and Its Impact on Clinical Dentistry. *Journal of Dental Education* 65**,** 896-905.
SIMMER, J. P., RICHARDSON, A. S., HU, Y.-Y., SMITH, C. E. & HU, J. C.-C. 2012. A post-classical theory of enamel biomineralization... and why we need one. *International Journal of Oral Science* 4**,** 129-134.
SISCHO, L. & BRODER, H. L. 2011. Oral Health-related Quality of Life: What, Why, How, and Future Implications. *Journal of Dental Research,* 90**,** 1264-1270.
SKAARE, A. B., AAS, A. M. & WANG, N. J. 2015. Enamel defects on permanent successors following luxation injuries to primary teeth and carers' experiences. *International Journal of Paediatric Dentistry* 25**,** 221-228.
SLADE, G. D. 1997. Measuring Oral Health and Quality of Life. *In:* SLADE, G. D. (ed.). Department of Dental Ecology, School of Dentistry, University of North Carolina.
SMITH, C. E. & NANCI, A. 1995. Overview of morphological changes in enamel organ cells associated with major events in amelogenesis. *Int J Dev Biol,* 39**,** 153-161.
SMITH, C. E., POMPURA, J. R., BORENSTEIN, S., FAZEL, A. & NANCI, A. 1989. Degradation and loss of matrix proteins from developing enamel. *The Anatomical Record,* 224**,** 292-316.
SMITH, R. N., LATH, D. L., RAWLINSON, A., KARMO, M. & BROOK, A. H. 2008. Gingival inflammation assessment by image analysis: measurement and validation. *Int J Dent Hyg,* 6**,** 137-42.
SONMEZ, H., YILDIRIM, G. & BEZGIN, T. 2013. Putative factors associated with molar incisor hypo mineralisation: an epidemiological study. *Eur Arch Paediatr Dent,* 14**,** 375-380.
SOUZA, J. F., COSTA-SILVA, C. M., JEREMIAS, F., SANTOS-PINTO, L., ZUANON, A. C. C. & CORDEIRO, R. C. L. 2012. Molar Incisor Hypomineralisation: Possible etiological factors in children from urban and rural areas. *European Archives of Paediatric Dentistry* 13**,** 164-170.
SPALJ, S., SLAJ, M., VARGA, S. & STRUJIC, M. 2010. Perception of orthodontic treatment need in children and adolescents. *Eur J Orthod,* 32**,** 387-94.
STEFFEN, R., KRAMER, N. & BEKES, K. 2017. The Wurzburg MIH concept: the MIH treatment need index (MIH TNI) : A new index to assess and plan treatment in patients with molar incisior hypomineralisation (MIH). *Eur Arch Paediatr Dent,* 18**,** 355-361.
SUBKA, S., RODD, H., NUGENT, Z. & DEERY, C. 2019. In vivo validity of proximal caries detection in primary teeth, with histological validation. *Int J Paediatr Dent,* 29**,** 429-438.
SUBRAMANIAM, P., GIRISH BABU, K. L. & LAKHOTIA, D. 2014. Evaluation of penetration depth of a commercially available resin infiltrate into artificially created enamel lesions: An in vitro study. *Journal of conservative dentistry,* 17**,** 146-149.
SUCKLING, G. 1980. Defects of enamel in sheep resulting from trauma during tooth development. *Journal of Dental Research,* 59**,** 1541-1548.

SUCKLING, G., HERBISON, G. P. & BROWN, R. H. 1987. Etiological factors influencing the prevalence of developmental defects of dental enamel in nine-year-old New Zealand children participating in a health and development study. *Journal of Dental Research,* 66**,** 1466-1469.

SUCKLING, G. & PEARCE, E. I. F. 1984. Developmental defects of enamel in a group of New Zealand children: their prevalence and some associated etiological factors. *Community Dentistry and Oral Epidemiology,* 12**,** 177-184.

SUCKLING, G. W., NELSON, D. G. & PATEL, M. J. 1989. Macroscopic and scanning electron microscopic appearance and hardness values of developmental defects in human permanent tooth enamel. *Advances in Dental Research,* 3**,** 219-233.

SUGA, S. 1989. Enamel Hypomineralization Viewed From the Pattern of Progressive Mineralization of Human and Monkey Developing Enamel. *Advances in Dental Research,* 3, 188-198**.,** 188-198.

SUI, W., BOYD, C. & WRIGHT, J. T. 2003. Altered pH Regulation During Enamel Development in the Cystic Fibrosis Mouse Incisor. *J Dent Res* 82**,** 388-392.

SUJAK, S. L., ABDUL KADIR, R. & DOM, T. N. 2004. Esthetic perception and psychosocial impact of developmental enamel defects among Malaysian adolescents. *J Oral Sci* 46**,** 221-226.

SUNDFELD, R. H., RAHAL, V., CROLL, T. P., DE AALEXANDRE, R. S. & BRISO, A. L. F. 2007. Enamel Microabrasion Followed by Dental Bleaching for Patients after Orthodontic Treatment—Case Reports. *J Esthet Restor Dent,* 19**,** 71-78.

SUNDFELD, R. H., SUNDFELD-NETO, D., MACHADO, L. S., FRANCO, L. M., FAGUNDES, T. C. & BRISO, A. L. F. 2014. Microabrasion in tooth enamel discolouration defects: three cases with long-term follow-ups. *J Appl Oral Sci,* 22**,** 347-354.

SUNFELD, R. H., SUNFELD-NETO, D., MACHADO, L. S., FRANCO, L. M., FAGUNDES, T. C. & BRISO, A. L. F. 2014. Microabrasion in tooth enamel discolouration defects: three cases with long-term follow-ups. *J Appl Oral Sc,* 22**,** 347-354.

TAPIAS-LEDESMA, M. A., JIMÉNEZ, R., LAMAS, F. & GONZÁLEZ, A. 2003. Factors associated with first molar dental enamel defects: a multivariate epidemiological approach. *Journal of dentistry for children (Chicago, Ill.),* 70**,** 215-220.

TAYLOR, G. D. 2017. Molar incisor hypomineralisation. *Evid Based Dent,* 18**,** 15-16.

TEIXEIRA, R. J. P. B., ANDRADE, N. S., QUEIROZ, L. C. C., MENDES, F. M., MOURA, M. S., MOURA, L. & LIMA, M. D. M. 2017. Exploring the association between genetic and environmental factors and molar incisor hypomineralization: evidence from a twin study. *Int J Paediatr Dent*.

TEN CATE, J. M., HOFMAN, A., VEERKAMP, J. S. J., ELFRINK, M. E. C., MOLL, H. A. & JADDOE, V. W. V. 2012. Deciduous Molar Hypomineralization and Molar Incisor Hypomineralization. *Journal of Dental Research,* 91**,** 551-555.

THIRUVENKADAM, G., ASOKAN, S., JOHN, J. B., GEETHA PRIYA, P. R. & PRATHIBA, J. 2015. Oral health-related quality of life of children seeking orthodontic treatment based on child oral health impact profile: A cross-sectional study. *Contemp Clin Dent,* 6**,** 396-400.

TIRLET, G., CHABOUIS, H. F. & ATTAL, J. P. 2013. Infiltration, a new therapy for masking enamel white spots: a 19-month follow-up case series. *Eur J Esthet Dent,* 8**,** 180-90.
TOMARKEN, A. J. & WALLER, N. G. 2005. Structural equation modeling: strengths, limitations, and misconceptions. *Annu Rev Clin Psychol,* 1**,** 31-65.
TORRES, C. R. & BORGES, A. B. 2015. Color masking of developmental enamel defects: a case series. *Oper Dent,* 40**,** 25-33.
TUNG, K., FUJITA, H., YAMASHITA, Y. & TAKAGI, Y. 2006. Effect of turpentine-induced fever during the enamel formation of rat incisor. *Archives of Oral Biology* 51**,** 464-470.
ULUSOY, A. T., TUNC, E. S., BAYRAK, S. & ONDER, H. 2016. A Comparative Study of Oral Health Parameters in Molar Incisor Hypomineralization and High-Caries-Risk Children Aged 8–11 Years. *Med Princ Pract,* 25**,** 85-89.
VALINOTI, A. C., DA SILVA PIERRO, V. S., DA SILVA, E. M. & MAIA, L. C. 2011. In vitro alterations in dental enamel exposed to acidic medicines. *International Journal of Paediatric Dentistry,* 21**,** 141-150.
VARGAS-FERREIRA, F. & ARDENGHI, T. M. 2011. Developmental enamel defects and their impact on child oral health-related quality of life. *Braz Oral Res,* 25**,** 531-537.
VELANDIA, L. M., ALVAREZ, L. V., MEJIA, L. P. & RODRIGUEZ, M. J. 2018. Oral health-related quality of life in Colombian children with Molar-Incisor Hypomineralization. *Acta Odontol Latinoam,* 31**,** 38-44.
VETTORE, M. V., AHMAD, S. F. H., MACHUCA, C. & FONTANINI, H. 2019. Socio-economic status, social support, social network, dental status, and oral health reported outcomes in adolescents. *Eur J Oral Sci,* 127**,** 139-146.
WADE, D. T. & HALLIGAN, P. W. 2004. Do biomedical models of illness make for good healthcare systems? *British Medical Journal* 329**,** 1398-1401.
WAGGONER, W. F., JOHNSTON, W. M., SCHUMANN, S. & SCHIKOWSKI, E. 1989. Microabrasion of human enamel in vitro using hydrochloric acid and pumice. *Pediatric Dentistry,* 11**,** 319-323.
WALTERS, S. J. 2009. *Quality of life outcomes in clinical trials and health-care evaluation. A practical guide to analysis and interpretation,* School of Health and Related Research, University of Sheffield, John Wiley and Sons Ltd.
WARWICK-BOOTH, L., CROSS, R. & LOWCOCK, D. 2012. What is Health? *Contemporary Health Studies: An Introduction.* Polity Press.
WEERHEIJM, K. L. 2003. Molar Incisor Hypomineralisation (MIH). *European Journal of Paediatric Dentistry,* 4**,** 115-120.
WEERHEIJM, K. L. 2004. Molar Incisor Hypomineralization (MIH):Clinical Presentation, Aetiology and Management. *Dental Update,* 31**,** 9-12.
WEERHEIJM, K. L., DUGGAL, M., MEJÀRE, I., PAPAGIANNOULIS, L., KOCH, G., MARTENS, L. C. & HALLONSTEN, A.-L. 2003. Judgement criteria for molar incisor hypomineralisation (MIH) in epidemiologic studies: a summary of the European meeting on MIH held in Athens. *European Journal of Paediatric Dentistry,* 4**,** 110-113.

WEERHEIJM, K. L., GROEN, H. J., BEENTJES, V. E. & POORTERMAN, J. H. 2001a. Prevalence of cheese molars in eleven-year-old Dutch children. *ASDC J Dent Child,* 68**,** 259-262.
WEERHEIJM, K. L., JÄLEVIK, B. & ALALUUSUA, S. 2001b. Molar-incisor hypomineralisation. *Caries research,* 35**,** 390-391.
WEERHRIJM, K. L. & MEJARE, I. 2003. Molar incisor hypomineralization: a questionnaire inventory of its occurrence in member countries of the European Academy of Paediatric Dentistry (EAPD). *International Journal of Paediatric Dentistry* 13**,** 411-416.
WESTLAND, S., LUO, W., ELLWOOD , R., BRUNTON, P. & PRETTY , I. 2007. Colour Assessment in Dentistry *Annals of the BMVA* 2007**,** 1-10.
WHATLING, R. & FEARNE, J. M. 2008. Molar incisor hypomineralization: a study of etiological factors in a group of UK children*. *International Journal of Paediatric Dentistry* 18**,** 155-162.
WHO, W. H. O. 2006. Constitution of the World Health Organization. Available: WHO. Constitution of the World Health Organization. 2006. http://www.who.int/governance/eb/Available: who_constitution_en.pdf.
WHOQOL 1995. The World Health Organization quality of life assessment (WHOQOL): Position paper from the World Health Organization. *Social Science & Medicine,* 41**,** 1403-1409.
WILLIAM, V., BURROW, M. F., PALAMARA, J. E. A. & MESSER, L. B. 2006a. Microshear Bond Strength of Resin Composite to Teeth Affected by Molar Hypomineralization Using 2 Adhesive Systems. *Pediatric Dentistry* 28**,** 233-241.
WILLIAM, V., MESSER, L. B. & BURROW, M. F. 2006b. Molar Incisor Hypomineralization: Review and Recommendations for Clinical Management. *Pediatric Dentistry* 28**,** 224-232.
WILLMOTT, N. S., BRYAN, R. A. E. & S., D. M. 2008. Molar-Incisor-Hypomineralisation: A literature review. *European Archives of Paediatric Dentistry* 9**,** 172-179.
WILSON, I. B. & CLEARY, P. D. 1995. Linking clinical variables with healthy-related quality of life: A conceptual model of patient outcomes. *Journal of American Medical Association (JAMA),* 273**,** 59-65.
WONG, A. T., MCMILLAN, A. S. & MCGRATH, C. 2006. Oral health-related quality of life and severe hypodontia. *J Oral Rehabil,* 33**,** 869-73.
WONG, F. & WINTER, G. 2002. Effectiveness of microabrasion technique for improvement of dental aesthetics. *British Dental Journal,* 193**,** 155-158.
WONG, H. 2014. Aetiological Factors for Developmental Defects of Enamel. *Austin J Anat* 1**,** 1003.
WONG, H., PENG, S.-M., WEN, Y. F. & KING, N. M. 2014. Risk Factors of Developmental Defects of Enamel-A Prospective Cohort Study. *PloS one,* 9**,** e109351.
XIE, Z., KILPATRICK, N. M., SWAIN, M. V., MUNROE, P. R. & HOFFMAN, M. 2008. Transmission electron microscope characterisation of molar-incisor hypomineralisation. *Journal of Material Science: Material Medicine* 19**,** 3187-3192.

YUSUF, H., GHERUNPONG, S., SHEIHAM, A. & TSAKOS, G. 2006. Validation of an English version of the Child-OIDP index, an oral health-related quality of life measure for children. *Health and Quality of Life Outcomes,* 4**,** 1-7.
ZHAO, D., DONG, B., YU, D., REN, Q. & SUN, Y. 2018. The prevalence of molar incisor hypomineralization: evidence from 70 studies. *Int J Paediatr Dent,* 28**,** 170-179.

List of appendices

APPENDIX 17

Completion of study report which was sent out to all participants

APPENDIX 18

Abstract submitted, British Society of Paediatric Dentistry conference, 2019

APPENDIX 19

Thank you card from a participant

APPENDIX 1

Molar Hypomineralisation Severity Index (Oliver et al., 2014)

i) MHSI (Tooth Scores)

MHSI Tooth Scores	Description	Management
Mild (scores 1-3)	Intact coloured defects, usually on smooth or occlusal surfaces	Provide preventive therapy with FS and remineralisation (with fluoride or CPP-ACP) or GICs if defects are in areas of occlusal load. Adhesive restorations if teeth become carious or develop PEB.
Moderate (scores 7-9)	Yellow or brown defects on occlusal or cuspal surfaces which may have atypical or previous restorations, PEB, or sensitivity.	Provide adhesive restorations particularly when PEB is present. Consider SSC if PEB is extensive. Stabilise enamel surfaces using remineralisation (with fluoride or CPP-ACP), FS, and/or GICs. Consider MHSI dentition score also. If defect is extensive, consider optimal timed extraction with orthodontic advice to encourage space closure.
Severe (scores 10-13)	Brown or yellow defects with a combination of PEB, sensitivity, and atypical restorations or previous restorations.	Consider remineralisation (with fluoride or CPP-ACP). Stabilise enamel surfaces with GIC until a definitive treatment plan is made or while waiting optimal timed extraction with orthodontic advice. Provide adhesive restorations or extraction. If FPMs have been restored unsuccessfully on multiple occasions, place SSCs or extract.

ii) MHSI (Dentition Scores)

MHSI Dentition Scores	Description	Management
Mild (scores 5-20)	One to all first permanent molars (FPMs) mildly affected by MIH OR One severely affected FPM	Preventive therapy with fissure sealant (FS) and remineralisation (with fluoride or CPP-ACP) for mild defects and unaffected FPMs. Treat severe defects according to MHSI tooth score
Moderate (scores 21-36)	Dentitions with two to four mild/moderately affected FPMs, or up to two severely affected FPMs.	Preventive therapy with FS and remineralisation (with fluoride or CPP-ACP) for mild defects and unaffected FPMs. Stabilise enamel surface with GIC or SSC until a definitive treatment plan is made or while awaiting optimal timed extraction following Orthodontic consultation. Provide adhesive restorations, particularly when PEB is present; consider SSC if PEB is extensive.
Severe (scores 37-52)	-All four FPMs severely affected	Provide adhesive restorations or extraction for one or more affected teeth. Consult orthodontist to check suitability and timing for extractions, particularly for scores of 45–52. If FPMs have been restored unsuccessfully on multiple occasions, place SSCs or extract.

APPENDIX 2

Health Research Authority approval letter

Mrs Noren N Hasmun
School of Clinical Dentistry, The University of Sheffield
Academic Unit of Oral Health and Development, School of Clinical Dentistry
Claremont Crescent
Sheffield
S10 2TA

Email: hra.approval@nhs.net

27 April 2017

Dear Mrs Hasmun

Letter of HRA Approval

Study title:	**Predictors of clinical- and patient-reported outcomes for management of Molar Incisor Hypomineralisation in young patients**
IRAS project ID:	**220083**
Protocol number:	**STH19676**
REC reference:	**17/WA/0096**
Sponsor	**Sheffield Teaching Hospitals NHS Foundation Trust**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices

The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators",* issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices

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In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
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Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

APPENDIX 3

Research ethics approval confirmation

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

Gwasanaeth Moeseg Ymchwil
Research Ethics Service

Ariennir gan Lywodraeth Cymru
Funded by Welsh Government

Wales REC 6
First Floor
Institute of Life Science 2
Swansea University
Singleton Park
Swansea
SA2 8PP

Telephone : 01792 606334
E-mail : penny.beresford@wales.nhs.uk
Website : www.hra.nhs.uk

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

20 April 2017

Mrs Noren N Hasmun
PhD Candidate
School of Clinical Dentistry, The University of Sheffield
Academic Unit of Oral Health and Development, School of Clinical Dentistry
Claremont Crescent
Sheffield
S10 2TA

Dear Mrs Hasmun

Study title:	**Predictors of clinical- and patient-reported outcomes for management of Molar Incisor Hypomineralisation in young patients**
REC reference:	**17/WA/0096**
Protocol number:	**STH19676**
IRAS project ID:	**220083**

Thank you for your email of 18/04/2017, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact please contact hra.studyregistration@nhs.net outlining the reasons for your request.
Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).
Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.
There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Poster to advertise research project]	Version 1	09 January 2017
Covering letter on headed paper [Response to ethics committee]		18 April 2017
IRAS Application Form [IRAS_Form_17032017]		17 March 2017
IRAS Application Form XML file [IRAS_Form_17032017]		17 March 2017

IRAS Checklist XML [Checklist_17032017]		17 March 2017
IRAS Checklist XML [Checklist_18042017]		18 April 2017
Letter from funder [funding letter]		27 March 2017
Letter from funder [affidavit 1]		27 March 2017
Letter from funder [affidavit 2]		27 March 2017
Letters of invitation to participant [Cover letter for follow-up questionnaire]	Version 1	09 January 2017
Other [Safeguarding protocol]	Version 1	13 April 2017
Other [CCDH safeguarding pathway (existing policy document)]	N/A	13 April 2017
Other [DNA pathway-CCDH June 2015 (existing policy document)]	N/A	13 April 2017
Other [CP1515 Managing domestic abuse affecting children and adults at risk policy (existing policy document)]	N/A	13 April 2017
Other [Multi-Agency Confirmation Form (existing policy document)]	N/A	13 April 2017
Participant consent form [Tracked participant assent form age 8-10 years]	Version 2	06 April 2017
Participant consent form [Clean participant assent form age 8-10 years]	Version 2	06 April 2017
Participant consent form [Tracked participant assent form age 11-16 years]	Version 2	06 April 2017
Participant consent form [Clean participant assent form age 11-16 years]	Version 2	06 April 2017
Participant consent form [Tracked parent/caregiver consent form]	Version 2	06 April 2017
Participant consent form [Clean parent/caregiver consent form]	Version 2	06 April 2017
Participant information sheet (PIS) [Tracked Information sheet for participant age 8-10 years]	Version 2	06 April 2017
Participant information sheet (PIS) [Clean Information sheet for participant age 8-10 years]	Version 2	06 April 2017
Participant information sheet (PIS) [Tracked Information sheet for participant age 11-16 years]	Version 2	06 April 2017
Participant information sheet (PIS) [Clean Information sheet for participant age 11-16 years]	Version 2	06 April 2017
Participant information sheet (PIS) [Tracked Information sheet for parent or caregiver]	Version 2	06 April 2017
Participant information sheet (PIS) [Clean Information sheet for parent or caregiver]	Version 2	06 April 2017
Referee's report or other scientific critique report [Lead reviewer report and responses]		09 January 2017
Referee's report or other scientific critique report [Second reviewer report and responses]		09 January 2017
Research protocol or project proposal [Research Protocol]	Version 1	09 January 2017
Summary CV for Chief Investigator (CI) [Summary CV for CI]		09 January 2017
Summary CV for student [Summary of CV for CI]		09 January 2017
Summary CV for supervisor (student research) [Summary of CV Main Supervisor]		09 January 2017
Summary CV for supervisor (student research) [Summary CV Co-Supervisor 1]		09 January 2017
Summary CV for supervisor (student research) [Summary CV Co-Supervisor 2]		09 January 2017
Validated questionnaire [Baseline questionnaire 8-10 years]		
Validated questionnaire [Baseline questionnaire 11-16 years]		
Validated questionnaire [Tracked baseline questionnaire 8-10 years]		
Validated questionnaire [Clean baseline questionnaire 8-10 years]		
Validated questionnaire [Tracked baseline questionnaire 11-16 years]		

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Validated questionnaire [Clean baseline questionnaire 11-16 years]		
Validated questionnaire [Tracked 1 month follow-up questionnaire 8-10 years]		
Validated questionnaire [Clean 1 month follow-up questionnaire 8-10 years]		
Validated questionnaire [Tracked 1 month follow-up questionnaire 11-16 years]		
Validated questionnaire [Clean 1 month follow-up questionnaire 11-16 years]		
Validated questionnaire [Tracked 6 months follow-up questionnaire 8-10 years]		
Validated questionnaire [Clean 6 months follow-up questionnaire 8-10 years]		
Validated questionnaire [Tracked 6 months follow-up questionnaire 11-16 years]		
Validated questionnaire [Clean 6 months follow-up questionnaire 11-16 years]		

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance

We are pleased to welcome researchers and R & D staff at our RES Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

17/WA/0096	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp
Dr M J Lawrence
Vice Chair

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Enclosures:	*"After ethical review – guidance for researchers" [SL-AR2]*
Copy to:	*Mrs Samantha Walmsley, Sheffield Teaching Hospitals NHS FT*

APPENDIX 4

Information sheet for participants aged 7-10 years

The University Of Sheffield.

Information Sheet for Children 7-10 years

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?

Hello!
I am Noren Hasmun. I am a children's dentist and I am doing a project at the University of Sheffield. This is me.

What is the study about and why we are doing it?

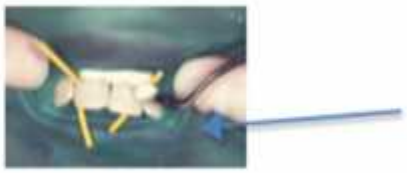
We are doing this study to better understand how children feel about their teeth and themselves. By answering the quiz, you will help us learn more about your (children's) experience of having marks on your front teeth (like the one in the photo). We are interested to know if things are any different after the marks on your front teeth have been treated. The Wales Research Ethics 6 Proportionate Review Sub-Committee has checked and approved this study.

Who can join in?

Children aged 8-16 years who have marks on their front teeth and who would like to have some treatment for these marks.

What will happen?

We will ask you to fill in a quiz. It will take about 15 minutes and an adult can help you! It is not a test, there are no right or wrong answers. Then we need to take a picture of your front teeth (not your face, as in photo above) so that we know how they looked before and after we mended them. You might have a special cleaning paste on the tooth with a protective cover on them – like in this photo.



This picture shows some front teeth being treated for marks; the green sheet is wrapped round them to keep them dry. This is a normal treatment provided for children with marks on their front teeth, like you.
If your tooth has deep marks, we might see you again and mend your tooth with the cleaning paste again or a dental filling to make it look whiter. We will see you again one and 6 months later to check if everything is ok and take a picture of your teeth again. We will ask you to fill in the quiz again. But it is up to you if you want to do this or not!
We will send you a letter at the end of the project to tell you all about our findings, but your name won't be on any of the things we say!

How can I take part?
Just tell us, or any of the dentists or nurses on the children's dental department if you would like to join in. We can answer any questions you might have. If you do not wish to participate, you do not need to.

What if you don't want to join in anymore?
If you want to stop doing the research at any time, you can stop without giving a reason. Your treatment will still be the same. Just tell us, or your parent/guardian. That is fine with everybody. No one will be cross.

What happens after?
The details about you and your answers will be kept private so no-one outside of the research team will know it is you. Afterwards, we will write about what I have found out from the research. You will get a letter to tell you what we have found.

What if there is a problem?
We can't see anything going wrong during this project but if you or your parents feel unhappy about anything to do with the research, we are very happy to talk to you at any time. Please just contact us (or ask your parent/guardian to talk to us):

1: Noren Hasmun
Telephone: 0114 2717877 (9.00 am-5.00 pm) or email:
nnhasmun1@sheffield.ac.uk OR
2: My supervisor Professor Helen Rodd on 0114 271 7814 (9.00 am-5.00 pm) or email: h.d.rodd@sheffield.ac.uk OR
3. Independent contact for complaints: Kathryn Allred (Service Manager Charles Clifford Dental Services on 0114 271 7806 (9.00 am-5.00 pm) or email: Kathryn.Allred@sth.nhs.uk

Thank you for reading this

APPENDIX 5

Information sheet for participants aged 11-16 years

The University Of Sheffield.

Information Sheet for Children 11-16 years

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?

Hello!
I am Noren Hasmun. I am a children's dentist and I am doing some research at the University of Sheffield.

What is the study about and why we are doing it?

We are doing this study to better understand how children feel about their teeth and themselves. By answering the questionnaire, you will help us learn more about your (children's) experience of having marks on their front teeth, like the ones in this picture. We are interested to know if things are any different after the marks on your front teeth have been treated. The Wales Research Ethics 6 Proportionate Review Sub-Committee has checked and approved this study.

Who can join in this study?

Children aged 8-16 years who have marks on their front tooth or teeth because their enamel didn't grow properly, and who would like to have some treatment for these marks.

What will happen during the study?

This study will involve your front teeth being photographed so we can measure the colour and size of the marks on a computer. Your face won't be on these photos! We will also ask you to fill in a questionnaire, about your teeth, about your feelings and what the treatment was like to improve the appearance of your front teeth. You will get the same dental treatment whether you are in the study or not, the only difference is that we will ask you to fill in some questionnaires. Each treatment session will last about an hour. The first step is to put a special paste on your teeth and protect them with a rubber sheet to keep them dry (like in this photo). This is a normal treatment provided for children with marks on their front teeth, like you.

If your tooth has deep marks, we may need to see you again to put the special paste again or cover the marks with dental filling. We will see you again one month and six months after the dental treatment to see how things are. Your teeth will be photographed again so that we can compare how it looks before and after the dental treatment. We will also ask you to fill in the questionnaire again during these visits.
All the information you give us will be kept private. No one else will be able to look at it apart from the researchers working with me on this study. Your name or anything else that identifies you will not be used in any reports of the project. We will send you a letter at the end of the project to tell you all about our findings!

How can I take part?
Taking part in this study is voluntary, which means it is your decision to take part or not. If you are interested in taking part, just tell us, or any of the dentists or nurses on the children's dental department if you would like to join in. If you have any question about the research, you can call me, Noren Hasmun on 0114 2717877 (9.00 am-5.00 pm) or email: nnhasmun1@sheffield.ac.uk.
If you do not wish to participate, you do not need to.

What if you don't want to join in anymore?
You may change your mind at any time without giving any reason. This will not affect any treatment or care you have in the future. There is no need to worry about stopping and that is fine with everybody here.

What happens after?
The details about you and your answers will be kept private so no-one outside of the research team will know it is you. Afterwards, we will write about what we have found out from the research. You will get a letter to tell you what we have found.

What should you do if there is a problem?

If you have any problems or feel you need to ask questions, please contact:

1: Noren Hasmun
Telephone: 0114 2717877 (9.00 am-5.00 pm) or email: nnhasmun1@sheffield.ac.uk OR

2: My supervisor Professor Helen Rodd on 0114 271 7814 (9.00 am- 5.00 pm) or email: h.d.rodd@sheffield.ac.uk OR

3. Independent contact for complaints: Kathryn Allred (Service Manager Charles Clifford Dental Services on 0114 271 7806 (9.00 am-5.00 pm)or email: Kathryn.Allred@sth.nhs.uk

Thank you very much for your help

APPENDIX 6

Information sheet for parents/carers

Information Sheet for Parent/Guardian

How do children feel about having marks on their front teeth? Does our dental treatment make a difference?

Your child has been invited to take part in a study to find out how they feel about having marks on their front teeth, caused by a condition called Molar Incisor Hypomineralisation (MIH). We are also interested to find out about their experience of the treatment we provide to improve the appearance of these marks. You can take as much time as you like to consider if both your child and you are happy to participate in this study. This information leaflet gives you details of what will be involved if you decide to participate and also who to contact if you have any question or would like to discuss any aspect of study. Please read the information leaflet carefully. We hope it helps you to make the decision whether to take part or not.

What is the study about?

This study is about a condition called Molar Incisor Hypomineralisation (MIH), which means the enamel of the permanent incisor and first molar teeth has not formed properly. This condition may present as white chalky spots, or yellow-brown areas on teeth. The cause of this condition is still unclear, but it has been associated with problems around the time of birth and illnesses during early childhood. This study will involve children aged 8-16 years old with visible marks on their front tooth or teeth (incisors) due to MIH. This study is looking at how children feel about having these marks on their front teeth. We are also interested to know if the treatment we provide to improve the appearance of the mark makes any difference to the children's lives. We hope with this knowledge we will be able to provide better treatment for children with this condition. The Wales Research Ethics 6 Proportionate Review Sub-Committee has reviewed and approved this study.

What is involved?

This study involves you and your child signing a consent form to confirm your child's participation in this study. Your child will be asked to complete a questionnaire. Then your child will have a check up to look at the overall condition and position of their teeth. Your child's front teeth will be photographed, to record how they look before (and after) treatment. Their face will not be photographed. Finally, the marks on their front teeth will be treated to improve the appearance. This will be undertaken by Noren Hasmun, who is specialist paediatric dentist currently doing research at the University of Sheffield, or a staff member at the paediatric dentistry clinic. The actual treatment is just the same as it would be by anybody else in the clinic, it is what we normally do. Each treatment visit will last approximately 1 hour: 15-20 minutes to fill in questionnaire, 10 minutes for photographs and 30 minutes for the dental examination and treatment.

The first treatment is just to have an acid paste rubbed into the front teeth. But if your child has a deep mark on their tooth or teeth, they will be given another appointment to further improve the appearance by re-applying the acid paste or using a dental filling. Your child will be seen again one and six months later. It is important that we know whether the improvement in appearance is long lasting. We will repeat the photograph and at these follow-up appointments, and ask your child to complete the same questionnaire again. The follow-up appointments will take approximately 30 minutes each. If you are unable to attend these appointments, we will send your child the questionnaire in the post to fill in and return to us, if they are happy to do so. We will send you a summary of the results at the end of the study, which will be December 2018.

Benefits, risks and safety

We do not anticipate any risks from this study as it involves normal clinical treatments that we routinely provide. The questionnaires do ask personal questions about how your child feels about him/herself, which we have used with study participants before and have not experienced any upset. You child will however benefit from receiving quicker appointments for their treatment. The information that we obtain from this study will help us to better understand what impacts MIH may have on children's lives and help us to provide better information and treatment options for children with similar conditions.

Confidentiality

All information gathered is confidential and nothing which identifies your child will be stored on a computer. All information from the research will be kept securely at the School of Clinical Dentistry, University of Sheffield. No one will have access to the material apart from the research team. Your child will not be identified in any reports produced from the research project. The results will be shared by being presented at dental conferences and published in scientific journals.

What will happen after the research finished?

All research data will be stored for 5 years following completion of the study at which time it will then be destroyed. No identifiable personal data will be used in the publication of results.

Participation

Taking part in this study is entirely voluntary. If you and your child decide to take part, you may change your mind and if so you can withdraw at any time without giving a reason. Your decision will not affect any ongoing or future dental care in any way.

After your initial assessment with a consultant, your child will be made an appointment with Noren or a staff member at the paediatric dentistry clinic to have the treatment on their front teeth. At this appointment you and your child can decide whether or not you would like to be in this study and can ask us any further questions you may have. If you would like to take part, you and your child will be asked to sign a consent form. You are both free to withdraw from the study at any time, without having to give a reason.
If you and your child do not wish to participate, you do not need to. Your child's treatment will be just the same.

I will also ask your permission to keep your child's contact details for a period of three years, as it may be desirable to contact you again in the future, to clarify information or to invite them to consider participating in further research related to this condition.
If you have any problems or feel you would like to know more, please contact any of the following:

- Principal Investigator: Mrs Noren Hasmun
  Telephone: 0114 2717877 (9.00 am-5.00pm)
  Email: nnhasmun1@sheffield.ac.uk
- Supervisors: Professor Helen Rodd (Tel: 0114 421 7814 (9.00 am-5.00 pm); email:h.d.rodd@sheffield.ac.uk)
  Dr Mario Vettore and Dr Claire Elcock
  Academic Unit of Oral Health and Development
  School of Clinical Dentistry, Claremont Crescent, S10 2TA, Sheffield
- Independent contact for complaints: Kathryn Allred (Service Manager Charles Clifford Dental Services on 0114 271 7806 (9.00 am- 5.00 pm) or email: Kathryn.Allred@sth.nhs.uk

Thank you for reading this

APPENDIX 7

Assent forms for children aged 7-10 years

I.D. Number:

Participant Assent Form (7-10 years)

How do children feel about having marks on their front teeth? Does our dental treatment make a difference?

Name of young person to be involved in the research:

_____

Name of parent/carer:

_____

	Please put a circle round the one you agree with:
1. Have you read, or an adult read to you, the information about this study dated **06th April 2017** (version **2**)?	Yes / No
2. Has someone told you what this study is about?	Yes / No
3. Do you understand what this study is about?	Yes / No
4. Have you asked all the questions you want?	Yes / No
5. Have your questions been answered OK?	Yes / No
6. Do you understand it's OK to stop taking part at any time?	Yes / No
7. Are you happy to take part?	Yes / No

If any answers are 'no' or you don't want to take part, don't write your name!

If you do want to take part, you can write your name below:

Name of child (please PRINT name)	Date	Child to write name here
Name of person taking consent	Date	Signature

1 copy for parent/guardian, 1 for researcher

APPENDIX 8

Assent forms for children aged 11-16 years

The University Of Sheffield.

I.D. Number:

Participant Assent Form (11-16 years)

How do children feel about having marks on their front teeth? Does our dental treatment make a difference?

Thank you for completing this sheet.

Name of young person to be involved in the research:

_____

Name of parent/carer:

_____

Please tick the box if you agree with the sentence:

1. I have read and understood the information sheet for this project dated **06th April 2017** (version **2**) and that I have had the opportunity to ask questions. ☐

2. I understand that joining in this study is up to me and I am free to stop being in the study at any time, without giving a reason and without my dental care being affected. ☐

3. I understand that any information will be used for research purposes only; including research publications and reports. My privacy will be kept at all times. ☐

4. I give my permission to be contacted again within a three year period ☐

5. I agree to take part ☐

_____	_____	_____
Name of Young Person	Date	Signature
_____	_____	_____
Name Researcher	Date	Signature

1 copy for parent/guardian, 1 for researcher

APPENDIX 9

Parents' consent form

I.D. Number:

Parent Consent Form

How do children feel about having marks on their front teeth? Does our dental treatment make a difference?

Study Number: _____

Name of Researcher: Mrs Noren Hasmun

Name of young person to be involved in the research: _____

Name of parent/carer: _____

Parent or carer, please complete this sheet

Please initial all boxes

1. I confirm that I have read and understand the information sheet dated **06th April 2017** (version **2)** for the above study. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that any information will be used for research purposes only, including research publications and reports. Anonymity and confidentiality will be preserved at all times. ☐
4. I give permission for my child to be contacted again within a three year period ☐
5. I agree to my child taking part in this study. ☐

Name of Parent/Guardian	Date	Signature
Name Researcher	Date	Signature

1 copy for parent/guardian, 1 for researcher

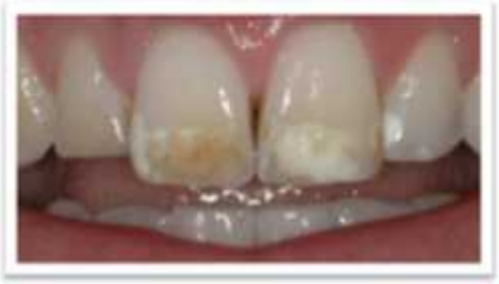
APPENDIX 10

Baseline questionnaire for children aged 7-10 years

The University Of Sheffield.

I.D. Number:

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?



Questionnaire Booklet 1
(Baseline for 7-10 year olds)

Investigator: Mrs Noren Hasmun
Co-Investigators: Professor Helen Rodd, Dr Mario Vettore & Dr Claire Elcock
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Claremont Crescent
S10 2ST
Sheffield

Hello

Thank you for taking part in this study. We are doing this study to better understand how children feel about their teeth and themselves. By answering the quiz, you will help us learn more about your (children's) experience of having marks on their front teeth. We are interested to know if things are any different before and after the marks on your front teeth have been treated.

Before you start, can you and your parent/guardian please tick mark (√) in the boxes below if you agree with the statements:

	Child	Parent/ Guardian
I am happy for the information given in this study to be used for research purposes	☐	☐
I am happy for the information about my/my child's treatment to be collected without my name being passed on (anonymously) to help with the research project only	☐	☐

Please remember:

- Do not write your name on the quiz
- This is not a test. There are no right or wrong answers
- Read each question carefully and answer the questions as honestly as you can
- If you do not understand a question, please ask for help.

Here are some questions for you to answer:

1. Please enter today's date e.g 0 6 0 9 2 0 1 6

☐☐☐☐☐☐☐☐

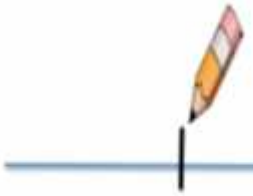
2. Are you a boy or a girl? ☐ Boy ☐ Girl (please tick √)

3. How old are you (in whole years)? Please circle your age below.

7 8 9 10 11 12 13 14 15 16

LET'S START!

How do I feel about my front teeth?



On the lines below please can you put a mark like this

to tell us how you feel about the marks on your front teeth **today**.

1. How worried are you about the marks on your front teeth?

I am very worried — I am not worried at all

2. How embarrassed are you about the marks on your front teeth?

I am very embarrassed — I am not embarrassed at all

3. How 'chalky' or discoloured do you think your front teeth are?

Very 'chalky'/discoloured — Not 'chalky' at all /discoloured

4. How happy are you with your front teeth?

I am very unhappy — I am very happy

How do I feel about my teeth, mouth and face?

We want to know how you felt about your **teeth, mouth and face in the past 3 months (before you came for treatment)**. Before you answer, ask yourself if this happens because of my teeth, mouth or face? Please put a tick mark (√) in the box that matches to the answer that best describes you.

1. In the past 3 months, how often have you had pain in your teeth/toothache?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

2. In the past 3 months, how often have you had crooked teeth or spaces between your teeth?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

3. In the past 3 months, how often have you had discoloured teeth or spots/marks on your teeth?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

4. In the past 3 months, how often have you had bad (smelly) breath?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

5. In the past 3 months, how often have you had bleeding gums?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

6. In the past 3 months, how often have you been unhappy or sad because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

7. In the past 3 months, how often have you missed school for any reason because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

8. In the past 3 months, how often have you been confident because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

9. In the past 3 months, how often have you had difficulty eating foods you would like to because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

Thanks for answering those questions - now please go to the next page

How do I feel about myself?

We would like to know how you feel about your **teeth, mouth and face** in the **past 3 months (before you came for treatment)**. Before you answer, ask yourself if this happens because of my teeth, mouth or face?

After reading each question, put a tick mark (√) in the box that matches to the answer that best suits you.

1. In the past 3 months, how often have you felt worried or anxious because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

2. In the past 3 months, how often have you not wanted to speak/read out loud in class?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

3. In the past 3 months, how often have you avoided smiling or laughing with other children because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

4. In the past 3 months, how often have you had trouble sleeping because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

5. In the past 3 months, how often have you been teased, bullied or called names by other children because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

6. In the past 3 months, how often have you felt that you were attractive (good looking) because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

7. In the past 3 months, how often have you felt that you look different because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

Please go to the next page

8. In the past 3 months, how often have you had difficulty saying certain words?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

9. In the past 3 months, how often have you had difficulty keeping your teeth clean?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

10. In the past 3 months, how often have you been worried about what other people think about your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

11. Overall, how healthy do you think your teeth are?

- ☐ Poor
- ☐ Fair
- ☐ Average
- ☐ Good
- ☐ Excellent

Please go to the next page

Who Am I Like?

I would rather play outdoors

I would rather watch TV

The following sentences in white boxes describe two kinds of kids – on the LEFT or on the RIGHT. Please read each sentence carefully. Choose which kid seems MOST like you. Once you have decided you are most like the kids on the left or right white box, go to that side of the sentence. You have to decide whether that is only *sort of true for you*, or *really true for you*. If it's only sort of true, then put a cross (X) in the box under "Sort of true for me"; if it's really true for you, then put a cross (X) in that box, under "Really true for me". The first one has been filled out to show you how.

You only put a cross (X) on **one** box for each sentence. **DON'T PUT A CROSS (X) ON BOTH SIDES, JUST THE ONE SIDE MOST LIKE YOU.** There is no right or wrong answer. We are only interested in which kids are most like you. Please look at the "EXAMPLE" below.

"EXAMPLE"

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
Example You would put an "x" here if you are someone who always liked playing outdoors	X		Some kids would rather play outdoors in their spare time	BUT	Other kids would rather watch T.V.		

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
1.	☐	☐	Some kids find it hard to make friends	BUT	Other kids find it's pretty easy to make friends	☐	☐
2.	☐	☐	Some kids are happy with the way they look	BUT	Other kids are not happy with the way they look	☐	☐
3.	☐	☐	Some kids are often unhappy with themselves	BUT	Other kids are pretty pleased with themselves	☐	☐
4.	☐	☐	Some kids know how to make classmates like them	BUT	Other kids don't know how to make classmates like them	☐	☐
5.	☐	☐	Some kids are happy with their height and weight	BUT	Other kids wish their height or weight were different	☐	☐
6.	☐	☐	Some kids don't like the way they are leading their life	BUT	Other kids do like the way they are leading their life	☐	☐
7.	☐	☐	Some kids don't have the social skills to make friends	BUT	Other kids do have the social skills to make friends	☐	☐
8.	☐	☐	Some kids wish their body was different	BUT	Other kids like their body the way it is	☐	☐
9.	☐	☐	Some kids are happy with themselves as a person	BUT	Other kids are often not happy with themselves	☐	☐

Please turn over for a few more

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
10.	☐	☐	Some kids understand how to get peers (people of same age) to accept them	BUT	Other kids don't understand how to get peers (people of same age) to accept them	☐	☐
11.	☐	☐	Some kids wish their physical appearance (how they look) was different	BUT	Other kids like their physical appearance the way it is	☐	☐
12.	☐	☐	Some kids like the kind of person they are	BUT	Other kids often wish they were someone else	☐	☐
13.	☐	☐	Some kids wish they knew how to make more friends	BUT	Other kids know how to make as many friends as they want	☐	☐
14.	☐	☐	Some kids wish something about their face or hair looked different	BUT	Other kids like their face and hair the way they are	☐	☐
15.	☐	☐	Some kids are very happy being the way they are	BUT	Other kids wish they were different	☐	☐
16.	☐	☐	Some kids know how to become popular	BUT	Other kids do not know how to become popular	☐	☐
17.	☐	☐	Some kids think that they are good looking	BUT	Other kids think that they are not very good looking	☐	☐
18.	☐	☐	Some kids are not very happy with the way they do a lot of things	BUT	Other kids think the way they do things is fine	☐	☐

Please go to the next page - nearly finished

How Do I Feel About My General Health?

NEXT, we would like to know how you feel about your health in general. Please tick (√) one from the following options.

Overall, would you say your general health is?

☐	☐	☐	☐	☐
Poor	Fair	Good	Very good	Excellent

NEARLY FINISHED... only one more page!

How Do I Feel About the Hospital?

Finally, we would like to know what you think about this dental hospital.....

I would say this is a good dental hospital for my friends and family to be looked after in, if they needed similar treatment or care to me

Please tick (√) one only

- ☐ I agree a lot
- ☐ I agree a bit
- ☐ I disagree a bit
- ☐ I disagree a lot
- ☐ I can't decide/ I don't know

Please tell us more about your dental hospital visit

What was good?	

What could we do better?	

There, it's FINISHED!!
We REALLY appreciate the time and thought you have given to this study.

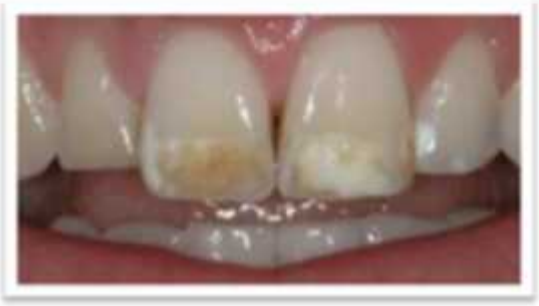
APPENDIX 11

Baseline questionnaire for children aged 11-16 years

The University Of Sheffield.

I.D. Number:

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?



Questionnaire Booklet 1
(Baseline for 11-16 year olds)

Investigator: Mrs Noren Hasmun
Co-Investigators: Professor Helen Rodd, Dr Mario Vettore & Dr Claire Bcock
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Claremont Crescent
S10 2ST
Sheffield

Hello

Thank you for taking part in this study. We are doing this study to better understand how children feel about their teeth and themselves. By answering the questionnaire, you will help us learn more about your (children's) experiences of having marks on their front teeth. We are interested to know if things are any different before and after the marks on your front teeth have been treated.

Before you start, can you and your parent/guardian please tick mark (√) in the boxes below if you agree with the statements:

	Child	Parent/ Guardian
I am happy for the information given in this study to be used for research purposes	☐	☐
I am happy for the information about my/my child's treatment to be collected without my name being passed on (anonymously) to help with the research project only	☐	☐

Please remember:

- Do not write your name on the questionnaire
- This is not a test. There are no right or wrong answers
- Read each question carefully and answer the questions as honestly as you can
- If you do not understand a question, please ask for help.

Please answer the following questions:

1. Please enter today's date e.g 0 6 0 9 2 0 1 6

☐☐☐☐☐☐☐☐

2. Are you a boy or a girl? ☐ Boy ☐ Girl (please tick √)

3. How old are you (in whole years)? Please circle your age below.

7 8 9 10 11 12 13 14 15 16

LET'S START!

How do I feel about my front teeth?

On the lines below please can you put a mark like this

to tell us how you feel about the marks on your front teeth **today**.

1. How worried are you about the marks on your front teeth?

0 — 10

I am very worried — I am not worried at all

2. How embarrassed are you about the marks on your front teeth?

0 — 10

I am very embarrassed — I am not embarrassed at all

3. How 'chalky' or discoloured do you think your front teeth are?

0 — 10

Very 'chalky'/discoloured — Not 'chalky' at all /discoloured

4. How happy are you with your front teeth?

0 — 10

I am very unhappy — I am very happy

How do I feel about my teeth, mouth and face?

From the following questions, we are interested to know how you felt about your **teeth, mouth and face in the past 3 months (before you came for treatment)**. Before you answer, ask yourself if this happens because of my teeth, mouth and face? Choose the answer that best describes you in the past 3 months.

After reading each question, please put a tick mark (√) in the box that matches the answer that best suits you.

Questions	Never	Almost never	Sometimes	Fairly often	Almost all the time
1. In the past 3 months, how often have you had pain in your teeth/toothache?	☐	☐	☐	☐	☐
2. In the past 3 months, how often have you had crooked teeth or spaces between your teeth?	☐	☐	☐	☐	☐
3. In the past 3 months, how often have you had discoloured teeth or spots/marks on your teeth?	☐	☐	☐	☐	☐
4. In the past 3 months, how often have you had bad (smelly) breath?	☐	☐	☐	☐	☐
5. In the past 3 months, how often have you had bleeding gums?	☐	☐	☐	☐	☐
6. In the past 3 months, how often have you been unhappy or sad because of your teeth, mouth or face?	☐	☐	☐	☐	☐
7. In the past 3 months, how often have you missed school for any reason because of your teeth, mouth or face?	☐	☐	☐	☐	☐
8. In the past 3 months, how often have you been confident because of your teeth, mouth or face?	☐	☐	☐	☐	☐
9. In the past 3 months, how often have you had difficulty eating foods you would like to because of your teeth, mouth or face?	☐	☐	☐	☐	☐

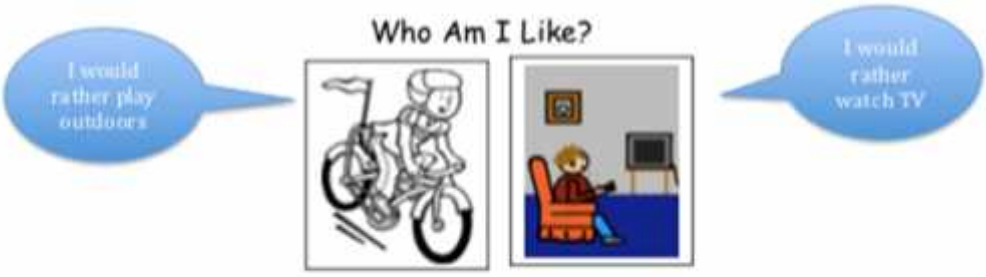
Thanks for answering those questions - now please go to the next page

How do I feel about myself?

From the following questions, we are interested to know how you feel about your **teeth, mouth and face** in the **past 3 months (before you came for treatment)**. Before you answer, ask yourself if this happens because of my teeth, mouth and face? After reading each question, place a tick mark ☑ in the box that matches the answer that best suits you.

Questions	Never	Almost never	Sometimes	Fairly often	Almost all the time
1. In the past 3 months, how often have you felt worried or anxious because of your teeth, mouth or face?	☐	☐	☐	☐	☐
2. In the past 3 months, how often have you not wanted to speak/read out loud in class?	☐	☐	☐	☐	☐
3. In the past 3 months, how often have you avoided smiling or laughing with other children because of your teeth, mouth or face?	☐	☐	☐	☐	☐
4. In the past 3 months, how often have you had trouble sleeping because of your teeth, mouth or face?	☐	☐	☐	☐	☐
5. In the past 3 months, how often have you been teased, bullied, or called names by other children because of your teeth, mouth or face?	☐	☐	☐	☐	☐
6. In the past 3 months, how often have you felt that you were attractive (good looking) because of your teeth, mouth or face?	☐	☐	☐	☐	☐
7. In the past 3 months, how often have you felt that you look different because of your teeth, mouth or face?	☐	☐	☐	☐	☐
8. In the past 3 months, how often have you had difficulty saying certain words?	☐	☐	☐	☐	☐
9. In the past 3 months, how often have you had difficulty keeping your teeth clean?	☐	☐	☐	☐	☐
10. In the past 3 months, how often have you been worried about what other people think about your teeth, mouth or face?	☐	☐	☐	☐	☐
11. Overall, how healthy do you think your teeth are?	Poor ☐	Fair ☐	Average ☐	Good ☐	Excellent ☐

Who Am I Like?



The following sentences in white boxes describe two kinds of kids – on the LEFT or on the RIGHT. Please read each sentence carefully. Choose which kid seems MOST like you. Once you have decided you are most like the kids on the left or right white box, go to that side of the sentence. You have to decide whether that is only *sort of true for you*, or *really true for you*. If it's only sort of true, then put a cross (X) in the box under "Sort of true for me"; if it's really true for you, then put a cross (X) in that box, under "Really true for me". The first one has been filled out to show you how.

You only put a cross (X) on **one** box for each sentence. **DON'T PUT A CROSS (X) ON BOTH SIDES, JUST THE ONE SIDE MOST LIKE YOU**. There is no right or wrong answer. We are only interested in which kids are most like you. Please look at the "EXAMPLE" below.

"EXAMPLE"

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
Example you would put an "x" here if you are someone who always liked playing outdoors	X		Some kids would rather play outdoors in their spare time	BUT	Other kids would rather watch T.V.		

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
1.	☐	☐	Some kids find it hard to make friends	BUT	Other kids find it's pretty easy to make friends	☐	☐
2.	☐	☐	Some kids are happy with the way they look	BUT	Other kids are not happy with the way they look	☐	☐
3.	☐	☐	Some kids are often unhappy with themselves	BUT	Other kids are pretty pleased with themselves	☐	☐
4.	☐	☐	Some kids know how to make classmates like them	BUT	Other kids don't know how to make classmates like them	☐	☐
5.	☐	☐	Some kids are happy with their height and weight	BUT	Other kids wish their height or weight were different	☐	☐
6.	☐	☐	Some kids don't like the way they are leading their life	BUT	Other kids do like the way they are leading their life	☐	☐
7.	☐	☐	Some kids don't have the social skills to make friends	BUT	Other kids do have the social skills to make friends	☐	☐
8.	☐	☐	Some kids wish their body was different	BUT	Other kids like their body the way it is	☐	☐
9.	☐	☐	Some kids are happy with themselves as a person	BUT	Other kids are often not happy with themselves	☐	☐

Please turn over for a few more

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
10.	☐	☐	Some kids understand how to get peers (people of same age) to accept them	BUT	Other kids don't understand how to get peers (people of same age) to accept them	☐	☐
11.	☐	☐	Some kids wish their physical appearance (how they look) was different	BUT	Other kids like their physical appearance the way it is	☐	☐
12.	☐	☐	Some kids like the kind of person they are	BUT	Other kids often wish they were someone else	☐	☐
13.	☐	☐	Some kids wish they knew how to make more friends	BUT	Other kids know how to make as many friends as they want	☐	☐
14.	☐	☐	Some kids wish something about their face or hair looked different	BUT	Other kids like their face and hair the way they are	☐	☐
15.	☐	☐	Some kids are very happy being the way they are	BUT	Other kids wish they were different	☐	☐
16.	☐	☐	Some kids know how to become popular	BUT	Other kids do not know how to become popular	☐	☐
17.	☐	☐	Some kids think that they are good looking	BUT	Other kids think that they are not very good looking	☐	☐
18.	☐	☐	Some kids are not very happy with the way they do a lot of things	BUT	Other kids think the way they do things is fine	☐	☐

Please go to the next page - nearly finished

How Do I Feel About My General Health?

NEXT, we would like to know how you feel about your health in general. Please tick (√) one from the following options.

Overall, would you say your general health is?

☐ Poor ☐ Fair ☐ Good ☐ Very good ☐ Excellent

NEARLY FINISHED... only one more page!

How Do I Feel About the Hospital?

Finally, we would like to know your opinion about this dental hospital.....

I would say this is a good dental hospital for my friends and family to be looked after in, if they needed similar treatment or care to me

Please tick (√) one only

- ☐ I agree a lot
- ☐ I agree a bit
- ☐ I disagree a bit
- ☐ I disagree a lot
- ☐ I can't decide/ I don't know

Please tell us more about your dental hospital visit

What was good?	

What could we do better?	

There, it's FINISHED!!
We REALLY appreciate the time and thought you have given to this study.

APPENDIX 12

One month follow-up questionnaire for children aged 7-10 years

The University Of Sheffield.

I.D. Number:

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?

Questionnaire Booklet 2
(1 month follow-up for 7-10 year olds)

Investigator: Mrs Noren Hasmun
Co-investigators: Professor Helen Rodd, Dr Mario Vettore & Dr Claire Elcock
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Claremont Crescent
S10 2ST
Sheffield

Hello

Thank you for taking part in this study. We are doing this study to better understand how children feel about their teeth and themselves. By answering the quiz, you will help us learn more about your (children's) experience with marks on their front teeth. We are interested to know if things are any different before and after the mark/s on your tooth/teeth has been treated.

Before you start, can you and your parent/guardian please tick mark (√) in the boxes below if you agree with the statements:

	Child	Parent/ Guardian
I am happy for the information given in this study to be used for research purposes	☐	☐
I am happy for the information about my/my child's treatment to be collected without my name being passed on (anonymously) to help with the research project only	☐	☐

Please remember:

- Do not write your name on the questionnaire
- This is not a test. There are no right or wrong answers
- Read each question carefully and answer the questions as honestly as you can
- If you do not understand a question, please ask for help.

Here are some questions for you to answer:

1. Please enter today's date e.g 0 6 0 9 2 0 1 6

☐☐☐☐☐☐☐☐

2. Are you a boy or a girl? ☐ Boy ☐ Girl (please tick √)

3. How old are you (in whole years)? Please circle your age below.

7 8 9 10 11 12 13 14 15 16

LET'S START!

How do I feel about my front teeth?

On the lines below please can you put a mark like this

to tell us how you feel about any marks that you still have on your teeth today .

1. How worried are you about the marks on your front teeth?

0 10

I am very worried I am not worried at all

2. How embarrassed are you about the marks on your front teeth?

0 10

I am very embarrassed I am not embarrassed at all

3. How 'chalky' or discoloured do you think your front teeth are?

0 10

Very 'chalky'/discoloured Not 'chalky' at all /discoloured

4. How happy are you with your front teeth?

0 10

I am very unhappy I am very happy

How do I feel about my teeth, mouth and face?

We want to know how you feel about your **teeth, mouth and face since the treatment for marks on your tooth 1 month ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face? Please put a tick mark (√) in the box that matches to the answer that best describes you.

1. In the past 1 month, how often have you had pain in your teeth/toothache?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

2. In the past 1 month, how often have you had crooked teeth or spaces between your teeth?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

3. In the past 1 month, how often have you had discoloured teeth or spots/marks on your teeth?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

4. In the past 1 month, how often have you had bad (smelly) breath?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

5. In the past 1 month, how often have you had bleeding gums?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

6. In the past 1 month, how often have you been unhappy or sad because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

7. In the past 1 month, how often have you missed school for any reason because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

8. In the past 1 month, how often have you been confident because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

9. In the past 1 month, how often have you had difficulty eating foods you would like to because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

Thanks for answering those questions - now please go to the next page

How do I feel about myself?

We would like to know how you feel about your **teeth, mouth and face** since you had **the treatment for marks on your tooth 1 month ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face?

After reading each question, put a tick mark (√) in the box that matches to the answer that best suits you.

1. In the past 1 month, how often have you felt worried or anxious because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

2. In the past 1 month, how often have you not wanted to speak/read out loud in class?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

3. In the past 1 month, how often have you avoided smiling or laughing with other children because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

4. In the past 1 month, how often have you had trouble sleeping because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

5. In the past 1 month, how often have you been teased, bullied, or called names by other children because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

6. In the past 1 month, how often have you felt that you were attractive (good looking) because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

7. In the past 1 month, how often have you felt that you look different because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

8. In the past 1 month, how often have you had difficulty saying certain words?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

9. In the past 1 month, how often have you had difficulty keeping your teeth clean?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

10. In the past 1 month, how often have you been worried about what other people think about your teeth, mouth or face?
    - ☐ Never
    - ☐ Almost never
    - ☐ Sometimes
    - ☐ Fairly often
    - ☐ Almost all the time

11. Overall, how healthy do you think your teeth are?
    - ☐ Poor
    - ☐ Fair
    - ☐ Average
    - ☐ Good
    - ☐ Excellent

Please go to the next page

Who Am I Like?

The following sentences in white boxes describe two kinds of kids – on the LEFT or on the RIGHT. Please read each sentence carefully. Choose which kid seems MOST like you. Once you have decided you are most like the kids on the left or right white box, go to that side of the sentence. You have to decide whether that is only *sort of true for you*, or *really true for you*. If it's only sort of true, then put a cross (X) in the box under "Sort of true for me"; if it's really true for you, then put a cross (X) in that box, under "Really true for me". The first one has been filled out to show you how.

You only put a cross (X) on **one** box for each sentence. **DON'T PUT A CROSS (X) ON BOTH SIDES, JUST THE ONE SIDE MOST LIKE YOU.** There is no right or wrong answer. We are only interested in which kids are most like you. Please look at the "EXAMPLE" below.

"EXAMPLE"

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
Example you would put an "x" here if you are someone who always liked playing outdoors	X	☐	Some kids would rather play outdoors in their spare time	BUT	Other kids would rather watch T.V.	☐	☐

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
1.	☐	☐	Some kids find it hard to make friends	BUT	Other kids find it's pretty easy to make friends	☐	☐
2.	☐	☐	Some kids are happy with the way they look	BUT	Other kids are not happy with the way they look	☐	☐
3.	☐	☐	Some kids are often unhappy with themselves	BUT	Other kids are pretty pleased with themselves	☐	☐
4.	☐	☐	Some kids know how to make classmates like them	BUT	Other kids don't know how to make classmates like them	☐	☐
5.	☐	☐	Some kids are happy with their height and weight	BUT	Other kids wish their height or weight were different	☐	☐
6.	☐	☐	Some kids don't like the way they are leading their life	BUT	Other kids do like the way they are leading their life	☐	☐
7.	☐	☐	Some kids don't have the social skills to make friends	BUT	Other kids do have the social skills to make friends	☐	☐
8.	☐	☐	Some kids wish their body was different	BUT	Other kids like their body the way it is	☐	☐
9.	☐	☐	Some kids are happy with themselves as a person	BUT	Other kids are often not happy with themselves	☐	☐

Please turn over for a few more

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
10.	☐	☐	Some kids understand how to get peers (people of same age) to accept them	BUT	Other kids don't understand how to get peers (people of same age) to accept them	☐	☐
11.	☐	☐	Some kids wish their physical appearance (how they look) was different	BUT	Other kids like their physical appearance the way it is	☐	☐
12.	☐	☐	Some kids like the kind of person they are	BUT	Other kids often wish they were someone else	☐	☐
13.	☐	☐	Some kids wish they knew how to make more friends	BUT	Other kids know how to make as many friends as they want	☐	☐
14.	☐	☐	Some kids wish something about their face or hair looked different	BUT	Other kids like their face and hair the way they are	☐	☐
15.	☐	☐	Some kids are very happy being the way they are	BUT	Other kids wish they were different	☐	☐
16.	☐	☐	Some kids know how to become popular	BUT	Other kids do not know how to become popular	☐	☐
17.	☐	☐	Some kids think that they are good looking	BUT	Other kids think that they are not very good looking	☐	☐
18.	☐	☐	Some kids are not very happy with the way they do a lot of things	BUT	Other kids think the way they do things is fine	☐	☐

Please go to the next page - nearly finished

How Do I Feel About My General Health?

NEXT, we would like to know how you feel about your health in general. Please tick (√) one from the following options.

1. Overall, would you say your general health is?

☐ Poor ☐ Fair ☐ Good ☐ Very good ☐ Excellent

2. Overall, how has your general health changed since our last meeting 1 month ago?

Please tick (√) one from the following options.

☐ Much Worse ☐ Worse ☐ Same ☐ Better ☐ Much Better

NEARLY FINISHED...only one more page!

How Do I Feel About the Hospital?

Finally, we would like to know your opinion about this dental hospital .....

I would say this is a good dental hospital for my friends and family to be looked after in, if they needed similar treatment or care to me

Please tick (√) one only

- ☐ I agree a lot
- ☐ I agree a bit
- ☐ I disagree a bit
- ☐ I disagree a lot
- ☐ I can't decide/ I don't know

Please tell us more about your dental hospital visit

What was good?	

What could we do better?	

There, it's FINISHED!!
We REALLY appreciate the time and thought you have given to this study.

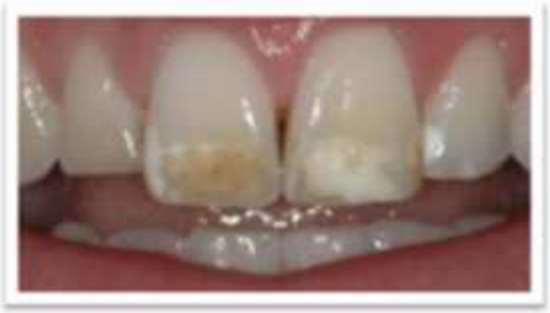
APPENDIX 13

One month follow-up questionnaire for children aged 11-16 years

The University Of Sheffield.

I.D. Number:

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?



Questionnaire Booklet 2
(1 month follow-up for 11-16 year olds)

Investigator: Mrs Noren Hasmun
Co-Investigators: Professor Helen Rodd, Dr Mario Vettore & Dr Claire Bcock
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Claremont Crescent
S10 2ST
Sheffield

Hello

Thank you for taking part in this study. We are doing this study to better understand how children feel about their teeth and themselves. By answering the questionnaire, you will help us learn more about your (children's) experience with marks on their front teeth. We are interested to know if things are any different before and after the mark/s on your tooth/teeth has been treated.

Before you start, can you and your parent/guardian please tick mark (√) in the boxes below if you agree with the statements:

	Child	Parent/ Guardian
I am happy for the information given in this study to be used for research purposes	☐	☐
I am happy for the information about my/my child's treatment to be collected without my name being passed on (anonymously) to help with the research project only	☐	☐

Please remember:

- Do not write your name on the questionnaire
- This is not a test. There are no right or wrong answers
- Read each question carefully and think about how feel since the treatment you had 1 month ago.
- If you do not understand a question, please ask for help.

Please answer the following questions:

1. Please enter today's date e.g 0 6 0 9 2 0 1 6

☐☐☐☐☐☐☐☐

2. Are you a boy or a girl? ☐ Boy ☐ Girl (please tick √)

3. How old are you (in whole years)? Please circle your age below.

7 8 9 10 11 12 13 14 15 16

LET'S START!

How I feel about my front teeth

On the lines below please can you put a mark like this

to tell us how you feel about any marks that you still have on your teeth today

1. How worried are you about the marks on your front teeth?

0 — 10

I am very worried — I am not worried at all

2. How embarrassed are you about the marks on your front teeth?

0 — 10

I am very embarrassed — I am not embarrassed at all

3. How 'chalky' or discoloured do you think your front teeth are?

0 — 10

Very 'chalky'/discoloured — Not 'chalky' at all /discoloured

4. How happy are you with your front teeth?

0 — 10

I am very unhappy — I am very happy

How do I feel about my teeth, mouth and face?

From the following questions, we are interested to know how you feel about your **teeth, mouth and face since the treatment for marks on your tooth 1 month ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face? Choose the answer that best describes you in the past 1 month.

After reading each question, please put a tick mark (√) in the box that corresponds to the answer that best suits you.

Questions	Never	Almost never	Sometimes	Fairly often	Almost all the time
1. In the past 1 month, how often have you had pain in your teeth/toothache?	☐	☐	☐	☐	☐
2. In the past 1 month, how often have you had crooked teeth or spaces between your teeth?	☐	☐	☐	☐	☐
3. In the past 1 month, how often have you had discoloured teeth or spots/marks on your teeth?	☐	☐	☐	☐	☐
4. In the past 1 month, how often have you had bad (smelly) breath?	☐	☐	☐	☐	☐
5. In the past 1 month, how often have you had bleeding gums?	☐	☐	☐	☐	☐
6. In the past 1 month, how often have you been unhappy or sad because of your teeth, mouth or face?	☐	☐	☐	☐	☐
7. In the past 1 month, how often have you missed school for any reason because of your teeth, mouth or face?	☐	☐	☐	☐	☐
8. In the past 1 month, how often have you been confident because of your teeth, mouth or face?	☐	☐	☐	☐	☐
9. In the past 1 month, how often have you had difficulty eating foods you would like to because of your teeth, mouth or face?	☐	☐	☐	☐	☐

Thanks for answering those questions - now please go to the next page

How do I feel about myself?

From the following questions, we would like to know **how you feel about yourself generally after you had your treatment for marks on your tooth 1 month ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face?

After reading each question, place a tick mark (√) in the box that corresponds to the answer that best suits you.

Questions	Never	Almost never	Sometimes	Fairly often	Almost all the time
1. In the past 1 month, how often have you felt worried or anxious because of your teeth, mouth or face?	☐	☐	☐	☐	☐
2. In the past 1 month, how often have you not wanted to speak/read out loud in class?	☐	☐	☐	☐	☐
3. In the past 1 month, how often have you avoided smiling or laughing with other children because of your teeth, mouth or face?	☐	☐	☐	☐	☐
4. In the past 1 month, how often have you had trouble sleeping because of your teeth, mouth or face?	☐	☐	☐	☐	☐
5. In the past 1 month, how often have you been teased, bullied, or called names by other children because of your teeth, mouth or face?	☐	☐	☐	☐	☐
6. In the past 1 month, how often have you felt that you were attractive (good looking) because of your teeth, mouth or face?	☐	☐	☐	☐	☐
7. In the past 1 month, how often have you felt that you look different because of your teeth, mouth or face?	☐	☐	☐	☐	☐
8. In the past 1 month, how often have you had difficulty saying certain words?	☐	☐	☐	☐	☐
9. In the past 1 month, how often have you had difficulty keeping your teeth clean?	☐	☐	☐	☐	☐
10. In the past 1 month, how often have you been worried about what other people think about your teeth, mouth or face?	☐	☐	☐	☐	☐
11. Overall, how healthy do you think your teeth are?	Poor ☐	Fair ☐	Average ☐	Good ☐	Excellent ☐

Who Am I Like?

I would rather play outdoors

I would rather watch TV

The following sentences in white boxes describe two kinds of kids - on the LEFT or on the RIGHT. Please read each sentence carefully. Choose which kid seems MOST like you. Once you have decided you are most like the kids on the left or right white box, go to that side of the sentence. You have to decide whether that is only *sort of true for you*, or *really true for you*. If it's only sort of true, then put a cross (X) in the box under "Sort of true for me"; if it's really true for you, then put a cross (X) in that box, under "Really true for me". The first one has been filled out to show you how.

You only put a cross (X) on **one** box for each sentence. **DON'T PUT A CROSS (X) ON BOTH SIDES, JUST THE ONE SIDE MOST LIKE YOU.** There is no right or wrong answer. We are only interested in which kids are most like you. Please look at the "EXAMPLE" below.

"EXAMPLE"

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
Example you would put an "x" here if you are someone who always liked playing outdoors	X	☐	Some kids would rather play outdoors in their spare time	BUT	Other kids would rather watch T.V.	☐	☐

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
1.	☐	☐	Some kids find it hard to make friends	BUT	Other kids find it's pretty easy to make friends	☐	☐
2.	☐	☐	Some kids are happy with the way they look	BUT	Other kids are not happy with the way they look	☐	☐
3.	☐	☐	Some kids are often unhappy with themselves	BUT	Other kids are pretty pleased with themselves	☐	☐
4.	☐	☐	Some kids know how to make classmates like them	BUT	Other kids don't know how to make classmates like them	☐	☐
5.	☐	☐	Some kids are happy with their height and weight	BUT	Other kids wish their height or weight were different	☐	☐
6.	☐	☐	Some kids don't like the way they are leading their life	BUT	Other kids do like the way they are leading their life	☐	☐
7.	☐	☐	Some kids don't have the social skills to make friends	BUT	Other kids do have the social skills to make friends	☐	☐
8.	☐	☐	Some kids wish their body was different	BUT	Other kids like their body the way it is	☐	☐
9.	☐	☐	Some kids are happy with themselves as a person	BUT	Other kids are often not happy with themselves	☐	☐

Please turn over for a few more

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
10.	☐	☐	Some kids understand how to get peers (people of same age) to accept them	BUT	Other kids don't understand how to get peers (people of same age) to accept them	☐	☐
11.	☐	☐	Some kids wish their physical appearance (how they look) was different	BUT	Other kids like their physical appearance the way it is	☐	☐
12.	☐	☐	Some kids like the kind of person they are	BUT	Other kids often wish they were someone else	☐	☐
13.	☐	☐	Some kids wish they knew how to make more friends	BUT	Other kids know how to make as many friends as they want	☐	☐
14.	☐	☐	Some kids wish something about their face or hair looked different	BUT	Other kids like their face and hair the way they are	☐	☐
15.	☐	☐	Some kids are very happy being the way they are	BUT	Other kids wish they were different	☐	☐
16.	☐	☐	Some kids know how to become popular	BUT	Other kids do not know how to become popular	☐	☐
17.	☐	☐	Some kids think that they are good looking	BUT	Other kids think that they are not very good looking	☐	☐
18.	☐	☐	Some kids are not very happy with the way they do a lot of things	BUT	Other kids think the way they do things is fine	☐	☐

Please go to the next page - nearly finished

How Do I Feel About My General Health?

NEXT, we would like to know how would you feel about your health in general. Please tick (√) one from the following options.

1. Overall, would you say your general health is?

☐	☐	☐	☐	☐
Poor	Fair	Good	Very good	Excellent

2. Overall, how has your general health changed since our last meeting 1 month ago?

Please tick (√) one from the following options.

☐	☐	☐	☐	☐
Much Worse	Worse	Same	Better	Much Better

NEARLY FINISHED... only one more page!

How Do I Feel About the Hospital?

Finally, we would like to know your opinion about this dental hospital .....

I would say this is a good dental hospital for my friends and family to be looked after in, if they needed similar treatment or care to me

Please tick (√) one only

- ☐ I agree a lot
- ☐ I agree a bit
- ☐ I disagree a bit
- ☐ I disagree a lot
- ☐ I can't decide/ I don't know

Please tell us more about your dental hospital visit

What was good?	

What could we do better?	

There, it's FINISHED!!
We REALLY appreciate the time and thought you have given to this study.

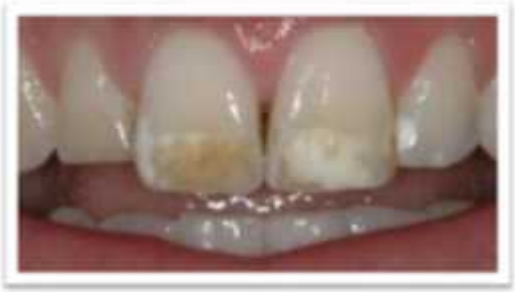
APPENDIX 14

Six month follow-up questionnaire for children aged 7-10 years

The University Of Sheffield.

I.D. Number:

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?



Questionnaire Booklet 3
(6 months follow-up for 7-10 year olds)

Investigator: Mrs Noren Hasmun
Co-Investigators: Professor Helen Rodd, Dr Mario Vettore & Dr Claire Bicock
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Claremont Crescent
S10 2ST
Sheffield

Hello

Thank you for taking part in this study. We are doing this study to better understand how children feel about their teeth and themselves. By answering the quiz, you will help us learn more about your (children's) experience with marks on their front teeth. We are interested to know if things are any different before and after the mark/s on your tooth/teeth has been treated.

Before you start, can you and your parent/guardian please tick mark (√) in the boxes below if you agree with the statements:

	Child	Parent/ Guardian
I am happy for the information given in this study to be used for research purposes	☐	☐
I am happy for the information about my/my child's treatment to be collected without my name being passed on (anonymously) to help with the research project only	☐	☐

Please remember:

- Do not write your name on the questionnaire
- This is not a test. There are no right or wrong answers
- Read each question carefully and answer the questions as honestly as you can
- If you do not understand a question, please ask for help.

Here are some questions for you to answer:

1. Please enter today's date e.g 0 6 0 9 2 0 1 6

☐☐☐☐☐☐☐☐

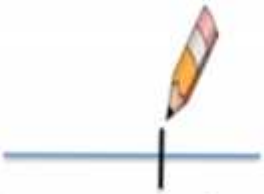
2. Are you a boy or a girl? ☐ Boy ☐ Girl (please tick √)

3. How old are you (in whole years)? Please circle your age below.

7 8 9 10 11 12 13 14 15 16

LET'S START!

How do I feel about my front teeth?

On the lines below please can you put a mark like this 

to tell us how you feel about any marks that you still have on your teeth today .

1. How worried are you about the marks on your front teeth?

0 — 10

I am very worried — I am not worried at all

2. How embarrassed are you about the marks on your front teeth?

0 — 10

I am very embarrassed — I am not embarrassed at all

3. How 'chalky' or discoloured do you think your front teeth are?

0 — 10

Very 'chalky'/discoloured — Not 'chalky' at all /discoloured

4. How happy are you with your front teeth?

0 — 10

I am very unhappy — I am very happy

How do I feel about my teeth, mouth and face?

We want to know how you feel about your **teeth, mouth and face since the treatment for marks on your tooth 6 months ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face? Please put a tick mark (√) in the box that matches to the answer that best describes you.

1. In the past 6 months, how often have you had pain in your teeth/toothache?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

2. In the past 6 months, how often have you had crooked teeth or spaces between your teeth?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

3. In the past 6 months, how often have you had discoloured teeth or spots/marks on your teeth?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

4. In the past 6 months, how often have you had bad (smelly) breath?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

5. In the past 6 months, how often have you had bleeding gums?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

6. In the past 6 months, how often have you been unhappy or sad because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

7. In the past 6 months, how often have you missed school for any reason because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

8. In the past 6 months, how often have you been confident because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

9. In the past 6 months, how often have you had difficulty eating foods you would like to because of your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

Thanks for answering those questions - now please go to the next page

How do I feel about myself?

We would like to know how you feel about your **teeth, mouth and face since the treatment for marks on your tooth 6 months ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face?

After reading each question, put a tick mark (√) in the box that matches to the answer that best suits you.

1. In the past 6 months, how often have you felt worried or anxious because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

2. In the past 6 months, how often have you not wanted to speak/read out loud in class?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

3. In the past 6 months, how often have you avoided smiling or laughing with other children because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

4. In the past 6 months, how often have you had trouble sleeping because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

5. In the past 6 months, how often have you been teased, bullied, or called names by other children because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

6. In the past 6 months, how often have you felt that you were attractive (good looking) because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

7. In the past 6 months, how often have you felt that you look different because of your teeth, mouth or face?
   - ☐ Never
   - ☐ Almost never
   - ☐ Sometimes
   - ☐ Fairly often
   - ☐ Almost all the time

8. In the past 6 months, how often have you had difficulty saying certain words?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

9. In the past 6 months, how often have you had difficulty keeping your teeth clean?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

10. In the past 6-months, how often have you been worried about what other people think about your teeth, mouth or face?

- ☐ Never
- ☐ Almost never
- ☐ Sometimes
- ☐ Fairly often
- ☐ Almost all the time

11. Overall, how healthy do you think your teeth are?

- ☐ Poor
- ☐ Fair
- ☐ Average
- ☐ Good
- ☐ Excellent

Please go to the next page

Who Am I Like?

The following sentences in white boxes describe two kinds of kids – on the LEFT or on the RIGHT. Please read each sentence carefully. Choose which kid seems MOST like you. Once you have decided you are most like the kids on the left or right white box, go to that side of the sentence. You have to decide whether that is only *sort of true for you*, or *really true for you*. If it's only sort of true, then put a cross (X) in the box under "Sort of true for me"; if it's really true for you, then put a cross (X) in that box, under "Really true for me". The first one has been filled out to show you how.

You only put a cross (X) on **one** box for each sentence. **DON'T PUT A CROSS (X) ON BOTH SIDES, JUST THE ONE SIDE MOST LIKE YOU**. There is no right or wrong answer. We are only interested in which kids are most like you. Please look at the "EXAMPLE" below.

"EXAMPLE"

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
Example you would put an "x" here if you are someone who always liked playing outdoors	X		Some kids would rather play outdoors in their spare time	BUT	Other kids would rather watch T.V.		

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
1.	☐	☐	Some kids find it hard to make friends	BUT	Other kids find it's pretty easy to make friends	☐	☐
2.	☐	☐	Some kids are happy with the way they look	BUT	Other kids are not happy with the way they look	☐	☐
3.	☐	☐	Some kids are often unhappy with themselves	BUT	Other kids are pretty pleased with themselves	☐	☐
4.	☐	☐	Some kids know how to make classmates like them	BUT	Other kids don't know how to make classmates like them	☐	☐
5.	☐	☐	Some kids are happy with their height and weight	BUT	Other kids wish their height or weight were different	☐	☐
6.	☐	☐	Some kids don't like the way they are leading their life	BUT	Other kids do like the way they are leading their life	☐	☐
7.	☐	☐	Some kids don't have the social skills to make friends	BUT	Other kids do have the social skills to make friends	☐	☐
8.	☐	☐	Some kids wish their body was different	BUT	Other kids like their body the way it is	☐	☐
9.	☐	☐	Some kids are happy with themselves as a person	BUT	Other kids are often not happy with themselves	☐	☐

Please turn over for a few more

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
10.	☐	☐	Some kids understand how to get peers (people of same age) to accept them	BUT	Other kids don't understand how to get peers (people of same age) to accept them	☐	☐
11.	☐	☐	Some kids wish their physical appearance (how they look) was different	BUT	Other kids like their physical appearance the way it is	☐	☐
12.	☐	☐	Some kids like the kind of person they are	BUT	Other kids often wish they were someone else	☐	☐
13.	☐	☐	Some kids wish they knew how to make more friends	BUT	Other kids know how to make as many friends as they want	☐	☐
14.	☐	☐	Some kids wish something about their face or hair looked different	BUT	Other kids like their face and hair the way they are	☐	☐
15.	☐	☐	Some kids are very happy being the way they are	BUT	Other kids wish they were different	☐	☐
16.	☐	☐	Some kids know how to become popular	BUT	Other kids do not know how to become popular	☐	☐
17.	☐	☐	Some kids think that they are good looking	BUT	Other kids think that they are not very good looking	☐	☐
18.	☐	☐	Some kids are not very happy with the way they do a lot of things	BUT	Other kids think the way they do things is fine	☐	☐

Please go to the next page - nearly finish

How Do I Feel About My General Health?

NEXT, we would like to know how would you feel about your health in general. Please tick (√) one from the following options.

1. Overall, would you say your general health is?

☐ Poor ☐ Fair ☐ Good ☐ Very good ☐ Excellent

2. Overall, how has your general health changed since our last meeting 6 months ago?

Please tick (√) one from the following options.

☐ Much Worse ☐ Worse ☐ Same ☐ Better ☐ Much Better

NEARLY FINISHED...only one more page!

How Do I Feel About the Hospital?

Finally, we would like to know your opinion about this dental hospital ....

I would say this is a good dental hospital for my friends and family to be looked after in, if they needed similar treatment or care to me

Please tick (√) one only

- ☐ I agree a lot
- ☐ I agree a bit
- ☐ I disagree a bit
- ☐ I disagree a lot
- ☐ I can't decide/ I don't know

Please tell us more about your dental hospital visit

What was good?	

What could we do better?	

There, it's FINISHED!!
We REALLY appreciate the time and thought you have given to this study.

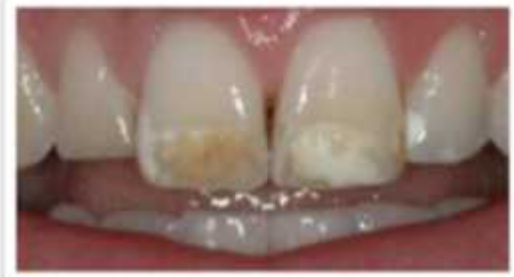
APPENDIX 15

Six month follow-up questionnaire for children aged 11-16 years

The University Of Sheffield.

I.D. Number:

How do you feel about having marks on your front teeth? Does our dental treatment make a difference?



Questionnaire Booklet 3 (6 months follow-up for 11-16 year olds)

Investigator: Mrs Noren Hasmun
Co-Investigators: Professor Helen Rodd, Dr Mario Vettore & Dr Claire Elcock
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Claremont Crescent
S10 2ST
Sheffield

Hello

Thank you for taking part in this study. We are doing this study to better understand how children feel about their teeth and themselves. By answering the questionnaire, you will help us learn more about your (children's) experience with marks on their front teeth. We are interested to know if things are any different before and after the mark/s on your tooth/teeth has been treated.

Before you start, can you and your parent/guardian please tick mark (√) in the boxes below if you agree with the statements:

	Child	Parent/ Guardian
I am happy for the information given in this study to be used for research purposes	☐	☐
I am happy for the information about my/my child's treatment to be collected without my name being passed on (anonymously) to help with the research project only	☐	☐

Please remember:

- Do not write your name on the questionnaire
- This is not a test. There are no right or wrong answers
- Answer the questions as honestly as you can
- Read each question carefully and think about how feel since the treatment you had 6 months ago.
- If you do not understand a question, please ask for help.

Please answer the following questions:

1. Please enter today's date e.g 0 6 0 9 2 0 1 6

☐☐☐☐☐☐☐☐

2. Are you a boy or a girl? ☐ Boy ☐ Girl (please tick √)

3. How old are you (in whole years)? Please circle your age below.

7 8 9 10 11 12 13 14 15 16

LET'S START!

How I feel about my front teeth

On the lines below please can you put a mark like this

to tell us how you feel about any marks that you still have on your teeth today

1. How worried are you about the marks on your front teeth?

0 10

I am very worried I am not worried at all

2. How embarrassed are you about the marks on your front teeth?

0 10

I am very embarrassed I am not embarrassed at all

3. How 'chalky' or discoloured do you think your front teeth are?

0 10

Very 'chalky'/discoloured Not 'chalky' at all /discoloured

4. How happy are you with your front teeth?

0 10

I am very unhappy I am very happy

How do I feel about my teeth, mouth and face?

From the following questions, we are interested to know how you feel about your **teeth, mouth and face since the treatment for marks on your tooth 6 months ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face? Choose the answer that best describes you in the past 6 months.

After reading each question, please put a tick mark (√) in the box that corresponds to the answer that best suits you.

Questions	Never	Almost never	Sometimes	Fairly often	Almost all the time
1. In the past 6 months, how often have you had pain in your teeth/toothache?	☐	☐	☐	☐	☐
2. In the past 6 months, how often have you had crooked teeth or spaces between your teeth?	☐	☐	☐	☐	☐
3. In the past 6 months, how often have you had discoloured teeth or spots/marks on your teeth?	☐	☐	☐	☐	☐
4. In the past 6 months, how often have you had bad (smelly) breath?	☐	☐	☐	☐	☐
5. In the past 6 months, how often have you had bleeding gums?	☐	☐	☐	☐	☐
6. In the past 6 months, how often have you been unhappy or sad because of your teeth, mouth or face?	☐	☐	☐	☐	☐
7. In the past 6 months, how often have you missed school for any reason because of your teeth, mouth or face?	☐	☐	☐	☐	☐
8. In the past 6 months, how often have you been confident because of your teeth, mouth or face?	☐	☐	☐	☐	☐
9. In the past 6 months, how often have you had difficulty eating foods you would like to because of your teeth, mouth or face?	☐	☐	☐	☐	☐

Thanks for answering those questions - now please go to the next page

How do I feel about myself?

From the following questions, we would like to know **how you feel about yourself generally after you had your treatment for marks on your tooth 6 months ago**. Before you answer, ask yourself if this happens because of my teeth, mouth and face?
After reading each question, place a tick mark (√) in the box that corresponds to the answer that best suits you.

Questions	Never	Almost never	Sometimes	Fairly often	Almost all the time
1. In the past 6 months, how often have you felt worried or anxious because of your teeth, mouth or face?	☐	☐	☐	☐	☐
2. In the past 6 months, how often have you not wanted to speak/read out loud in class?	☐	☐	☐	☐	☐
3. In the past 6 months, how often have you avoided smiling or laughing with other children because of your teeth, mouth or face?	☐	☐	☐	☐	☐
4. In the past 6 months, how often have you had trouble sleeping because of your teeth, mouth or face?	☐	☐	☐	☐	☐
5. In the past 6 months, how often have you been teased, bullied, or called names by other children because of your teeth, mouth or face?	☐	☐	☐	☐	☐
6. In the past 6 months, how often have you felt that you were attractive (good looking) because of your teeth, mouth or face?	☐	☐	☐	☐	☐
7. In the past 6 months, how often have you felt that you look different because of your teeth, mouth or face?	☐	☐	☐	☐	☐
8. In the past 6 months, how often have you had difficulty saying certain words?	☐	☐	☐	☐	☐
9. In the past 6 months, how often have you had difficulty keeping your teeth clean?	☐	☐	☐	☐	☐
10. In the past 6 months, how often have you been worried about what other people think about your teeth, mouth or face?	☐	☐	☐	☐	☐
11. Overall, how healthy do you think your teeth are?	Poor ☐	Fair ☐	Average ☐	Good ☐	Excellent ☐

Who Am I Like?

The following sentences in white boxes describe two kinds of kids – on the LEFT or on the RIGHT. Please read each sentence carefully. Choose which kid seems MOST like you. Once you have decided you are most like the kids on the left or right white box, go to that side of the sentence. You have to decide whether that is only *sort of true for you*, or *really true for you*. If it's only sort of true, then put a cross (X) in the box under "Sort of true for me"; if it's really true for you, then put a cross (X) in that box, under "Really true for me". The first one has been filled out to show you how.

You only put a cross (X) on **one** box for each sentence. **DON'T PUT A CROSS (X) ON BOTH SIDES, JUST THE ONE SIDE MOST LIKE YOU.** There is no right or wrong answer. We are only interested in which kids are most like you. Please look at the "EXAMPLE" below.

"EXAMPLE"

	Really true for me	Sort of true for me	SENTENCES LEFT		SENTENCES RIGHT	Sort of true for me	Really true for me
Example you would put an "x" here if you are someone who always liked playing outdoors	X	☐	Some kids would rather play outdoors in their spare time	BUT	Other kids would rather watch T.V.	☐	☐

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
1.	☐	☐	Some kids find it hard to make friends	BUT	Other kids find it's pretty easy to make friends	☐	☐
2.	☐	☐	Some kids are happy with the way they look	BUT	Other kids are not happy with the way they look	☐	☐
3.	☐	☐	Some kids are often unhappy with themselves	BUT	Other kids are pretty pleased with themselves	☐	☐
4.	☐	☐	Some kids know how to make classmates like them	BUT	Other kids don't know how to make classmates like them	☐	☐
5.	☐	☐	Some kids are happy with their height and weight	BUT	Other kids wish their height or weight were different	☐	☐
6.	☐	☐	Some kids don't like the way they are leading their life	BUT	Other kids do like the way they are leading their life	☐	☐
7.	☐	☐	Some kids don't have the social skills to make friends	BUT	Other kids do have the social skills to make friends	☐	☐
8.	☐	☐	Some kids wish their body was different	BUT	Other kids like their body the way it is	☐	☐
9.	☐	☐	Some kids are happy with themselves as a person	BUT	Other kids are often not happy with themselves	☐	☐

Please turn over for a few more

	Really true for me	Sort of true for me	SENTENCES LEFT		RIGHT	Sort of true for me	Really true for me
10.	☐	☐	Some kids understand how to get peers (people of same age) to accept them	BUT	Other kids don't understand how to get peers (people of same age) to accept them	☐	☐
11.	☐	☐	Some kids wish their physical appearance (how they look) was different	BUT	Other kids like their physical appearance the way it is	☐	☐
12.	☐	☐	Some kids like the kind of person they are	BUT	Other kids often wish they were someone else	☐	☐
13.	☐	☐	Some kids wish they knew how to make more friends	BUT	Other kids know how to make as many friends as they want	☐	☐
14.	☐	☐	Some kids wish something about their face or hair looked different	BUT	Other kids like their face and hair the way they are	☐	☐
15.	☐	☐	Some kids are very happy being the way they are	BUT	Other kids wish they were different	☐	☐
16.	☐	☐	Some kids know how to become popular	BUT	Other kids do not know how to become popular	☐	☐
17.	☐	☐	Some kids think that they are good looking	BUT	Other kids think that they are not very good looking	☐	☐
18.	☐	☐	Some kids are not very happy with the way they do a lot of things	BUT	Other kids think the way they do things is fine	☐	☐

Please go to the next page - nearly finished

How Do I Feel About My General Health?

NEXT, we would like to know how would you feel about your health in general. Please tick (√) one from the following options.

1. Overall, would you say your general health is?

☐	☐	☐	☐	☐
Poor	Fair	Good	Very good	Excellent

2. Overall, how has your general health changed since our last meeting 6 months ago?

Please tick (√) one from the following options.

☐	☐	☐	☐	☐
Much Worse	Worse	Same	Better	Much Better

NEARLY FINISHED.. only one more page!

How Do I Feel About the Hospital?

Finally, we would like to know your opinion about this dental hospital .....

I would say this is a good dental hospital for my friends and family to be looked after in, if they needed similar treatment or care to me

Please tick (√) one only

- ☐ I agree a lot
- ☐ I agree a bit
- ☐ I disagree a bit
- ☐ I disagree a lot
- ☐ I can't decide/ I don't know

Please tell us more about your dental hospital visit

What was good?	

What could we do better?	

There, it's FINISHED!!
We REALLY appreciate the time and thought you have given to this study.

APPENDIX 16

Data collection form

Patient ID ☐☐☐

The University Of Sheffield.

How do children feel about having marks on their front teeth? Does our dental treatment make a difference?

First treatment visit (T_0) – Page 1 to be completed for all booked patients

1. Date..... (dd.mm.yy)

2. Participation/attendance record
   1 ☐ was not brought
   2 ☐ cancelled appointment
   3 ☐ attended but found not to meet inclusion criteria..... (specify)
   4 ☐ attended but declined participation
   5 ☐ attended and consented to participate

3. Gender
   1 ☐ Male
   2 ☐ Female

4. Age..... yrs

5. Postcode.....
   (IMD Score and Deprivation Decile to be computed)
6. Ethnicity
   1 ☐ White English/Welsh/Scottish/Northern Irish/British
   2 ☐ Any other White
   3 ☐ Any ethnic minority group

Page 2 onwards to be completed for participants only

Patient ID ☐☐☐

Checks

Consent and assent signed	Yes ☐	No ☐ (do not proceed)
Pre-op photographs taken	Yes ☐	No ☐ ..... (why not)
T_0 questionnaire completed	Yes ☐	No ☐ ..... (why not)

Caries experience (data extrapolated from existing clinical records)

7. Radiographs used for caries diagnosis 1 ☐ Yes 2 ☐ No
8. Number of decayed primary teeth.....
9. Number of restored (due to caries) primary teeth.....
10. Number of extracted (due to caries) primary teeth.....
11. dmft..... (to be computed)
12. Number of decayed permanent teeth.....
13. Number of restored (due to caries) permanent teeth
14. Number of extracted (due to caries) permanent teeth.....
15. DMFT.....(to be computed)
16. dmft+DMFT .....(to be computed)

Orthodontic status

17. Aesthetic Component (AC) score undertaken 1 ☐ Yes 2 ☐ No

(if no, specify why not).....

AC Treatment Need score (1-3) .....

1 ☐ No/slight need for treatment

2 ☐ Moderate/borderline need

3 ☐ Need for orthodontic treatment

Sensitivity due to MIH

Ask for:

18. Sensitive front teeth

    0 ☐ No

    1 ☐ Yes

19. Sensitive back teeth

    0 ☐ No

    1 ☐ Yes

Severity of MIH (tick status of each tooth)

Characteristics	Severity of Characteristics	16	12	11	21	22	26	36	32	31	41	42	46
Eruption status	**0** Unerupted												
	1 Erupted												
Colour of most severe defect	**0** None												
	1 White												
	2 Cream/Yellow												
	3 Orange/Brown												
Location of most severe defect	0 None												
	1 Smooth surface												
	2 Occlusal surface (FPMs)												
	2 Incisal surface (PIs)												
	3 Cuspal involve (FPMs)												
Atypical restorations (prior to study entry)	**0** None												
	1 Present												
Post eruptive enamel breakdown (PEB)	**0** None												
	1 Present												
Stainless steel crown (SSC)	**0** None												
	7 Yes (7)												
Extraction	**0** None												
	8 Yes (8)												
Unable to score	99												

Patient ID ☐☐☐

Treatment completed at T_0

20. Any previous treatment on hypomineralised incisor/s?
    0 ☐ No
    1 ☐ Yes (specify what type of previous treatment)……

21. Number of teeth having treatment (please circle each affected tooth)

22. Treatment undertaken at T0 (specify which tooth)
    1 ☐ Microabrasion
    2 ☐ ICON

23. Details of treatment (please √)

Treatment T0	12	11	21	22	32	31	41	42
Microabrasion								
ICON								

Note any clinical observations about treatment and outcomes here

Check: Post-op photographs taken Yes ☐ No ☐ …… (why not)

Patient ID ☐☐☐

Interim visit, Ti (If needed)

24. Date..... ....(dd.mm.yy)

25. Attendance record

1 ☐ was not brought (send new appointment and complete new sheet next time)
2 ☐ cancelled appointment (complete new sheet next time)
3 ☐ attended but decline further study participation
4 ☐ attended and happy to continue in study

26. Details of treatment (please √)

1 ☐ Microabrasion
2 ☐ ICON
3 ☐ Tooth whitening
4 ☐ Composite restoration

Treatment Ti	12	11	21	22	32	31	41	42
Microabrasion								
ICON								
Tooth whitening								
Composite restoration								

Note any clinical observations about treatment and outcomes – include exact details of composite shades and use of opaquers

Check: Post-op photographs taken Yes ☐ No ☐ ..... (why not)

Patient ID ☐☐☐

1 month review T_1

30. Date..... (dd.mm.yy)

31. Attendance record
- 1 ☐ was not brought (send new appointment and complete new T_1 next time)
- 2 ☐ cancelled appointment (complete new T_1 next time)
- 3 ☐ attended but declined further study participation
- 4 ☐ attended and happy to continue in study

32. Outcome of review
- 1 ☐ patient happy with outcome no further interventions
- 2 ☐ patient not happy with outcome, further intervention required
- 3 ☐ other (specifiy eg clinician not happy).....

Note any clinical observations eg lost restoration

Checks

Post-op photographs taken Yes ☐ No ☐ ..... (why not)
T_1 questionnaire completed Yes ☐ No ☐ ..... (why not)

Patient ID ☐☐☐

6 months review T_2

33.Date……

34.Attendance record

1 ☐ was not brought (send new appointment and complete T_2 sheet again)
2 ☐ cancelled appointment (complete new T_2 sheet next time)
3 ☐ attended but declined further study participation
4 ☐ attended and happy to continue in study

35. Outcome of review

1 ☐ patient happy with outcome no further interventions
2 ☐ patient not happy with outcome, further intervention required
3 ☐ other (specifiy eg clinician not happy)……

Note any clinical observations eg lost restoration

Checks

Post-op photographs taken Yes ☐ No ☐ …… (why not)

T_2 questionnaire completed Yes ☐ No ☐ …… (why not)

Follow up postal T_2 questionnaire sent Yes ☐ No ☐ Date……
Postal T_2 questionnaire returned Yes ☐ No ☐ Date……

Data record for image analysis complete a table for each individual tooth treated

Note: analysis needs to be repeated on 10% of tooth samples to check intra-examiner repeatability

Tooth…………………	Visit 1 T_0 (pre-op)	Visit 1 T_0 (post-op)	Visit Ti	1 month review T_1	6 months review T_2
Area of labial surface					
Area of opacity					
% area of tooth occupied by opacity					
Difference in colour contrast between unaffected enamel vs opacity					

Tooth…………………	Visit 1 T_0 (pre-op)	Visit 1 T_0 (post-op)	Visit Ti	1 month review T_1	6 months review T_2
Area of labial surface					
Area of opacity					
% area of tooth occupied by opacity					
Difference in colour contrast between unaffected enamel vs opacity					

Tooth…………………	Visit 1 T_0 (pre-op)	Visit 1 T_0 (post-op)	Visit Ti	1 month review T_1	6 months review T_2
Area of labial surface					
Area of opacity					
% area of tooth occupied by opacity					
Difference in colour contrast between unaffected enamel vs opacity					

Patient ID ☐☐☐

Tooth……	Visit 1 T_0 (pre-op)	Visit 1 T_0 (post-op)	Visit Ti	1 month review T_1	6 months review T_2
Area of labial surface					
Area of opacity					
% area of tooth occupied by opacity					
Difference in colour contrast between unaffected enamel vs opacity					

APPENDIX 17
Completion of study report which was sent out to all participants

The University Of Sheffield.

How do children feel about having marks on their teeth? Does our dental treatment make a difference?

The project

We did a research project with children like you whose front teeth grew with marks on them, like the ones in this photograph. We wanted to find out what children feel about having teeth like this, and how it might affect them? We also wanted to find out if our treatment makes a difference.

These teeth didn't form properly, that's why they have coloured marks on them

Who took part in this study?

- 103 children who have marks on their front teeth (because their enamel didn't form properly) aged between 7 and 16 years participated and had their treatment. 86 children completed attended their one-and six-month review visits.

What we did?

- We assessed your teeth and discussed appropriate treatment with you and your parents.
- Most children received a combination of scrubbing (microabrasion) and resin treatment. Some children had tooth whitening, and some had composite filling after the scrubbing and resin treatment

What we found from the results?

- Children reported that they were less worried and less embarrassed about the 'marks' on their front teeth after the treatment. They also reported that their teeth were less yellow/discoloured and that they were happy with their teeth after the treatment.
- Children also reported that our dental treatment has improved their self-esteem.
- All children would recommend our dental hospital if their friends and family required the same dental treatment

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APPENDIX 18

Abstract submitted, British Society of Paediatric Dentistry conference, 2019

Assessment of clinical outcomes for the aesthetic improvement of incisor opacities

Jennifer A. Lawson. Sheffield Teaching Hospitals NHS Foundation Trust. StR in Paediatric Dentistry
Laura Timms. Sheffield Teaching Hospitals NHS Foundation Trust. Dental Core Trainee
Noren Hasmun. School of Clinical Dentistry, University of Sheffield. PhD student
Helen D. Rodd. School of Clinical Dentistry, University of Sheffield. Professor and Honorary Consultant in Paediatric Dentistry

Background

A variety of minimally invasive dental treatments can be offered to children with visible incisor opacities, which have positive impact on oral health-related quality of life. However, no measure currently exists to assess clinical outcomes.

Aim

To determine the effectiveness of micro-invasive treatment in reducing the visibility of anterior enamel opacities.

Method

Participants included children, with a diagnosis of molar incisor hypomineralisation (MIH), referred to our unit for management of incisor opacities. Standardised clinical photographs were taken pre- and post-treatment of children who underwent a variety of interventions including: tooth whitening, microabrasion, resin infiltration and composite resin restoration. The team developed a simple outcome measure, following training and calibration, based on a 5-point scale (with accompanying descriptive criteria): excellent outcome; good outcome; some improvement; no improvement and worse outcome. Two investigators then assessed the change in pre- and post-treatment tooth appearance using this scale. Intra- and inter-examiner repeatability was determined on five cases.

Results

Images from 60 children, involving 129 treated teeth, were evaluated. The majority of teeth were rated as having an excellent/good clinical outcome following treatment (79.1%), thus not warranting further treatment. 19.4% were assessed as having some improvement but 1.6% showed no improvement/worse outcome. There was perfect agreement for both inter- and intra-examiner ratings (κ=1.0).

Conclusion

It was encouraging to find a good clinical outcome in 80% of cases. However, further research is needed to identify which regimen, and opacity characteristics are likely to result in optimum clinical outcomes, to aid decision-making and manage patient/parent expectation

APPENDIX 19

Thank you card from a study participant