



**Does Orthodontic Treatment Improve the Oral Health Related Quality of Life
of Young People? A Longitudinal, Cohort Study**

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ABSTRACT

Objectives: To examine the impact of orthodontic treatment completion on the Oral Health-Related Quality of Life (OHRQoL) of adolescents aged 11-16 years, and to explore factors that may be associated with any changes observed in OHRQoL.

Background: Whilst numerous studies have explored the impact of malocclusion on OHRQoL, few have investigated how completing orthodontic treatment affects OHRQoL. Moreover, the studies that do exist have methodological limitations.

Methods: A longitudinal, prospective cohort study, conducted across 11 sites in the United Kingdom, following two groups: an Orthodontic Treatment Group (OTG), and a Waiting List Control Group (WLCG). In the OTG, OHRQoL was assessed before treatment (T1), 6 weeks to 9 months post-treatment (T2), and 9 to 32 months post-treatment (T3). In the WLCG, OHRQoL was assessed at the start (T1) and a minimum of 12 months after (T2) placement on the waiting list. The Malocclusion Impact Questionnaire (MIQ), and Child Oral Health Impact Profile Short Form-19/Oral Health Impact Profile-14 were used to measure OHRQoL. Socio-demographic, clinical, and psychosocial data were collected. Data analyses included independent samples t-test, Wilcoxon signed rank tests, and ANCOVA with bootstrapping.

Results: The study recruited 596 participants in the OTG, with 222 and 57 followed up at T2 and T3, respectively. The WLCG recruited 376 participants, with 177 followed up at T2. OHRQoL changes from T1 to T2, in the OTG and WLCG were significantly different ($p < 0.001$) with a large effect size (1.6). ANCOVA revealed that participants with lower self-esteem, better life satisfaction, and higher OHRQoL, at baseline, were more likely to experience better OHRQoL following treatment.

Conclusions: Orthodontic treatment during adolescence significantly improved OHRQoL, whilst waiting for treatment caused deterioration. This study highlights the benefits of orthodontics in improving OHRQoL and supports the effectiveness of the MIQ as a reliable tool in assessing this.

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“And still, after all this time, The sun never says to the
earth, "You owe Me." Look what happens with A love
like that, It lights the Whole Sky.”

Hāfez-e Shīrāzī

(AD 1325-1390)

14th century Persian poet

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LIST OF ABBREVIATIONS AND SYMBOLS

AC	Aesthetic component
AJO-DO	American Journal of Orthodontics and Dentofacial Orthopedics
ANCOVA	Analysis of Covariance
BCSQ	Bristol Condition-Specific Questionnaire for hypodontia
Child-OIDP	Child Oral Impacts on Daily Performance
CHQ-CF87	Child Health Questionnaire
CI	Confidence Interval
COHIP	Child Oral Health Impact Profile
COHIP-SF 19	Child Oral Health Impact Profile – Short Form 19
CPQ	Child Perception Questionnaire
CPQ₁₁₋₁₄-ISF:16	16-Item Shortened version of the Child Perception Questionnaire
DAI	Dental Aesthetic Index
DHC	Dental Health Component
DMFT	Decayed, Missing and Filled Teeth
EWB	Emotional Wellbeing
FWB	Functional Wellbeing
GDPR	General Data Protection Regulation
GOH	Global Oral Health
GTJ	Global Transition Judgement
HRA	Health Research Authority
HRQoL	Health-Related Quality of Life
ICD-11	International Classification of Diseases 11 th Revision
ICO	Information Commissioner's Office
ICON	Index of Complexity, Outcome and Need
IMD	Index of Multiple Deprivation
IOTN	Index of Orthodontic Treatment Need
IRAS	Integrated Research Application System
LLS	Lower Labial Segment
MID	Multiple Index of Deprivation

MIQ	Malocclusion Impact Questionnaire
NHS	National Health Service
NIHR	National Institute for Health and Care Research
NSA	Non-Substantial Amendment
OASIS	Orthodontic Aesthetic Subjective Impact Score
OHRQoL	Oral Health-Related Quality of Life
OIDP	Oral Impacts on Daily Performance
OR	Odds Ratio
OTG	Orthodontic Treatment Group
OS	Oral Symptoms
PAR	Peer Assessment Rating
PBMA	Program Budgeting Marginal Analysis
PCPQ	Parent-Child Perception Questionnaire
PI	Principle Investigator
PIL	Patient Information Leaflet
PROM	Patient Reported Outcome Measure
PWB	Psychological Wellbeing
QoL	Quality of Life
REC	Research Ethics Committee
SA	Substantial Amendment
ScWB	Social Wellbeing
SEM	Structural Equation Modelling
SES	Socioeconomic Status
SLSS	Student Life Satisfaction Scale
SOC	Sense of Coherence
STH	Sheffield Teaching Hospital
SWB	Subjective Wellbeing
TMD	Temporomandibular Disorders
UK	United Kingdom
ULS	Upper Labial Segment
US	United States

WHO	World Health Organisation
WHOQoL	World Health Organisation Quality of Life
WLCG	Waiting List Control Group
WTP	Willingness to Pay

DECLARATION

I, the author, confirm that the Thesis is my own work. I am aware of the University's Guidance on the Use of Unfair Means (www.sheffield.ac.uk/ssid/unfair-means). This work has not been previously been presented for an award at this, or any other, university.

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Chapter 1

Introduction

Beauty is considered subjective in nature and the concept that ‘beauty is in the eyes of the beholder’ is one that has been ingrained in society for hundreds, if not thousands of years.

***“Everything that is made beautiful and fair and lovely is made for
the eye of one who sees.”***

Jalāl ad-Dīn Muhammad Rūmī
(AD 1207-1273)
13th Century Persian poet

Whilst individuals may have different opinions on what they consider to be attractive, there is undoubtedly a significant role that cultural and societal norms can play in influencing such views (Coetzee et al., 2014). Crucially, in an era where digital technology has capitalised so many aspects of our everyday lives, the impact of social media and online platforms in influencing ‘attractive’ norms cannot be refuted (Batres and Perrett, 2014). This is of particular importance in reference to ‘Generation Z’, a generation that have never known a world without the Internet and are often considered to be true digital natives.

From an ethical perspective, whilst we may argue that on a societal level, we should refrain from judging an individual based on their level of ‘attractiveness’, the realists amongst us would maintain that there is perhaps no human characteristic that is more desired and rewarded in our society. The influence and impact of ‘attractiveness’ has been demonstrated from birth, right through to adulthood. Infant attractiveness has been shown to influence maternal behaviours, with mothers of more attractive infants found to be increasingly affectionate and playful when compared to mothers of less attractive infants (Langlois et al., 1995). Teachers have been shown to rate the academic ability of students they perceive to be more attractive, as higher, than those whom they perceive as being less attractive (Hansen, 2016). Unsurprisingly perhaps, attractiveness has also been shown to play an important role in both romantic relationships and friendships (Sprecher and Regan, 2002), and whilst this may not be an unexpected finding, the impact of attractiveness has been shown to go beyond relational relationships. Research literature has now clearly demonstrated the significant career advantages that physically attractive

individuals can experience, from more favourable employment interview outcomes (Gilmore et al., 1986), higher pay (Judge et al., 2009, French, 2002), as well as an increased likelihood of promotion (Morrow et al., 1990). Remarkably, even in university settings, attractive professors have been shown to receive significantly higher student evaluations than their less attractive counterparts (Riniolo et al., 2006, Bonds-Raacke and Raacke, 2007).

Superficially, an assumption can be made that the relationship between ‘attractiveness’ and favourable outcomes is simple; that these are a direct result of bias that occurs in the process of social evaluation and judgement. However, this relationship is likely to be more complex. It is not unreasonable to theorise that perhaps the positive bias experienced by attractive individuals encourages them to develop traits such as power and non-verbal presence, and in turn, it is these traits that lead to more favourable career outcomes (Tu et al., 2022). With such a large body of research evidence demonstrating the significant role of ‘attractiveness’ in the lives of individuals, it is crucial to question what makes an individual ‘attractive’?

Facial attractiveness has been shown to predict overall attractiveness more strongly than body attractiveness (Peters et al., 2007). Additionally, the act of smiling is thought to play an important role in the perception of facial attractiveness (Golle et al., 2014). The only facial component that has demonstrated significant correlation with the attractiveness of a smiling face is ‘smile attractiveness’ (Godinho et al., 2020). A socially perceived ‘attractive smile’ can be influenced by features of malocclusion such as dental crowding, midline discrepancies, occlusal canting, as well as the presence of spacing (Parrini et al., 2016, Yabe et al., 2021). For many individuals, the key motivating factor in seeking orthodontic treatment for ‘correction’ of malocclusion and elimination of such features, is improved smile aesthetics (Samsonyanova and Broukal, 2014). As such, it is imperative that the risks and benefits of orthodontic treatment are carefully balanced, and any claims made are supported by high quality research. The need to establish the benefits of orthodontic treatment are even more crucial in countries such as the United Kingdom (UK), where treatment is state-funded and provided by the National Health Service (NHS). It is a well-known that the NHS is very much an over-stretched and underfunded resource and thus,

the use of its' funds must be questioned and justified appropriately. It is also well recognised that patients should form the central pillar of any healthcare system and there is a growing realisation that assessment of treatment outcomes should undoubtedly be patient centred. Such outcomes form powerful tools for all stakeholders including policy-makers (Black, 2013). It is the need for high quality research, exploring the benefits of orthodontic treatment, with a particular focus on Patient-Reported Outcome Measures (PROMs), which justifies the need to explore this subject area in greater depth. Therefore, the aim of this research was to explore the impact of the completion of orthodontic treatment on the Oral Health-Related Quality of Life (OHRQoL) of adolescents aged 11-16 years. This thesis is structured into nine chapters:

Chapter 2 provides a review of the literature surrounding malocclusion, as well as the concepts of orthodontic treatment 'need' and 'demand'. Following this, the benefits of orthodontic treatment are explored, with a particular focus on dental health, function, bullying, and wellbeing. The review then moves on to define key concepts such as Quality of Life (QoL), Health-Related Quality of Life (HRQoL), and OHRQoL, providing clarity on how in particular, OHRQoL is used in healthcare, especially in orthodontics. Instruments for assessing OHRQoL in children and adolescents are discussed, alongside both clinical (including malocclusion) and non-clinical determinants that have been found to influence OHRQoL. The review then examines the literature in relation to the impact of orthodontic appliances on OHRQoL during treatment. Finally, existing research studies that have investigated the influence of completed orthodontic treatment on OHRQoL are discussed, and their limitations are comprehensively explored.

Chapter 3 describes the rationale for this research, together with the aims and objectives.

Chapter 4 describes the methods used in the research. The study design is presented, together with the methods used to recruit participants. The outcome measures and the handling of this data is described. The ethical approval and research governance requirements are outlined. Finally, the methods of statistical analysis are presented.

Chapter 5 reports the results of the study. It outlines the flow of participant recruitment and highlights the number of participants followed up at each stage of the study. It provides a descriptive analysis of the data comparing those in the two groups of the study, as well as those who completed the study to T2, compared to those who were lost to follow-up. The data analysis then provides a psychometric analysis of the Malocclusion Impact Questionnaire (MIQ). The analysis moves on to address the first research question focusing on whether there is a difference in OHRQoL change from T1 to T2, between the two groups of the study. The final analysis relates to the second research question which explores the impact that different characteristics may have on the OHRQoL observed.

Chapter 6 is a discussion of the results in relation to the aims and objectives of the study, and the two research questions the research is aiming to address. The limitations and strengths of the research are discussed.

Chapter 7 provides the conclusions of the research and makes recommendations for future clinical practice and research.

Chapter 8 contains the Bibliography.

Chapter 9 contains the Appendices.

Chapter 2

Literature Review

2.1: Introduction

Malocclusion is often considered a variation or deviation from 'ideal' occlusion. The International Classification of Diseases 11th Revision (ICD-11), which came into effect from January 2022, has included 'Malocclusion', 'Anomalies of dental arch relationship' and 'Anomalies of tooth position' under the heading of 'Dentofacial anomalies' (WHO, 2021). Undoubtedly, one could argue that the inclusion of these within the ICD-11 reflects their acceptance as diseases/health problems and further extrapolate that their treatment may help establish a state of 'health'. Of course, these are merely assumptions, which may be incorrect or misguided, and it is important that such theories are explored appropriately. One of the fundamental challenges in determining whether a 'condition' is considered a disease or health problem is that there is no universally accepted definition of disease (Scully, 2004). The assumption that disease is simply the opposite of health is also fraught with difficulties as health is equally difficult to define. Whilst the World Health Organisation (WHO) has defined health as "a state of complete physical, mental and social well-being, not merely the absence of disease or infirmity" (WHO, 1948), there is an argument that notions of health are very much context dependent and can vary significantly based on cultural and social constructs. The importance of appropriately defining and determining what a disease is, goes beyond academic interest- it also serves a practical purpose.

Whilst our medical armamentarium has vastly increased over the years, there is a fundamental need to establish which treatments and interventions should be provided, particularly in countries such as the UK, where a state-funded National Health Service (NHS) exists. The UK was, for many years, considered to be a pioneer in providing healthcare for its population. It was the first large country to provide a comprehensive range of healthcare services 'free at the point of use' using a model that is taxpayer funded. As the NHS approached its 75th anniversary, there was a significant reflection and interest in its performance, particularly compared to the healthcare systems of other countries. In 2023, the King's Fund published the results of a review comparing the NHS healthcare system to the healthcare systems of 18 other countries. The results were somewhat disappointing; the UK was found to lag other countries in relation to capital

investment into the service, as well as having low levels of key clinical staff (including doctors and nurses). Its performance on many measures of health status and health care outcomes (such as cancer survival) were also substantially poorer than other countries. Whilst the report highlighted the good protection that the population have in relation to the potentially catastrophic costs of ill health, it also emphasised that this financial protection is weaker for services such as dental care, where only 46% was covered by the NHS. The struggles of the NHS, and particularly, NHS dentistry, have been widely publicised and there is no doubt that some form of major reform is required if the system is to have any chance of functioning in the future (Hunter, 2023). Given the clear constraints that currently exist within the service, when it comes to the justification of providing orthodontic treatment on the NHS, it is imperative that we establish the prevalence of malocclusion, the 'demand' and 'need' for orthodontic treatment, and the benefits that such treatment can provide.

2.2: Prevalence of Malocclusion

There are several cross-sectional studies that have explored and attempted to quantify the prevalence of malocclusion in different population groups. The prevalence rates reported in the literature are widespread, and often range from 20% (Kumar et al., 2013) to 99.7% (Eslamipour et al., 2018). Some of the reasons for this variation include the use of different classifications and definitions of malocclusion, exploration of prevalence rates amongst dissimilar age groups, as well as a genuine difference in prevalence amongst various population groups. A systematic review combined data from 53 different studies to determine the distribution of malocclusion traits worldwide in both the mixed and permanent dentition (Alhammadi et al., 2018). The results of this review found that particular types of malocclusions were indeed more prevalent in different population groups. Whilst in Europe, Class II malocclusions made up 33.5% (SD. 17.7) of all types of malocclusion, in Africa this was only 11.5% (SD. 9.1) (Alhammadi et al., 2018). There were also significant differences found between various racial backgrounds, with Class II malocclusions affecting 22.9% (SD 14.1) of Caucasians, but only 6.8% (SD 5.0) of Africans (Alhammadi et al., 2018). Such data undoubtedly suggests that when considering the

generalizability of results from studies involving malocclusion and/or orthodontic treatment, due regard must be given to the population and geographical location from which the data is obtained.

Unarguably, the prevalence of malocclusion in most contexts is reported as being high. However, it is important to note that the presence of a malocclusion does not always necessitate the need for orthodontic treatment to 'correct' it. Whilst malocclusion can be considered a broad umbrella term used to describe a deviation from ideal occlusion, there are several distinct traits of malocclusion, such as dental crowding, spacing and impacted teeth, which may occur either alone or in combination. The impact that such individual traits may have, and therefore the benefits that may occur as a result of treatment, can vary greatly. This is further compounded by the fact that 'orthodontic treatment need' can be considered from different perspectives; 'normative' versus 'subjective need', 'clinician-assessed need' versus 'child or parent assessed need'. A number of studies have attempted to look at the possible associations between 'orthodontic needs' as assessed using different measures/groups, but the results have been highly variable (Livas and Delli, 2012). To add a further layer of complication, it is also now well established that 'orthodontic treatment need' and 'orthodontic treatment demand' are two distinct entities and there is conflicting evidence about whether these two always correlate (Ingervall and Hedegard, 1974, Ingervall et al., 1978, Taghavi Bayat et al., 2017a, Sam et al., 2015). The next section of this literature review will explore 'orthodontic treatment need', followed by 'orthodontic treatment demand' in more detail.

2.3: Orthodontic Treatment Need

Need is an important notion in public health, but as a multi-faceted concept it still lacks a universally accepted definition. A search of the literature highlights the difficulty posed in defining the term 'need' with numerous definitions now present (Asadi-Lari et al., 2003). Often, different stakeholders have different opinions on which populations and individuals have the capacity to benefit from various healthcare services, therefore influencing the

value that they associate with each of these. This is reflected clearly in Bradshaw's Taxonomy of Need (Bradshaw, 1972), which outlines different categories:

- *Normative need*: This is need as defined by experts. It is essentially based on what healthcare specialists would view as a desirable standard that individuals should be provided with in any given situation. Normative needs are not absolute, and it may be that different experts lay down different standards.
- *Felt need*: This is need as perceived by an individual. Felt needs are limited by individual perceptions and knowledge of services.
- *Expressed need*: This is a felt need that results in action.
- *Comparative needs*: This is need identified by comparing the services received by one group of individuals with those received by another comparable group.

There are a number of countries such as the UK, where healthcare, including orthodontic treatment, is state funded. Given the tax-funded nature of the NHS, there is a moral obligation to ensure that resources are used as efficiently and effectively as possible. With limited budgets, it is paramount that these resources are used, not only to provide forms of treatment or care that have demonstrable benefits for patients, but to ensure that such treatment is prioritised (and perhaps ring-fenced) for those that are likely to benefit the most. In a hypothetically, idealistic world, where budgets are non-existent and resources unlimited, orthodontic treatment could be provided to all who want it (provided of course, that the benefits of treatment still outweigh the risks). But the pragmatists amongst us acknowledge that such a hypothetical circumstance is far from reality, and healthcare commissioners will continue to face the challenges and dilemmas of deciding which services to fund. With so many definitions of 'need', and with the knowledge that various stakeholders will have different opinions on which 'needs' should be prioritised, how do healthcare systems decide which services (including orthodontic treatment) to provide?

The NHS Act was introduced in 1948, and the provision of orthodontic treatment has been within its remit from inception. However, as malocclusion is considered a 'variation of ideal occlusion', defining a threshold at which patients should be offered treatment, and

moreover, identifying those that will benefit the most from treatment, is undoubtedly a complex task. Over the years, various occlusal indices have been designed to help produce a hierarchy representative of malocclusion severity. One such index was the Index of Orthodontic Treatment Need (IOTN) which was produced in the UK (Brook and Shaw, 1989) , in response to what was known as the 'Schanschieff report' (Schanschieff S, 1986). In the mid-1980s, an enquiry into the provision of NHS dental treatment led to the publication of the 'Schanschieff report', which confirmed initial concerns that orthodontic patients were being treated in high volume caseloads, and these were often associated with poor or unnecessary treatment (Schanschieff S, 1986). The IOTN was subsequently designed to assess the need for orthodontic treatment based on the highest potential risk to the integrity of the existing teeth or supporting structures from the malocclusion. The IOTN is comprised of two components; a dental health component (DHC) that is designed to provide an objective measure of malocclusion traits, and an aesthetic component (AC), which aims to provide a subjective measure of the aesthetic impact of the malocclusion. Today, the IOTN is widely used in the UK to identify those aged 17 years and under, who are entitled to undergo orthodontic treatment funded by the NHS. Pre-determined thresholds have been established whereby patients who score a DHC of 4 or 5, (or DHC of 3 with an AC of 6 or more) are eligible for NHS funded treatment. So, if this is the threshold that is used by the NHS today to determine eligibility for NHS orthodontic treatment, it is important to explore the proportion of the population that would meet this criteria, in order to estimate the 'treatment need' within the population.

In the UK, the Child Dental Health Survey which was carried out in 2013, and was commissioned by the Health and Social Care Information Centre, provided invaluable statistical information on the dental health of 5-, 8-, 12- and 15-year-old children nationally (Office for National Statistics, 2015). These surveys are carried out every ten years and first started in 1973. The survey data are based on dental examinations that are carried out on a stratified and clustered random sample of children in different schools by calibrated dentists and nurses and can provide information about the need and demand for orthodontic treatment. Whilst different methods have been used over the years to assess the 'orthodontic condition' of children, data from the surveys suggest that approximately 30%, 32% and 36% of 15-year-olds had undergone orthodontic treatment

or had a brace fitted, in the 1993, 2003 and 2013 survey respectively (Murray et al., 2015). In the 2013 survey, 44% of 12-year-olds and 28% of 15-year-olds reported that they would like to have their teeth straightened. The reason for this difference in proportion may be that at the age of 15 years, many of those requiring orthodontic treatment are likely to be undergoing this or have already completed this treatment. A thought-provoking observation in the survey was that children from more economically deprived families, had a higher perceived need for orthodontic treatment (based on the child's desire to have straight teeth), when compared to those from more affluent backgrounds. It is challenging to hypothesize why such a difference was observed, but it likely reflects the complexity and multifaceted nature that determines an individual's desire to undergo treatment. Interestingly, the perceptions of orthodontic treatment need of the children and their parents, did not show a high level of agreement with the assessment of treatment need using IOTN. This is perhaps, a further demonstration of how our clinician-based methods of treatment need, do not necessarily correlate with patient perceived needs.

Analysis of data from the Child Dental Health Survey in 2013 also suggested that in the UK, only about half of the orthodontic treatment need is being met (Murray et al., 2015). Possible explanations for this may be lack of access to or availability of orthodontic care, or perhaps a lack of desire to undergo orthodontic treatment, but exact reasons are difficult to establish. Within the context of orthodontics, there are usually four categories of patients; those with an objective need for orthodontic treatment who undergo treatment, those with an objective need who do not undergo treatment (either because they do not want to have treatment, or because they may have other forms of dental disease which prevent them from undergoing orthodontic treatment), those without an objective need who undergo treatment, and those without an objective need who do not undergo treatment. The reasons why individuals who have an objective need for orthodontic treatment but chose not to undergo this (even though it is state funded), is of particular interest, but is very difficult to establish, as this group are unlikely to present in orthodontic settings. Often, in national surveys such as the Child Dental Health Survey, objective orthodontic treatment need is assessed using IOTN, and whilst this considers the severity of the malocclusion, it does not take account of other dental variables such as

oral hygiene and dental caries, which are important pre-requisites for orthodontic treatment provision. So, whilst such patients may theoretically qualify for NHS orthodontic treatment, it may be that this is not provided due to other dental health related issues. Such is the complexity of these decision-making processes, that exploring them within population-based cohort or cross-sectional studies is challenging, as exploration of such details in large samples can be difficult.

Although the IOTN has been used in the UK for several years to identify patients that are eligible for NHS orthodontic treatment, there are undoubtedly elements of weakness associated with the index. Firstly, many of the objective thresholds used to determine scores, and therefore treatment need, are not necessarily supported by research evidence. The Index was drawn together and published over 30 years ago, and whilst it was a significant development in the orthodontic speciality at the time, there has invariably been a substantial body of evidence published since, assessing the impact of various traits of malocclusion on the dental health of individuals. In ideal circumstances therefore, it would be prudent to ensure that the objective thresholds used to determine eligibility, are supported and justified using high quality research data.

“The good physician treats the disease; the great physician treats the patient who has the disease.”

Sir William Osler

(AD 1849-1919)

Canadian physician

Arguably, a second weakness of the Index is that it fails to fully consider the patients' perspective or consider the impact that their malocclusion has on them when determining their level of treatment need. In an era where we are striving to ensure that the services we provide within the NHS are maximised and are used to provide the most significant benefit to our patients, it is crucial that the opinions and experiences of these very patients are heard and are used to shape the framework of care provided. Moreover, there is now a substantial body of evidence to suggest there is a significant difference in what orthodontic clinicians would consider to be a definitive need for treatment, when

compared to the opinions and views of patients themselves (Hamdan, 2004, McKeta et al., 2012). In a cross-sectional study carried out in an orthodontic clinic in the UK, 187 children aged 11-16 years were recruited and data was collected on their OHRQoL, demographics, perceived need for orthodontic treatment, and objective need for orthodontic treatment (IOTN) (de Oliveira et al., 2008). The study found that the participants' perceived need for treatment was supported by OHRQoL measures, but not by IOTN, clearly demonstrating the discrepancy that exists between clinical and child perceived need for orthodontic treatment. This discrepancy clearly echoes the findings of the data obtained in the Child Dental Health survey (Office for National Statistics, 2015). So, whilst the IOTN has become firmly built into the infrastructure of our orthodontic service provision in the UK, it is certainly not without limitations, and the demands for treatment may be influenced by factors that go far beyond the objective measures of orthodontic treatment need. As such, the next section of the literature review will explore the concept of orthodontic treatment 'demand', the factors that may influence this, and the commissioning challenges faced in meeting orthodontic treatment 'needs' and 'demands'.

2.4: Orthodontic Treatment Demand & Commissioning

The demand for orthodontic treatment appears to have increased over the years. Possible reasons for this increase are thought to include heightened awareness of dental health, an improvement in the aesthetics of orthodontic appliances, as well as greater social acceptance of orthodontic appliances (Jawad et al., 2015). That said, the demand for orthodontic treatment is complex and can also be influenced by several individual factors such as self-esteem, perceived malocclusion and perceived functional limitation (Taghavi Bayat et al., 2017b). However, one major factor that is known to significantly influence the demand for treatment is a country's financial model for the provision of such care. In some countries, such as the UK (where IOTN eligibility criteria are met) orthodontic treatment is fully state-funded for those 17 years of age or younger, whilst in other countries, such as the United States (US), treatment costs may only be part-subsidised by assistance programs for lower income families. Such can be the effect of this on orthodontic demand, that a study was carried out to explore the effects of the so-called 'Great Recession', when

there was a marked decline in the global economy between 2007 and 2009, on the demand for general oral health care and orthodontic care in the US (Guay and Blatz, 2019). The study found that the number of general dental visits and orthodontic visits declined during the Great Recession, but by 2017, whilst the number of orthodontic visits had recovered, the number of general dental visits had not. Such data reflects the important role that economic factors can play in the demand for orthodontic care, and that the use of study data exploring the demand for orthodontic treatment should be interpreted and applied within the national/state context in which the data were collected.

In England, the latest figures published suggest that in 2022-2023, the cost of orthodontic treatment in the NHS was in the region of £294 million, equating to approximately 10% of the NHS' annual expenditure on dentistry (NHS Business Services Authority, 2024). It cannot be denied that the NHS is currently experiencing challenging times. Only recently, a report published following Lord Darzi's investigation into the NHS, explicitly stated that 'the NHS is in serious trouble' (Darzi, 2024), and there are now intense calls to reform the service. There is simply no doubt that in response to some of the issues raised in the report, the services currently offered within the NHS will have to be stringently analysed, and orthodontic treatment provision may well be one of these services. Even prior to the publication of the report, we had already witnessed the scrutinization of commissioning of orthodontic treatment by the NHS. The Resource Allocation in NHS Dentistry: Recognition of Societal Preferences (RAINDROP) study was a National Institute of Health Research (NIHR) funded research project that aimed to work with dental commissioners in NHS England to utilise economic-based tools in their priority setting activities (Vernazza et al., 2018). A major part of the project was the use of a program budgeting marginal analysis (PBMA) (Vernazza et al., 2023). The PBMA was undertaken by a selected panel of 11 (including three local dental network chairs, two dental commissioners, two dental public health consultants, one health economist, one dental academic and two patient/public members). The project was the first of its' kind to incorporate patient and public values into a PBMA, and it did so by using two avenues: the inclusion of the two patient/public members on the panel, as well as data from a Willingness to Pay (WTP) survey. The panel were tasked with reviewing current allocations and generating a set of weighted criteria to which services could be evaluated against. The panel then determined which services

should receive new investments, those which should be disinvested, and those where targeted efficiency improvements should be made. Interestingly, amongst a number of different recommendations made as a result of the PBMA process, the panel recommended the disinvestment of a large proportion of orthodontic treatment, with only those scoring a DHC of 5 being eligible for NHS funded treatment (Vernazza et al., 2023). Whilst this was a thought-provoking conclusion, one could argue that the results should be considered with caution. Though there will always be ongoing debate with regards to which stakeholders should be consulted and which models should be used in determining the commissioning of services within the NHS, there is little doubt that patient/public opinion should play a significant role in the process. Whilst this PBMA attempted to do this utilising WTP survey data, the panel only apportioned a small proportion of the overall score to the WTP survey data, and so its role in the final conclusions/recommendations made are likely to be very limited. Furthermore, whilst early initial methodological testing of the WTP survey data revealed limited distinction between the WTP values in the different programs (Carr et al., 2021), subsequent data collected indicated higher values for the appearance-based program components (such as orthodontic treatment), and lower values for some of the access related program components. This was in stark contrast to the final recommendations that were made by the panel, and does cast doubt on whether sufficient consideration was equated to the opinion of patients/public (Vernazza et al., 2023). Interestingly, one criterion considered by the panel was 'benefit' of the service, including the evidence base for this, and the impact it has in relation to Quality of Life (QoL) improvement. In many ways, this is a testament of how important it is that the benefits of all forms of service/treatment are established, as they play a significant role in determining whether such services should be funded by the NHS. As such, it is therefore crucial that we evaluate the potential benefits of orthodontic treatment.

2.5: The Benefits of Orthodontic Treatment

Whilst establishing the benefits of orthodontic treatment is important for healthcare commissioners and policymakers, it is also important for our individual patients. It allows clinicians to provide accurate information to patients and ensure that any claims made

regarding the benefits of treatment, are substantiated and supported by research evidence. This in turn allows patients to make an informed decision about whether they wish to undergo treatment. Given that most orthodontic treatment provided is elective in nature, the importance of this in orthodontics cannot be stressed enough. Any practicing orthodontist will know that some patients will present with what is objectively measured as a severe form of malocclusion, but the patient may have very little regard and desire to undergo orthodontic treatment. In such circumstances, communicating the potential benefits of treatment may play an important role in the final decision made by the patient.

***“It’s far more important to know what person the disease has
than what disease the person has.”***

Hippocrates of Kos

(460 BC- 370 BC)

Greek physician

Like all patients receiving healthcare treatment, those considering orthodontic care should be provided with a balanced and pragmatic account of the risks and benefits of treatment. Whilst the risks of orthodontic treatment are well documented (Travess et al., 2004) the benefits are less well-founded. Tsihlaki and Fleming (Tsihlaki and Fleming, 2019) have indicated a need to establish these using not only clinician-derived outcome measures, but also Patient-Reported Outcome Measures (PROMs).

2.5.1. Clinician versus Patient-Reported Outcome Measures

In the medical and dental world, all stakeholders within the healthcare system, including providers and policy makers would agree that patients should form the core pillar of the system. Historically, research from both disciplines was inundated with studies that focused exclusively on clinician-derived outcome measures. Lord Darzi’s report in 2008 highlighted the importance of assessing health outcomes and experiences from the perspective of the patients themselves (Department of Health, 2008) and in the last two decades, there has been a significant drive to use more encompassing PROMs. The use of

appropriately developed and validated PROMs helps provide patients with a voice and allows their opinions, priorities and experiences to be used in a way that can help shape the future of healthcare. Moreover, it also helps ensure that the finite resources used to provide healthcare are utilised in the best way possible. The drive to use PROMs in orthodontics has been encouraged for a number of years (Cunningham and Hunt, 2001), and the benefits of their use have been highlighted (Tsihlaki and Fleming, 2019). When it comes to determining the benefits of orthodontic treatment, it is therefore important that these are considered from not only the perspective of the clinician, but also from the viewpoint of our patients.

2.5.2. The Benefits of Orthodontic Treatment: Dental Health & Function

Traditionally, orthodontic treatment was thought to provide oral health benefits. Such benefits included reducing susceptibility to dental caries, periodontal disease, temporomandibular disorders (TMD), traumatic dental injuries, the sequelae of impacted teeth, as well as improving speech or mastication. The aim of this section is to explore all these areas in detail.

2.5.2.1. Dental Caries

Historically, it was hypothesized that poor teeth alignment was a risk factor for developing dental caries, as it facilitated the accumulation of bacterial plaque and made its removal more challenging. As such, several studies have attempted to explore the impact of malocclusion (particularly dental crowding) on dental caries, and whilst some have found an association between the two (Feldens et al., 2015, Kolawole and Folayan, 2019) others have not (Helm and Petersen, 1989a). Not only have the results of individual studies been conflicting, so too have the results obtained from systematic reviews in the subject area. Hafez et al (2012) conducted a systematic review evaluating the potential causal relationship between dental crowding and dental caries, placing no age restriction on the participants recruited in relevant studies. Overall, the review identified eight studies for

inclusion, but the authors were not able to carry out a meta-analysis due to significant heterogeneity and limitations in the quality of the included studies. In conclusion, the authors stated that there were no high quality studies to determine whether an association exists between dental crowding and dental caries (Hafez et al., 2012). A subsequent systematic review published by Sa-Pinto et al (2018) investigated the association between malocclusion (not just dental crowding) and dental caries in individuals aged 11-20 years. This review identified four cross-sectional studies for inclusion, three of which were included in a meta-analysis. All four studies assessed malocclusion using the Dental Aesthetic Index (DAI), and all were judged to be at high risk of bias. Overall, the authors concluded that the results of the meta-analysis suggested an association between malocclusion and dental caries, as those with a lower DAI score also had a lower Decayed, Missing and Filled Teeth (DMFT) index (Sa-Pinto et al., 2018). However, it is important to note that all the studies included were at high risk of bias, and the authors very clearly highlighted the need for longitudinal studies to be conducted, controlling for potential, yet significant confounding factors, such as socioeconomic status (SES).

When interpreting the results of studies in this subject area, it is crucial this is carried out appropriately and the temptation to make unsubstantiated assumptions is avoided. It is well documented in the literature that the presence of an association does not imply causation (Altman and Krzywinski, 2015), and the possible association of malocclusion and dental caries is a perfect example of this. Whilst some studies have considered malocclusion to be an independent variable, and dental caries a dependent variable, it is very much a reality that children experiencing high caries rates may well experience early loss of primary teeth which itself can lead to the development of malocclusion (Bhujel et al., 2016). This is even more complex as the development of dental caries is multifactorial and significantly influenced by individual susceptibility to caries, oral hygiene practices, dietary habits, as well fluoride exposure. If these elements are optimised, individuals have a reduced risk of developing dental caries. This area of research is also further complicated by the increasing number of confounding factors that are known to influence caries experience, such as SES/deprivation and type of school attended (Wang et al., 2021). To date therefore, it is unsurprising that the evidence regarding the impact of

malocclusion on the incidence of dental caries is contradictory and, given the multi-factorial nature of caries development, and the possible two-way association between dental caries and malocclusion, it is unlikely that high quality evidence will ever be able to demonstrate that malocclusion is a casual factor in the development of dental caries on a population level.

Whilst some research has focused on examining the impact of malocclusion on the incidence of dental caries, when it comes to determining the benefits of orthodontic treatment, it is perhaps more appropriate to explore caries incidence in those that have completed orthodontic treatment versus those who have not. A recent cross-sectional study conducted in South Australia compared DMFT scores in a sample of 30-year-olds (n=448), over a third of whom had previously undergone orthodontic treatment (Doğramacı and Brennan, 2019). The study found no significant difference in the long-term caries experience of the study population based on previous orthodontic treatment. Given the multi-factorial aetiology of dental caries, such findings are unsurprising. Additionally, any practicing orthodontic clinician will agree that a pre-requisite to undergoing orthodontic treatment is that a patient must be free of active caries. Orthodontic appliances themselves can in fact act as plaque retentive factors and therefore increase the risk of demineralisation and dental caries occurring. To this effect, many studies have investigated the impact of orthodontic treatment/appliances on the development of caries or demineralisation, and have explored methods to reduce the risk of this occurring (Enerbäck et al., 2018, Benson et al., 2019b). It is due to these risks therefore that clinicians consider it paramount that patients can maintain a sufficient level of oral hygiene and appropriate diet, prior to, and throughout orthodontic treatment. And whilst some types of malocclusions such as dental crowding may make achieving optimal oral hygiene levels more difficult, they do not make it unachievable.

Based on the evidence to date and the reasons highlighted, it is only reasonable to assume that on a population level, high quality research is unlikely to ever be able to demonstrate the benefits of orthodontic treatment in reducing the incidence of dental caries.

2.5.2.2. Periodontal Disease

Previously, it was hypothesised that the alignment of crowded teeth would improve access to all their surfaces and therefore help reduce the likelihood of developing periodontal disease. A systematic review exploring the association between periodontal disease and malocclusion concluded that there was a correlation between the two factors, and that subjects with greater malocclusion have more severe periodontal disease (Bollen, 2008). Whilst classified as a 'systematic review', a fundamental methodological flaw associated with the review included a lack of quality assessment of included studies. As such, the results or conclusion of the study cannot be adequately relied upon. Much like dental caries, studies investigating the association of periodontal disease and malocclusion are complex; the primary aetiological factor in the development of periodontal disease is the presence of pathogenic microflora in the dental biofilm sitting in close contact with the gingival margins (Socransky and Haffajee, 1992), with individuals displaying various levels of susceptibility. The main objective of periodontal disease prevention and treatment is the removal and disruption of this biofilm through adequate oral hygiene. Orthodontic treatment itself can exacerbate periodontal disease if the disease has not been stabilised prior to the start of orthodontic treatment (Willmot, 2008), and as such, orthodontic treatment is not routinely commenced until periodontal disease has been treated and stabilised.

In the presence of an inadequate level of oral hygiene, orthodontic appliances themselves can encourage plaque accumulation and lead to deterioration in periodontal health. As such, oral hygiene and adequate plaque control are often a pre-requisite of orthodontic treatment. It is therefore unsurprising that studies that have found an improvement in periodontal health following orthodontic treatment, have concluded that this improvement was likely due to a more effective oral hygiene regime being established during the orthodontic treatment, rather than the alignment of the teeth themselves (Helm and Petersen, 1989b, Sadowsky and BeGole, 1981). The exception to this is the presence of an anterior cross-bite when associated with an occlusal deviation on biting together, where labial displacement of the crown of a lower incisor from the line of the

dental arch can lead to periodontal bone loss around the tooth, and orthodontic treatment to correct this form of malocclusion, has obvious periodontal health benefits.

Much like dental caries, the complex and multi-factorial aetiology of periodontal disease make it unlikely that, on a population level, orthodontic treatment can be shown to have significant periodontal health benefits.

2.5.2.3. Temporomandibular Disorders

Several observational studies have associated TMD with various occlusal traits including crossbites, anterior open bites, and increased or reverse overjets (Egermark et al., 2003, Carlsson et al., 2002). In addition, the impact of orthodontic treatment on the incidence of TMD has been a subject of contention, with some claiming that treatment can lead to the development of TMD, and others advocating an improvement in TMD following treatment. Given there is a high prevalence of TMD in the general population, with some studies reporting prevalence rates as high as 30% amongst children and adolescents (Christidis et al., 2019), it is not surprising that the impact of orthodontic treatment on TMD has been explored. A systematic review evaluating the possible association between malocclusion, orthodontic treatment and TMD identified nine relevant articles (Fernandez-Gonzalez et al., 2015). Careful assessment of these led the authors to conclude that there is no evidence for a cause-effect relationship between malocclusion, orthodontic treatment and TMD, or that such treatment may help improve or prevent TMD from occurring. These conclusions echo those of a previously conducted Cochrane systematic review that found insufficient evidence to determine the relationship between malocclusion, orthodontic treatment and TMD, and described the need for high quality randomized controlled trials in the subject area to allow for appropriate evidence-based guidance to be established (Luther et al., 2010). A more recent systematic review of the subject area has also concluded that these correlations between malocclusion and TMD are minimal and unlikely to be of any clinical significance (Manfredini et al., 2017), further reinforcing the conclusion of previous systematic reviews in the subject area. They also

stress that it is important to appreciate that the presence of a correlation does not necessarily imply causation.

It is evident that beliefs linking orthodontic treatment to the development of TMD are based on long held opinions, or studies that have been found to lack basic methodological quality principles. Lack of control groups, the absence of power calculations to determine appropriate sample sizes to detect statistical significance, and unreported methods of randomization of study subjects, are some of the problems associated with studies carried out in this subject area. TMD is a condition that fluctuates throughout the lifetime of an individual, and without the presence of high-quality evidence, it is impossible to confidently state whether orthodontic treatment can help improve this. In a recent commemorative article published in the American Journal of Orthodontics and Dentofacial Orthopedics (AJO-DO) (Kandasamy et al., 2022), a reflection was made on what had been learnt about orthodontics and TMD over the last 30 years. Crucially, the authors highlighted that based on a large amount of evidence-based data that had been collated over the years, the overall conclusion now resides in the belief that conventional orthodontic treatment (with or without dental extractions), does not cause or cure TMD, and as such, orthodontic treatment should not be provided as a form of treatment for TMD.

2.5.2.4. Dental Trauma

The risk of sustaining traumatic dental injuries is thought to significantly increase in the presence of an increased overjet (Jarvinen, 1978), particularly in the presence of incompetent lips. A recent Cochrane systematic review (Batista et al., 2018) pooled the results of three randomised controlled trials assessing the impact of early treatment of large overjets on the prevention of such trauma (two-phase versus one-phase treatment) (Koroluk et al., 2003, O'Brien et al., 2009, Chen et al., 2011). The results found that a small, but statistically significant difference (OR 0.56, 95% CI 0.33-0.95) with patients who had undergone two-phase treatment (including a phase of early treatment) experiencing fewer traumas. Whilst the authors of the review publicised these results extensively,

(Macey et al., 2020, Thiruvengkatachari et al., 2015, Batista et al., 2018) the large confidence interval associated with this difference must be noted and the result interpreted cautiously. In addition to this, the authors highlighted that the evidence was deemed to be of low to moderate quality (Thiruvengkatachari et al., 2015, Batista et al., 2018). It is also important to note that patients receiving treatment at such an early stage are likely to require further orthodontic treatment in the future. Considering that most of the trauma experienced is minor, the cost-effectiveness of such an approach is debatable (Koroluk et al., 2003), and due regard must be given to the possibility of losing patient motivation when faced with such a burdensome, two-phased approach to treatment. As such, in the UK, it is widely accepted that two-phase treatment should only be considered in exceptional cases and is not considered routine practice.

2.5.2.5. Sequelae of Impacted Teeth

There are a number of occlusal anomalies such as impacted teeth, which can, if left untreated, lead to dental caries, periodontal bone loss and root resorption of adjacent teeth (Sarica et al., 2019). The impacted teeth themselves can also become cystic in nature. The benefits of treating such anomalies cannot be refuted and are evidently clear. However, the management of such impacted teeth may involve surgical removal of the tooth itself, and their management does not always necessitate the need for orthodontic treatment.

2.5.2.6. Speech

It has been established that speech is a complex interaction between the higher brain functions and the various components of the oral cavity. The production of sounds requires various degrees of articulation, for example, the tongue raising and contacting the palatal aspect of the upper incisors helps produce consonants such as 't' and 'd'. Similarly, patients that present with significant anterior open bites can at times demonstrate a significant lisp and misarticulate sounds such as 's' (Laine, 1992). It could

therefore be hypothesised that articulatory speech disorders can be expected in patients with significant malocclusions. Some traits of malocclusion that have been most commonly associated with speech problems include Class III malocclusions, increased overjets and spacing (Johnson and Sandy, 1999) and in particular, anterior open bites (Johnson and Sandy, 1999, Leavy et al., 2016). However, the general consensus is that even in the presence of a malocclusion, individuals tend to compensate articulatory sounds, as speech is often established at a young age. The exact mechanisms underlying this compensation is still poorly understood (Doshi and Bhad-Patil, 2011), but as no direct cause-and-effect relationship between malocclusion and speech has been established, there is little evidence that orthodontic treatment will help resolve such articulatory problems (Doshi and Bhad-Patil, 2011).

2.5.2.7. Mastication

The dentition plays a crucial role in masticatory performance, and it is reasonable to theorize the malocclusion may have a detrimental impact on masticatory performance and function. Key determinants in masticatory performance have been found to include age, body size, bite force, as well the number of functional tooth units (Hatch et al., 2001, Julien et al., 1996, Toro et al., 2005). However, these variables may not all be independent and the relationships between them may be complex. Whilst poor masticatory performance has been found to have a significant relationship with being underweight (de Moraes Tureli et al., 2010), it is difficult to establish the direction of a cause-effect relationship. Does being underweight lead to a reduced bite force and therefore reduced masticatory performance, or does having a reduced masticatory performance lead to being underweight? The research evidence to date has not yet established this with any certainty.

The impact of malocclusion on masticatory performance has been investigated amongst children and adolescents, and the results have been contradictory. Whilst some studies have found a difference between different types of malocclusion and masticatory performance, with Class III malocclusion subjects reporting the greatest difficulties,

followed by Class II, Class I and subjects with normal occlusion (English et al., 2002), other studies have found no significant difference between normal occlusion and Class II malocclusions (Toro et al., 2005). To date, malocclusion type and severity have failed to demonstrate or explain the variation seen in masticatory performance in children and adolescents.

The impact of orthodontic treatment on mastication has also been investigated. A longitudinal, prospective, cohort study evaluated self-perceived masticatory ability and tested masticatory efficiency, in three groups of age matched adolescent girls (65 Class II subjects who received fixed orthodontic appliance treatment, 58 untreated Class II group, and 60 subjects with normal occlusion). The study found that regardless of occlusal status, masticatory efficiency increased with age during adolescence (Henrikson et al., 2009). Furthermore, the normal occlusion group presented better masticatory efficiency than both other groups, at both time points (Henrikson et al., 2009).

The IOTN clearly distinguishes the DHC score awarded for Class III malocclusions (reverse overjet) based on the presence of masticatory or speech difficulties, which can have a significant impact on whether a patient is deemed eligible for NHS orthodontic treatment or not. To date however, there is still no substantial body of evidence to support an improvement in either masticatory function or speech following orthodontic treatment and differentiation in eligibility for treatment based on such a variable, is questionable.

2.5.3. The Benefits of Orthodontic Treatment: Bullying

The impact of malocclusion on teasing and bullying in children and adolescents has been explored in a number of different countries (Shaw et al., 1980b, Seehra et al., 2011, Al-Bitar et al., 2013). Investigations into bullying have found that teeth are often the most common feature identified as a target (Al-Bitar et al., 2013). In particular, this has been associated with the presence of spacing/missing teeth, shape or colour of the teeth, and prominent maxillary anterior teeth (Al-Bitar et al., 2013). A recent systematic review exploring the relationship between malocclusion and bullying in schoolchildren and

adolescents identified nine studies for inclusion, eight of which were cross-sectional in design and one that was a cohort based study (Tristão et al., 2020). Based on these, the authors concluded that malocclusion and in particular, malocclusion traits including increased overjets/overbites, anterior spacing or missing teeth were all associated with bullying, but this evidence was of low quality (Tristão et al., 2020). A recent cross-sectional study in the South East of the UK, explored the prevalence of bullying in 10- to 14-year-olds (DiBiase et al., 2024). In total, the authors collected data from 698 participants and found the prevalence of bullying to be 9.7%. Higher rates of bullying were found amongst participants with an increased overjet ($p=0.02$), and those who had a greater need for treatment as measured by IOTN DHC ($p=0.01$) and clinician-assessed AC ($p=0.01$).

From the literature published to date, there is a general consensus that teasing and bullying frequently occur due to the presence of an unattractive arrangement of teeth, but there is still little evidence to demonstrate the role of orthodontic treatment in reducing the incidence or severity of bullying. This can be difficult to determine as orthodontic treatment is often carried out during adolescence, and bullying is frequently found to be most severe during the ages of 11 to 13 years (Eslea and Rees, 2001). In addition to this, bullying and the impact it has on individuals is complex, with bullied individuals reporting a diverse range of psychological impacts and developing various coping mechanisms (Chan et al., 2017). One follow-up study, based in the UK, attempted to assess the impact of interceptive orthodontic treatment in the self-reported bullying of orthodontic patients who had previously been identified as being bullied (Seehra et al., 2012). A total of 27 participants were included at the outset of the study, and at follow-up, 21 participants reported that they were no longer being bullied due to the presence of their malocclusion. However, the time point at which follow-up of the participants was carried out was not after the completion of orthodontic treatment, and many of the participants were still wearing some form of orthodontic appliance (Seehra et al., 2012). Given the small sample size, lack of sample size calculation, and some participants still undergoing orthodontic treatment and wearing appliances, the results of the study must be interpreted with caution and cannot be used to make any substantial claims regarding the benefits of orthodontic treatment in reducing bullying (Seehra et al., 2012).

2.5.4. The Benefits of Orthodontic Treatment: Wellbeing

As a practicing clinician, it is not uncommon to see orthodontic patients for their initial assessment and find that their presenting complaint is based on concerns regarding the impact of their malocclusion on their daily interactions. This includes acts such as smiling or having their photograph taken, as well as interacting with their peers and others within society. Their desire to undergo orthodontic treatment often revolves around the idea of improving their dental or smile aesthetics, and there is now evidence in the literature to support this (Prabakaran et al., 2012). Similarly, when reviewing patients following the completion of orthodontic treatment, patients often report an improved sense of happiness or wellbeing and discuss ways in which the treatment has altered their life. It is therefore important that if such improvements do occur following the completion of orthodontic treatment, they are captured and measured appropriately. This in and of itself poses difficulties; with so many different outcome measures and synonyms including happiness, wellbeing and QoL, how do we decide which outcome measure to use?

For the novice researcher in the field, understanding the conceptual distinctions between happiness, wellbeing and QoL is challenging (Park et al., 2023). This is not least because the terms can represent very different connotations depending on the context in which they are being considered. There is no doubt that happiness is subjective in nature and can mean very different things to different people; whilst behavioural scientists may consider happiness to be a compound of emotions experienced when an individual achieves something good or positive, neurologists view happiness as a vast release of hormones, such as serotonin in the brain as a reward for positive actions or achievements. To further complicate matters, 'happiness' and 'wellbeing' are sometimes used synonymously in the literature, so to truly understand these concepts, it is important to explore the theoretical constructs that underpin the concept of 'wellbeing'. In the last few decades, there has been significant and widespread interest in the measurement of wellbeing including, but not limited to, health researchers, policy makers and even politicians. In 2006, David Cameron, the UK Conservative leader at the time, famously stated in one of his speeches that;

"Wellbeing can't be measured by money or traded in markets. It's about the beauty of our surroundings, the quality of our culture and, above all, the strength of our relationships. Improving our society's sense of wellbeing is, I believe, the central political challenge of our times."

David Cameron (2006)

Former UK Conservative leader

Even amid a world-changing pandemic, at a time when governments were burdened with making unprecedented restrictions on the free movement of individuals in an attempt to limit the spread of the notorious COVID-19, the importance of maintaining wellbeing was not neglected. Whilst announcing these restrictions, the UK Prime Minister, Boris Johnson, emphasised this in his statement on the 22nd of March 2020:

"Of course, I want people to be able to go to the parks and open spaces and to enjoy themselves- it is crucial for health and mental and physical wellbeing'.

Boris Johnson (2020)

Former UK Prime Minister

It is obviously crucial that if we are to measure wellbeing, we must first establish how wellbeing is defined. One of the fundamental problems when reading the literature on wellbeing is that there are many 'definitions' and 'descriptions' of the construct, often with very little differentiation between the two. Despite this however, in behavioural sciences, wellbeing research is often described as reflecting two broad, but old philosophical orientations, known as *hedonic* and *eudaimonic* wellbeing. The core philosophy of *hedonism* is that the objective of life is to experience the greatest amount of pleasure and is based on pursuing happiness and a pleasant life (Diener, 1984). In the field of modern psychology, the predominant concept that stems from *hedonism* is 'subjective wellbeing' (SWB). SWB is a multi-dimensional construct, composed of three distinct, but inter-related components; presence of positive affects, relative lack of negative affects, and people's cognitive evaluations of their life circumstances (life satisfaction). Despite the wide use of this conceptualisation of wellbeing, some academics have emphasised a different perspective of wellbeing, often referred to as *eudaimonic* wellbeing. This form of wellbeing is centred on the fulfilment of human potential and a

meaningful life. It involves perceived thriving in the face of life challenges, including pursuing important goals, growing and developing as a person, and establishing quality ties to others (Ryff and Keyes, 1995). To differentiate it from the more *hedonistic* form of SWB, it is often referred to as 'psychological wellbeing' (PWB).

2.5.4.1. Psychological Wellbeing

Carol Ryff, one of the most prominent advocates of this form of wellbeing has proposed a six-factor model of PWB (Ryff, 1989) which includes:

- Self-acceptance
- Personal growth
- Purpose in life
- Environmental mastery
- Autonomy
- Positive relations with others

Understanding the conceptual distinction between these two types of wellbeing is challenging; on one hand, some of the literature suggests that SWB and PWB encompass distinct aspects of wellbeing (Diener et al., 2018), whilst other areas of the literature claim that the two are simply different approaches to the study and assessment of wellbeing, and are thus more similar than they are different (Chen, 2013). Attempts have been made to help address this conundrum. A recent bifactor analysis of PWB and SWB found that when wellbeing is tested at a general level, the two constructs are more similar than they are different, therefore supporting the notion that that the two are similar constructs (Chen, 2013). However, when wellbeing was examined with the specific components of PWB and SWB, the two constructs demonstrated distinctness. Based on this, the authors concluded that both perspectives have merit, and this is very much influenced by the level of analysis (Chen, 2013).

Previously, there was speculation that perhaps the presence of malocclusion may have a negative impact on wellbeing, including PWB (O'Brien et al., 2003). If this is true, it could be hypothesised that correction of malocclusion using orthodontic treatment can lead to improvements in PWB. When we consider the impact of malocclusion on PWB, one of the largest landmark studies of its' time, was published over 40 years ago evaluating the psychological effects of malocclusion on a sample of 1018, 11- to 12 -year-olds in the UK (Kenealy et al., 1989). The study found no strong evidence that children with a malocclusion were psychologically disadvantaged. However, the authors drew attention to the fact that the measures used to assess psychological status, may not have been suited to detect impact on those with a malocclusion (Kenealy et al., 1989). The follow-up of this longitudinal study also found that orthodontic treatment had no long-term impact on PWB (Kenealy et al., 2007, Shaw et al., 2007). The lack of association between malocclusion and PWB, and subsequent orthodontic treatment and PWB may lie in the complex and dynamic nature of PWB.

PWB is a concept that is based on how content an individual feels with him- or herself (self-esteem), and is a combination of feeling good and functioning effectively (Huppert, 2009). The concept of feeling good is not only based on happiness and contentment, but also emotions such as interest, engagement, confidence and affection. Functioning effectively on the other hand, is centred on the development of an individuals' potential, having a control over their life, having a sense of purpose and experiencing positive relationships (Huppert, 2009). Research has suggested that positive emotions lead to positive cognitions and behaviours and increased cognitive capability. In turn, these are thought to stimulate positive emotions (Fredrickson and Joiner, 2002), which suggests there is a vicious cycle phenomenon.

There has been debate about whether PWB can be considered a trait that is generally stable over time, or whether it fluctuates in response to change in circumstances. Exploration of this requires an understanding of factors that are known to influence and determine PWB levels. Such factors can include an individuals' environment, actions and personality. Early research on personality traits led to the emergence of the Big Five traits of neuroticism, extraversion, openness, agreeableness and conscientiousness (Fiske,

1949). When these five traits are considered, low levels of neuroticism and high levels of extraversion have been found to strongly correlate with high levels of PWB (Kokko et al., 2013). Furthermore, traits such as conscientiousness, openness and agreeableness are also linked to PWB (Kokko et al., 2013). These findings echo those found in previous studies (Siegler and Brummett, 2000, Grant et al., 2009). Since the introduction of the Big Five traits, a more recent model known as HEXACO has emerged as an alternative (Lee and Ashton, 2004). HEXACO is an acronym for the six broad traits of Honesty-Humility, Emotionality, Extraversion, Agreeableness, Conscientiousness, and Openness. Each of these six factors is associated with a range of facets (For example, Extraversion is associated with social self-esteem, social boldness, sociability and liveliness). An excellent, comprehensive meta-analysis was recently published that explored the relationship between the domains and facets of the Big Five and HEXACO personality models, with SWB and PWB (Anglim et al., 2020). Despite the difficulties previously discussed in defining and differentiating between SWB and PWB, the authors of the study clearly stated that they were using the three dimensions of life satisfaction, positive affect and negative affect to represent SWB, and the six dimensions of positive relations, autonomy, environmental mastery, personal growth, purpose in life and self-acceptance to reflect PWB. In the meta-analysis, large correlations were found between PWB and environmental mastery, personal growth and self-acceptance, whilst smaller correlations were found for life satisfaction and autonomy. In the HEXACO framework, extraversion demonstrated the most significant correlation with PWB. Strong correlations were also found between openness and personal growth, as well as conscientiousness and purpose in life (Anglim et al., 2020). In the Big Five framework, lower levels of neuroticism were strongly correlated with higher levels of PWB (Anglim et al., 2020). Overall, the authors concluded that personality is crucial to the experience of SWB and PWB, but that personality traits can change throughout life. It is therefore important to explore the factors that may influence personality.

“As to the mental essence, we find it in infants devoid of every mental form”.

Ibn Sīna (Latinized: Avicenna)

(AD 980-1037)

Persian physician-polymath

It is recognised that personality is greatly influenced by both genetic and environmental factors (Bouchard and Loehlin, 2001) . However, the extent to which each factor plays a contributory role is a subject of great research interest. Previously published twin studies have suggested that approximately half the variance observed in personality can be attributed to genetics, whilst the other half is influenced by environmental variation (Lykken et al., 1993). A significant assumption that was made by such historical studies is that the level of variation is a constant across the entire population, though the use of statistical models has challenged this. This area of research is particularly complicated, as it is now recognised that the distinct traits of personality, such as those described in the HEXACO model, can show different genetic and environmental variance, at different ages, throughout the lifespan of an individual (Kandler et al., 2021). The extent of genetic variance in extraversion, agreeableness and openness for example, has shown a reverse 'U-shaped' pattern across age, whilst it appears to decline for honesty-humility and conscientiousness (Kandler et al., 2021). The development and use of new statistical models have allowed academics to assess the impact that environmental variables such as parental relationship, can have on this genetic-environmental interaction. It has been found that parental relationship itself can both enhance and lessen the impact of genetics on establishing personality (Krueger et al., 2008). Interestingly, studies have found that once personality traits are established, individuals experience an increased level of self-confidence, warmth, self-control and emotional stability, and this tends to increase with age (Roberts and Mroczek, 2008). It has also been found that whilst individuals demonstrate unique patterns of development during the different stages of life, these patterns can be strongly influenced by individual life experiences (Krueger et al., 2008).

One of the strongest predictors of PWB is considered to be levels of self-esteem (Diener and Diener, 1995). Self-esteem is defined as a person's subjective evaluation of his or her worth as a person (Du et al., 2017). It includes feelings of self-acceptance and having a positive attitude towards oneself and is one of the facets of extraversion in the HEXACO model of personality. Determining the factors that help establish levels of self-esteem and the subsequent fluctuations that occur over an individual's lifetime are important. Research evidence suggest that self-esteem is a key player in many aspects of life,

including social relationships, school, education, work, physical health, as well as mental health (Orth et al., 2012). Over the last two decades, longitudinal evidence has found that self-esteem has similar characteristics to personality traits such as emotional stability and conscientiousness (Orth et al., 2010) and there has been great debate about the patterns of fluctuation that occur in self-esteem levels over an individuals' life span. In an attempt to address this, a recent meta-analysis combined longitudinal data on mean-level change in self-esteem, assessing the development of self-esteem from the age of 4 to 94 years (Orth et al., 2018). This generated a significant data set, combining the data from 331 independent samples (164,868 participants). Interestingly, the results showed that self-esteem levels increased between the ages of 4 to 11 years, remained stable between 11 to 15 years. and increased significantly until the age of 30 years. Between 30 and 60 years, levels continued to increase, reaching a peak at the age of 60 years. From the age of 70 years onwards, levels began to decline. Remarkably, this pattern of mean-level change was consistent across gender, country, ethnicity, sample type and birth cohort. Of particular note is that the results of this meta-analysis challenge the previously held beliefs that self-esteem is least stable during adolescence and only stabilises after this time period (Orth et al., 2010, Trzesniewski et al., 2003). In fact, the results of the meta-analyses suggest that self-esteem is largely stable between the ages of 11 and 15 years, which is particularly important, as this is the age at which most orthodontic treatment is carried out.

Decades of research exploring PWB have demonstrated the complexity of this form of wellbeing, with several factors acting and interacting to influence the levels of PWB individuals' experience. Predictors of PWB have even been explored during the COVID-19 pandemic, where dramatic shifts were observed in daily life (Tuason et al., 2021). A total of 938 volunteers based in the US completed an online questionnaire during April 2020. The study found that PWB was significantly predicted by factors such as physical health, spirituality, emotional and social loneliness and job security (Tuason et al., 2021).

With so many different factors influencing PWB, it is unsurprising that no definitive, evidence-based conclusions regarding the impact of malocclusion on PWB can be established. This is further complicated when considering the impact of orthodontic

treatment on PWB, as this form of treatment often occurs during adolescence when individuals are experiencing significant physical and psychological changes. When it comes to the study of PWB and malocclusion/orthodontic treatment, one could argue that the direction of research in the field has changed over the years; whilst previously it was speculated that malocclusion could perhaps have a negative impact on PWB, the latest research in the field suggests that it is in fact PWB levels that influence how an individual is affected by their malocclusion, and in turn the benefit they may experience following their orthodontic treatment (Agou et al., 2011, Deng et al., 2018). This is an area that will be explored in more detail in later sections of this literature review.

Based on the evidence to date, there is a general consensus that on a population level, orthodontic treatment is unlikely to improve levels of PWB (Benson et al., 2015b). But where do we stand when it comes to determining the impact of malocclusion/orthodontic treatment on the SWB of individuals? A search of the literature reveals that no studies specifically assessing the impact of malocclusion/orthodontic treatment on SWB as a single construct have been reported. One possible reason for the lack of studies utilising SWB in this field may be that whilst some authors believe SWB and QoL are two separate constructs (Skevington and Bohnke, 2018), others believe that QoL is composed of various objective and subjective indicators, and that SWB is merely one element of the subjective components (Costanza et al., 2007). It is factors such as this that perhaps make QoL a fundamental and more important player in orthodontic outcome measures.

2.6: Quality of Life

The multidimensional concept of QoL has generated a great deal of interest. Whilst historically, emphasis was exclusively directed towards mortality and morbidity, advances in medical fields such as dialysis and transplantation, have encouraged a shift in focus and a drive towards a more pragmatic and well-balanced assessment of impact, with a particular focus on QoL. As a medical term, QoL was first introduced into the literature in the 1960s, although early notions of QoL can be dated back to philosophers such as

Aristotle (384-322 B.C.) who wrote about the concepts of 'good life' and 'living well' (Aristotle and Browne, 1853).

"I would rather have a short life with width rather than a narrow one with length."

Ibn Sīna (Latinized: Avicenna)

(AD 980-1037)

Persian physician-polymath

In the 1930s, academics, as well as clinicians, expressed a great deal of interest in the concept of QoL, and various attempts were made to define, measure and investigate the subject. However, it was during the second half of the twentieth century when it became evident that QoL can be influenced by factors other than material wealth, including health, education and welfare. By the 1990s, several large research centres had been set up to investigate the QoL of populations and there was a significant increase in the amount of research in this field. These included the World Health Organisation Quality of Life (WHOQoL) group who formally defined QoL as:

"An individuals' 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. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment." (WHOQOL, 1995).

2.7: Health-Related Quality of Life

Although there are several factors that can impact on QoL, it is well recognised that health and disease can play a significant role.

"A wise man should consider that health is the greatest of human blessings, and learn how by his own thought to derive benefit from his illnesses".

Hippocrates of Kos

(460 BC- 370 BC)

Greek physician

When considered in this context, the term 'Health-Related Quality of Life' (HRQoL) is used as an attempt to differentiate it from other aspects of QoL. However, some of the literature suggests that the distinction between 'QoL' and 'HRQoL' is problematic, as definitions of HRQoL fail to sufficiently differentiate it from QoL (Karimi and Brazier, 2016). Despite the lack of agreement on the definitions and dimensions of HRQoL, there is a consensus that it is a multidimensional construct and includes physical, mental, emotional and social functioning. It is also well recognised that research in HRQoL should be based on conceptual models as these can help enhance our understanding of the relationships between the dimensions of HRQoL and other variables or constructs that can influence these (Bakas et al., 2012). One such theoretical model of HRQoL has been designed by Wilson and Cleary (Wilson and Cleary, 1995). This model conceptualizes the relationships between clinical factors, characteristics of an individual and their environment. It has been found to be the most commonly used model in health research (Bakas et al., 2012) and clearly illustrates the way in which the assessment of interventions has shifted from a bio-medical model of health, where disease is simply viewed as a pathological process, to a bio-psychosocial model where disease is assessed based on its impact on physical functioning and wellbeing (Bowling and Ebrahim, 2001). In the model (Figure 1), a taxonomy of different health outcomes is proposed, namely, biological and physiological, symptoms, functioning, general health perceptions, and overall QoL. The model highlights the influential role that characteristics of an individual and the environment can have, either directly, or as mediators, on each of these outcomes.

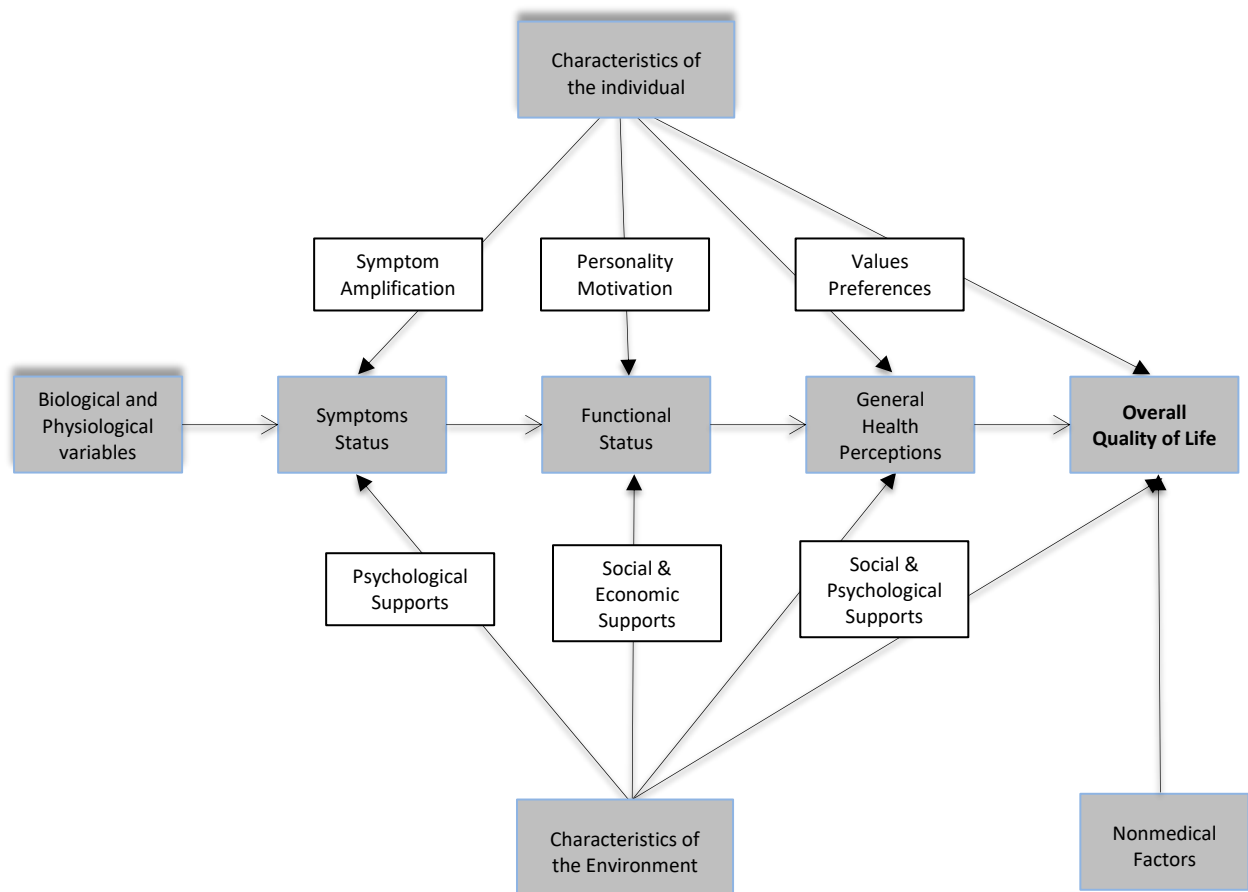


Figure 1: The Wilson-Cleary model of patient-centred outcomes
Reproduced from Wilson and Cleary (1995).

One feature of this model that is particularly noteworthy, is that it can to be applied to all individuals irrespective of age, health, disease condition and culture (Bakas et al., 2012). In addition to this, it has been shown to demonstrate good features for the evaluation of HRQoL in chronic diseases (Ojelabi et al., 2017).

It is widely accepted that oral health problems are very rarely life threatening. However, the importance of oral health cannot be refuted, as there is now a growing body of evidence to demonstrate the way in which oral health is closely related to systemic health (Dorfer et al., 2017). As such, oral health can be considered to play a significant role in HRQoL, and this is where OHRQoL becomes a key player.

2.8: Oral Health-Related Quality of Life

The WHO defines oral health as ‘a state of being free from chronic mouth and facial pain, oral and throat cancer, oral infection and sores, periodontal (gum) disease, tooth decay, tooth loss, and other diseases and disorders that limit an individual’s capacity in biting, chewing, smiling, speaking, and psychosocial wellbeing’ (WHO, 2003). As such, oral health and its associated problems can have physical, social, economic and psychological consequences and can therefore impact significantly on HRQoL.

Although OHRQoL is a concept that has only emerged over the last few decades, it plays a significant role in general health and wellbeing. The underlying principles of OHRQoL are based on the interactions that occur between and among oral health conditions, social and contextual factors, as well as the rest of the body. Whilst oral health provides a description of an individual’s oral status, OHRQoL aims to provide a subjective evaluation of that status. In order to reflect this, Locker and Allen (Locker and Allen, 2007) have published what is now a universally accepted definition of OHRQoL:

“The impact of oral diseases and disorders on everyday life that a patient or person values, that are of sufficient magnitude, in terms of frequency, severity or duration to affect their experience and perceptions of their life overall.”

OHRQoL measures are an invaluable tool in assessing the impact of adverse oral health conditions on the lives of children and their families (Cunningham and Hunt, 2001). Moreover, similar to other HRQoL measures, they can serve as an adjunct to objectively measured clinical outcomes when evaluating different treatments. In addition to this, they can be useful in the development of clinical guidelines and policies, as well as the prioritisation of healthcare (Bennadi and Reddy, 2013).

Whilst there is agreement that OHRQoL is a multidimensional attribute, there is still some variation in the literature about what dimensions these are. Some studies have demonstrated that OHRQoL is composed of four main dimensions of oral function, orofacial pain, social impact and psychological impact (John, 2007), whilst other studies

state that these four dimensions are oral function, orofacial pain, orofacial appearance and psychosocial impact (John, 2021). This demonstrates the variability in findings that may be found when using different instruments when measuring OHRQoL.

2.8.1. The Assessment of Oral Health-Related Quality of Life

Many instruments have been designed to assess OHRQoL. These are often designed for use in specific age groups, but as the majority of patients undergoing orthodontic treatment are children or adolescents, this literature review will specifically explore some of the instruments that have been designed for use in this age group.

2.8.1.1 Generic OHRQoL Instruments for Children and Adolescents

Any instrument used to assess OHRQoL must be standardised, valid and reliable, so that any data obtained is comprehensive and relevant. The importance of measuring OHRQoL outcomes in orthodontic patients, particularly children or adolescents, is well publicised (Cunningham and Hunt, 2001). However, the assessment of OHRQoL in this age group has traditionally been fraught with difficulties. Concerns have included the cognitive capacity and communication skills of children when completing OHRQoL questionnaires and for this reason, historically, parents' views were sought instead (Barbosa and Gavião, 2008a). However, the appropriateness of this has been questioned, and discrepancies have been observed in levels of OHRQoL reported between children and their parents, particularly in the emotional and social dimensions (Barbosa and Gavião, 2008c). As a result of this, several instruments for measuring OHRQoL in children and adolescents have now been designed and validated. In a recent systematic review, nine instruments were identified as being used in the assessment of OHRQoL in schoolchildren and adolescents, and of these, the CPQ₁₁₋₁₄ was rated highly (Zaror et al., 2019).

Child Perception Questionnaire (CPQ)

The Child Oral Health Quality of Life Questionnaire is a generic instrument designed to assess the adverse impacts of oral conditions on children. It consists of a questionnaire for children known as the Child Perception Questionnaire (CPQ), as well as a questionnaire for parents (Parents Perception Questionnaire). This is also complimented by a Family Impact Scale, which is also completed by parents (Jokovic et al., 2002, Jokovic et al., 2003, Locker et al., 2002).

The CPQ has three versions for different age groups: 6- to 7-year-olds, 8- to 10-year-olds, and 11- to 14-year-olds. CPQ₁₁₋₁₄, which is designed for use in 11- to 14-year-olds (which is the age range when most orthodontic treatment is provided) consists of 37 questions across four dimensions; six based on oral symptoms (OS), nine centered on functional limitations (FL), nine to assess emotional wellbeing (EWB) and 13 questions measure social wellbeing (ScWB) (Jokovic et al., 2004, Foster Page et al., 2005). The questions ask about the frequency of events experienced by a child in the last 3 months, and the sum of the responses generate domain scores and an overall CPQ₁₁₋₁₄ score. Higher scores of CPQ₁₁₋₁₄ are associated with poorer OHRQoL levels. A large number of studies have tested the validity of this instrument including one conducted by O'Brien et al (O'Brien et al., 2007). This was a cross-sectional study and based on children aged 11 to 14 years in the UK. The study included two groups; a malocclusion group made up of children with either dental crowding, an increased overjet, or hypodontia, who were due to commence orthodontic treatment, and a second group of children (non-malocclusion) with IOTN scores of 1 or 2 and a DMFT_≤2. The authors found a statistically significant difference in CPQ₁₁₋₁₄ scores between the malocclusion and the non-malocclusion group. As such, they concluded that the instrument was valid for use in similar patient cohorts.

Child-Oral Impacts on Daily Performance (Child-OIDP)

The Child-OIDP is also an instrument that has been used extensively in children (Gherunpong et al., 2004). It was based on the original Oral Impacts on Daily Performance

(OIDP) index and was developed and tested among children aged 11 to 12 years, using interviews. It assesses oral impacts on the daily life of a child and focuses on eight daily performances: Eating, speaking, cleaning the mouth, sleeping, smiling, studying, emotion, and social contact. The frequency and severity of the impacts are each recorded on a scale of 0 to 3, and the total impact for each daily performance is calculated by multiplying the two scores in each category. The overall Child-OIDP score is based on the total sum of the scores for each impact (0 to 72), multiplied by 100 and divided by 72. Evidently, the higher the Child-OIDP scores, the more detrimental the impact on OHRQoL.

A study assessing the quality of OHRQoL measures in children, found limited positive evidence to support the construct validity, reliability and interpretability of the Child-OIDP (Gilchrist et al., 2014). The authors also noted that although the instrument has been used longitudinally, it has not in fact been validated for use in this way and therefore caution must be exercised if it is used in the same individuals over time (Gilchrist et al., 2014).

Child Oral Health Impact Profile (COHIP)

The Child Oral Health Impact Profile (COHIP) is similar to the CPQ but also includes positive health constructs (Broder et al., 2007) and is designed for use in 8- to 17-year-olds. This instrument is a questionnaire and is composed of 34 questions across 5 domains: Oral health, functional wellbeing, social/emotional wellbeing, school environment and self-image. Subjects are asked to rate responses based on their experiences over the last three months on a five-point Likert scale that is scored from 0 to 4. The negative items have their scores reversed and therefore unlike CPQ, the higher the COHIP scores, the better the levels of OHRQoL. This instrument has been found to show adequate content and construct validity, but there is limited evidence of its reliability (Gilchrist et al., 2014).

These instruments are some of the most used in children and adolescents, and all seek to measure the impact of oro-facial conditions on OHRQoL and its' contributing dimensions. Although they have been used in the assessment of orthodontic patients previously, they have not been designed specifically for use in this population group. Concerns have been

raised that many of the generic OHRQoL instruments designed for use in dentistry are not applicable to orthodontic patients. This is often attributed to the fact that orthodontics is aimed at the treatment of malocclusion, and malocclusion itself is a condition that is often asymptomatic and primarily concerned with aesthetics (O'Brien et al., 1998).

Consequently the need to develop and validate condition and age-specific measures of OHRQoL for orthodontic research has been highlighted (Cunningham and Hunt, 2001). It is thought that such a measure helps focus on problems that are relevant to the condition, and their specific nature means that they are more likely to respond to change, however subtle these may be (Robinson, 2016). In light of this, a malocclusion-specific OHRQoL instrument has now been developed to help overcome these concerns (Benson et al., 2016, Patel et al., 2016).

2.8.1.2. Malocclusion-Specific OHRQoL Instruments for Children and Adolescents

Malocclusion Impact Questionnaire (MIQ)

The MIQ is a condition-specific measure that has been recently developed to assess the impact of malocclusion on young people (10- to 16-years-old) (Benson et al., 2016, Patel et al., 2016). The MIQ consists of 17-items, with each item scored based on a 3-point severity scale (0-2). The scores for each item are added together to obtain a total score, with higher scores indicating poorer levels of OHRQoL. The questions are centred on the specific impacts that malocclusion may have on emotional wellbeing, social interactions, functioning as well as oral symptoms. This new measure has been shown to demonstrate good construct validity, internal reliability and test-retest reliability using cross-sectional evaluation when tested in the UK (Benson et al., 2016, Patel et al., 2016). More recently, the MIQ has been tested in a population of young people attending an orthodontic clinic in New Zealand, where it was found to perform similarly (Benson et al., 2019a). It is the first instrument of its kind, and its' responsiveness or ability to respond to change over time have yet to be tested and demonstrated.

The MIQ is aimed at assessing OHRQoL in 10- to 16-year-olds only, as this age group make up the majority of patients undergoing orthodontic treatment. However, there is evidence that orthodontic treatment is now becoming increasingly popular in the adult population, and no doubt, the development and testing of an appropriate instrument for assessment of OHRQoL in this patient cohort will be in the pipeline for future orthodontic research.

Whilst there have been significant advancements in the development and testing of instruments assessing OHRQoL, it is important to note that in the theoretical model produced by Wilson and Cleary (1995), it is clear that both clinical and non-clinical factors can have a significant influence on OHRQoL. In order to correctly interpret the results of studies examining OHRQoL, it is therefore important to appreciate the impact that such factors may have.

2.8.2. Clinical Determinants of OHRQoL in Children and Adolescents

2.8.2.1. Health Conditions

Much in the way that oral health can impact on the general health of individuals (Dorfer et al., 2017), there is emerging evidence that various health conditions can also impact on the OHRQoL of children and adolescents. A team in Brazil, assessing the impact of HIV-1 on OHRQoL in individuals aged 1 to 18 years, carried out a cross-sectional study using validated questionnaires (Rovaris et al., 2014). The most significant impacts on OHRQoL were found in those aged 12 years and over, as well as those who presented with a high need for dental treatment. It could be theorised that the negative impact of HIV-1 on OHRQoL is primarily due to the oral conditions that HIV-1 can cause such as candidiasis and gingivitis, and in turn, it is these that attribute to the negative impacts on OHRQoL observed. To this end, calls have been made to ensure that care programmes for children with HIV include dental protocols to help improve their OHRQoL (Lauritano et al., 2020).

Patients with chronic conditions such as juvenile idiopathic arthritis, immunodeficiency, inflammatory bowel disease, epilepsy, as well as learning disabilities such as Down's

syndrome, are often considered as being at an increased risk of dental caries (Foster and Fitzgerald, 2005) and therefore lower levels of OHRQoL. However, the negative impact that systemic health conditions may have on OHRQoL can be more complex than this; though, some conditions may have oral manifestations that cause impact, other conditions may simply make maintaining oral health difficult or accessing adequate dental care more challenging (Espinoza and Heaton, 2016). To complicate matters further, there is some evidence to suggest that more deprived populations may have a higher risk of congenital anomalies of non-chromosomal origin (Vrijheid et al., 2000). Given that the increased prevalence of dental caries in lower socio-economic groups is well documented (Verlinden et al., 2019), there is undoubtedly various factors that can act both directly and indirectly to influence the OHRQoL levels of those with systemic health conditions.

2.8.1.2. Oral Conditions

A number of dental and oral conditions have been associated with poor levels of OHRQoL (Barbosa and Gaviao, 2008b). In particular, dental caries, fluorosis, periodontal problems and craniofacial conditions such as cleft lip and/or palate have all been shown to correlate with worse OHRQoL, and evidence in the form of systematic reviews now supports this (Barbosa and Gaviao, 2008b, Moghaddam et al., 2020, Alvarez-Azaustre et al., 2021). The review by Barbosa and Gaviao (2008b) did note that a number of the studies only demonstrated a weak relationship between children's oral health and OHRQoL, and it was difficult to ascertain whether this was due to low levels of disease in the study samples, the low level of impact that the conditions truly had on OHRQoL, or simply differences in cultural or educational levels.

There has been significant research interest in not only exploring the impact of dental appearance on OHRQoL, but also investigating the mechanisms, including different clinical and non-clinical variables, that may mediate or moderate such relationships. Rodd et al (2011) conducted a cohort study investigating the OHRQoL of children in relation to dental appearance and educational transition. Ninety-two children aged 10 to 11 years were recruited and the participants were divided based on whether they had a visible dental difference (abnormal incisor aesthetics which included trauma, enamel defects, gross

caries, hypodontia, abnormal morphology and/or orthodontic malocclusion) or no visible difference. OHRQoL and participant satisfaction were measured at baseline, and at follow-up (three months after they had started secondary school). At baseline, of the 92 participants recruited, 52 were classified as having a visible dental difference. At follow-up, 71 participants completed the questionnaires, and of these, 9 participants had undergone dental treatment, which may have changed their dental appearance. Statistical analysis of the results found that at both baseline and follow-up, children with a visible dental difference reported significantly worse OHRQoL than those with no difference, and interestingly, it was the domains of EWB and ScWB that were most significantly affected. At follow-up, although OHRQoL levels were still significantly different between the two groups, OHRQoL in both groups showed an improvement, regardless of whether dental treatment had been undertaken to improve the visible dental difference or not (Rodd et al., 2011). This finding is particularly interesting as it contributes to the body of evidence, which suggests that OHRQoL, particularly in this age group, is not a stable construct and appears to improve over time. This theory will be discussed in more detail later in this review.

The impact of hypodontia on the OHRQoL in adolescents aged 11 to 18 years has also been investigated in a cross-sectional study based in a UK hospital clinic (Johal et al., 2021). A total of 97 participants with hypodontia were recruited, 56 of which had mild hypodontia, and 39 subjects with moderate to severe hypodontia. OHRQoL was assessed using the CPQ₁₁₋₁₄, with scores found to be significantly higher in those with moderate/severe hypodontia, indicating poorer OHRQoL, particularly in the dimensions of EWB and SWB. The study also used a new, condition-specific measure of QoL designed for use in patients with hypodontia known as the Bristol condition-specific questionnaire for hypodontia (BCSQ) (Akram et al., 2013). The results of this measure also demonstrated a significantly higher level of negative impact in those with moderate/severe hypodontia, when compared to those with mild hypodontia.

Though cross-sectional studies have suggested an association between visible dental abnormalities/defects and a negative impact on OHRQoL, there is a fundamental need to establish whether treatment of such defects can lead to an improvement in OHRQoL. One

such study was published recently where 103 participants, aged 7 to 16 years, underwent treatment for incisor opacities (Hasmun et al., 2020). OHRQoL was measured before and after treatment, with only 17 participants lost to follow-up. Both total and domain scores of OHRQoL improved significantly following treatment, which suggests that such treatment can have significant benefits. However, such longitudinal improvements in OHRQoL must be interpreted with caution as OHRQoL has been shown to improve over time in this age group, regardless of oral health status or treatment (Benson et al., 2015a). As such, if OHRQoL improvements are to be attributed to a particular form of treatment, it is imperative that such studies employ a similar control/comparator group to ensure that any improvements observed in OHRQoL are due to the treatment alone, and not natural improvements in OHRQoL.

There are clearly several studies that have identified a significant association between visible dental defects and negative OHRQoL. As orthodontics is concerned with the correction of malocclusion, it is imperative that this association between malocclusion and OHRQoL is explored in greater depth.

2.8.1.3. Malocclusion

The impact of malocclusion on OHRQoL has been explored extensively over the last decade, and the number of studies published in this area of research has increased exponentially. One of the first literature reviews exploring the social effects of malocclusion was conducted in the 1970's (Shaw et al., 1980a). When determining the impact of malocclusion on PWB, the authors found 'social response' and 'self-esteem' as two factors that could potentially be influenced. However, based on the literature that was published up until that time point, there was no evidence that children with a malocclusion would be emotionally handicapped. This review was pivotal in highlighting the need for further research in this subject area. Not long after the publication of this review, a prospective longitudinal cohort study was conducted specifically to investigate the effects of malocclusion on oral health and PWB (Shaw et al., 1986). The study recruited a total of 1018 participants, aged 11 to 12 years, from various schools in South

Wales, UK. The children were recruited in 1981, and they underwent extensive health and PWB assessments. The study was observational in design and aimed to follow up the participants for a substantial period. The initial results of the study supported a previously proposed relationship between attractiveness and self-esteem (Kenealy et al., 1991). However, it provided little evidence to support the notion that children with malocclusions were psychologically disadvantaged. From the initial cohort of participants, 337 presented for follow-up at 20 years. Though the drop-out rate of participants was significant, the longitudinal nature of the study, spanning over a 20-year period was remarkable and the authors should be applauded for their ability to re-assess this number of participants after such a long period. At follow-up, the authors found that participants who had presented with an orthodontic treatment need at baseline, and had subsequently undergone orthodontic treatment, had better tooth alignment, increased satisfaction with their occlusion, higher self-esteem and HRQoL compared to those who did not seek treatment. More importantly however, detailed analysis of the results found that when baseline scores of self-esteem was accounted for, no significant difference between the two groups was demonstrated (Kenealy et al., 2007). The results revealed that those who had undergone orthodontic treatment, had in fact reported higher levels of self-esteem at baseline, compared to those who had not. These results led the authors to conclude that orthodontic treatment was thought to have an insignificant impact on long-term psychological health, and that lack of treatment when a prior need for treatment was determined, is unlikely to impact negatively on PWB (Kenealy et al., 2007). To date, this study is one of the most significant in this field of research and the considerable dataset it has generated is invaluable. However, it must be noted that the study did have some limitations. Firstly, no power calculations were presented, and the possibility of attrition bias resulting from the large drop-out rate (67%) and the subsequent impact this may have had on the results observed cannot be excluded. Secondly, the conclusions drawn in relation to psychological health must be interpreted with caution. One of the scales used to assess QoL was the WHOQoL-BREF. This instrument was not available to the authors at the start of the study, and was only used at follow-up. To this effect, the data obtained with this instrument cannot be considered truly 'longitudinal' in nature. Moreover, this is a generic instrument that has not been validated for use in patients with a malocclusion/orthodontics.

There is a drive to improve the quality of research in this field and to ensure that studies conducted produce results that are valid, reliable and generalizable to appropriate populations. As discussed previously, one study that assessed the validity of the CPQ₁₁₋₁₄ in orthodontic patients was O'Brien et al. (2007). In this study, when individual OHRQoL domains were assessed, the malocclusion and non-malocclusion groups differed significantly in EWB ($p=0.006$) and ScWB ($p=0.001$), whilst no significant difference was observed in the OS and FL domains. The results also illustrated a significant correlation between total CPQ₁₁₋₁₄ scores and overall wellbeing and patient satisfaction. Overall, the authors concluded that malocclusion has a negative impact on the OHRQoL of adolescents. Interestingly however, no statistically significant difference between the different malocclusion subgroups (crowding, increased overjet and hypodontia) and OHRQoL was found. One possible reason for the lack of significance demonstrated may have been because the study was not powered to detect a significant difference at this subgroup level. Another reason may have been that the CPQ₁₁₋₁₄ simply lacks the ability discriminate between the different types of malocclusions, or that different malocclusions do truly have similar impacts on OHRQoL.

The impact of specific types of malocclusions on OHRQoL is a subject of interest. The findings of the O'Brien et al. (2007) study have been supported by some (Johal et al., 2007) and contradicted by others (Sardenberg et al., 2013). In 2007, Johal et al., recruited 90 participants aged 13 to 15 years. The sample was composed of 30 participants with an increased overjet, 30 participants with a spaced dentition, and 30 participants with a class I incisal relationship and a well aligned upper labial segment as a control group. Each participant and their parent were asked to complete the CPQ₁₁₋₁₄ and parent-CPQ (PCPQ) respectively. Although the results of the study indicated a statistically significant difference between the OHRQoL scores of the participants in the control group and those with an increased overjet ($p=0.002$) or spaced dentition ($p< 0.001$), there was no difference in OHRQoL between those with an increased overjet and those with a spaced dentition ($p=0.5$). Parents of children with an increased overjet or spaced dentition were also found to report statistically significantly worse OHRQoL for their children than those with children in the control group. Interestingly, no significant difference was found

between the parental reported OHRQoL in the increased overjet versus spaced dentition group. Overall, the study suggested that both an increased overjet and a spaced dentition could have a significantly negative impact on the OHRQoL of adolescents as reported by themselves and by their parents. Although we cannot assume that worse OHRQoL due to the presence of a malocclusion is an indicator for a greater desire to undergo orthodontic treatment (or vice versa), this may indicate that perhaps the parents of children presenting with such malocclusions may have an increased inclination to seek, encourage and support their child to undergo orthodontic treatment, if they believe that malocclusion may have a negative impact on the OHRQoL of their child.

Sardenberg et al. (2013) conducted a cross-sectional study sampling 1204 Brazilian school children aged 8 to 10 years. The authors used the CPQ₈₋₁₀ to measure OHRQoL, and the DAI to assess malocclusion. The DAI data was dichotomized and scores <25 were classified as indicating the absence of malocclusion and scores ≥ 25 as the presence of a malocclusion. Similarly, CPQ₈₋₁₀ scores were also dichotomized and those with a median score of ≤ 10 were assessed as having a low impact, and those scoring > 10 as having a high impact on OHRQoL. The results of this study found that schoolchildren with a malocclusion were 1.3 times (95%CI: 1.15-1.46; $P < 0.001$) more likely to suffer a negative impact on OHRQoL. Further analysis of the results also revealed that anterior spacing, maxillary overjet and reverse overjet all had a negative impact on OHRQoL. Confounding factors including gender, caries and socio-economic factors were considered and a Poisson regression analysis conducted. Interestingly, the authors found that schoolchildren with malocclusion who were from lower socioeconomic backgrounds were more likely to experience a negative impact on OHRQoL than those from higher socioeconomic backgrounds.

Whilst some researchers have attempted to establish the impact of different occlusal traits on OHRQoL, others have investigated the impact of varying levels of occlusal complexity or severity on OHRQoL. Foster Page et al. (2005) conducted a cross-sectional observational study on a random sample of 599, 12- and 13-year-old adolescents in New Zealand. They assessed malocclusion using the DAI and OHRQoL using the CPQ₁₁₋₁₄. The results demonstrated a striking relationship; as the level of orthodontic treatment need

increased, overall CPQ₁₁₋₁₄ scores also increased (indicating worse OHRQoL levels). Interestingly, this was not reflected in all four dimensions of OHRQoL. In fact, no statistically significant relationship was observed in the dimensions of OS or FL, with only the EWB and ScWB domains showing a significant relationship. These results have also been echoed in studies published more recently. In 2013, Ukra et al. published the results of their study based on a sample of 12- and 13-year-olds also residing in New Zealand (Ukra et al., 2013). The authors used data from two separate cross-sectional studies; One carried out in Tararua in 2003 and the other from Otago in 2010. In total, the study was based on data from 738 adolescents. OHRQoL was assessed using the short-form CPQ₁₁₋₁₄, and clinical examinations were used to establish caries experience and DAI scores. Based on DAI scores, participants' malocclusion or treatment need severity was defined as minor (score ≤ 25), definite (score 26-30), severe (score 31-35) or handicapping (score >36). Overall, the authors found a distinct gradient in mean CPQ₁₁₋₁₄ scores and severity of malocclusion. Those with a 'handicapping' malocclusion demonstrated higher CPQ₁₁₋₁₄ scores. The domains of OHRQoL that were significantly impacted on were ScWB and EWB. Linear regression modelling of the results found that even when caries experience and socio-demographic characteristics were controlled for, malocclusion severity (and female gender) was still positively associated with higher CPQ₁₁₋₁₄ scores (worse OHRQoL). One of the strengths of this study was that the authors clearly identified potential confounding factors such as gender, caries and socio-economic factors and accounted for these by conducting multiple linear regression analyses. The results of these two studies, both of which were based on populations in New Zealand, have also been reproduced in studies conducted in other geographical locations such as the UK (O'Brien et al., 2006). In this study, 525 school children aged 11 to 12 years from Greater Manchester and Lancashire, UK, were recruited and 325 of these were followed up three years later. At baseline, calibrated examiners recorded the IOTN AC and DHC for all participants. The children's self-perceived IOTN AC scores were also recorded. At follow-up, the children were asked to complete the CPQ₁₁₋₁₄. The main finding of this study was that CPQ₁₁₋₁₄ scores corresponded to differences in orthodontic treatment need as assessed by the IOTN. However, when individual dimensions of OHRQoL were assessed, it was once again the EWB and ScWB dimensions that were significantly affected.

Whilst the results of these aforementioned studies have provided some evidence to support similar conclusions, other studies have produced conflicting results. Heravi et al. (2011) conducted a cross-sectional study recruiting 120 male students from high schools in Mashhad, Iran. Clinical assessment of malocclusion was carried out using the Index of Complexity, Outcome and Need (ICON), and a modified version of the CPQ to determine OHRQoL. The results of this study are in stark contrast to others; whilst a statistically significant relationship between ICON and CPQ scores were demonstrated, the only OHRQoL domain that significantly correlated with ICON scores was OS. Evidently the sample was based on males only, which may account for the results observed. Alternatively, the different impact that malocclusion had on the OHRQoL of participants in this cohort may have truly been as a result of cultural and environmental factors (Wilson and Cleary, 1995).

Based on published literature to date, it is evident that many studies have explored the impact of malocclusion on OHRQoL. These studies have involved the use of different designs, malocclusion indices, OHRQoL outcome measures, as well as different population groups. In an attempt to collate this information and help establish appropriate conclusions, several systematic reviews and meta-analyses have been conducted. One such systematic review was published in 2009 and looked at the impact of malocclusion/orthodontic treatment need on OHRQoL (Liu et al., 2009). This review presented a clear search strategy with concise inclusion/exclusion criteria, together with appropriate methodology for determining the quality of the included studies. The authors identified 20 studies that met their inclusion criteria, and though they were unable to conduct a meta-analysis due to significant heterogeneity, a modest association between malocclusion and poor OHRQoL was found. Whilst they placed no limits on the age range of participants included, similar results have been echoed in other systematic reviews on this subject area where participant age has been restricted. Andiappan et al (2015) investigated the impact of malocclusion on OHRQoL across studies that used the OHIP-14 in individuals aged 15 years and over. In total, they identified 25 studies for inclusion, with data from seven of these being used in different meta-analyses (Andiappan et al., 2015). The identified studies fell into one of three groups: those comparing the same group before and after orthodontic treatment, those comparing participants with and without a

malocclusion, and those comparing an orthodontically treated group with an untreated group. Overall, whilst the authors reported a high degree of heterogeneity and publication bias amongst the studies included, they concluded that OHRQoL was significantly better amongst those without a malocclusion and those who had undergone orthodontic treatment for correction of their malocclusion.

A more recent review, focused exclusively on the impact of malocclusion on OHRQoL in children and adolescents, identified six cross-sectional studies for inclusion (Dimberg et al., 2015). Four studies were assessed as being high quality. They reported that the presence of a malocclusion in the anterior region has a negative impact on OHRQoL. The remaining two studies were classified as being of moderate quality and reported that an increased orthodontic treatment need was found to have a negative impact on OHRQoL. Overall, the authors concluded that there was high quality evidence that malocclusions, particularly when present in the aesthetic zone, have a negative impact on OHRQoL in children and adolescents, especially in the dimensions of ScWB and EWB. A similar systematic review, focusing on the impact of malocclusion on OHRQoL in children only, was also published recently (Kragt et al., 2016). This review identified 40 cross-sectional studies for inclusion in a meta-analysis. They combined data from 9293 individuals with malocclusions and 10,717 individuals without malocclusion. They found that those with malocclusion were 1.74 times more likely to have a negative impact on their OHRQoL, and that OHRQoL was significantly lowered in those with malocclusions. They also highlighted that the strength of association between malocclusion and OHRQoL was influenced by age and cultural environment, further confirming the mediating role of non-clinical variants on OHRQoL.

An ambitious systematic review was recently published by Macey et al. (2020), which sought to determine the impact of malocclusion and orthodontic treatment on oral health. The authors of the review concluded that, with the exception of dental trauma, there is an absence of evidence on the effects of malocclusion on oral health (including OHRQoL) (Macey et al., 2020). Given the vast number of studies that have now been published in this subject area, this conclusion was clearly inaccurate.

Whilst many of the studies discussed so far have used generic measures of OHRQoL, it is promising to see that more recent studies have started to use condition-specific measures of OHRQoL to assess the impact of malocclusion on OHRQoL. The impact of malocclusion on OHRQoL in adolescents aged 11 to 14 years in Nigeria was explored using the CPQ as well the MIQ (Kolawole and Ayodele-Oja, 2021). This was a cross-sectional study with a total of 200 participants recruited from secondary schools (those with a history of orthodontic treatment, or, who were undergoing treatment, were not included). Malocclusion was assessed using the IOTN AC. The study found that sex, SES and malocclusion severity had no significant impact on OHRQoL. The only variable that did show a significant impact was that of age, where older individuals were found to have significantly better OHRQoL than those who were younger. Whilst the results of this study suggest that malocclusion severity has no impact on OHRQoL, the results must be interpreted with caution. Of the participants recruited, 87% reported no need for orthodontic treatment based on the IOTN AC. This of course is significant and may explain why malocclusion severity was not found to impact on OHRQoL. It has been shown that self-perceived malocclusion can influence OHRQoL (Tajudin et al., 2021), so having a large proportion of the sample who reported no need for orthodontic treatment, may well significantly influence the OHRQoL demonstrated. The MIQ has now been adapted and validated for use in Morocco (Bourzgui et al., 2020), China (Li et al., 2020) and Chile (Hope et al., 2020). The use of the MIQ in the assessment of OHRQoL has gained significant momentum, and there is no doubt that there will be an exponential increase in the use of this instrument over the coming years.

Many of the studies assessing the impact of malocclusion on OHRQoL have correctly identified that there are many non-clinical factors that can play a role in this relationship. It is imperative that these factors are identified, their mediating/modifying roles established, and they are appropriately accounted for in studies of malocclusion/orthodontic treatment and OHRQoL.

2.8.3. Non-Clinical Determinants of OHRQoL in Children and Adolescents

2.8.3.1 Individual Characteristics: Gender

A recent systematic review and meta-analysis exploring the potential determinants of OHRQoL in children, found various factors, including gender, to play a significant role (Moghaddam et al., 2020). Within the review, the authors identified three cross-sectional studies that examined the association between gender and OHRQoL among 12-year-old adolescents (Paula et al., 2012b, de Paula et al., 2013, Piovesan et al., 2010). Two of these studies were considered to be of high quality. Overall, the meta-analysis conducted by the authors of the systematic review found that female adolescents were 1.14 times more likely to have poor OHRQoL when compared to male adolescents (Moghaddam et al., 2020). The reasons for this may be complex; whilst at face value, it could be assumed that it is gender itself that has a direct impact on OHRQoL, more critical exploration suggests that the relationship observed may be more compound and indirect. It is well-established that gender can have an impact on psychological constructs such as self-esteem, and that in turn can influence OHRQoL. Females have been found to report lower self-esteem than males within Western cultures (Helwig and Ruprecht, 2017). As such, one could argue that it is the impact of gender on these psychological variables, that in turn play a role in OHRQoL. It is therefore imperative to explore the research evidence exploring the impact of these variables on OHRQoL.

2.8.3.2. Individual Characteristics: Self-esteem

The effect of self-esteem on OHRQoL in adolescents has been widely explored using different research methodologies, including systematic reviews and meta-analyses. A recent study aimed to identify the associations between dental anxiety, self-esteem and OHRQoL in children and adolescents, with a particular focus on establishing the strength of these associations, should they exist (Alharbi et al., 2021). Overall, the authors identified four studies which explored the influence of self-esteem on OHRQoL, and whilst a high degree of heterogeneity between the studies was identified ($I^2 = 88.7\%$), a

meta-analysis demonstrated a moderate relationship between the two (Alharbi et al., 2021). Based on the results observed between OHRQoL and self-esteem, the authors concluded that some health improvement interventions may have a direct effect on improving OHRQoL, and an indirect effect on improving self-esteem. However, it is likely that the relationship between OHRQoL and self-esteem is not a simple, linear relationship, and is more complex in nature. Whilst there appears to be an association between the two, it is not possible to conclude from the results of this meta-analysis, whether it is self-esteem levels that influence OHRQoL, or vice versa. This is particularly important when considering the impact of a condition on the OHRQoL of an individual, as well as the benefit they may experience from treatment.

The role of self-esteem as a mediating factor in OHRQoL in orthodontic patients has been investigated by Agou et al. (2008) using a cross-sectional study. The researchers evaluated OHRQoL levels using the CPQ₁₁₋₁₄, self-esteem using the subscale of the child health questionnaire, and orthodontic treatment need using the DAI. The authors found that the variance in OHRQoL scores explained by malocclusion was relatively small, whilst it was much more significant for self-esteem. The authors therefore concluded that the impact of malocclusion on OHRQoL in children with low self-esteem is significant. The relationship between self-esteem and OHRQoL has also been investigated in a cohort of adolescents in the UK (Benson et al., 2015a). The participants were assessed at the age of 11 to 12 years, and then followed up three years later. OHRQoL levels were found to improve over time, and significant associations between the change in OHRQoL and self-esteem were found, regardless of whether individuals had undergone any form of intervention (such as orthodontic treatment). The results of such studies suggest there may be an association between OHRQoL and self-esteem, and as such, self-esteem must be considered a possible mediating factor in studies exploring OHRQoL.

2.8.3.3. Individual Characteristics: Sense of Coherence

A systematic review by Barbosa and Gaviao (2008b) found an association between oral conditions and OHRQoL, but found some of these relationships to be weak. They

suggested that one of the reasons for this may be the inter- and intra-personal variation of subjects in the studies included. This certainly supports the principles established in the Wilson-Cleary model (1995) that describes personal characteristics as direct or mediating factors in different health outcomes and QoL. Based on this theoretical model, Baker et al. (2010) carried out a prospective longitudinal study recruiting 439 Malaysian participants, aged 12 to 13 years, for a period of six months. They examined the role of psychosocial factors in adolescents' oral health status, health perceptions and OHRQoL outcomes. When controlling for all pre-determined confounding factors, the authors found that the individual factor to have greatest influence on children's OHRQoL was Sense of Coherence (SOC). SOC is defined as;

'A global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that (1) the stimuli deriving from one's internal and external environments in the course of living are structured, predictable, and explicable (comprehensibility); (2) the resources are available to one to meet the demands posed by these stimuli (manageability); and (3) these demands are challenges, worthy of investment and engagement (meaningfulness)' (Antonovsky, 1987).

Children with higher SOC levels at baseline were found to have better OHRQoL at 6-month follow-up compared to those with lower levels. A similar relationship between SOC and OHRQoL was also found in a study of 510 Thai children aged 10 to 14 years (Gururatana et al., 2014). Whilst these studies have found an association between SOC and OHRQoL, a more recent systematic review was published specifically exploring influence of SOC on OHRQoL (Gomes et al., 2018). Although the review placed no restriction on inclusion of studies based on a specific age range, it did discuss the results based on different age groups. When considering adolescents only, the review identified five studies for inclusion, including two studies previously discussed (Baker et al., 2010, Gururatana et al., 2014). Whilst the authors concluded that the five studies demonstrated an inverse relationship between SOC and OHRQoL (i.e. a lower SOC is associated with a greater impact on OHRQoL), they advised caution due to the risks of selection bias in three of the studies which were cohort in design, with participants selected from distinct populations/centers. It is important to be mindful that whilst it is becoming increasingly

evident that SOC may well play a role in the OHRQoL of children and adolescents (and those with a strong SOC may be better equipped to respond to health conditions that may arise), such relationships are rarely direct, and there are often several other mediating factors which may play both direct and indirect roles. These are thought to be factors such as age, gender, SES, parental education, amongst other variables, all of which may play a significant role in establishing SOC (Langeland et al., 2022). As such, like many psychological variables that are influenced by other mediating factors, it can be challenging to determine the extent to which SOC plays a role in the OHRQoL of adolescents.

2.8.3.3. Individual Characteristics: Psychological Wellbeing

The impact of PWB on OHRQoL has also been explored. Foster Page et al. (2013) conducted a cross-sectional study of 358 adolescents in Dunedin. Participants were asked to complete questionnaires detailing their socio-demographic and psychosocial characteristics including PWB. The orthodontic needs of participants were assessed clinically using the DAI, and OHRQoL was determined using a 16-item shortened version of the CPQ₁₁₋₁₄ (CPQ₁₁₋₁₄-ISF:16). Overall, the authors found that all psychosocial variables, except for self-esteem, were strongly associated with CPQ₁₁₋₁₄ scores. Of note, PWB was the strongest predictor, which supports the proposed mediator role that PWB may play on OHRQoL. The results of this study very much supported those established in a cohort study of 11 to 14 year olds (74 undergoing orthodontic treatment, and 44 on an orthodontic treatment waiting list), where OHRQoL and PWB were measured at baseline and following the completion of treatment (and the equivalent time interval for the control group subjects) (Agou et al., 2011). The results of the study suggested that adolescents with better levels of PWB were overall more likely to report better OHRQoL levels regardless of their orthodontic treatment status, and vice versa. The results from studies such as these very much confirm the mediating role that PWB can play in the OHRQoL of individuals, particularly those with a malocclusion or undergoing orthodontic treatment.

2.8.3.4. Environmental and Social Characteristics: Socio-economic status

There are suggestions that environmental and social factors such as culture, education levels, SES and family structure can influence OHRQoL in children and adolescents (Paula et al., 2012a).

A systematic review assessing the impact that paternal SES and home environment can have on children's OHRQoL, found evidence that children from families with a high income and parental education had better OHRQoL (Kumar et al., 2014). They also found evidence to suggest that as maternal age decreased, children had poorer levels of OHRQoL. Additionally, as household crowding and the presence of siblings increased, children's OHRQoL was also negatively influenced. Due to significant heterogeneity in the population's studied, paternal characteristics investigated, and methods and statistical tests used, the authors of the systematic review were unable to carry out a meta-analysis. The authors therefore highlighted the limit this imposed on their ability to draw definitive conclusions.

There has been significant interest in the exploration of SES as a mediating or moderating factor between dental status and OHRQoL. This of course is particularly important to healthcare professionals and policymakers alike. A recent study, analysing data drawn from the Brazilian Oral Health Survey, analysed data from 5445 adolescents aged 15 to 19 years (Mohamed and Vettore, 2019). Data analysed included clinical variables such the number of decayed and missing teeth, gingivitis and malocclusion, as well as OHRQoL, SES, age and gender. A significant correlation was found between the oral clinical variables, OHRQoL and SES, with the impact of all the oral conditions on adolescent's OHRQoL being less in those from lower socioeconomic backgrounds, when compared to those with higher socioeconomic backgrounds (Mohamed and Vettore, 2019). Such findings demonstrate that, whilst it is well established that SES can play a significant role in the development of dental disease such as dental caries, the impact of these conditions on OHRQoL can also be mediated significantly by SES, and as such, must be given appropriate consideration when exploring the impact of various oral conditions on OHRQoL.

Structural Equation Modeling (SEM) has been used increasingly over the last few years to identify demographic predictors of OHRQoL. A recent cohort study was carried out in Hong Kong, with a cluster-randomised sample of 12-year-olds (n=589), who were then followed up at the age of 15 years (n=331) (Sun et al. 2021). The variables in the study included OHRQoL, which was measured using the CPQ₁₁₋₁₄, periodontal status, caries and malocclusion. The other potential predictors of OHRQoL that were measured included age, gender, father's education, mother's education and household income. The authors reported that the degree of malocclusion, caries and periodontal status worsened from age 12 to 15 years. More severe malocclusion was associated with worse OHRQoL, and age, gender, as well as maternal education were all found to influence OHRQoL.

There is a consensus that OHRQoL instruments must be appropriate for the cultural environment in which they are used. However, there has been little research exploring the impact of culture on children's and adolescent's OHRQoL. That said, the impact of clinical, environmental and individual factors on OHRQoL has been explored in different cultures, and related findings have demonstrated that such impacts are often consistent across the different settings (Baker et al., 2010, Nammontri et al., 2013, Gururatana et al., 2011).

Based on the evidence presented so far, there is a significant body of evidence that demonstrates the detrimental impact that malocclusion can have on the OHRQoL of children and adolescents, particularly in the dimensions of EWB and ScWB. We have explored the complexities around investigating OHRQoL in this age group, particularly in relation to possible direct and indirect mediators which may influence the OHRQoL levels observed. It is important to acknowledge that orthodontic treatment itself can affect an individual's OHRQoL. Consequently, the next section of this literature review examines the impact of orthodontic appliances on OHRQoL, along with the evidence surrounding this topic.

2.8.4. Impact of Orthodontic Appliances on OHRQoL

Orthodontic treatment is often considered to be elective in nature, so it is only reasonable that clinicians fully appreciate the impact that orthodontic appliances can have on the

OHRQoL of patients. It is imperative that the research data we have in this field is interpreted correctly and in a manner that can be discussed with patients and/or their parents where appropriate. It is important now more than ever, that patients are fully informed of the risks of any treatments they are offered and are made aware of the availability of any reasonable alternatives. The impact that an orthodontic appliance can have on the OHRQoL of a patient is clearly no exception to this. Often, there are likely to be different options available for the management of an orthodontic patient, and these must be thoroughly explored and discussed to ensure that an informed consent process has taken place. Over the last decade, there has been a significant volume of research published that has sought to assess the impact of fixed appliances on OHRQoL (Chen et al., 2010, Zhang et al., 2008, Feu et al., 2013). This has included several cross-sectional and longitudinal studies.

Costa et al. (2011) carried out a cross-sectional study to assess the impact of fixed orthodontic appliances on the OHRQoL of Brazilian schoolchildren. A total of 579 participants aged 11 to 14 years were recruited. Participants were selected from public and private schools in Brumadinho, Brazil. The participants included two groups of individuals: those wearing an orthodontic appliance (n=160) and those not wearing an appliance (n=419). The participants were assessed using the DAI and OHRQoL was established using the Brazilian short version of the CPQ₁₁₋₁₄. The results of the study showed that children wearing fixed appliances reported significantly higher total CPQ₁₁₋₁₄ scores, than those not wearing a brace ($p=0.002$). Interestingly, this was true for three dimensions of OHRQoL including FL ($p=0.005$), EWB ($p=0.006$) and ScWB ($p=0.003$). No statistically significant difference was observed in OS ($p=0.124$). Confounding factors including age, gender and type of school were controlled for using multiple logistic regression models. Gender was found to be a modifying factor with females 1.8 times more likely to report poorer levels of OHRQoL than males. Although the authors collected data for malocclusion using the DAI, they failed to report the details of these data in their study. They did explain that as very few children with a malocclusion were found not to be wearing fixed appliances, they were unable to exclude malocclusion as a confounding factor. Evidently, a major drawback of this study was its' inability to determine whether the difference observed in OHRQoL between the two groups was due to the presence of a

fixed appliance, the presence of a malocclusion, or in fact the presence of any other dental anomaly or condition.

When assessing the impact of orthodontic appliances on OHRQoL, longitudinal studies can provide an excellent method of assessing the level of impact at different time points during treatment. This is particularly important as treatment can often take in the region of 2 years to complete, and OHRQoL levels are likely to fluctuate and alter throughout this time period (Tsichlaki et al., 2016). Zhang et al. (2007) carried out a study examining the expectations and experiences of patients wearing fixed orthodontic appliances over a 6-month period. A total of 217 participants who were about to undergo fixed orthodontic appliance therapy were recruited from the Faculty of Dentistry, The University of Hong Kong. The mean age of participants was 13.1 years, 47% of whom were males. The individuals were asked to complete the CPQ₁₁₋₁₄ at six different time points: at pre-treatment screening, before treatment to assess anticipated change in OHRQoL as a result of wearing fixed orthodontic appliances, and at 1 week, 1 month, 3 months and 6 months after the start of treatment. The total response rate of the study was reasonable, with a drop-out rate of 9%. Overall, the authors reported that participants expected wearing fixed appliances to have a detrimental impact on their OHRQoL ($p < 0.001$). However, the inference of this must be interpreted with caution as CPQ₁₁₋₁₄ is not designed to assess expectations or the impacts of treatments and should only be used to determine the impact of dental conditions on OHRQoL. Further data collected suggested that OHRQoL became worse at 1-week post fixed appliance placement but subsequently improved as treatment progressed. Interestingly, improvements were observed in EWB during treatment, and possible reasons for this could be factors such as the increased popularity and social acceptance of fixed appliances.

One of the important factors that must be considered when interpreting results from studies using OHRQoL measures is the socio-demographic and socio-economic setting in which participants for the study were recruited from, as this will significantly influence the generalizability of the results. This may explain the difference observed in the overall OHRQoL changes found in the study by Zhang et al. (2007), compared to those in a similar study conducted by Abreu et al. (2013). Abreu et al. (2013) carried out a longitudinal study

to evaluate the OHRQoL of adolescents during the first month of fixed orthodontic appliance therapy. The study was based on 96 children aged 11 to 12 years undergoing orthodontic treatment at the Federal University of Minas Gerais, Brazil. The CPQ₁₁₋₁₄ (Brazilian version) was used and participants were asked to complete the questionnaire before the start of treatment and one month after the placement of fixed appliances. The overall response rate was good (97.9%), and 47.9% of participants were male. Interestingly, in this study, the results showed a statistically significant improvement in OHRQoL scores at one month post fixed appliance placement ($p=0.032$), particularly in the EWB domain ($p<0.001$). The difference observed in OS, FL and ScWB prior to starting treatment, and one month after placement of fixed appliances, were not significantly different. Although the EWB domain of OHRQoL appeared to show a similar trend and improved in both the Abreu et al. (2013) and Zhang et al. (2007) study, the overall OHRQoL scores in Abreu et al. (2013) demonstrated a significant improvement at one month, whilst those from Zhang et al. (2007) suggested a negative impact on OHRQoL at one month, though this change observed was not statistically significant.

The impact of orthodontic appliances over longer periods of time have also been investigated using longitudinal methodology. Brosens et al. (2014) assessed changes in OHRQoL in children undergoing orthodontic treatment over a 12-month period and explored the possible role that self-esteem may play on this. A total of 138 adolescents aged 11 to 16 years who were about to undergo orthodontic treatment at the University Hospital of Leuven (Belgium) were recruited. All participants were asked to complete the CPQ₁₁₋₁₄ at baseline and at one-year after the start of orthodontic treatment, to assess OHRQoL at these time points. The Dutch version of Harter's self-perception Profile for Adolescents was used to assess self-esteem, and IOTN was used as a method of determining orthodontic treatment need. Overall, 29 (21%) participants dropped out of the study. Unsurprisingly, the results of the study found that the DHC and AC of IOTN scores decreased significantly ($p<0.0001$) during treatment. There was a significant ($p<0.0001$) increase in the overall CPQ scores during treatment, indicating a significant negative impact on OHRQoL during the first year of orthodontic treatment. The increase observed in the OS, FL and ScWB domains of OHRQoL were all significant ($p<0.001$), whilst EWB scores decreased, though not to a degree of statistical significance. These

trends were similar to those observed by Zhang et al. (2007), though their study had a follow-up period of six months. Patients reporting higher baseline levels of self-esteem demonstrated significantly ($p=0.0066$) lower variability in OHRQoL one year after the start of treatment, though the correlation observed was weak ($p=-0.26$). When analysing the separate domains, significant correlations were observed with self-esteem scores and total change in FL ($p=0.0378$), EWB ($p=0.0225$) and ScWB ($p=0.0043$). A correlation was also found between self-esteem and OS, but this was not significant ($p=0.1046$). Whilst the results of this study follow the trend of similar studies conducted, the study itself does suffer from a few methodological limitations. Firstly, the study used CPQ₁₁₋₁₄ that is a validated instrument for assessing OHRQoL in 11- to 14-year-olds. However, this study also included children aged 15 and 16 years of age, and it could be argued that this instrument was not valid for use in this age group. The study also had a reasonable proportion of participants who were lost to follow-up (21%), which could affect the validity of the results through attrition bias. In addition to these drawbacks, the study also failed to control for the type of orthodontic appliance used which may cause significant variability in the results obtained. Fixed, functional and removable appliances were all used and the impact that these may have on OHRQoL may be significantly different.

With the publication of so many studies, a systematic review is an ideal method of collectively assessing and combining this research data. A systematic review that attempted to do this was published in 2014 and included studies assessing OHRQoL during and after orthodontic treatment, in both children and adults (Zhou et al., 2014a). The authors of this review identified 11 studies; Three of the studies had short-term (during orthodontic treatment), and six had long-term (after completion of orthodontic treatment) follow up periods. Overall, the authors found evidence that a patient's OHRQoL is often worse during treatment, particularly in the domains of OS and FL. Whilst the dimension of EWB seemed to improve. These findings were particularly true during the first month of treatment, but thereafter, the detrimental effects on OHRQoL seemed to reduce as treatment continued.

Since the publication of this systematic review, further studies in this area have been published including a longitudinal study in the UK (Johal et al., 2014). This study examined

OHRQoL levels in adolescents aged 11 to 14 years at baseline, 6-weeks and 3-months after the placement of fixed orthodontic appliances and compared these to OHRQoL levels of similarly aged participants who were on a waiting list for treatment. The results of this study mirrored those of the systematic review (Zhou et al., 2014a). Fixed orthodontic appliance treatment was found to impact negatively on OHRQoL during the early stages of treatment, with significant impacts witnessed in OS and FL.

With our orthodontic armamentarium continually evolving, it is imperative that new forms or protocols of treatment are thoroughly evaluated, not only with regards to clinical efficiency and efficacy, but also in terms of PROMs. A recent study compared the effect of twin block functional appliances versus fixed orthodontic appliances on the OHRQoL of adolescents undergoing treatment for a class II division 1 incisor relationship (Alzoubi et al., 2017). The authors assessed OHRQoL levels before, during, and at the end of treatment. The patterns of OHRQoL were similar in both groups; OHRQoL became worse during the initial stages of treatment and then improved as treatment progressed, with no significant differences found between the two groups, compelling the authors to conclude that either approach to the management of such malocclusions was equally acceptable to patients (Alzoubi et al., 2017).

The introduction of new brackets systems into the orthodontic world is frequently accompanied by various marketing claims, and the resurgence of self-ligating brackets over the last 30 years is no exception to this. This has included claims of superior clinical outcomes such as reduced treatment times, as well improved patient comfort and QoL. For such claims of superiority to be made, they must be substantiated and demonstrated through high quality research. Where OHRQoL is concerned, a longitudinal cohort study following Chinese adolescent participants undergoing orthodontic treatment using either conventional brackets or self-ligating brackets was conducted (Zhou et al., 2014b). The OHRQoL of participants was measured using OHIP-14, and this was completed at 1-week, 1-, 3-, 6-months after appliance placement, as well after treatment completion. The authors found no significant difference in OHRQoL between the two groups, but did find that OHRQoL was significantly worse at 1- week and 1-month compared to other time

points, in both groups. Overall, the study concluded that there was no significant difference in the impact of the different brackets types on OHRQoL (Zhou et al., 2014b).

As the variety of orthodontic appliances continues to grow and develop, it is important that the literature exploring these is also continuously updated. As such, a recent systematic review and meta-analysis exploring the impact of orthodontic appliances on the OHRQoL of children and adolescents was published (Vidigal et al., 2022). The review sought to identify studies exploring the impact of any form of orthodontic intervention on OHRQoL and included both randomised and non-randomised controlled trials. In total, the authors identified 20 studies for inclusion, with the data from 11 of these being deemed appropriate for use in various meta-analyses. Interestingly, the authors found that in most of the identified eligible studies, negative impacts were observed in both the FL and OS dimensions of OHRQoL, especially on the first day, first week and first month of orthodontic treatment. None of the four domains of OHRQoL showed a significant impact at either six or twelve months into treatment, when compared to baseline levels of OHRQoL.

Based on the evidence available to date, it would appear that orthodontic appliances have a negative impact on the OHRQoL of children and adolescents, particularly during the initial stages of treatment. However, this appears to only be temporary in nature, and with time, OHRQoL levels appear to improve. Importantly, a crucial question remains- does the completion of orthodontic treatment lead to an improvement in OHRQoL? The next section of this literature review will thoroughly examine this topic and explore the evidence surrounding this area of research.

2.8.5. The OHRQoL Benefits of Orthodontic Treatment

As there is now evidence that malocclusion can impact negatively on the OHRQoL of young people, it could be argued that perhaps orthodontic treatment can lead to an improvement in OHRQoL following treatment. However, such conclusions can never simply be extrapolated based on mere assumptions, especially given the complex

interactions that can occur both directly and indirectly in the establishment of psychological constructs such as OHRQoL.

“An ignorant doctor is the aide-de-camp of death”.

Ibn Sīna (Latinized: Avicenna)

(AD 980-1037)

Persian physician-polymath

Several studies have been conducted and published in the last two decades that have sought to determine whether orthodontic treatment does in fact lead to a change in OHRQoL. A systematic review and meta-analysis addressing this specific research question has previously been published (Javidi et al., 2017). The review identified 13 studies, six of which were included in various meta-analyses, assessing the impact of orthodontic treatment on the OHRQoL of young people, following the completion of treatment (Javidi et al., 2017). The studies included in the review were all assessed as being of low or moderate quality. Using data from 243 participants, within a meta-analysis, a moderate improvement in OHRQoL was observed following the completion of orthodontic treatment. The standardized mean difference was -0.75 (95% CI, -1.15 to -0.36). The greatest improvements were seen in the dimensions of EWB and ScWB. As such, the authors concluded that there was some evidence to suggest that orthodontic treatment can lead to a moderate improvement in OHRQoL, but this evidence was of low and moderate quality.

One of the studies included in the review was a longitudinal cohort study that sought to determine whether individual psychological characteristics affect changes in OHRQoL reports following the completion of orthodontic treatment (Agou et al., 2011). Children aged 11 to 14 years were recruited from the graduate orthodontic clinic at the University of Toronto. Participants in the treatment group were all managed using fixed appliances and the control group was composed of individuals on the orthodontic treatment waiting list. The CPQ₁₁₋₁₄ was used to determine OHRQoL in all the subjects. Overall, the results of the study found that subjects who had undergone orthodontic treatment had significantly

better OHRQoL at follow-up, and this improvement was significantly better than the changes that occurred in the control group.

The authors did however find that individual PWB levels significantly influenced OHRQoL changes. When PWB was controlled for, the impact of orthodontic treatment was only significant for the EWB dimension of OHRQoL. PWB was also dichotomised into 'low' and 'high' levels, and it was found that children with better levels of PWB, generally reported better OHRQoL regardless of their orthodontic treatment status. However, children with low PWB who did not receive orthodontic treatment reported lower levels of OHRQoL compared to those who received treatment. Although the study was well designed and included an untreated waiting list control group, there were a number of methodological concerns. The authors stated that data collection was carried out at two time-points, namely, baseline (T1) and at the first retention check appointment (T2), yet they failed to describe how soon after completion of treatment this appointment was. Moreover, 199 children were recruited at the start of the study, but only 118 were successfully followed up, equating to 41% of participants lost to follow-up. The authors attempted to overcome the influence of this large drop-out on their results by contrasting the baseline data of the original cohort and the retained cohort and reported no statistically significant differences between the two in both the treatment and the control group. It is important to note that the loss to follow-up in the treatment group and control group were 24.5% and 56.4%, respectively. The authors stated that the reason for such a high attrition rate in the control group was that some patients sought alternative care. Given that the attrition rate in the control group was so high, and that only 44 subjects were followed up, this may have detrimentally impacted the internal validity of the study and therefore the conclusions drawn. Unfortunately, attrition is one of the main problems associated with longitudinal studies as it can lead to bias if those who drop out share common characteristics. Nevertheless, the study presented data in relation to the OHRQoL of subjects before and after orthodontic treatment, as well as a control group, and they must be commended for this study design.

Another study identified in the systematic review by Javidi et al. (2017) was a longitudinal cohort study that recruited 374 adolescents aged 11 to 12 years, from different schools in

the UK (Benson et al., 2015a). All the participants were followed up for three years. Data at baseline and follow-up were collected for OHRQoL using the CPQ₁₁₋₁₄-ISF:16, self-esteem using the self-esteem subscale of the Child Health Questionnaire-Child Form 87 (CHQ-CF87), clinical and self-assessed normative measures of IOTN, DMFT and SES using the Index of Multiple Deprivation. At follow-up, subjects were asked about whether they had undergone orthodontic treatment in the last three years. Although OHRQoL was found to improve from baseline to follow-up, there was no statistically significant difference between the improvements observed in those who had undergone orthodontic treatment (mean improvement of 3.2, S.D.= 6.9) and those who had not (mean improvement of 2.4, S.D.= 8.8). The proportion of participant drop-outs for the study was 31% at follow-up, which is comparable to other longitudinal studies (Shaw et al., 2007). The authors had reported a sample size calculation, based on the estimation that 32% of the participants at follow-up (15 years old) will have undergone and completed orthodontic treatment. They calculated that a sample of 198 at follow-up would be required, and accounting for expected dropout rates, they aimed to recruit 400 participants at baseline. However, although their sample at follow-up included 258 participants, only 35 of these had reported undergoing orthodontic treatment, which limited the data available to answer the question if orthodontic treatment leads to an improvement in OHRQoL.

One of the problems highlighted in QoL research, including OHRQoL, is that condition-specific measures should be used if we are to truly establish the impact of conditions and/or their treatments on the lives of individuals. With the introduction of the MIQ, it is encouraging to see that studies have now started using this outcome measure to investigate the impact of orthodontic treatment on OHRQoL. A recent cross-sectional study evaluating the impact of Class II division 1 malocclusion on OHRQoL recruited 241 participants from a university hospital in the UK (Tsichlaki et al., 2021). Of the participants recruited, 121 had not yet undergone treatment, and 120 participants had completed orthodontic treatment of their malocclusion. Occlusal severity and outcome were assessed using the Peer Assessment Rating (PAR) scores, and OHRQoL was measured using the MIQ and the short form of the COHIP. Overall, the authors concluded that increased overjet (Class II division 1 malocclusion) was associated with impaired OHRQoL,

when compared to those who had completed treatment for the increased overjet. Interestingly, the MIQ scores in the post-treatment group were 11.35 times lower than the pre-treatment group, even after adjusting for age and sex. Whilst the results of the study could not be used to determine whether orthodontic treatment of Class II division 1 malocclusion can lead to improvements in OHRQoL due to the cross-sectional nature of the study, the authors were able to conclude that such malocclusions were associated with impaired OHRQoL, and this impairment was particularly evident when the condition-specific measure of MIQ was used. To determine whether treatment can lead to improvements in OHRQoL, the authors rightly highlighted that further evaluation using longitudinal methodology was needed.

It is promising to see that condition-specific measures such as MIQ are now being used in longitudinal orthodontic based research, with a recent, 3-year prospective longitudinal cohort study recently published assessing whether orthodontic treatment improves OHRQoL (Peter et al., 2023). The study was based in Kerala, India, and recruited 210 participants, under the age of 18 years, who were about to start orthodontic treatment. Participants were asked to complete the MIQ before the start of treatment and one month after the completion of treatment, with IOTN and PAR scores also being collected at the same time points. Overall, the authors observed a large reduction in MIQ scores from baseline (mean = 28.1, SD = 6.1) to post-treatment (mean = 3.7, SD = 2.6), and concluded that a significant improvement in OHRQoL had been observed following orthodontic treatment. Whilst this is encouraging, detailed critique of the study design does suggest that a number of methodological flaws are evident which may affect the validity of the results observed. In particular, the study failed to recruit an appropriate control group, and as such, it is not possible to ascertain whether the results observed were due to the orthodontic treatment alone, or whether they were due to natural fluctuations in OHRQoL that are observed in this age group (Benson et al., 2015a). Furthermore, despite the large number of confounding factors that may influence OHRQoL which are now well established in the research literature, such as SOC, self-esteem and PWB, the authors did not control for any of these variables, and only controlled for age, gender and SES. As such, the improvements in OHRQoL demonstrated in the results may not be entirely attributable to the orthodontic treatment alone.

2.9: Summary of Literature Review Findings

Based on the review of the literature to date, significant advances have been made in the field of OHRQoL. There is now a substantial body of research evidence exploring the different variables that may influence OHRQoL levels observed, using health belief models and appropriate mathematical equations to establish the possible significance of these, and help determine the extent of the roles they may play. Academics and clinicians are now in a considerably better position to utilise these when using OHRQoL as an outcome measure in their research studies.

It is encouraging to observe a marked increase in the use of OHRQoL measures in orthodontic research over the last two decades. A growing body of evidence now supports the conclusion that malocclusion has a negative impact on OHRQoL, particularly in the dimensions of EWB and ScWB. Several studies have also explored the effect of orthodontic appliances on OHRQoL. Many of these have reported short-term declines in OHRQoL, especially in the dimensions of FL and OS during the initial stages of treatment; however, these negative effects have been found to diminish over time, with OHRQoL generally improving as treatment progresses. While much of the existing research has relied on generic OHRQoL instruments such as the CPQ₁₁₋₁₄, it is promising to see the orthodontic world responding to the need for condition-specific tools. The development of the MIQ represents a significant advancement in this area. The increasing adoption of the MIQ in cross-sectional orthodontic studies, and its more recent, albeit limited, use in prospective cohort research, marks a positive step towards enhancing the quality and relevance of evidence in this field.

Whilst to date, orthodontic treatment continues to be provided on the NHS within the UK, there is a clear need to establish the benefits of this treatment using high-quality research methodology. Based on the literature to date, there is little evidence that orthodontic treatment leads to significant dental health benefits on a population level, and we are yet to determine, with clear certainty, whether orthodontic treatment can lead to an improvement in OHRQoL.

Chapter 3

Rationale, Aim & Objectives

3.1: Rationale for the Project

In the UK, the NHS funds orthodontic treatment for those who meet pre-defined thresholds based on the IOTN. Given the current economic climate and the financial constraints that no doubt faces the NHS at present and in the future, it is important now, more than ever, that the benefits of all forms of treatments/services are carefully established and analysed, to ensure that these finite resources are used appropriately. Orthodontic treatment is no exception to this.

To date, on a population level, published literature has failed to demonstrate any significant oral health benefits in the treatment of malocclusion using orthodontic treatment. Where wellbeing is concerned, in particular PWB, evidence from the literature suggests that this is complex and influenced by various factors such as personality, the environment and self-esteem. It is therefore unlikely that correction of malocclusion will lead to significant benefits in such forms of wellbeing. However, the last two decades has witnessed a significant increase in the number of studies exploring the impact of malocclusion on OHRQoL, and there is now a substantial body of evidence, particularly in the form of systematic reviews, that demonstrate the negative impact that malocclusion can have on this PROM. This is especially true in the dimensions of ScWB and EWB. Likewise, there is now evidence that wearing orthodontic appliances can have a detrimental effect on OHRQoL, and one could argue that this is perhaps unsurprising as most forms of dental treatment are likely to have a negative impact during the treatment period itself. It is logical to assume that it is, in fact, the subsequent improvement in OHRQoL, on completion of treatment, which motivates patients to seek and undergo such care.

The systematic review and meta-analysis by Javidi et al. (2017) sought to determine whether orthodontic treatment in children and adolescents leads to an improvement in OHRQoL. Though the review found some evidence to suggest that moderate improvements occur, particularly in the dimensions of ScWB and EWB, this evidence was of low and moderate quality. The review found that the studies identified were either cross-sectional or longitudinal study design. Evidently, cross-sectional studies simply offer

a single snapshot at a particular moment in time and are unable to offer any information regarding treatment-and-effect relationships. Some of the existing studies also failed to recruit an untreated control group. It is crucial that a comparative prospective untreated control group is recruited to the study (Such as participants with malocclusion who do not receive corrective treatment for their malocclusion over a period of time) to help establish if any differences in changes over time between the treated and untreated participants can be reasonably attributed to the treatment itself, and not a natural change. This is particularly relevant for orthodontic treatment, which can take 2-3 years to complete. Furthermore, the systematic review called for future studies to use malocclusion-specific measures of OHRQoL to ensure that any changes that do occur, are detected appropriately. A randomised controlled trial where participants on an orthodontic waiting list are randomised into an orthodontic treatment arm or continue on the waiting list, together with a malocclusion-specific OHRQoL outcome measure, would form the basis of an ideal study design, to determine definitively whether orthodontic treatment leads to an improvement in OHRQoL. One of the difficulties in conducting such a trial, using randomised controlled trial methodology, is that it can be fraught with ethical dilemmas. One could argue that participants who are randomised into the treatment arm of the study may be seen to have bypassed the waiting list, and those who remain on the waiting list may in turn, be perceived as being disadvantaged. Moreover, the practical implications of running such a trial are difficult, as study sites would need to have the capacity to provide treatment immediately to those participants randomised into the treatment arm of the study, and this may not be possible in many settings. Based on these difficulties, it is not practical to carry out an interventional randomised controlled trial to address what is evidently an important research question. However, it is possible to carry out a longitudinal prospective cohort study, together with an appropriate control group, and it is this, that has led to the development of this project.

3.2: Aim

The primary aim of this study was to examine the impact of the completion of orthodontic treatment on the OHRQoL of adolescents aged 11 to 16 years. The secondary aim was to explore the factors that were associated with any observed changes in OHRQoL.

3.3: Objectives

The objectives of this study were:

- To recruit a sample of adolescents aged 11 to 16-years in primary and secondary orthodontic care settings, who qualified for NHS Orthodontic treatment. These comprised a cohort of adolescents that are about to undergo orthodontic treatment, and a cohort of adolescents that are about to be placed on an orthodontic treatment waiting list (which had to be a minimum of 12 months).
- To collect data for the cohort of adolescents undergoing orthodontic treatment at time-point 1 (pre-treatment), time-point 2 (6 weeks up to 9 months post-treatment), and time-point 3 (9 months up to 32 months post-treatment).
- To collect data for the cohort of adolescents being placed on an orthodontic treatment waiting list at time-point 1 (just before they were placed on the waiting list) and time-point 2 (just as they were coming off the waiting list).
- To describe the socio-demographic, clinical, psychosocial and OHRQoL of participants recruited.
- To determine the responsiveness and longitudinal construct validity of the MIQ.
- To analyse the OHRQoL of adolescents aged 11 to 16 years, before and after the completion of orthodontic treatment compared to adolescents on the orthodontic treatment waiting list.
- To examine the socio-demographic, clinical and psychosocial variables that may predict OHRQoL levels following the completion of orthodontic treatment.



Chapter 4

Methods



4.1: Research Questions

The study was designed to address two main research questions:

1. Are there differences in the changes observed in the OHRQoL of young people aged 11 to 16 years who receive orthodontic treatment versus those who are still waiting for treatment?
2. If there is an improvement in OHRQoL following orthodontic treatment, can specific characteristics be identified that can predict which individuals will benefit the most from treatment?

4.2: Study Design

This study was a multi-centre, longitudinal, prospective, clinical cohort study, based on the comparison of two cohorts of participants:

- An **Orthodontic Treatment Group (OTG)** cohort. This cohort of participants were due to undergo orthodontic treatment.
- A **Waiting List Control Group (WLCG)** cohort. This cohort of participants were due to be placed on an orthodontic treatment waiting list which had to be a minimum of 12 months.

The overall design of the study, together with specific time-points for data collection, are illustrated in Figure 2.

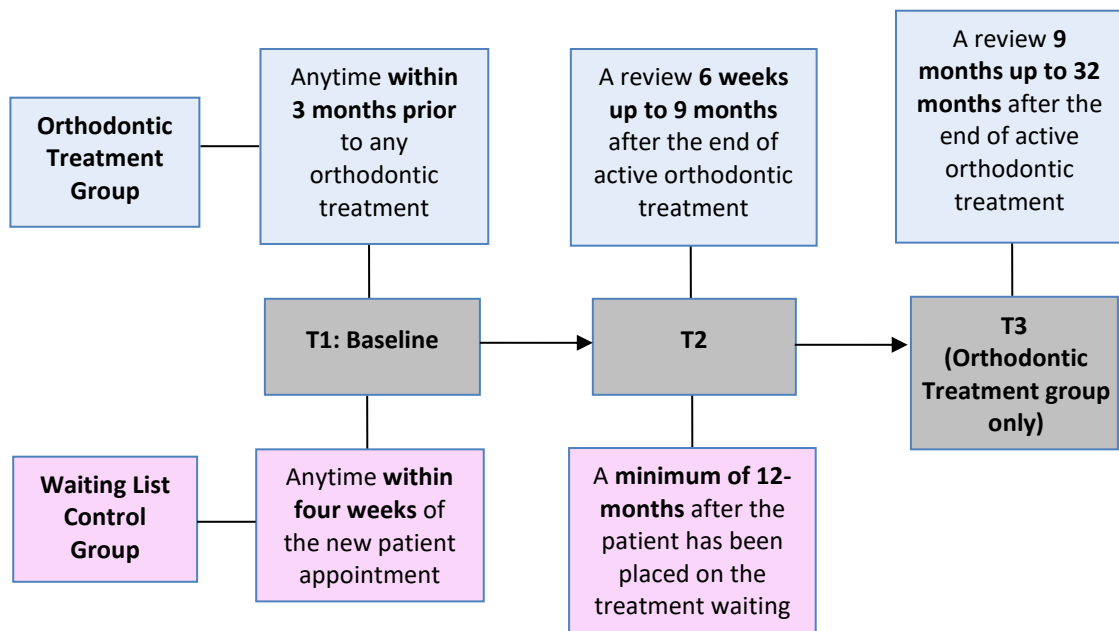


Figure 2: An illustration of the overall study, with the time-points for data collection in the Orthodontic Treatment Group, and the Waiting List Control Group. Please note that T3 was only applicable to the Orthodontic Treatment Group.

The specific data collected at each time point is discussed in detail in Section 4.6.

4.3: Study Sample

The participants selected for the two cohorts of the study were based upon specific inclusion and exclusion criteria.

4.3.1. Inclusion Criteria

- Aged 11 to 16 years (inclusive) at the start of treatment or when placed on an orthodontic treatment waiting list.
- A measurable need for orthodontic treatment based on the IOTN (DHC grades 3 [AC 6 - 10], 4 or 5).

- About to commence orthodontic treatment (OTG cohort) **or** to be placed on a treatment waiting list (WLCG) for any orthodontic intervention, using any type of appliance or auxiliary.
- Dentally fit to commence orthodontic treatment (including no active caries and good oral hygiene).
- To have the cognitive ability and sufficient knowledge of the English language to complete the questionnaires.

4.3.2. Exclusion Criteria

- Cleft of the lip or palate, or other facial deformity or craniofacial syndromes that require surgical correction.
- Medical condition(s) that might prevent comprehensive orthodontic treatment.
- Cognitive impairment and inability to complete questionnaires.

4.3.3. Sample Size Calculations

A systematic review examining the literature for changes in OHRQoL following orthodontic treatment (Javidi et al., 2017), found evidence of moderate to large effect sizes (SMD 0.75; 95% CI 0.36 to 1.15) for the overall improvement in OHRQoL before and after orthodontic treatment. This was derived from four longitudinal studies, involving 243 participants. Taking the lower value for the effect size confidence interval (0.36), a minimum sample size of 450 participants would be required to detect a significant difference, with a power ($1-\beta$) of 0.90 and significance level (α) of 0.01. Assuming a 30% dropout rate over 4 years, (including those who have their fixed appliances removed, retainers fitted and who do not return for a retainer review) we required a minimum sample size of 585 participants in the OTG.

Unpublished data from a longitudinal cohort study (Benson et al., 2015a) found that there was a mean improvement in the OHRQoL scores (reduction in the Total CPQ₁₁₋₁₄-ISF:16)

of 3% (95% CI 1% to 5%) in a group that reported no change in their global oral health after 3 years. This compared to a mean improvement of 8% (95% CI 5% to 11%) in those who reported better global oral health after 3 years. Assuming similar proportional improvements in OHRQoL between the WLCG and OTG, an equivalence margin (δ) of 10%, a power of 0.80 and a significance level (α) of 0.05, using sample size calculator software (Powerandsamplesize.com) we estimated that 320 participants would be required in the WLCG to test for equivalence with the OTG. Accounting for a 20% dropout over one year, it was determined that a minimum sample size of 384 participants was required in the WLCG.

Based on the Agou et al., (2011) study, the difference in change in the OHRQoL between the orthodontic treatment group, and the waiting list control group at follow-up was 4. The data provided by the authors can be used to estimate a pooled standard deviation of change scores to be 14.0. Assuming a power of 80% ($1-\beta$) and a significance level (α) of 0.05, approximately 350 participants (175 participants per group) would be required to detect a statistically significant difference between the two groups. Assuming a 30% dropout rate over 4 years in the OTG and a 20% dropout in the WLCG, a total of 228 participants would need to be recruited into the OTG, and 210 into the WLCG.

As the second sample size calculation (between group comparison of OHRQoL change) was based on limited data, and smaller than the first sample size calculation (based on the testing of equivalence in OHRQoL between the two groups), it was determined that the first sample size calculation would be used to recruit an appropriate number of participants into the study.

Based on these calculations, it was therefore determined that a total of 585 participants would need to be recruited into the OTG, and 384 participants into the WLCG.

4.4: Study Setting

Multiple centres were used to recruit appropriate participants. These were purposefully selected to include primary and secondary care orthodontic services, and included

teaching hospitals, district general hospitals and specialist orthodontic practices throughout the UK. This was done to ensure that a range of participants with varying orthodontic treatment needs could be recruited, enabling the generalisability of any findings. The settings selected for the recruitment of participants for the OTG cohort were:

- **Site 1:** Orthodontic Department, Charles Clifford Dental Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, 76 Wellesley Road, Sheffield, S10 2SZ.
- **Site 2:** Orthodontic Department, Royal National ENT and Eastman Dental Hospitals, University College London Hospitals NHS Foundation Trust, 47-49 Huntley Street, London, WC1E 6DG.
- **Site 3:** Orthodontic Department, Northampton General Hospital NHS Trust, Cliftonville, Northampton, NN1 5BD.
- **Site 4:** The Specialist Orthodontic Practice, 117 High Street, Epping, Essex, CM16 4BD.
- **Site 5:** The Orthodontic Practice, 19 Woodhouse Road, Mansfield, Nottingham, NG18 2AF.
- **Site 6:** Orthodontic Department, UHNM NHS Trust, Royal Stoke University Hospital, Newcastle Road, Stoke-on-Trent, ST4 3SA.
- **Site 7:** Orthodontic Department, Royal Devon & Exeter Hospital, Royal Devon University Healthcare NHS Foundation Trust, Exeter, EX2 5DW.

The settings selected for the recruitment of participants for the WLCG group cohort were:

- **Site 8:** No1 The Orthodontic Specialists, 1 Station Road, Derby, DE3 9GH.
- **Site 9:** Crystal Peaks Orthodontics, 15 Peaks Mount, Sheffield, S20 7HZ.
- **Site 10:** The Orthodontic Centre, 498 Ecclesall Road, Ecclesall, Sheffield, S11 8PY.
- **Site 11:** Orthodontic Department, Charles Clifford Dental Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, 76 Wellesley Road, Sheffield, S10 2SZ.

4.5: Methods of Recruitment of Participants

Consecutive, eligible patients at the various centres, were planned to be recruited over a two-year period. At the inception of the study, the recruitment rate was felt to be realistic as each centre had a minimum number of 100 young people starting orthodontic treatment per year.

Visits were carried out by the PI (HJ) to all the sites that were involved in the study to provide the support necessary to participate and recruit participants. A member of the patient's existing clinical care team at each centre was tasked with identifying potential participants, through convenience sampling, using the study inclusion and exclusion criteria. Potential participants and their parents (when applicable) were subsequently approached to ask if they would be willing to talk to a specified person at each site, who was trained to provide information about the study. This specified person then explained the study and provided written information sheets (Appendix 1) to reinforce the verbal discussion. Potential participants were given sufficient time to consider whether they wished to take part. If they agreed, then written consent was obtained from participants and where applicable, their parents, by the trained individual. Where participants were aged 16 years, they were asked to complete the specific consent form for participants aged 16 years (Appendix 2). Where participants were aged 15 years or under, the participant was asked to complete an assent form, and their parent, a consent form (Appendix 2). Recruited participants were each allocated a 'Participant ID' number, and this reference was used and shared with the host site (Sheffield Teaching Hospital). All data was pseudonymised using this Participant ID number. All sites were provided with screening logs and subject enrolment logs (Appendix 3). As the screening logs and subject enrolment logs contained patient identifiable data, they were kept secure within each site and were not shared with the host site.

4.6: Measures

All data were collected using a data collection sheet which was completed by the treating clinician (Appendix 4), in addition to a participant questionnaire (Appendix 5). Printed copies of the data collection sheets were provided to all the sites and these were completed manually. These sheets were later collected by the PI of the study (H.J), for data analysis and storage at the host site.

The participant questionnaires were administered electronically for all sites, except for site 6. At this site, there was no Wi-Fi access, and participants were asked to complete the participant questionnaire manually. Later, members of the research team at this site transferred this data and submitted it using the electronic participant questionnaire link provided. All the sites were provided with Amazon Kindle tablets, and the electronic participant questionnaires were administered using a Google form. This data was pseudonymised using the participant ID number, and the Google drive was administered and stored on the encrypted network hosted by the University of Sheffield. A screenshot of the Google form used can be found in Appendix 5.

Several measures were used throughout the study to collect relevant data. The primary outcome for the study was OHRQoL, and as such, appropriate OHRQoL outcome measures were used (Section 4.5.4). Based on the literature review presented in Chapter 2, it is evident that various socio-demographic, clinical and psychosocial factors may play a role in the OHRQoL levels observed. The Wilson-Cleary model also hypothesises that such variables may influence overall QoL (Wilson and Cleary, 1995). As such, appropriate measures were used to obtain data on environmental (Index of Multiple Deprivation) and individual (gender, age, ethnicity, self-esteem) factors. Table 1 provides an overview of the different measures that were used at T1, T2 and T3. The details for all these measures are described in this Section (4.6).

Table 1: Measures used to collect data and the time-points (T1, T2, and T3) in which this was collected.

Measures	T1	T2	T3 (Treatment Group only)
Socio-demographic:			
Date of birth	X		
Gender	X		
Postcode	X		
Ethnicity		X	
Clinical:			
Participant's main complaint	X		
Clinical measurements of malocclusion	X		
Type of brace/treatment to be provided	X		
Clinician-assessed IOTN DHC	X		
Self-assessed IOTN AC	X	X	X
Oral Health-Related Quality of Life & Psychosocial:			
Malocclusion Impact Questionnaire	X	X	X
Child Oral Health Impact Profile Short Form-19/ Oral Health Impact Profile-14	X	X	X
Self-esteem scale of the 87-item Child Health Questionnaire-Child Form	X	X	X
Students' Life Satisfaction Scale	X	X	X
Global Oral Health Question 1	X	X	X
Global Oral Health Question 2	X	X	X
Global Oral Health Question 3	X	X	X
Global Oral Health Question 4	X	X	X
Global Oral Health Question 5	X	X	X
Global Transition Judgement Question 1		X	X
Global Transition Judgement Question 2		X	X

4.6.1. Socio-Demographic Measures

All data on socio-demographic variables were collected using the data collection sheet (Appendix 4) which was completed by the clinician, at T1, except for ethnicity. Data on participant ethnicity was collected using the participant questionnaire at T2. The reason for this was that soon after the study had started, it was determined that ethnicity would

be an important variable to consider in the analysis of the data (Abdelrahim et al., 2017), and as such, as part of a substantial amendment that was submitted for the study (see Section 4.7), data for ethnicity was to be captured by including it in the participant questionnaire at T2. Table 2 highlights the socio-demographic measures used, the method used to obtain this data, and the way in which the responses were coded. The difference between the date of birth of participants and date at T1, T2 and T3 (where applicable), were used to calculate participant age at T1, T2 and T3 (where applicable) in years. The postcode of participants was used to determine their Index of Multiple Deprivation (IMD) decile. The IMD decile was derived using the Ministry of Housing, Communities & Local Government English indices of deprivation 2019 (<https://imd-by-postcode.opendatacommunities.org/imd/2019>). Whilst data on the ranking of each postcode is available, it is generally recommended that IMD data should be presented and analysed using deciles rather than individual rankings (Ministry of Housing, 2019).

Table 2: Socio-demographic measures used, the methods of response collection, and the coding approach for the responses.

Data collected	Response options in questionnaire	Coding of responses
Date of birth	Narrative, free text	Age presented in years.
Gender	Narrative, free text	Male: 1 Female: 2
Postcode	Narrative, free text	Index of Multiple Deprivation Deciles: 1-10
Ethnicity	White British White Irish Any other White background Pakistani Indian Bangladeshi Any other Asian background White and Asian White and Black African White and Black Caribbean Any other Mixed background African Caribbean Any other Black background Chinese Any other ethnic group Prefer not to say	White British: 1 White Irish: 2 Any other White background: 3 Pakistani: 4 Indian: 5 Bangladeshi: 6 Any other Asian background: 7 White and Asian: 8 White and Black African: 9 White and Black Caribbean: 10 Any other Mixed background: 11 African: 12 Caribbean: 13 Any other Black background: 14 Chinese: 15 Any other ethnic group: 16 Prefer not to say: 17

4.6.2. Clinical Measures of Malocclusion and Features of the Dentition

Except for self-assessed IOTN AC, the rest of the data on measures of malocclusion (including participants main complaint) was recorded by the clinician using the data collection sheet (Appendix 4). Self-assessed IOTN AC was included within the participant questionnaire. Table 3 demonstrates the different features of malocclusion for which data was collected and outlines the way these data were subsequently coded.

Table 3: Clinical measures of the malocclusion, the response options for each measure, and the coding method used for the responses.

Data collected	Response options in questionnaire	Coding of responses
Participants main complaint	Narrative, free-text response	Increased overjet: 1 Overbite: 2 Crowding: 3 Spacing: 4 Function: 5 No concerns: 6 Other: 7
Incisor relationship	Class I Class II Div 1 Class II Div 2 Class III	Class I: 1 Class II Div 1: 2 Class II Div 2: 3 Class III: 4
Overjet	Measured (mm)	N/A
Overbite	Average Increased Reduced Anterior open bite Incomplete Complete to hard tissue Complete to soft tissue	Average: 1 Increased: 2 Reduced: 3 Anterior open bite: 4 Incomplete: 1 Complete to hard tissue: 2 Complete to soft tissue: 3
Spacing in the upper labial segment	Combined total (mm) Single largest (mm)	N/A
Spacing in the lower labial segment	Combined total (mm) Single largest (mm)	N/A
Dental irregularity in the upper labial segment	Combined total (mm) Single largest (mm)	N/A
Dental irregularity in the lower labial segment	Combined total (mm) Single largest (mm)	N/A
Developmentally absent teeth (excluding 8's)	No Yes	No: 0 Yes: 1
Presence of Impacted teeth (excluding 8's)	Nomenclature of which tooth/teeth	Nomenclature of which tooth/teeth: Recoded according to the Federation Dentaire International Tooth Numbering System
IOTN DHC	IOTN DHC Grade	1-5
Self-assessed IOTN AC	IOTN AC Grade	1-10
Other dental conditions (e.g. trauma)	Narrative, free-text response	No other condition: 0 Presence of other condition: 1

4.6.3. Type of Orthodontic Treatment provided

In both the OTG and the WLCG, data on the type of treatment that the clinician was planning to provide for the participant was collected using the data collection sheet (Appendix 4). Clinicians at each site were to provide treatment as per their standard protocol. The details of the response options within the questionnaire for this data, together with the coding of these responses are outlined in Table 4.

Table 4: Data collected on the type of orthodontic treatment provided to study participants, together with the coding method used to represent these.

Data collected	Response options in questionnaire	Coding of responses
Type of brace/ treatment	Removable appliance Functional appliance Fixed appliance Extraction (s) Other (please specify)	Fixed appliance(s) +/- extraction(s): 1 Functional, fixed appliance(s) +/- extraction (s): 2 Removable, fixed appliance(s) +/- extraction (s): 3 Removable, functional, fixed appliance(s) +/- extraction(s): 4

4.6.4. Oral Health-Related Quality of Life (Primary Outcome)

The data on the OHRQoL of participants was collected using the participant questionnaire, and both generic and condition-specific OHRQoL measures were used.

4.6.4.1. Generic Oral Health-Related Quality of Life Measures

The two generic OHRQoL measures that were used included:

- **Child Oral Health Impact Profile – Short Form 19 Questionnaire (COHIP-SF 19):** This was developed for use in a wide range of oral conditions, including malocclusion, in patients aged 8 to 17 years (Broder et al., 2007, Broder et al., 2012). The COHIP-SF 19 is composed of 19 questions, with a 5-point Likert scale. The questionnaire contains 17 negatively worded questions and two positively worded questions. The instructions for the items in the questionnaire were 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.’.

- **Oral Health Impact Profile-14 (OHIP-14):** This was designed for patients aged 18 years or over (Slade, 1997). This questionnaire was used at T2 or T3, where participants were aged 18 years or over, instead of the COHIP-SF 19. There are 14 questions, with a 5-point Likert scale. Whilst the instructions for the original OHIP-14 questionnaire are as follows: ‘How frequently have you experienced the following impacts in the preceding 12 months?’, this was deemed too long to use in the context of this study at T2 or T3, and, as such, the instructions provided for participants in this study were as follows: ‘The next few questions are about your oral health. For each question, please select the answer that best applies to you during the past month’.

The reason for choosing COHIP-SF 19 as the generic measure of OHRQoL, rather than the commonly used CPQ₁₁₋₁₄, was that COHIP-SF 19 was developed for use with young people in the age range of this study (8 to 17 years). It also allowed possible follow-up with the adult OHIP-14 (Slade and Spencer, 1994, Slade, 1997) in young people who were outside the range of COHIP-SF 19 when they finished their orthodontic treatment. In contrast, the CPQ was developed for 11- to 14-year-olds and there was no suitable questionnaire to use with young people, who are usually older than 14 years when their orthodontic appliance is removed.

The response options for each questionnaire, their interpretation, and the coding of these responses are demonstrated in Table 5.

Table 5: Response options and coding for the Child Oral Health Impact Profile-Short Form 19 (COHIP-SF 19) and the Oral Health Impact Profile-14 (OHIP-14) questionnaires.

Questionnaire	Response options and coding	Interpretation of scores
Child Oral Health Impact Profile-Short Form 19 (COHIP-SF 19)	Never: 0 Almost never: 1 Sometimes: 2 Fairly often: 3 Almost all the time: 4 For the 17 negatively worded questions, these scores were reversed.	Scores of all 19 items were added together to produce a total score ranging from 0 to 76. Higher scores reflect better OHRQoL.
Oral Health Impact Profile-14 (OHIP-14)	Never: 0 Hardly ever: 1 Occasionally: 2 Fairly often: 3 Very often: 4	Scores of all 14 items were added together to produce a total score ranging from 0 to 56. Higher scores reflect poorer OHRQoL.

4.6.4.2. Condition-specific Oral Health-Related Quality of Life Measure

The Malocclusion Impact Questionnaire (MIQ) is a unidimensional measure, and is the only condition-specific instrument that has been developed, specifically for use in young people with malocclusion (Benson et al., 2016, Patel et al., 2016). This was the first time the MIQ was to be used in a longitudinal study in the UK (at the time of start-up), and its' longitudinal construct validity was therefore to be investigated. The questionnaire contains 17 questions, with responses on a scale ranging from 0 to 2. Where the change in OHRQoL following treatment is required, the authors recommend the conversion of ordinal raw scores to an interval scale score, and advise that both the ordinal raw scores and the interval scores should be presented (Benson et al., 2016). As such, both the raw and interval scores for MIQ were used.

The response options for the MIQ together with its' interpretation, and the coding of the responses are demonstrated in Table 6.

Table 6: Response options and coding for the Malocclusion Impact Questionnaire (MIQ).

Questionnaire	Response options and coding	Interpretation of score
Malocclusion Impact Questionnaire	For negatively worded questions: Don't or Doesn't: 0 A bit: 1 Very or A lot: 2 For positively worded questions: Don't or Doesn't: 2 A bit: 1 Very or A lot: 1	Scores of all 17 items were added together to produce a total score ranging from 0 to 34. Higher scores reflect poorer OHRQoL.

4.6.5. Global Oral Health & Transition Judgement

The data on global oral health was obtained using the participant questionnaires. An overall Global Oral Health (GOH) question was used at all time points, including T1, T2 and T3 (where applicable):

- **(GOH1):** How would you describe the overall health of your teeth and mouth today?

In addition to the 17-questions in the MIQ (see Section 4.6.4.2), the MIQ questionnaire also contains two global questions which were included in the participant questionnaire:

- **(GOH2):** Overall, how does the appearance of your teeth, as they are now, upset you?
- **(GOH3):** Overall, how does the appearance of your teeth, as they are now, affect your life in a negative way?

To determine whether the aesthetics of the occlusion, or in fact the function of the occlusion, played a contributory role to the OHRQoL of participants, two additional GOH questions were also used:

- **(GOH4):** Overall, does the way your teeth bite, as they do now, upset you?

- **(GOH5):** Overall, does the way your teeth bite, as they do now, affect your life in a negative way?

To test the responsiveness of the MIQ questionnaire (which at the conception of the study, had not been tested longitudinally), two Global Transition Judgement (GTJ) questions were included in the participant questionnaire, and used at T2 and T3 (where applicable) only:

- **(GTJ1):** Overall, has the appearance of your teeth changed since you last filled out the questionnaire?
- **(GTJ2):** Overall, has the bite of your teeth changed since you last filled out the questionnaire?

The responses of all these global oral health questions/judgements were based on a Likert scale. The response options, scores, and coding, and timepoint within the study in which each of these questions were administered in shown in Table 7.

Table 7: Response options, coding of responses, and the time points in the study at which the Global Oral Health and Global Transition Judgement questions were included in the participant questionnaires.

Global Oral Health Questions	Timepoint (T1, T2, T3)	Response options and coding
(GOH1): How would you describe the overall health of your teeth and mouth today?	T1 T2 T3	Poor: 0 Fair: 1 Average: 2 Good: 3 Excellent: 4
(GOH2): Overall, how does the appearance of your teeth, as they are now, upset you?	T1 T2 T3	Not at all: 0 A little: 1 Somewhat: 2 Quite a bit: 3 Very much: 4
(GOH3): Overall, how does the appearance of your teeth, as they are now, affect your life in a negative way?	T1 T2 T3	Not at all: 0 A little: 1 Somewhat: 2 Quite a bit: 3 Very much: 4
(GOH4): Overall, does the way your teeth bite, as they do now, upset you?	T1 T2 T3	Not at all: 0 A little: 1 Somewhat: 2 Quite a bit: 3 Very much: 4
(GOH5): Overall, does the way your teeth bite, as they do now, affect your life in a negative way?	T1 T2 T3	Not at all: 0 A little: 1 Somewhat: 2 Quite a bit: 3 Very much: 4
(GTJ1): Overall, has the appearance of your teeth changed since you last filled out the questionnaire?	T2 T3	Worsened a lot: 0 Worsened a little: 1 Stayed the same: 2 Improved a little: 3 Improved a lot: 4
(GTJ2): Overall, has the bite of your teeth changed since you last filled out the questionnaire?	T2 T3	Worsened a lot: 0 Worsened a little: 1 Stayed the same: 2 Improved a little: 3 Improved a lot: 4

4.6.6. Life Satisfaction (Overall Quality of Life)

The measure used to assess life satisfaction (overall QoL), was the Students' Life Satisfaction Scale (SLSS) (Huebner, 1991). This questionnaire contained 7 items, each of which were scored on a 4-point Likert scale (Table 8) and was administered in the electronic participant questionnaire.

Table 8: Response options and coding for the Students' Life Satisfaction Scale.

Questionnaire	Response options and coding	Interpretation of score
Students' Life Satisfaction Scale (SLSS)	Never: 1 Sometimes: 2 Often: 3 Almost always: 4 For the two negatively worded questions, these scores were reversed.	Scores of all seven items were added together to produce a total score ranging from 7 to 28. Higher scores reflect better life satisfaction.

4.6.7. Self-Esteem

Self-esteem was measured using the Self-esteem scale of the 87-item Child Health Questionnaire-Child Form (CHQ-CF87) (Landgraf et al., 1998). This questionnaire contained 14 items, each scored on a 5-point Likert scale (Table 9), and was administered in the electronic participant questionnaire. The standardised scores for this were calculated according to the guidelines provided for the questionnaire (Landgraf et al., 1998). Further details of this cannot be reproduced in this thesis due to licencing restrictions.

Table 9: Response options and coding for the self-esteem scale of the CHQ-CF87.

Questionnaire	Response options and coding	Interpretation of score
Self-esteem scale of the 87-item Child Health Questionnaire-Child Form (CHQ-CF87)	Very badly: 1 Somewhat badly: 2 Neither good or bad: 3 Somewhat good: 4 Very good: 5	Standardised scores ranging from 0 to 100. Higher scores reflect better self-esteem.

4.7: Ethical and Research Governance Approval

Protocol V7 (27.01.17) for this study was approved by the North West – Preston Research Ethics Committee (REC reference:17/NW/0204) on the 16th of March 2017 (Appendix 6). Following this, a Substantial Amendment (SA1) was submitted to include the addition of a WLCG. Protocol V8 (16.05.17) was subsequently approved by North West – Preston Research Ethics Committee (REC reference:17/NW/0204) on the 5th of June 2017. A further Non-Substantial Amendment (NSA1) was submitted on 18th August 2017 for the addition of a further site to the WLCG (Appendix 6). Health Research Authority (HRA) approval was obtained, based on the SA1, on the 5th of September 2017 (IRAS project ID: 214707) (Appendix 6). The project was sponsored by Sheffield Teaching Hospital NHS Foundation Trust (STH Project Reference number 19669), and the study started recruitment on the 16th of October 2017.

Throughout the course of the study, various challenges were encountered (discussed in Section 6.5) which resulted in several changes being made to the study and the need to seek appropriate approvals for these amendments. A Non-Substantial Amendment (NSA2) was issued on the 2nd of April 2018, to permit the inclusion of one orthodontic practice in the OTG and another in the WLCG (Appendix 6). A third Non-Substantial Amendment (NSA3) was made on the 25th of May 2018, to add two more sites to the WLCG and to change the Principal Investigator (PI) at one of the sites (Appendix 6).

A Substantial Amendment (SA2) was submitted and approved by the North West – Preston Research Ethics Committee (REC reference:17/NW/0204) on the 30th of October 2018 (Appendix 6). This amendment was to allow for the removal of wording within the Patient Information Leaflets (PILs) prescribing a 7-day window to consider whether patients would like to enrol on the study, the follow-up questionnaires were to include ethnicity data, and the new PILs were amended to ensure they were GDPR compliant. HRA for this amendment was obtained the 8th of January 2019.

During and after the COVID-19 pandemic, further requests to amend the study were made. A Non-Substantial Amendment (NSA4) was made on the 20th of April 2020 to

change the time-points for follow-up of participants in the OTG at T2 from 6 to 15 weeks after the end of active orthodontic treatment, to 6 weeks up to 9 months after the end of active orthodontic treatment. The time-points for T3 were changed from 9 to 15 months after the end of active orthodontic treatment, to 9 months up to and including 18 months post-orthodontic treatment (Appendix 6). A Non-Substantial Amendment (NSA5) was submitted on the 1st of December 2020 to allow for participants to be contacted for follow-up either via phone, mail or email. A final, Non-Substantial Amendment (NSA6) was made on the 4th of March 2022 to allow for extension and change of the follow-up of participants in the OTG at T3 from 9 up to 32 months (Appendix 6).

Insurance for the study was obtained from the University of Sheffield (Appendix 6).

4.8: Data Transfer

All electronic participant questionnaire data was downloaded into a Microsoft Excel spreadsheet. This data was then imported into IBM SPSS Statistics 29.0, and the data from the data collection sheet was then entered manually into IBM SPSS Statistics 29.0. All data analysis was carried out using IBM SPSS Statistics 29.0.

4.9: Statistical Analysis Plan

The response data for all the participant questionnaires were managed, as previously described, using the recommended methods for each questionnaire. At T2 and T3, there was a combination of COHIP SF-19 and OHIP-14 data. The COHIP SF-19 data and the OHIP-14 data were standardised on a scale of 0-100, and the OHIP-14 scores reversed, to allow the amalgamation of the data from these questionnaires at T2 and T3 (where applicable). As such, higher scores of the standardised and combined COHIP SF-19 and OHIP-14 scores were considered to represent better levels of OHRQoL.

The statistical analysis for the study was carried out in five phases.

4.9.1. Phase 1: Descriptive and Psychometric Analysis

This included a descriptive analysis of the socio-demographic, clinical, OHRQoL and psychosocial data of all the participants who were recruited into the study at T1 (baseline). Appropriate measures of central tendency, spread and proportions were used to analyse the data. Data for the OTG and the WLCG were presented separately to allow the detection of any obvious differences. No hypothesis testing of this data was carried out as the study was not powered to detect differences at baseline.

To assess the responsiveness and longitudinal construct validity of the MIQ (which has not previously been carried out using such a large sample size), data from both the WLCG and the OTG were analysed together, using MIQ scores at T1 and T2, along with the two GTJ questions, 'Overall, how has the appearance of your teeth changed from before you started treatment or last filled out the questionnaire?' (GTJ1) and 'Overall, how has the bite of your teeth changed from before you started treatment or last filled out the questionnaire?' (GTJ2). By analysing this data and using the GTJ questions as an external validation measure, it was possible to assess whether the MIQ score changes from T1 to T2 were sensitive to and correlated with participants' self-reported changes in dental appearance and bite.

The difference in MIQ scores from T1 and T2, provided an indication of whether OHRQoL improved, stayed the same, or become poorer. The responsiveness of the MIQ was assessed using standardised effect sizes, which can be used to determine the magnitude of the change (Cohen, 2013). These are considered small (0.2-0.5), moderate (0.5-0.8), or large depending on their values (greater than 0.8) (Cohen, 2013). In accordance with previous studies (Peter et al., 2023, Locker et al., 2004), the statistical significance of within-subject change in MIQ scores for those who reported worsening of OHRQoL (worsened a lot, or worsened a little), those who reported an improvement in OHRQoL (improved a lot or improved a little) and those who reported no change in their OHRQoL, was assessed using paired samples *t*-tests (Locker et al., 2004, Peter et al., 2023). If the MIQ is responsive, the former two should be statistically significant, whilst the latter should be non-significant. A *p*-value below 0.05 was considered statistically significant.

The Minimal Important Difference (MID) for the MIQ was calculated using the anchor method by subtracting the mean change (from T1 to T2) in the MIQ score of participants who reported to have experienced no change in their OHRQoL, from the mean change in MIQ score of participants who had reported a little improvement in their OHRQoL, and those that reported their OHRQoL to worsen a little (Masood et al., 2014, Revicki et al., 2008). The two were then pooled together to produce a MID (Revicki et al., 2008). This was calculated for both GTJ1 and GTJ2.

The association between changes in MIQ (from T1 to T2), and GTJ1 and GTJ2, were assessed using a One-way Analysis of Variance (ANOVA). If the MIQ is considered to demonstrate good longitudinal construct validity, then participants who reported an improvement in response to the GTJ questions, would demonstrate this with a decrease in MIQ scores, and vice versa. The use of regression, including ANOVA, to assess the responsiveness of a new measure/tool is well recognised in the literature (Husted et al., 2000). Furthermore, a recently published 3-year longitudinal cohort study, (with a total of 162 participants followed-up one month after the completion of orthodontic treatment) assessing the impact of orthodontic treatment on OHRQoL using the MIQ, used a similar methodology to determine the longitudinal construct validity of the MIQ (Peter et al., 2023).

4.9.2. Phase 2: Descriptive Analysis of those Lost to Follow-up Versus those who Completed the Study to T2

This included a descriptive analysis of the socio-demographic, clinical, OHRQoL and psychosocial data of the participants in the study at T1 (baseline), with data presented separately for participants who completed the study to T2, compared to participant who were lost to follow-up. Appropriate measures of central tendency, spread and proportions were used to analyse the data. No hypothesis testing of this data was carried out, as the study was not powered to detect differences at baseline.

4.9.3. Phase 3: Parametric and Non-Parametric Testing To Compare the Orthodontic Treatment Group and the Waiting List Control Group

This phase of the data analysis was aimed at addressing the first research question:

- Are there differences in the changes observed in the OHRQoL of young people aged 11 to 16 years who receive orthodontic treatment versus those who are still waiting for treatment?

An independent samples t-test was used to compare changes observed in MIQ scores from T1 to T2, in the OTG versus the WLCG. A p-value below 0.05 was considered statistically significant.

Wilcoxon Signed Rank tests were used to assess changes in responses to the GOH questions (GOH1-5) from T1 to T2. A p-value of less than 0.05 was considered statistically significant, indicating a meaningful change in responses.

4.9.4. Phase 4: Analysis of Covariance (ANCOVA)

This phase of the data analysis was aimed at addressing the second research question:

- If there is an improvement in OHRQoL following orthodontic treatment, can specific characteristics be identified that can predict which individuals will benefit the most from treatment?

An Analysis of Covariance (ANCOVA) was used to examine the effect of specific baseline factors, on the scores of MIQ at T2. The OTG and WLCG were used as the independent variables, and MIQ at T2 was inputted as the dependent variable. The covariates were selected based on factors which have previously been found to influence OHRQoL (Chapter 2), and those that are considered to be important. The covariates selected for the analysis were:

- **Socio-demographic:** Gender, age, IMD decile
- **Clinical:** Largest space and contact point displacement in the Upper Labial Segment (ULS), overjet, IOTN DHC grade, self-assessed IOTN AC grade.
- **Psychosocial:** Self-esteem scale of the CHQ-CF87, SLSS.

The MIQ interval scores at T1 were also included as a covariate. Where Levene's test for homogeneity was found to be statistically significant, bootstrapping methods were used (Freedman, 1981).

4.9.5. Phase 5: Visual Presentation of Orthodontic Treatment Group Data at T3

This phase of the data analysis was aimed at presenting the data collected in the OTG at T3.

4.9.6. Management of Missing Data

At the start of the study, the MIQ had undergone limited testing, and there was insufficient data to establish a threshold for missing data that would warrant participant exclusion from the analysis. Consequently, we decided to exclude participants from the analysis if five or more items were missing from the MIQ. Following the guidelines for the self-esteem scale of the CHQ-CF87, data were excluded if six or more items were missing (Landgraf et al., 1998). For the COHIP-SF 19 and OHIP-14, definitive thresholds for exclusion were not found in the literature. Therefore, drawing on previous studies (Benson et al., 2015a), we opted to exclude data if five or more items were missing. Similarly, for the SLSS, data were excluded if three or more items were missing. In cases where the missing data fell below these thresholds, predicted values were imputed using regression models (Papageorgiou et al., 2018).

Chapter 5

Results

5.1 Introduction

The first section of this Chapter outlines the flow of participants from recruitment through to follow-up in the study. The remaining five sections of the Chapter focus on the five phases of data analysis.

5.2 Recruitment of Participants

The recruitment flow charts (Figures 3 & 4) indicate that a total of 972 participants were recruited across all the study sites. These included 596 participants in the OTG, and 376 participants in the WLCG. The recruitment of participants started in October 2017 and finished in February 2020. At each site, potential participants were screened during their routine appointments in the orthodontic clinic. Where the inclusion criteria were met and the potential participant was willing to participate in the study, they were appropriately recruited. Due to data storage errors in one site, the screening logs could not all be retrieved, and so the total number of participants screened for the study cannot be presented. Due to administrative errors at some sites, a total of 11 participants had no clinical or questionnaire data at baseline, and so they were excluded from the study. Baseline data (T1) for a total of 596 participants in the OTG and 376 participants in the WLCG were available and analysed.

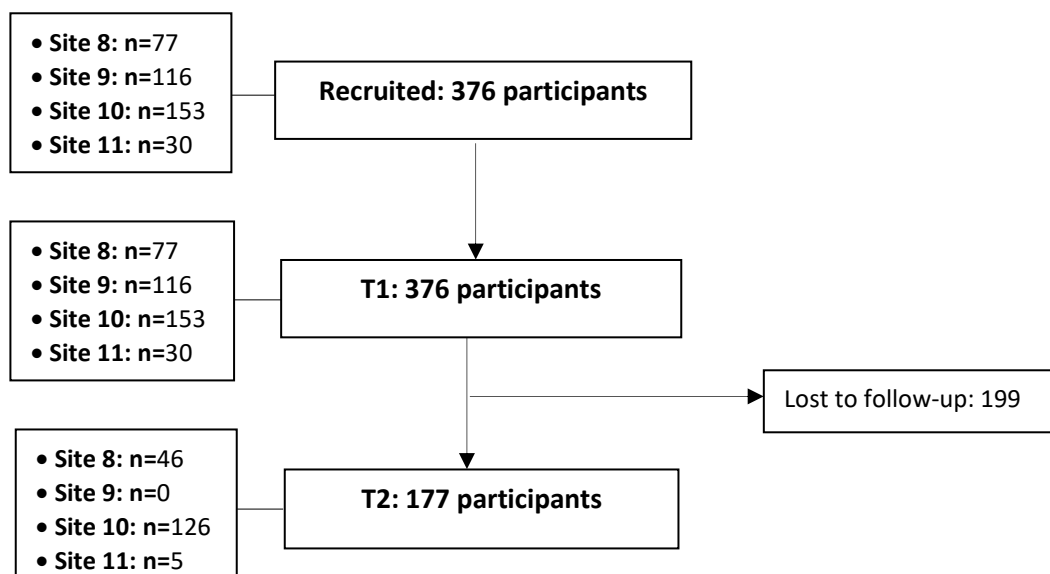


Figure 3: Participant flow chart in the Waiting List Control Group

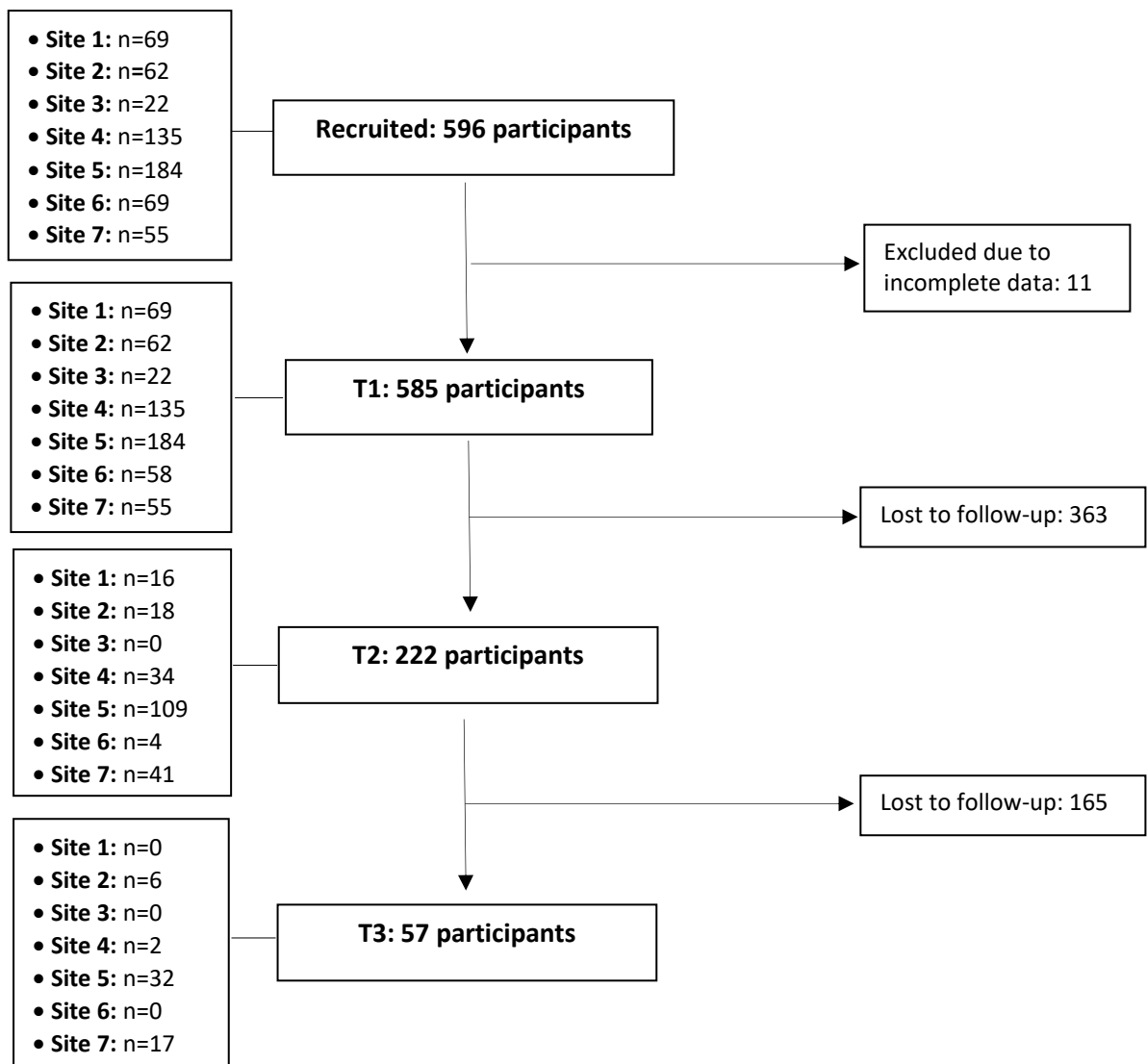


Figure 4: Participant flow chart in the Orthodontic Treatment Group

5.3 Phase 1: Descriptive and Psychometric Analysis

5.3.1 Socio-Demographic Characteristics

The demographic data of the participants in the OTG and the WLCG at baseline are demonstrated in Table 10. The percentage of missing data was slightly more in the OTG than the WLCG for all the socio-demographic variables. The reasons for this are discussed in Chapter 6. Despite this, the percentage of female participants in both groups were the same and equal to 50%. In relation to the age of participants, the majority (42%) of the participants in the OTG were aged 13 or 14 years, whilst the majority (71%) of

participants in the WLCG were aged 11 or 12 years at baseline. The data in relation to the IMD deciles, suggested that the deprivation of participants was well distributed, and similar patterns were seen in both the OTG and the WLCG.

Table 10: Socio-demographic data of participants in the Orthodontic Treatment Group and the Waiting List Control Group at T1 (percentage of participants).

Socio-Demographic Characteristics	Orthodontic Treatment Group (n=585) n (%)	Waiting List Control Group (n=376) n (%)
Gender		
Female	293 (50%)	189 (50%)
Male	221 (38%)	171 (45%)
Missing	71 (12%)	16 (4%)
Age (years)		
11 or 12	176 (30%)	267 (71%)
13 or 14	246 (42%)	79 (21%)
15 or 16	94 (16%)	11 (3%)
Missing	69 (12%)	19 (5%)
IMD (decile)		
1 or 2	70 (12%)	74 (20%)
3 or 4	105 (18%)	37 (10%)
5 or 6	94 (16%)	64 (17%)
7 or 8	94 (16%)	76 (20%)
9 or 10	70 (12%)	99 (26%)
Missing	152 (26%)	26 (7%)
Please note: Percentages may not total 100% due to rounding.		

Data on ethnicity was included in the questionnaires at T2 and is therefore limited. Table 11 highlights the data available for ethnicity, and based on the limited data available, most individuals were reported as being British in both the OTG (52%) and the WLCG (57%).

Table 11: Ethnicity of participants in the Orthodontic Treatment Group and the Waiting List Control Group at T2 (percentage).

Ethnicity	Orthodontic Treatment Group (n=222) n (%)	Waiting List Control Group (n=177) n (%)
African	3 (1%)	1 (1%)
Any other Asian background	3 (1%)	2 (1%)
Any other ethnic background	2 (1%)	2 (1%)
Any other White background	3 (1%)	4 (2%)
Any other Mixed background	3 (1%)	4 (2%)
Arabic	1 (1%)	1 (1%)
British	116 (52%)	101 (57%)
Bangladeshi	2 (1%)	0 (0%)
Indian	1 (1%)	2 (1%)
Pakistani	1 (1%)	3 (2%)
Prefer not to say	3 (1%)	18 (10%)
Missing	84 (38%)	39 (22%)

5.3.2 Clinical Characteristics

The clinical data in relation to the participants recruited into the OTG and WLCG of the study are outlined in Tables 12 and 13. Participants in both groups most frequently presented with Class II division 1 incisor relationships, increased overbites, and overjet between 2 to 4.9 mm. The least common incisor relationship in both groups was found to be Class III. A total of 65% and 64% of participants in the OTG and WLCG respectively, judged themselves to have an IOTN AC scores between 1-4. The most frequent IOTN DHC grade in both the OTG and the WLCG was grade 4. The distribution of spacing and dental irregularity in the ULS and Lower Labial Segment (LLS) were similar in both groups, as was the presence of impacted teeth. A slightly greater percentage of participants presented with hypodontia in the OTG (14%) compared to the WLCG (6%).

Table 12: Clinical characteristics of participants in the Orthodontic Treatment Group and the Waiting List Control Group of the study at T1 (percentage).

Clinical Characteristics	Orthodontic Treatment Group (n=585) n (%)	Waiting List Control Group (n=376) n (%)
Incisor relationship		
Class I	147 (25%)	77 (21%)
Class II div 1	227 (39%)	194 (52%)
Class II div 2	80 (14%)	50 (13%)
Class III	60 (10%)	36 (10%)
Missing	71 (12%)	19 (5%)
Overbite		
Average	157 (27%)	82 (22%)
Increased	239 (41%)	173 (46%)
Reduced	92 (16%)	96 (26%)
Anterior open bite	24 (4%)	6 (2%)
Missing	73 (12%)	19 (5%)
Overjet		
Less than 2mm	64 (11%)	30 (8%)
2 to 4.9mm	199 (34%)	128 (34%)
5 to 6.9mm	82 (14%)	71 (19%)
7mm or more	146 (25%)	109 (29%)
Missing	94 (16%)	38 (10%)
IOTN DHC Grade		
5	187 (32%)	89 (24%)
4	313 (54%)	261 (69%)
3	15 (3%)	8 (2%)
Missing	70 (12%)	18 (5%)
IOTN AC Grade		
1-4	384 (65%)	244 (65%)
5-8	155 (26%)	114 (30%)
9-10	33 (6%)	14 (4%)
Missing	13 (2%)	4 (1%)
Impacted teeth		
Yes	117 (20%)	54 (14%)
No	397 (68%)	305 (81%)
Missing	71 (12%)	17 (5%)
Hypodontia		
Yes	80 (14%)	24 (6%)
No	433 (74%)	335 (89%)
Missing	72 (12%)	17 (5%)

Table 13: Dental crowding and spacing present in the upper and lower labial segments of participants recruited into the Orthodontic Treatment Group and the Waiting List Control Group of the study at T1 (percentage).

Clinical Characteristics	Orthodontic Treatment Group (n=585) n (%)	Waiting List Control Group (n=376) n (%)
Total space ULS		
Less than 6mm	433 (74%)	315 (84%)
More than 6mm	82 (14%)	42 (11%)
Missing	70 (12%)	19 (5%)
Largest space ULS		
Less than 6mm	486 (83%)	346 (92%)
More than 6mm	29 (5%)	11 (3%)
Missing	70 (12%)	19 (5%)
Total space LLS		
Less than 6mm	486 (83%)	338 (90%)
More than 6mm	29 (5%)	19 (5%)
Missing	70 (12%)	19 (5%)
Largest space LLS		
Less than 6mm	509 (87%)	353 (94%)
More than 6mm	6 (1%)	4 (1%)
Missing	70 (12%)	19 (5%)
Total dental irregularity ULS		
Less than 6mm	216 (37%)	146 (39%)
More than 6mm	299 (51%)	210 (56%)
Missing	70 (12%)	20 (5%)
Largest contact point displacement ULS		
Less than 6mm	433 (74%)	320 (85%)
More than 6mm	82 (14%)	37 (10%)
Missing	70 (12%)	19 (5%)
Total dental irregularity LLS		
Less than 6mm	328 (56%)	196 (52%)
More than 6mm	187 (32%)	161 (43%)
Missing	70 (12%)	19 (5%)
Largest contact point displacement ULS		
Less than 6mm	486 (83%)	342 (9%)
More than 6mm	29 (5%)	15 (4%)
Missing	70 (12%)	19 (5%)

The main presenting complaint of participants were categorised, and the data for this in both the OTG and the WLCG is presented in Table 14. The data shows that the majority of participants in both the OTG and the WLCG were concerned about dental crowding (40%

and 41% respectively). The least common concern was in relation to function, which was reported in only 1% of participants in both the OTG, and the WLCG. One striking difference noted was that only 6% of participants in the OTG had no concerns regarding their teeth, whilst this was reported by 21% of participants in the WLCG.

Table 14: Participants main presenting complaint at baseline, both in the Orthodontic Treatment Group and the Waiting List Control Group (percentage).

Participants Main Complaint	Orthodontic Treatment Group (n=585) n (%)	Waiting List Control Group (n=376) n (%)
Increased overjet	88 (15%)	45 (12%)
Overbite	12 (2%)	7 (2%)
Dental crowding	234 (40%)	154 (41%)
Spacing	58 (10%)	19 (5%)
Functional concerns	6 (1%)	4 (1%)
No concerns	35 (6%)	79 (21%)
Other	41 (7%)	15 (4%)
Missing	111 (19%)	53 (14%)

The type of orthodontic treatment to be provided for participants in the OTG and WLCG are outlined in Table 15. Overall, the most common form of treatment provided in both groups was fixed appliances, either with or without dental extractions.

Table 15: Type of orthodontic treatment that was planned to be provided for participants in the Orthodontic Treatment Group and the Waiting List Control Group (percentage).

Type of Orthodontic Treatment to be provided	Orthodontic Treatment Group (n=585) n (%)	Waiting List Control Group (n=376) n (%)
Fixed appliance(s) +/- extraction(s)	345 (59%)	237 (63%)
Functional, fixed appliance(s) +/- extraction (s)	94 (16%)	105 (28%)
Removable, fixed appliance(s) +/- extraction (s)	12 (2%)	0 (0%)
Removable, functional, fixed appliance(s) +/- extraction(s)	12 (2%)	0 (0%)
Missing	122 (21%)	34 (9%)

Overall, when visually inspecting the data in relation to the clinical characteristics of the participants in the OTG and WLCG, with the exception of the increased proportion of participants reporting no concerns regarding their malocclusion in the WLCG compared to the OTG, and a slightly greater proportion of participants in the OTG presenting with hypodontia, there appears to be no significant differences between the two groups.

5.3.3 Oral Health-Related Quality of Life and Psychosocial Characteristics

The OHRQoL and psychosocial characteristics of participants in the OTG and WLCG at T1 are presented in Table 16. The total scores of COHIP SF-19 were similar between the two groups, as were the scores within the individual dimensions of COHIP SF-19. The mean and standard deviations (SD) of the participants in the OTG and WLCG was similar for MIQ, self-esteem scale of the CHQ-CF87 and SLSS.

Table 16: The Oral Health-Related Quality of Life and psychosocial characteristics of participants in the Orthodontic Treatment Group and the Waiting List Control Group at T1.

Oral Health-Related Quality of Life and Psychosocial Characteristics	Orthodontic Treatment Group Mean (SD)	Waiting List Control Group Mean (SD)
COHIP SF-19		
Oral Health Wellbeing	13.7 (3.0) n=574	13.4 (3.2) n=375
Functional Wellbeing	13.5 (2.3) n=574	13.4 (2.2) n=375
Socio-Emotional Wellbeing	23.3 (6.8) n=574	25.2 (6.1) n=375
Total	53.1 (10.6) n=574	54.8 (10.2) n=375
MIQ (raw scores)	11.9 (7.5) n=578	9.9 (6.8) n=371
Self-esteem scale of the CHQ-CF87	79.2 (17.0) n=562	83.7 (14.8) n=372
SLSS	22.6 (4.0) n=562	23.4 (4.1) n=373

5.3.4 Psychometric Analysis of the Malocclusion Impact Questionnaire (MIQ)

To assess the responsiveness and longitudinal construct validity of the MIQ (which has not previously been carried out using such a large sample size), data from both the WLCG and the OTG were combined and analysed, using the MIQ scores at T1 and T2, along with the two GTJ questions, 'Overall, how has the appearance of your teeth changed from before you started treatment or last filled out the questionnaire?' (GTJ1) and 'Overall, how has the bite of your teeth changed from before you started treatment or last filled out the questionnaire?' (GTJ2).

The responsiveness of the MIQ using GTJ1 and GTJ2, were assessed using standardised effect sizes, the results of which are outlined in Tables 17 and 18, respectively. The results in Table 17 show that in participants who reported that the appearance of their teeth had 'Worsened a lot', the increase in mean MIQ interval score from T1 to T2 was 6.3 (worsening of OHRQoL), whilst in those who reported that the appearance of their teeth had 'Improved a lot', the mean MIQ interval scores decreased by 9.4 (improvement in OHRQoL). The standardised effect size for these changes were 0.74 (medium) and -1.80 (large) respectively. For participants who reported that the appearance of their teeth stayed the same between T1 and T2, the mean change in MIQ score was an increase of 0.8 (indicating a worsening of OHRQoL), but the standardised effect size was very small at 0.15.

Table 17: Mean, standard deviation, and standardised effect size of the mean change in MIQ scores from T1 to T2, based on the different response options to Global Transition Judgement question 1.

Overall, how has the appearance of your teeth changed from before you started treatment or last filled out the questionnaire?" (GTJ1)	Change in MIQ scores from T1 to T2 Mean (SD)		Standardised effect size (Cohen's d) for interval score
	Raw score	Interval score	
Worsened a lot (n=9)	+9.1 (12.7)	+6.3 (10.1)	0.74
Worsened a little (n=32)	+4.0 (9.7)	+2.9 (7.5)	0.48
Stayed the same (n=107)	+1.3 (7.2)	+0.8 (6.2)	0.15
Improved a little (n=40)	-0.5 (8.3)	-0.8 (7.6)	-0.11
Improved a lot (n=198)	-9.6 (7.8)	-9.4 (6.6)	-1.80

Table 18: Mean, standard deviation, and standardised effect size of the mean change in MIQ scores from T1 to T2, for the different response options to Global Transition Judgement question 2.

Overall, how has the bite of your teeth changed from before you started treatment or last filled out the questionnaire?' (GTJ2)	Change in MIQ scores from T1 to T2 Mean (SD)		Standardised effect size (Cohen's d) for interval score
	Raw score	Interval score	
Worsened a lot (n=8)	+12.3 (13.6)	+8.2 (10.5)	1.15
Worsened a little (n=31)	+2.7 (9.7)	+2.3 (8.3)	0.37
Stayed the same (n=135)	+1.0 (6.9)	+0.4 (6.0)	0.09
Improved a little (n=57)	-6.7 (9.8)	-7.1 (8.4)	-1.14
Improved a lot (n=154)	-10.0 (7.6)	-9.7 (6.3)	-1.74

The results in Table 18 show that in participants who reported that their bite had ‘Worsened a lot’, the increase in mean MIQ interval score from T1 to T2 was 8.2 (worsening of OHRQoL), whilst in those who reported that their bite had ‘Improved a lot’, the mean MIQ interval scores decreased by 9.7 (improvement in OHRQoL). The standardised effect size for these changes were 1.15 and -1.74 respectively, both of which are large effect sizes. For participants who reported that their bite stayed the same between T1 and T2, the mean change in MIQ score was an increase of 0.4 (indicating a worsening of OHRQoL), but the standardised effect size was very small at 0.09.

The statistical significance of within-subject change in MIQ scores for those who reported worsening of OHRQoL (worsened a lot, or worsened a little), those who reported an improvement in OHRQoL (improved a lot or improved a little) and those who reported no change in their OHRQoL, was assessed using paired *t*-tests (Locker et al., 2004, Peter et al., 2023). If the MIQ is responsive, the former two should be statistically significant, whilst the latter should be non-significant. The results of these analyses for GTJ1 and GTJ2 are illustrated in Tables 19 and 20, respectively.

Table 19: Mean MIQ interval scores at T1 and T2 for each response option for Global Transition Judgement question 1. The change in MIQ interval scores from T1 to T2 is also presented, along with the results of the paired samples *t*-test comparing these changes.

Overall, how has the appearance of your teeth changed from before you started treatment or last filled out the questionnaire? (GTJ1)	T1 MIQ interval scores Mean (SD)	T2 MIQ interval scores Mean (SD)	Change in MIQ interval scores from T1 to T2 Mean (SD)	P-value
Worsened a lot or a little (n=41)	13.4 (5.5)	16.8 (7.4)	+3.4 (7.9)	0.009*
Stayed the same (n=107)	12.5 (5.0)	13.3 (5.9)	+0.8 (6.2)	0.204
Improved a little or a lot (n=238)	14.0 (6.1)	6.2 (5.9)	-7.8 (7.5)	<0.001*
*Significance p-value <0.05				

The results in Table 19 show that the change in MIQ interval scores from T1 to T2 in participants who reported the appearance of their teeth to have improved (a lot or a little), or to have worsened (a lot or a little), was statistically significant with p-values of <0.001 and 0.009 respectively. In participants who reported the appearance of their teeth to have stayed the same, the change in mean MIQ interval scores from T1 to T2 was not found to be statistically significant (0.204).

Table 20: Mean MIQ interval scores at T1 and T2 for each response option for Global Transition Judgement question 2. The difference between these scores is demonstrated (change in MIQ interval scores from T1 to T2), as well as the results of the paired samples t-test comparing these changes.

Overall, how has the bite of your teeth changed from before you started treatment or last filled out the questionnaire (GTJ2)	T1 MIQ scores Mean (SD)	T2 MIQ scores Mean (SD)	Change in MIQ scores from T1 to T2 Mean (SD)	P-value
Worsened a lot or a little (n=39)	13.1 (5.9)	16.5 (7.4)	+3.4 (8.8)	0.022*
Stayed the same (n=135)	12.2 (5.1)	12.7 (6.2)	+0.5 (5.9)	0.372
Improved a little or a lot (n=211)	14.4 (6.0)	5.7 (5.7)	-8.7 (7.1)	<0.001*
*Significance p-value <0.05				

The results in Table 20 show that the change in MIQ interval scores from T1 to T2 in participants who reported their bite had improved (a lot or a little), or to have worsened (a lot or a little), was statistically significant with p-values of <0.001 and 0.022 respectively. In participants who reported their bite to have stayed the same, the change in mean MIQ interval scores from T1 to T2 was not found to be statistically significant (0.372).

The Minimal Important Difference (MID) for the MIQ was calculated by subtracting the mean change (from T1 to T2) in the MIQ score of participants who reported to have experienced no change in their OHRQoL, from the mean change in MIQ score of participants who had reported a little improvement in their OHRQoL and a little

worsening in their OHRQoL (Masood et al., 2014, Revicki et al., 2008). The means of these were then calculated for both GTJ1 and GTJ2. Using the results from the GTJ1, the MID was calculated as 1.9, whilst using the results for the GTJ2, the MID was calculated as 4.7.

The association between changes in MIQ from T1 to T2, and GTJ1 and GTJ2, was assessed using a One-way ANOVA. The p-value for GTJ1 and GTJ2 was <0.001, which confirmed that participants who reported improvement in the GTJ questions have positive mean change in MIQ interval scores, those who reported worsening have a negative change in MIQ interval scores, and those who expressed no change showed little or no difference in scores. Overall, the results of the psychometric analysis of the MIQ demonstrated that the questionnaire is both responsive and has good longitudinal construct validity.

5.4 Phase 2: Descriptive Analysis of those Lost to Follow-up Versus those Who Completed the Study to T2

5.4.1 Socio-Demographic Characteristics

Overall, at T2, 399 participants (42%) completed the study and 562 (58%) did not. In the OTG, 222 participants (38%) were followed up at T2, and 57 participants (10%) were followed up at T3. Due to reasons outlined in Chapter 6, the loss-to-follow was significantly varied in the different sites, with two sites (site 3 & 9), being unable to follow-up any of the participants recruited at baseline at either T2 or T3. Given the relatively large loss to follow-up, the baseline data for those who completed the study to T2, and those who did not complete the study, was explored in detail to determine whether there were any differences observed between these participants at T1. The descriptive data in relation to this is presented in Tables 21, 22 and 23. It is important to note that as the study was not powered to detect differences at baseline, no hypothesis tests were carried out on this data as these were considered to be misleading.

Demographic data based on gender balance, age and SES were similar for participants completing and those not completing the study to T2 (Table 21). There were no significant differences noted between those who completed the study, and those who

were lost to follow-up with regards to gender, and this was evident in both the OTG and the WLCG. Whilst there appear to be some differences in the age groups between those who completed the study to T2 versus those that did not (51% were aged 11-12 year in the cohort of participants who completed the study versus 42% in those who did not), these differences were largely attributed to the increased percentage of missing data for some of the demographic variables, that were evident in the lost to follow-up cohort, compared to the cohort of participants who completed the study to T2. This trend in missing data was also seen in both the gender and IMD decile data. Overall, similar distributions in the IMD decile were demonstrated between those who completed the study to T2, and those who were lost to follow-up.

Table 21: Baseline socio-demographic characteristics of participants who completed the study to T2 and those who were lost to follow-up (percentage).

Socio-Demographic Characteristics	Total		Orthodontic Treatment Group		Waiting List Control Group	
	Completed to T2 (n=399) n (%)	Lost to follow-up (n=562) n (%)	Completed to T2 (n=222) n (%)	Lost to follow-up (n=363) n (%)	Completed to T2 (n=177) n (%)	Lost to follow-up (n=199) n (%)
Gender						
Female	208 (52%)	273 (49%)	119 (54%)	173 (48%)	87 (50%)	100 (50%)
Male	172 (43%)	220 (39%)	85 (38%)	136 (38%)	89 (49%)	84 (42%)
Missing	19 (5%)	69 (12%)	18 (8%)	53 (14%)	1 (1%)	15 (8%)
Age (Years)						
11 or 12	203 (51%)	238 (42%)	75 (34%)	98 (27%)	128 (72%)	140 (70%)
13 or 14	147 (37%)	175 (31%)	106 (48%)	136 (37%)	41 (23%)	39 (20%)
15 or 16	28 (8%)	76 (13%)	24 (11%)	71 (20%)	4 (2%)	5 (3%)
Missing	21 (5%)	73 (13%)	17 (8%)	58 (16%)	4 (2%)	15 (8%)
IMD (Decile)						
1 or 2	65 (16%)	77 (14%)	27 (12%)	41 (11%)	38 (21%)	36 (18%)
3 or 4	55 (14%)	91 (16%)	45 (20%)	64 (29%)	10 (6%)	27 (14%)
5 or 6	69 (18%)	89 (16%)	38 (17%)	56 (15%)	31 (17%)	33 (16%)
7 or 8	81 (21%)	87 (15%)	47 (21%)	45 (12%)	34 (19%)	42 (21%)
9 or 10	96 (23%)	73 (13%)	36 (16%)	34 (9%)	60 (34%)	39 (20%)
Missing	33 (8%)	145 (26%)	29 (13%)	123 (34%)	4 (2%)	22 (11%)
Please note: Percentages may not total 100% due to rounding.						

5.4.2 Clinical Characteristics

The clinical characteristics of participants who completed and did not complete the study to T2 are outlined in Table 22. These were all very similar between participants completing the study to T2, and those who did not complete the study. In both cohorts, participants most commonly presented with Class II division 1 incisor relationships, and the majority of participants had an overjet between 2 to 4.9mm. The most common IOTN

DHC grade in both groups was grade 4, and self-assessed IOTN AC score was between 1-4. There was no significant difference in the proportion of participants who presented with impacted teeth or hypodontia in the two groups. Similar to the demographic data, the percentage of missing data across all the variables was greater in the cohort of participants lost to follow-up. The reasons for this are discussed in Chapter 6.

Table 22: Baseline clinical characteristics of participants who completed the study to T2 and those who were lost to follow-up (percentage).

Clinical Characteristics	Total		Orthodontic Treatment Group		Waiting List Control Group	
	Completed to T2 (n=399) n (%)	Lost to follow-up (n=562) n (%)	Completed to T2 (n=222) n (%)	Lost to follow-up (n=363) n (%)	Completed to T2 (n=177) n (%)	Lost to follow-up (n=199) n (%)
Incisor relationship						
Class I	94 (24%)	130 (23%)	54 (24%)	93 (26%)	40 (23%)	37 (19%)
Class II div 1	197 (49%)	224 (40%)	97 (44%)	130 (36%)	100 (57%)	94 (47%)
Class II div 2	55 (14%)	75 (13%)	31 (14%)	49 (14%)	24 (14%)	26 (13%)
Class III	33 (8%)	63 (11%)	23 (10%)	37 (10%)	10 (6%)	26 (13%)
Missing	20 (5%)	70 (13%)	17 (8%)	54 (15%)	3 (2%)	16 (8%)
Overbite						
Average	107 (27%)	132 (24%)	62 (28%)	95 (26%)	45 (25%)	37 (19%)
Increased	183 (46%)	229 (41%)	96 (43%)	143 (39%)	87 (49%)	86 (43%)
Reduced	73 (18%)	114 (20%)	35 (16%)	56 (15%)	38 (22%)	58 (29%)
Anterior open bite	16 (4%)	14 (3%)	11 (5%)	13 (4%)	5 (3%)	1 (1%)
Missing	20 (5%)	73 (13%)	18 (8%)	56 (15%)	2 (1%)	17 (9%)
Overjet						
< 2mm	24 (6%)	54 (10%)	13 (6%)	36 (10%)	11 (6%)	18 (9%)
2 to 4.9mm	149 (37%)	182 (32%)	73 (33%)	128 (35%)	76 (43%)	54 (27%)
5 to 6.9mm	63 (16%)	91 (16%)	36 (16%)	47 (13%)	27 (15%)	44 (22%)
≥ 7mm	129 (32%)	144 (26%)	76 (34%)	87 (24%)	53 (30%)	57 (29%)
Missing	34 (9%)	91 (16%)	24 (11%)	65 (18%)	10 (6%)	26 (13%)
IOTN DHC						
5	104 (26%)	172 (31%)	65 (29%)	122 (34%)	39 (22%)	50 (25%)
4	260 (65%)	314 (56%)	131 (59%)	182 (50%)	129 (73%)	132 (66%)
3	16 (4%)	7 (1%)	9 (4%)	6 (2%)	7 (4%)	1 (1%)
Missing	19 (5%)	69 (12%)	17 (8%)	53 (15%)	2 (1%)	16 (8%)
IOTN AC						
1-4	271 (68%)	357 (64%)	154 (69%)	230 (63%)	117 (66%)	127 (64%)
5-7	63 (16%)	99 (18%)	27 (12%)	66 (19%)	36(20%)	33 (17%)
8-10	56 (14%)	98 (17%)	33 (15%)	62 (17%)	23 (13%)	36 (17%)
Missing	9 (2%)	8 (1%)	8 (4%)	5(1%)	1 (1%)	3 (2%)
Impacted teeth						
Yes	64 (16%)	107 (19%)	41 (19%)	76 (21%)	23 (13%)	31 (16%)
No	317 (79%)	385 (69%)	164 (74%)	233 (64%)	153 (86%)	152 (76%)
Missing	18 (5%)	70 (13%)	17 (8%)	54 (15%)	1 (1%)	16 (8%)
Hypodontia						
Yes	27 (7%)	77 (14%)	18 (8%)	62 (17%)	9 (5%)	15 (8%)
No	353 (89%)	415 (74%)	186 (84%)	247 (68%)	167 (94%)	168 (84%)
Missing	19 (4%)	70 (12%)	18 (8%)	54 (15%)	1 (1%)	16 (8%)

5.4.3 Oral Health-Related Quality of Life & Psychosocial Characteristics

The OHRQoL and psychosocial characteristics of participants who completed the study to T2, and those who were lost to follow-up are presented in Table 23. The OHRQoL and the psychosocial characteristics of both groups did not demonstrate any notable differences, with both groups showing similar levels of scores for the COHIP SF-10, MIQ, self-esteem scale of the CHQ-CF87, and SLSS.

Table 23: Oral Health-Related Quality of Life and psychosocial baseline characteristics of participants who completed the study to T2, and those who were lost to follow-up.

Oral Health-Related Quality of Life & Psychosocial Characteristics	Total		Orthodontic Treatment Group		Waiting List Control Group	
	Completed to T2 Mean (SD) n	Lost to follow-up Mean (SD) n	Completed to T2 Mean (SD) n	Lost to follow-up Mean (SD) n	Completed to T2 Mean (SD) n	Lost to follow-up Mean (SD) n
COHIP SF-19	54.3 (10.0) n=391	53.4 (10.8) n=549	53.7 (10.5) n=215	52.8 (10.7) n=351	60.8 (7.7) n=176	54.4 (10.9) n=198
MIQ	11.0 (7.3) n=389	11.1 (7.3) n=518	12.1 (7.7) n=213	11.8 (7.4) n=323	9.8 (6.5) n=176	10.0 (7.1) n=195
Self-esteem scale of the CHQ-CF87	81.5 (16.3) n=390	80.6 (16.2) n=543	79.7 (18.0) n=215	78.8 (16.3) n=347	83.6 (13.7) n=175	83.7 (15.7) n=196
SLSS	23.1 (4.1) n=390	22.8 (4.1) n=545	22.6 (4.1) n=215	22.6 (4.0) n=347	23.8 (4.0) n=175	23.1 (4.2) n=198

In summary, the two cohorts (participants who completed the study to T2, and those who were lost to follow-up) were considered similar in relation to socio-demographic, clinical, OHRQoL and psychosocial characteristics.

5.5 Phase 3: Parametric and Non-Parametric Testing Comparing the Orthodontic Treatment Group and the Waiting List Control Group

This phase of the data analysis was aimed at addressing the first research question:

- Are there differences in the changes observed in the OHRQoL of young people aged 11 to 16 years who receive orthodontic treatment versus those who are still waiting for treatment?

A total of 177 and 222 participants were followed up at T2 in the WLCG and OTG group, respectively. The mean time between T1 and T2 for the OTG group was 2.6 years (SD = 0.8), whereas for the WLCG group, it was 2.0 years (SD = 1.4). The mean age for these participants in the OTG at T1 was 13.5 years (SD=1.2), and at T2 was 16.0 years (SD=2.1). The mean age for participants at T1 in the WLCG was 12.6 years (SD=1.0), and at T2 was 14.6 (SD=1.7). The OHRQoL and psychosocial characteristics of participants in the WLCG and the OTG at T1 and T2 are outlined in Tables 24 and 25, respectively.

Based on the data in Table 24, it is evident that for participants in the WLCG, their OHRQoL, self-esteem, and life satisfaction (overall QoL) declined. The data in Table 25 shows that overall, in the OTG, participants' OHRQoL improved from T1 to T2, self-esteem showed a slight improvement, and life satisfaction (overall QoL) remained stable.

Table 24: Mean and standard deviation of the Oral Health-Related Quality of Life and psychosocial characteristics of participants in the Waiting List Control Group at T1 and T2, together with the change between the two time points.

Oral Health-Related Quality of Life & Psychosocial Characteristics	Waiting List Control Group T1 Mean (SD)	Waiting List Control Group T2 Mean (SD)	Waiting List Control Group Change T1 to T2 Mean (SD)
COHIP SF-19 & OHIP-14 (Standardised scores)	72.5 (12.4) n=175	66.4 (14.7) n=175	-6.11 (15.2) n=174
MIQ (raw scores)	9.8 (6.5) n=174	11.8 (8.5) n=174	+1.98 (8.0) n=173
MIQ (interval scores)	12.6 (5.4) n=174	14.1 (6.6) n=174	+1.4 (6.6) n=173
Self-esteem subscale of the CHQ-CF87	83.6 (13.7) n=175	77.5 (17.7) n=175	-6.1 (18.9) n=175
SLSS	23.8 (4.0) n=175	22.1 (4.2) n=175	-1.6 (4.4) n=173

Table 25: Mean and standard deviation of the Oral Health-Related Quality of Life and psychosocial characteristics of participants in the Orthodontic Treatment Group at T1 and T2, together with the change between the two time points.

Oral Health-Related Quality of Life and Psychosocial Characteristics	Orthodontic Treatment Group T1 Mean (SD)	Orthodontic Treatment Group T2 Mean (SD)	Orthodontic Treatment Group Change T1 to T2 Mean (SD)
COHIP SF-19 & OHIP-14 (Standardised scores)	70.6 (13.8) (n=212)	78.4 (10.1) (n=212)	+7.82 (15.8) (n=212)
MIQ (raw scores)	12.0 (7.7) (n=213)	3.1 (4.4) (n=213)	-8.92 (8.1) (n=212)
MIQ (interval scores)	14.2 (6.0) (n=213)	5.3 (5.1) (n=213)	-8.86 (6.9) (n=212)
Self-esteem subscale of the CHQ-CF87	79.7 (18.0) (n=214)	83.5 (16.1) (n=214)	+3.7 (20.5) (n=214)
SLSS	22.6 (4.1) (n=213)	22.6 (4.1) (n=213)	0.00 (4.4) (n=212)

5.5.1 Parametric Testing

Independent samples t-tests were conducted to compare the changes in OHRQoL from T1 to T2 in the OTG versus the WLCG. The results are presented in Table 26.

The results from the independent samples t-test show a statistically significant difference in the changes in scores between T1 and T2 for both OHRQoL measures (COHIP SF-19/OHIP-14 and MIQ) between the OTG and WLCG. The mean difference in COHIP SF-19/OHIP-14 scores was 13.5, which was statistically significant ($p < 0.001$). The effect size for this difference was 0.9, indicating a large effect. The mean differences in the MIQ raw scores and MIQ interval scores were -11.3 and -10.6, respectively, both of which were statistically significant ($p < 0.001$). These changes were associated with effect sizes of 1.4 and 1.6, suggesting large effects.

Table 26: Results of the independent samples t-test assessing the difference between the means in the measures of OHRQoL between T1 and T2 in the Orthodontic Treatment Group and the Waiting List Control Group.

Variables	Mean Difference (SE)	Two-sided p-value	Cohen's d (95% CI)
COHIP SF-19 & OHIP-14 (Standardised scores)	13.5 (1.4)	<0.001*	0.9 (0.7, 1.2)
MIQ (raw scores)	-11.3 (0.8)	<0.001*	-1.4 (-1.2, -1.6)
MIQ (interval scores)	-10.6 (0.7)	<0.001*	-1.6 (-1.3, -1.8)
*Significance p-value <0.05			

Overall, these results show significant differences in the mean changes observed between T1 and T2 in the OTG and WLCG. From T1 to T2, the OHRQoL of participants in the OTG improved, whilst it declined in the WLCG, with this difference being both statistically significant and large.

5.5.2 Non-Parametric Testing

Overall, there were five GOH questions that participants responded to at each of the time points in the study (GOH1-GOH5). These were designed to determine the perceptions of the participant regarding their occlusion, at that moment in time. The

results of these at both T1 and T2, in the OTG and the WLCG are demonstrated in Tables 27 and 28.

Table 27: Responses to the Global Oral Health questions 1-3, in the Orthodontic Treatment Group and the Waiting List Control Group, both at T1 and T2 (percentage).

Global Oral Health Question	Orthodontic Treatment Group T1 (n=222) n (%)	Orthodontic Treatment Group T2 (n=222) n (%)	Waiting List Control Group T1 (n=177) n (%)	Waiting List Control Group T2 (n=177) n (%)
GOH1: How would you describe the overall health of your teeth and mouth today?				
Poor	3 (1%)	1 (1%)	4 (2%)	3 (2%)
Fair	24 (11%)	7 (3%)	28 (16%)	21 (12%)
Average	74 (33%)	21 (10%)	75 (42%)	66 (37%)
Good	100 (45%)	132 (60%)	62 (35%)	78 (44%)
Excellent	13 (6%)	61 (28%)	7 (4%)	7 (4%)
Missing	8 (4%)	0 (0%)	1 (1%)	1 (1%)
GOH2: Overall, does the appearance of your teeth, as they are now, upset you?				
Not at all	41 (19%)	182 (82%)	36 (20%)	33 (19%)
A little	87 (39%)	27 (12%)	81 (46%)	55 (31%)
Somewhat	33 (15%)	8 (4%)	20 (11%)	36 (20%)
Quite a bit	39 (18%)	1 (1%)	33 (19%)	41 (23%)
Very much	15 (7%)	4 (2%)	6 (3%)	11 (6%)
Missing	7 (3%)	0 (0%)	1 (1%)	1 (1%)
GOH3: Overall, does the appearance of your teeth as they are now, affect your life in a negative way?				
Not at all	105 (47%)	208 (94%)	85 (48%)	71 (40%)
A little	59 (27%)	11 (5%)	64 (36%)	48 (27%)
Somewhat	24 (11%)	1 (1%)	14 (8%)	33 (19%)
Quite a bit	21 (10%)	0 (0%)	11 (6%)	19 (11%)
Very much	6 (3%)	1(1%)	2 (1%)	5 (3%)
Missing	7 (3%)	1 (1%)	1 (1%)	1 (1%)
Please note: Percentages may not total 100% due to rounding.				

Table 28: Responses to the Global Oral Health questions 4 & 5, in the Orthodontic Treatment Group and the Waiting List Control Group, both at T1 and T2. The results are presented as a percentage.

Global Oral Health Question	Orthodontic Treatment Group T1 (n=222) n (%)	Orthodontic Treatment Group T2 (n=222) n (%)	Waiting List Control Group T1 (n=177) n (%)	Waiting List Control Group T2 (n=177) n (%)
GOH4: Overall, does the way your teeth bite, as they do now, upset you?				
Not at all	86 (39%)	198 (89%)	102 (58%)	75 (42%)
A little	79 (36%)	15 (7%)	48 (27%)	44 (25%)
Somewhat	25 (11%)	4 (2%)	10 (6%)	31 (18%)
Quite a bit	20 (9%)	2 (1%)	15 (9%)	20 (11%)
Very much	5 (2%)	2 (1%)	1 (1%)	5 (3%)
Missing	7 (3%)	1 (1%)	1 (1%)	2 (1%)
GOH5: Overall, does the way your teeth bite, as they do now, affect your life in a negative way?				
Not at all	128 (58%)	211 (95%)	121 (68%)	89 (50%)
A little	51 (23%)	8 (4%)	36 (20%)	40 (23%)
Somewhat	20 (9%)	1 (1%)	13 (7%)	30 (17%)
Quite a bit	14 (6%)	1 (1%)	6 (3%)	14 (8%)
Very much	2 (1%)	1 (1%)	0 (0%)	3 (2%)
Missing	7 (3%)	0 (0%)	1 (1%)	1 (1%)
Please note: Percentages may not total 100% due to rounding.				

Wilcoxon signed rank tests were conducted to evaluate whether the changes in responses to GOH1-5 from T1 to T2 were statistically significant within the OTG and the WLCG. A p-value of less than 0.05 was considered statistically significant, indicating a meaningful change in responses. The results can be found in Table 29.

Table 29: Results of the Wilcoxon signed rank tests conducted to evaluate whether the changes in responses to GOH1-5 from T1 to T2 were statistically significant within the Orthodontic Treatment Group and the Waiting List Control Group.

Global Oral Health Question	Orthodontic Treatment Group		Waiting List Control Group	
	Z-value	P-value	Z-value	P-value
GOH1: How would you describe the overall health of your teeth and mouth today?	-8.16 (N=214)	<0.001*	-1.54 (N=174)	0.123
GOH2: Overall, does the appearance of your teeth, as they are now, upset you?	-10.11 (N=214)	<0.001*	2.89 (N=175)	<0.001*
GOH3: Overall, does the appearance of your teeth as they are now, affect your life in a negative way?	-8.61 (N=214)	<0.001*	3.30 (N=175)	<0.001*
GOH4: Overall, does the way your teeth bite, as they do now, upset you?	-8.93 (N=214)	<0.001*	4.02 (N=175)	<0.001*
GOH5: Overall, does the way your teeth bite, as they do now, affect your life in a negative way?	-7.38 (N=215)	<0.001*	4.57 (N=175)	<0.001*
* Significance of p <0.05				

Histograms outlining the change in responses in each group, with details of the proportions that remained the same, changed negatively or changed positively can be found in Appendix 7. The results indicate that in the OTG, responses to all five GOH questions (GOH1-5) showed significant improvement from T1 to T2 ($p < 0.001$). This suggests that, after orthodontic treatment, participants reported:

- An improvement in the overall health of their teeth and mouth
- A reduction in the upset caused by the appearance of the teeth
- A reduction in the negative way in which the appearance of the teeth affects their lives

- A reduction in the upset caused by the bite of the teeth
- A reduction in the negative way in which the bite of the teeth affects their lives

Conversely, the WLCG showed the opposite pattern for GOH2-5. Participants in this group reported a greater negative impact from the appearance of their teeth and their bite, as indicated by GOH2-GOH5, by the time they reached the end of the treatment waiting list (T2), compared to when they were initially placed on the list (T1). This change was statistically significant (<0.001) and suggests that the impact of malocclusion worsened over time for participants who did not receive treatment. There was no significant change in responses in GOH1 in the WLCG ($p=0.123$), indicating no significant changes in the overall health of the teeth and mouth of participants between T1 and T2.

5.6 Phase 4: Analysis of Covariance (ANCOVA)

This phase of the data analysis was aimed at addressing the second research question:

- If there is an improvement in OHRQoL following orthodontic treatment, can specific characteristics be identified that can predict which individuals will benefit the most from treatment?

An ANCOVA was used to examine the effect of specific baseline factors, on the scores of MIQ interval scores at T2. The covariates selected for the analysis were:

- **Socio-demographic:** Gender, age, IMD decile.
- **Clinical:** Largest spacing present in the ULS, largest contact point displacement in the ULS, overjet, IOTN DHC grade, self-assessed IOTN AC grade.
- **Psychosocial:** Self-esteem scale of the CHQ-CF87, SLSS.

The MIQ interval scores at T1 were also included as a covariate. As Levene's test was found to be statistically significant ($p\text{-value}=0.008$) for the analysis, this indicated that the

assumption of homogeneity of the variances was violated. Due to this, a bootstrapping procedure was employed to assess the significance of the covariates, and a total of 1000 resamples were used to estimate confidence intervals and p-values for these. The descriptive statistics for this are demonstrated in Table 30, and the results of the model are shown in Table 31.

Table 30: Bootstrap descriptive statistics of the MIQ interval scores at T2 for the Orthodontic Treatment Group and Waiting List Control Group.

Study Arm	Mean (SD)	Standard Error	95% Confidence interval
Orthodontic Treatment Group (n=181)	5.23 (5.16)	0.39	4.47, 6.04
Waiting List Control Group (n=156)	14.25 (6.60)	0.54	13.21, 15.27

Table 31: The results of the Analysis of Covariance using bootstrapping where the MIQ interval scores at T2 was the dependent variable and study arm (Orthodontic Treatment Group versus Waiting List Control Group) was the independent variable.

Variables	Beta Coefficient	Standard Error	P-value	95% Confidence interval	
				Lower	Upper
Intercept	10.573	4.963	0.034*	0.879	20.590
Age	-0.192	0.276	0.487	-0.741	0.370
Gender	0.462	0.663	0.459	-0.897	1.810
IMD (Decile)	0.070	0.098	0.475	-0.136	0.257
Largest space present in the upper labial segment	0.241	0.199	0.127	-0.234	0.540
Largest contact point displacement in the upper labial segment	0.142	0.153	0.334	-0.079	0.449
Overjet	0.43	0.122	0.701	-0.207	0.292
IOTN AC Grade at T1	-0.193	0.157	0.213	-0.487	0.141
IOTN DHC Grade	0.268	0.603	0.663	-0.976	1.456
Self-esteem scale of CHQ-CF87 at T1	0.048	0.023	0.032*	0.000	0.090
SLSS at T1	-0.201	0.090	0.027*	-0.388	-0.034
MIQ (interval score) at T1	0.358	0.084	<.001*	0.183	0.513
Study Group (Orthodontic Treatment group)	- 9.740	0.760	<.001*	-11.246	-8.249
Group sizes: WLCG (n=156), OTG (n=181)					
* Significance of p <0.05					

In the analysis (Table 31), the study arm (independent variable) was coded as a categorical variable, where the WLCG group served as the reference category, and the OTG was compared to this baseline. The model (Table 31) explored how various factors, including socio-demographic, clinical, and psychosocial variables, affected MIQ interval scores at T2 (where higher MIQ interval scores indicate poorer OHRQoL). The intercept (B

= 10.573) was statistically significant ($p = 0.034$), suggesting that, when all the independent variables were held constant at zero, a participant in the WLCG group would have an estimated MIQ interval score of 10.573. The model compared this to the OTG, which showed a significantly lower MIQ interval score at T2 ($B = -9.740$, $p < 0.001$), indicating that participants in the OTG, reported better OHRQoL at T2 compared to those in the WLCG.

Self-esteem at T1 (measured by the self-esteem scale of the CHQ-CF87) was a significant predictor of MIQ interval scores at T2 ($B = 0.048$, $p = 0.032$). The results suggest that those with higher self-esteem at baseline, are likely to have higher MIQ interval scores at T2, indicating poorer OHRQoL. This in turn suggests that those with lower self-esteem at baseline are likely to experience more significant benefits in OHRQoL at T2. Life satisfaction (QoL) at T1, measured by the SLSS, showed a statistically significant negative effect ($B = -0.201$, $p = 0.027$), suggesting that individuals with higher self-reported life satisfaction at T1 experienced lower MIQ scores (better OHRQoL) at T2. The MIQ interval scores at T1 had a highly significant positive effect on MIQ interval scores at T2 ($B = 0.358$, $p < 0.001$). This strong relationship suggested that individuals with poorer OHRQoL at T1 tended to have poorer OHRQoL at T2. Several other covariates, such as age, gender, IMD (Decile), overjet, displacement in the ULS, spacing in the ULS, IOTN DHC grade, and self-assessed IOTN AC grade, were not significant predictors of MIQ interval scores at T2, as their p -values were greater than 0.05. Orthodontic treatment itself remained the strongest predictor of MIQ interval scores at T2 ($B = -9.740$, $p < 0.001$), providing further evidence, that even when a number of covariates (or potential confounding factors) are controlled for, orthodontic treatment still results in improved levels of OHRQoL at T2.

In summary, the analysis demonstrated that the OTG reported better OHRQoL at T2 compared to the WLCG. Additionally, factors such as self-esteem, life satisfaction (overall QoL), and self-esteem were significant predictors of OHRQoL T2. The strongest predictor (with the exception of orthodontic treatment itself), however, was the MIQ interval scores at T1, which strongly predicted the MIQ interval scores at T2.

5.7 Phase 5: Visual presentation of Orthodontic Treatment Group data at T3

The reasons for the large drop-out rate in the study are highlighted in Section 6.5. In total, 57 participants were followed up at T3 in the OTG. The primary purpose of data collection at T3 was to determine whether any benefits in OHRQoL observed at T2 were maintained at T3.

The mean time from T2 to T3 in the 57 participants who completed the study to T3 was 0.9 years (S.D.=0.5). Overall, 31% of these participants were male, 63% female, and data in relation to gender was missing in 5% of cases. The mean age of these participants at T2 was 15.7 years (S.D.= 2.5), and 17.0 years (S.D. 1.2) at T3.

Overall, 57 participants provided MIQ data at both T2 and T3. At T2, the mean MIQ interval score was 5.8 (SD = 5.4), while at T3, it was 4.2 (SD=4.6). The line chart in Figure 5 demonstrates the change in the OHRQoL and psychosocial characteristics in the 57 participants who were followed up at T3, between timepoints T1-T3.

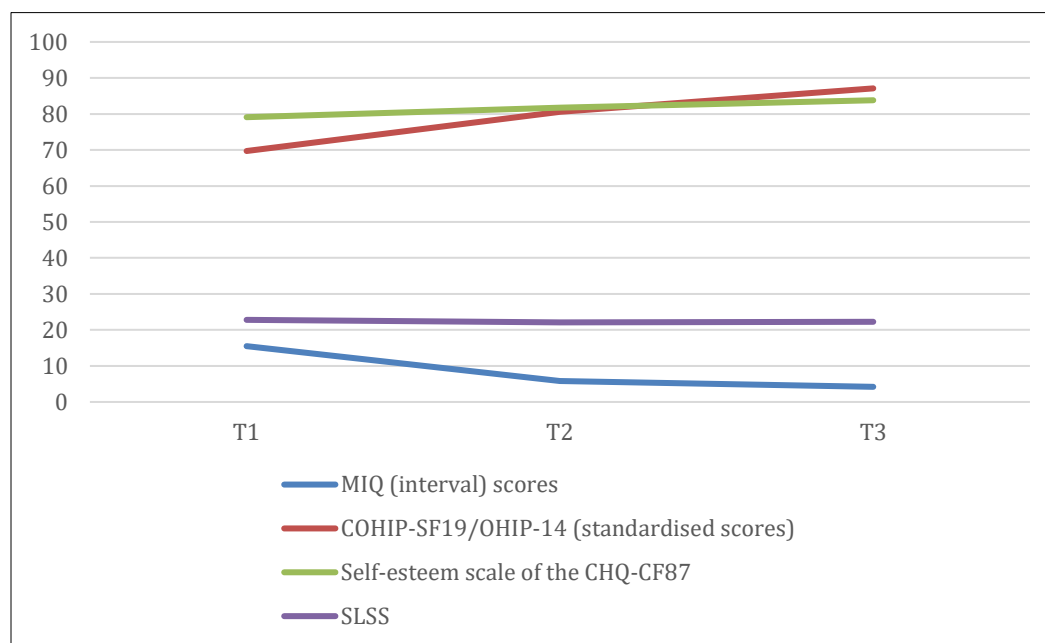


Figure 5: Line chart to demonstrate the change in the OHRQoL and psychosocial characteristics in the 57 participants who were followed up at T3, between timepoints T1-T3 in the Orthodontic Treatment Group.

The chart in Figure 5, suggests that OHQRoL improved following the completion of orthodontic treatment (based on both the MIQ interval scores and the COHIP-SF19/OHIP-14 standardised scores), and this improvement appears to have been maintained at T3. Self-esteem (measured by the self-esteem scale of the CHQ-CF87) appears to have marginally improved from T1 through to T2 and then T3, and life satisfaction (QoL), appears to have remained relatively stable throughout the study period.

Chapter 6

Discussion

6.1: Introduction

The primary aim of this research was to examine the impact of the completion of orthodontic treatment on the OHRQoL of adolescents aged 11 to 16 years. The secondary aim was to explore the factors that were associated with any observed changes in OHRQoL. The study was designed as a multi-centre, longitudinal study which followed two cohorts of participants: (1) A cohort undergoing orthodontic treatment, (2) A cohort being placed on an orthodontic treatment waiting list. In total, there were eleven sites that recruited participants into the study, and these included teaching hospitals, district general hospitals, and specialist orthodontic practices.

The study found that OHRQoL improved significantly in the OTG, whilst worsening in the WLCG. The difference between the change in OHRQoL that occurred in the OTG and WLCG was found to be statistically significant and associated with a large effect size.

The findings of this study will be discussed thoroughly as follows:

- Socio-demographic, clinical, OHRQoL and psychosocial characteristics of the study sample.
- Responsiveness and longitudinal construct validity of the MIQ.
- Research question 1: Are there differences in the changes observed in the OHRQoL of young people aged 11 to 16 years who receive orthodontic treatment versus those who are still waiting for treatment?
- Research question 2: If there is an improvement in OHRQoL following orthodontic treatment, can specific characteristics be identified that can predict which individuals will benefit the most from treatment?
- Challenges and limitations of the study (including COVID-19).
- Strengths of the study.

6.2: Socio-Demographic, Clinical, OHRQoL and Psychosocial Characteristics of the Study Sample.

Participants in this study were selected using convenience sampling, based on specific inclusion and exclusion criteria (Section 4.3.1, Section 4.3.2). A variety of recruitment sites, including teaching hospitals, district general hospitals, and specialist practices from different geographical regions (Section 4.4), were intentionally selected. The goal was to ensure that the participants accurately represented patients receiving or seeking NHS orthodontic treatment across the UK and ensure the generalisability of any findings. In the study sample, there was a slightly greater proportion of females than males, both in the OTG and the WLCG. This difference appears to reflect the difference observed in orthodontic practice, where females make up a larger proportion of patients undergoing orthodontic treatment within the UK (Rolland et al., 2016). As the prevalence and severity of malocclusion have not been found to significantly differ between the genders (Brunelle et al., 1996), it is thought that this difference is more likely due to the greater sensitivity that females have to features of malocclusion such as incisor irregularity (Harris and Glassell, 2011), and as such, accounts for their greater desire to have their teeth straightened at the age of 12 and 15 years, as found in the Children's Dental Health Survey 2013 (Rolland et al., 2016, Office for National Statistics, 2015). As such, the gender balance within the study was thought to accurately reflect that observed in practice.

Based on the participants recruited in the study, one difference that was evident between the socio-demographic characteristics of the OTG versus the WLCG, was age at baseline. In the OTG, most participants were aged 13 or 14 years (42%), whilst most participants in the WLCG were aged 11 or 12 years (71%). This difference is most likely due to the timing in which orthodontic treatment is usually provided, with orthodontic treatment commonly starting at the age of 13 to 14 years. In the Children's Dental Health Survey in 2013, only 9% of 12-year olds were found to be undergoing orthodontic treatment, whilst this was found to be in 18% of 15-year olds (Office for National Statistics, 2015). Though the difference in age at baseline was certainly considered as a potential confounding factor, this variable was not found to

be a significant factor in OHRQoL levels at T2 when it was controlled for in the bootstrapped ANCOVA (Section 5.6).

To date, there have been no multicentre, orthodontic-based studies that have been conducted in the UK, which have included both secondary and primary care providers, that have recruited adolescent participants qualifying for NHS orthodontic treatment, applied similar inclusion/exclusion criteria to this study, and collected data on clinical characteristics of the malocclusion such as IOTN DHC score and incisor relationship. However, a study looking at the factors that influence the uptake of orthodontic treatment in primary and secondary care services in the UK, found that 86% of those who were accepted for treatment had an IOTN DHC score of 4 or 5 (O'Brien et al., 1996). This is similar to our study sample, where 86% of participants in the OTG and 93% in the WLCG had IOTN DHC scores of 4 or 5. Therefore, it is reasonable to assume that the sample in this study reflects similar levels of malocclusion severity as the general population undergoing NHS orthodontic treatment in the UK.

A noticeable difference between the OTG and the WLCG in the study sample was the proportion of participants who had no reported concerns about their dentition. This was 6% in the OTG and 21% in the WLCG. While this difference is hard to fully explain, it could partially be attributed to the age differences between the participants in the OTG and WLCG at baseline. As mentioned earlier, the majority of participants in the WLCG were aged 11 or 12 years (71%) at baseline, whereas those in the OTG were aged 13 or 14 years (42%). The motivating factors for adolescents seeking orthodontic treatment have been explored in the literature, with the main motivating factor often focused on the desire for improved dental aesthetics (Prabakaran et al., 2012). However, it is also well documented, that in adolescents, it is not only their own, personal motivating factors that play a role, but crucially, that of their parents too. The study by Prabakaran et al. (2012) also explored the motivation for orthodontic treatment from the parents' perspective, and identified that an important factor for parents', was the desire for their child to undergo orthodontic treatment, to prevent problems in the future. Given that a much larger

proportion of participants in the WLCG were only aged 11 or 12 years old, compared to the OTG where most participants were aged 13 or 14 years, it may be that younger adolescents have less concern regarding their dentition at that stage, and the desire to undergo orthodontic treatment is increasingly driven by their parents. As adolescents become older, they may become more aware and conscious of their dentition, and this may explain why a greater proportion of participants in the OTG (which were older), reported concerns regarding their dentition compared to the WLCG.

The type of orthodontic treatment provided in both cohorts of this study were similar, with the most common form of treatment utilising fixed appliances (with or without dental extractions). This is similar to the findings of the Children's Dental Health Survey in 2013, which found fixed appliances to be the most common orthodontic appliance to be worn by children at the time of the survey examination (Office for National Statistics, 2015).

When considering the baseline levels of OHRQoL of participants in the study, these were assessed using both the COHIP-SF 19 and the MIQ. In the study by Broder et al. (2012), the reliability and validity of the COHIP-SF 19 was tested using three groups, namely, a paediatric sample, an orthodontic sample, and a sample of participants with craniofacial anomalies. The orthodontic sample was based on a group of adolescent orthodontic patients in New York, USA, who were seeking orthodontic treatment but had not yet started this treatment (Broder et al., 2012). In their sample, the orthodontic participants were found to have a mean total COHIP-SF 19 score of 57.8 (SD 10.3) (Broder et al., 2012). This score is not dissimilar to the mean scores in participant of this study sample, where baseline mean total COHIP-SF 19 scores were 53.1 (SD 10.6) and 54.8 (SD 10.2) in the OTG and WLCG respectively. Similarly, whilst the data on the more novel MIQ is limited, the MIQ scores obtained for 184 participants who were seeking orthodontic treatment in a dental hospital in the UK, within a study that was designed to examine the validity of the MIQ cross-sectionally (Benson et al., 2016), found that the mean total MIQ scores for the cohort to be 11.6 (SD 6.5). Again, this is similar to the findings for the sample in this study,

where baseline mean total scores of MIQ were 11.9 (SD 7.9) in the OTG, and 9.9 (SD 6.8) in the WLCG.

Self-esteem was measured using the self-esteem subscale of the CHQ-CF87, which was also a measure used in the longitudinal study by Benson et al. (2015), that followed a cohort of schoolchildren aged 11 to 12 years, for a 3-year period. In the sample recruited in that study, the mean baseline scores of the CHQ-CF87 were found to be 80.0 (SD 14.4), which is very similar to the results obtained in this current study. In the OTG, the mean score of the sample at baseline was 79.2 (SD 17.0), and in the WLCG, the respective figure was 83.7 (14.8). These findings suggest that the self-esteem characteristics of the sample in this study was representative of the general adolescent population within the UK.

Overall, based on the research evidence available for socio-demographic, clinical, OHRQoL and psychosocial characteristics within the orthodontic literature, particularly where available, data from the UK, it is reasonable to believe that the participants recruited into the study were a representative sample of the patients undergoing orthodontic treatment in the UK under the NHS. Furthermore, the orthodontic treatment that was delivered to those in the OTG and, was due to be delivered to participants in the WLCG, was illustrative of that which is typically delivered within the NHS. Whilst one of the largest limitations of this study was the number of participants who were lost to follow-up (Section 6.5), there were no striking differences between the characteristics of those who were followed up to T2, compared to those who were lost to follow-up. As such, it is believed that the sample was representative of young people receiving NHS orthodontic treatment within the UK.

6.3: Responsiveness and Longitudinal Construct Validity of the MIQ

At the inception of this study, the MIQ had undergone cross-sectional validation (Benson et al., 2019a), but its responsiveness and longitudinal construct validity had not yet been

explored. One of the objectives of this study was to explore this in detail. Using psychometric analysis methodology, based on two global transition judgement questions (GTJ1 and GTJ2) determining a change in the appearance of the teeth, and a change in bite, the MIQ was found to be responsive to change over time. Since the inception of this study, other authors have also attempted to assess the longitudinal construct validity of the MIQ (Peter et al., 2023). Peter et al. (2023) conducted a 3-year, longitudinal cohort study in India, which recruited 210 participants who were due to undergo orthodontic treatment (under the age of 18 years). Participants in the study completed the MIQ before the start of orthodontic treatment (T0), and one month after the completion of treatment (T1). In total, 162 participants were followed up at T1. The authors of the study used similar methodology to that used within our study to determine the responsiveness and longitudinal construct validity of the MIQ and found the questionnaire to perform well in both constructs. In this study however, the global transition question used was 'How do you rate the change in your oral health and related life quality after orthodontic treatment?'. Using an anchor-based method, centred on this question, the authors calculated the MID for the MIQ to be 7.7. The use of multiple independent anchors, and examination across multiple samples, to determine the MID is highly recommended (Revicki et al., 2008). As the study by Peter et al. (2023) did not have a control group, the authors found that no participants reported worsening of their OHRQoL in response to their global transition judgement question. As such, they were limited to calculating the MID using the difference in mean MIQ scores between those who reported 'no change' and those who reported their OHRQoL to have 'improved a little' following the completion of orthodontic treatment. This involved data from a total of 76 participants only. In our study, as a control group was recruited, a full range of responses to the two GTJ questions were observed. As such, the MID was calculated based on both a minimal improvement, and a minimal worsening in response to GTJ1, 'Overall, how has the appearance of your teeth changed from before you started treatment or last filled out the questionnaire?' and GTJ2, 'Overall, how has the bite of your teeth changed from before you started treatment or last filled out the questionnaire?'. Using this methodology, the MID for the MIQ based on GTJ1 and GTJ2 was 1.9 and 4.7 respectively. This suggests that a MID based on aesthetic change using the MIQ is 1.9, whilst the MID based on a change in the bite of a patient, is associated with a MID on 4.7. The MID calculated for GTJ1 was

based on data from 179 participants, and GTJ2 was based on 223 participants, both of which are significantly more than the study by Peter et al. (2023). It has been highlighted that MID's can vary depending on the population and the context of a study, and that the estimation of a MID for a specific measure, such as the MIQ, should be based on multiple approaches and a triangulation of methods (Revicki et al., 2008).

6.4: Research question 1: Are there differences in the changes observed in the OHRQoL of young people aged 11 to 16 years who receive orthodontic treatment versus those who are still waiting for treatment?

The results of this study found that OHRQoL improved in participants who received orthodontic treatment, whereas it declined in those waiting for treatment. A comparison of the changes in OHRQoL between the two groups demonstrated significant differences, and this was evidenced by both the condition-specific OHRQoL measure (MIQ) and the generic OHRQoL measures (COHIP-SF 19/OHIP-14). The difference between the two groups at T2 remained significant, even after controlling for several socio-demographic, clinical and psychosocial characteristics.

Many previous studies assessing the impact of orthodontic treatment on OHRQoL, are limited by shortcomings, including the generic nature of the OHRQoL instruments used, the follow-up time periods utilised, lack of appropriate control groups, together with methodological issues that have previously been discussed in Section 2.8.5 and Section 3.1. That said however, the findings for OHRQoL in relation to the orthodontic treatment group in the present study are somewhat similar to previous longitudinal studies.

The results of this study, particularly the changes observed in the OTG, echo those of a previous longitudinal cohort study. As previously discussed, (Section 2.8.5 and Section 6.3) the longitudinal study by Peter et al. (2023) used the MIQ to assess OHRQoL in a cohort of patients undergoing orthodontic treatment and found OHRQoL to improve following the completion of treatment. Whilst the study was novel in its' utilisation of the condition-specific MIQ, one of the significant limitations of this study was that a control

group was not recruited. Given that a previous study by Benson et al. (2015) has shown OHRQoL to improve between the ages of 12 to 15 years (in schoolchildren not undergoing orthodontic treatment), the absence of a control group makes it challenging to determine whether any improvements observed are due to the orthodontic treatment alone, or due to fluctuations and natural improvements in OHRQoL in this age group.

A similar, longitudinal 4-year cohort study was conducted in 19 specialist orthodontic practices throughout New Zealand, where 174 participants undergoing fixed orthodontic treatment were assessed before starting orthodontic treatment, immediately post-treatment (n=152) and at a later post-treatment period (mean 21 months after the immediate post-treatment assessment (n=104) (Healey et al., 2016). The authors of the study used the CPQ₁₁₋₁₄ to measure OHRQoL and found that the change in CPQ₁₁₋₁₄ score from pre-treatment to immediately post-treatment was minimal (mean of -0.3, SD 14.1), but this significantly improved at the later post-treatment follow-up period (mean change of 9.8, SD 14.6, effect size 0.7). This is unsurprising as immediately post-treatment the patient has not yet had any experience of their treated malocclusion without wearing an orthodontic appliance (which is known to have a negative impact on OHRQoL), and some time must lapse before the potential impact of improvement in the malocclusion can be determined. The improvement in OHRQoL after time had lapsed (mean 21 months) following the completion of orthodontic treatment, reflects the improvements seen in the OTG arm of this study.

A more recent, longitudinal cohort study carried out in Leuven, Belgium, investigated the changes in OHRQoL before, during and after orthodontic treatment, exploring the relationship with the initial treatment need, and evaluating the influence of self-esteem (Jaeken et al., 2018). The CPQ₁₁₋₁₄ was used to measure OHRQoL, self-esteem was assessed using the Dutch version of the Harter's Self-Perception Profile for Adolescents, and treatment need was determined using the IOTN. The perceived need for orthodontic treatment was determined using the OASIS. In total, 498 participants (aged 11 to 17 years) were recruited at baseline. The OHRQoL of participants was measured before the start of orthodontic treatment (T0), 1 year after the start of treatment (T1), and one

month after the completion of treatment (T2). In total, data from 215 participants at T2 was available. When focusing on the OHRQoL changes from T0 to T2 only (pre- and post-orthodontic treatment), the authors reported that OHRQoL significantly improved following the completion of orthodontic treatment (effect size 0.7), which is similar to the results observed in the OTG cohort of this study.

A meta-analysis and systematic review exploring the impact of the completion of orthodontic treatment on OHRQoL in children and adolescents, previously found orthodontic treatment to result in improvements in OHRQoL (Javidi et al., 2017). When comparing the pre- and post-orthodontic treatment OHRQoL scores, the improvement observed was associated with a medium effect size. As the authors of the review highlighted, only data from those undergoing treatment were included in the meta-analysis (Javidi et al., 2017), but the results of these mirror those that were observed in the OTG of this study.

Whilst changes were observed in OHRQoL in those undergoing orthodontic treatment, in the systematic review and meta-analysis by Javidi et al. (2017), as well as longitudinal studies such as Peter et al. (2023), Healey et al. (2016) and Jaeken et al. (2018), all these studies failed to recruit a control group. In the absence of a comparable control group, it is impossible to decipher whether the improvement observed in OHRQoL following the completion of orthodontic treatment in adolescents, is truly attributable to the orthodontic treatment alone, or whether they are due to the natural improvement in OHRQoL that may occur in this age group (Benson et al., 2015a). To the best of our knowledge, there is only one other longitudinal cohort study which did recruit a waiting list control group, in addition to a group undergoing orthodontic treatment (Agou et al., 2011). This study recruited 98 participants undergoing orthodontic treatment, and 101 participants who were on the waiting list for orthodontic treatment (control group). Participants were aged 11 to 14 years and were seeking treatment in the orthodontic clinic at the University of Toronto. In total, 74 of the participants in the orthodontic treatment group were followed up at the first retainer check appointment following the completion of orthodontic treatment, and 44 participants in the control group were

followed up at an equivalent time interval. The authors used the CPQ₁₁₋₁₄ as a measure of OHRQoL and found that those in the treatment group had significantly better OHRQoL scores at follow-up, compared to those in the waiting list control group. These results concur with the findings of our study. In the study by Agou et al. (2011) however, whilst those in the treatment group had significantly better overall OHRQoL scores at follow-up, compared to the waiting list control group, when PWB levels were controlled for, this difference was no longer found to be statistically significant (except for the EWB dimension of OHRQoL). Further analysis of the data by the authors found that PWB played a significant role, and those with high levels of PWB, were more like to report significant improvements in OHRQoL after treatment, when compared to those with low PWB levels. This will be discussed further in Section 6.5. One striking difference that was observed in the results of this study, and the study by Agou et al. (2011) was the change in OHRQoL that occurred in the waiting list group. In this study, the OHRQoL of those in the WLCG appeared to worsen over time, whilst this pattern was not observed in the study by Agou et al. (2011), where OHRQoL levels seemed to very marginally improve in this group of participants. Although the two studies used different instruments to measure OHRQoL, with the study by Agou et al. (2011) using the CPQ₁₁₋₁₄, and this study utilising the MIQ and the COHIP-SF 19/OHIP-14, this is unlikely to have influenced the pattern of changes observed. The worsening of OHRQoL in the WLCG in this study was demonstrated using both OHRQoL instruments. The difference in the observed results may in fact be due to the number of participants who were recruited, and subsequently followed-up in the two studies. In the study by Agou et al. (2011), 101 participants were initially recruited into the waiting list group, and 44 of these were followed up at T2 (43%). In this study, 376 participants were recruited into the WLCG, and 177 were followed up at T2 (47%). As such, it is possible that the larger number of followed-up participants in this study more accurately reflects the changes in OHRQoL occurring over time in individuals that have a malocclusion, but have not yet had orthodontic treatment; however, this requires further investigation.

In summary, the results of this study demonstrated significant improvements in OHRQoL following the completion of orthodontic treatment in adolescents starting treatment aged 11 to 16 years. This finding aligns with the results of several previous studies on the

subject. A unique aspect of this study was the inclusion of a large WLCG, consisting of participants who had malocclusion but had not yet received orthodontic treatment, who were assessed longitudinally over a reasonable time period. Using this cohort as a control group, enabled assessment of the impact of untreated malocclusion on OHRQoL over time, and helped establish a robust comparison to evaluate the true effects of completing orthodontic treatment. Where the results of this study differ from others, is in the findings from the WLCG. Not only did the OHRQoL not improve during the period participants were waiting for treatment, but it deteriorated over time. This highlights the potential impact of untreated malocclusion on adolescents' OHRQoL and underscores the improvement that can be achieved by undertaking orthodontic treatment.

6.5: Research question 2: If there is an improvement in OHRQoL following orthodontic treatment, can specific characteristics be identified that can predict which individuals will benefit the most from treatment?

It is now well-established that both clinical and non-clinical characteristics can influence an individual's OHRQoL (as discussed in Sections 2.8.2. and 2.8.3.). As such, an ANCOVA with bootstrapping was used, with MIQ interval scores at T2 as the dependent variable, treatment group allocation as the independent variable, with a number of socio-demographic, clinical and psychosocial characteristics as covariates. Despite controlling for all the covariates in the model, MIQ interval scores at T2 were still significantly lower in the OTG than in the WLCG, confirming the improvement in OHRQoL attributable to the orthodontic treatment. That said, there were also other covariates that demonstrated, smaller, but significant results. The first of these was MIQ interval scores at baseline (T1). This variable had a strong impact on the MIQ interval scores at T2, with higher scores at baseline being associated with higher scores at T2. This suggests that those with poorer OHRQoL at baseline, are likely to experience poorer OHRQoL at T2. These findings are similar to those observed in the Agou et al. (2011) study, where baseline scores of CPQ₁₁₋₁₄, were found to play a significant role in CPQ₁₁₋₁₄ scores at T2. With the exception of treatment group, and baseline MIQ interval scores, there were also two other covariates that

demonstrated significance in the model, namely, self-esteem and life satisfaction (overall QoL).

Two of the most common psychosocial characteristics that have been investigated in relation to their impact on OHRQoL in individuals with malocclusion and/or undergoing orthodontic treatment are self-esteem (Agou et al., 2008, Jaeken et al., 2018, Brosens et al., 2014) and PWB (Agou et al., 2011). The study by Agou et al. (2011) had produced particularly interesting results, as the authors carried out two ANCOVA models; one model evaluating the relationship between the provision of orthodontic treatment and the changes in OHRQoL, (represented by overall and individual CPQ₁₁₋₁₄ scores) while controlling for the CPQ₁₁₋₁₄ scores at T1, age, and malocclusion severity, and a similar second model, with PWB included as an additional covariate. Whilst the first model showed OHRQoL to significantly improve in those who had undergone orthodontic treatment, these differences diminished after accounting for PWB. Furthermore, when the authors dichotomised the participants based on high and low levels of PWB, they found that participants with better PWB were more likely to report better OHRQoL, regardless of their orthodontic treatment status, whilst participants with low PWB, who were on the waiting list, experienced worse OHRQoL compared with those who received treatment. The authors therefore concluded that adolescents with low PWB can benefit from undergoing orthodontic treatment (Agou et al., 2011). Such findings confirm the significant, mediating role that psychosocial parameters such as PWB can play in OHRQoL.

The number of studies exploring the influence of self-esteem on OHRQoL in patients with malocclusion, and those undergoing orthodontic treatment has increased over the last decade. Agou and colleagues report a cross-sectional study involving 199 young people aged 11 to 14 years, who were attending the orthodontic clinic in Faculty of Dentistry, University of Toronto (Agou et al., 2008). They evaluated the associations between OHRQoL (assessed using the CPQ₁₁₋₁₄), the self-esteem scale of the CHQ-CF87, and the DAI, and found that CPQ₁₁₋₁₄ scores were significantly related

to the self-esteem scores, and to a much lesser extent, to DAI ratings. Furthermore, the authors found that the impact of malocclusion on OHRQoL was greater in participants with low self-esteem (Agou et al., 2008).

The role of self-esteem on OHRQoL during orthodontic treatment itself, has also been explored using longitudinal methodology (Brosens et al., 2014). The team in Belgium report the findings of a longitudinal study involving participants aged 11 to 16 years undergoing orthodontic treatment. The aim of the study was to investigate any changes in OHRQoL during orthodontic treatment, and in particular, to determine the possible influence of self-esteem (Brosens et al., 2014). The OHRQoL of participants was measured using the Dutch version of the CPQ₁₁₋₁₄, and self-esteem was determined using the Dutch adaptation of the Harter's Self-Perception Profile for Adolescents. Participants were assessed prior to the start of orthodontic treatment, and one year after the start of treatment. In total, 138 participants started treatment at baseline, 109 of which were followed up one year into their orthodontic treatment. Unsurprisingly, the authors found that OHRQoL significantly declined during orthodontic treatment, but what was particularly noteworthy, was that those with a high self-esteem at baseline, showed significantly lower variability in OHRQoL at follow-up, and the authors concluded that self-esteem can be a protective factor in OHRQoL during orthodontic treatment (Brosens et al., 2014).

The relationship between self-esteem and OHRQoL has been explored not only in orthodontic patients but also in schoolchildren aged 11 to 12 years (Benson et al., 2015a). In this 3-year longitudinal cohort study, OHRQoL was found to improve over time (regardless of orthodontic treatment status), whilst self-esteem deteriorated over the same time period. At baseline, the results of a multivariate analysis indicated that participants with low self-esteem had poorer OHRQoL, and conversely, those with higher self-esteem had better OHRQoL. Additionally, the results of a multivariate analysis exploring longitudinal changes in adolescents, found that as self-esteem improved, so too did OHRQoL, and vice versa (Benson et al., 2015a).

Many studies exploring the relationship between orthodontics, self-esteem, and OHRQoL have typically focused on three key questions: firstly, how self-esteem changes over time; secondly, whether self-esteem influences OHRQoL; and thirdly, how varying levels of self-esteem impact the OHRQoL of individuals with malocclusion or undergoing orthodontic treatment. These questions are central to understanding the complex interplay between self-esteem and OHRQoL, particularly in the context of orthodontics. In this study, self-esteem was assessed using the self-esteem subscale of the CHQ-CF87. The findings showed that self-esteem improved in the OTG from T1 to T2, while it worsened in the WLCG during the same period. This was a unique finding, as the longitudinal cohort study by Agou et al. (2011), which also included a waiting list group, did not observe notable changes in PWB (which is often considered to have a high correlation to self-esteem), over time, between the orthodontic treatment and waiting list groups. Whilst it could be argued that the improvement in self-esteem observed in the OTG in this current study reflects the natural developmental progression seen in this age group (Benson et al., 2015a), the decline in self-esteem in the WLCG suggests that untreated malocclusion may have a negative impact self-esteem. The impact of self-esteem on MIQ interval scores at T2 was explored using an ANCOVA with bootstrapping, where self-esteem was included as a covariate. The results of the analysis found self-esteem to be a significant factor in determining MIQ interval scores at T2 (and therefore OHRQoL).

Where the results of this study were unique in relation to self-esteem, was in the finding that higher baseline levels of self-esteem were associated with higher MIQ interval scores at T2, indicating poorer OHRQoL. What the results suggest is that individuals with higher self-esteem at baseline are likely to experience less improvement in OHRQoL following orthodontic treatment, compared to those with lower levels of self-esteem. To date, there are no longitudinal studies that have employed a similar methodology to this study, specifically including a WLCG and measuring the same outcome variables. As such, it is difficult to directly compare this observation with findings from other research, as this study design and the use of the WLCG provide a unique perspective on the relationship between self-esteem and OHRQoL over time.

One theory that could explain the results observed in relation to self-esteem in this study draws upon the findings of Benson et al. (2015). In their study, a multivariate analysis at baseline revealed that participants with high self-esteem had better OHRQoL. Furthermore, their longitudinal analysis showed that as self-esteem improved over time, OHRQoL also improved, and vice versa. Based on these findings, one could hypothesise that individuals with high self-esteem at baseline may have less potential to experience significant improvements in self-esteem over time. This hypothesis is further supported by the results of a longitudinal study by Vulugundam et al. (2021), which explored whether orthodontic treatment was associated with changes in self-esteem during adolescence. The study analysed data from 2600 participants in a British Cohort Study, where the Lawrence Self-Esteem Questionnaire was completed at ages 10 and 16 years. Participants were divided into two groups based on parental reports of orthodontic treatment. Regression models were conducted, and included relevant covariates such as gender, ethnicity, and baseline self-esteem. Whilst the study found no evidence to suggest that orthodontic treatment was associated with changes in self-esteem during adolescence, the study did find that higher self-esteem at age 10 years was associated with a reduction in self-esteem over time, when compared to lower self-esteem at baseline (Vulugundam et al., 2021). This raises the important question of whether participants with higher self-esteem at baseline in this current study, experienced a reduction in self-esteem over time. Given the observed relationship between self-esteem and OHRQoL in the longitudinal study by Benson et al. (2015), it is reasonable to hypothesise that if individuals with higher baseline self-esteem did indeed experience a decline in self-esteem, the potential for significant improvement in OHRQoL would be limited. This may help explain the results observed in relation to self-esteem in the ANCOVA model, which suggested that individuals with higher self-esteem at baseline experienced higher total MIQ scores and hence poorer OHRQoL at T2. Overall, this suggests that individuals who have lower self-esteem at baseline, may benefit more from orthodontic treatment in terms of improved OHRQoL.

In the bootstrapped ANCOVA model, another covariate which demonstrated significant association with MIQ interval scores at T2 was life satisfaction (QoL) measured using the

SLSS. The model showed that those with higher levels of life satisfaction (QoL) at baseline, were likely to have lower MIQ interval scores at T2, and therefore better OHRQoL. To date, there appear to be no previous studies that have explored the impact of orthodontic treatment on OHRQoL longitudinally while collecting data on life satisfaction (QoL). This makes it difficult to corroborate and compare the results of this study directly with other studies in the existing literature. That said, the Wilson and Cleary model provides a taxonomy of different health outcomes, namely, biological and physiological, symptoms, functioning, general health perceptions, and highlights the influential role that characteristics of an individual and the environment can have, either directly, or as mediators, on each of these outcomes, including overall QoL (Wilson and Cleary, 1995). Previous studies using SEM have demonstrate the complex interplay between factors such as self-esteem, parental income, OHRQoL, and overall QoL in adolescents (Baker et al., 2010). It is therefore not surprising that in this study, overall QoL levels as baseline were found to have a significant association with OHRQoL levels at T2.

A systematic review by Dimberg et al. (2015) exploring the impact of malocclusion on OHRQoL, found high quality evidence that anterior malocclusions such as anterior crowding, spacing and increased overjet, have a detrimental impact on OHRQoL. With this mind, it was critical that data was collected and analysed on the various traits of malocclusion that may affect the anterior region, to determine whether any of these may influence the possible OHRQoL benefits that may be observed following orthodontic treatment. In the ANCOVA model with bootstrapping, IOTN DHC grade, self-assessed IOTN AC, overjet, the largest space and the largest contact point displacement present in the ULS, were all included as covariates. None of these clinical characteristics were found to have a significant impact on MIQ interval scores at T2. These findings are similar to those observed in the Agou et al. (2011) study, where the normative need for orthodontics, measured by the DAI, was not found to have a significant impact on overall OHRQoL levels observed at T2.

Other covariates in the model for this current study included gender, age and IMD (decile), all of which showed no significant associations with MIQ interval scores at T2. These were similar to the results observed in the study by Peter et al. (2023).

Overall, the analysis of the results from this current study suggested that individuals with lower self-esteem, and higher baseline levels of OHRQoL and life satisfaction (QoL), were more likely to experience better OHRQoL levels following orthodontic treatment.

6.6: Challenges & Limitations of the Study (including COVID-19)

The challenges of longitudinal study designs are well documented in the literature; they are considered time-consuming, costly in nature, and always run the risk of inevitable loss of participants as the study progresses (Liang, 2024).

This study was not without its challenges, many of which were unforeseen at the beginning. This section provides a thorough discussion of the obstacles encountered, the adjustments made to the study protocol to address these issues, and the limitations that emerged as a result of some of these challenges.

6.5.1. Study Design

The benefits of randomised controlled trials (RCTs) in assessing effectiveness are well-documented in the literature (Hariton and Locascio, 2018). Randomisation helps reduce bias and account for confounding factors, by balancing both observed and unobserved participant characteristics across groups, ensuring that any differences in outcomes are attributable to the intervention itself. Ideally, the potential benefit of orthodontic treatment in relation to OHRQoL would have been explored through this approach. However, due to practical and ethical considerations, this was not feasible in the current study. In sites where a waiting list for treatment exists, randomly assigning a participant to

either start their treatment immediately or remain on the waiting list might overcome some of the ethical arguments against randomisation, but in practice it might not be possible to arrange due to logistical constraints, such as limited manpower and chair availability. On the other hand, for sites without a waiting list, randomising participants into a group who must wait a minimum time for treatment to begin simply for research purposes, could potentially be viewed as unpopular with young people and their parents and unethical if there are good reasons to start their orthodontic treatment as soon as possible.

Given these ethical and practical challenges, it was determined that conducting a RCT within the current NHS orthodontic services in the UK would not be feasible. As a result, a longitudinal cohort study was undertaken, recruiting participants from sites with existing orthodontic waiting lists for the WLCG, and from other sites where participants were about to begin orthodontic treatment for the OTG. To increase the external validity of the study, efforts to recruit participants from a wide range of sites, including teaching hospitals, district general hospitals, and specialist practices, across various geographical locations. This approach helped ensure that the sample was more representative of the broader population. To assess whether the participants in the two cohorts were well balanced, the characteristics of participants in both groups were carefully examined. With the exception of age, the two groups appeared to be well balanced across other variables. Given this, despite the lack of randomisation, the differences between the groups were minimal and it is felt that these are unlikely to have had a significant impact on the results observed.

6.5.2. Introduction of the General Data Protection Regulation (GDPR)

This longitudinal study began in October 2017, and over a two-month period, all initial sites that agreed to participate were visited. Each site received packs containing PILs, assent forms, and consent forms. On the 28th of May 2018, the introduction and enforcement of GDPR by the Information Commissioner's Office (ICO) brought about changes to how data protection was managed. Consequently, the information within the PILs had to be updated to ensure compliance with the new GDPR regulations. These updated PILs had to then be re-printed and delivered to all recruiting sites.

6.5.3. Loss of Recruitment Sites

In total, three of the sites that had agreed to recruit participants for the study, failed to do so. Despite considerable effort in setting up the study at these units and practices, no participants were recruited from these three sites. At one site, the PI left their role before any recruitment could occur, and no suitable individual was available to take over as PI. At the other two sites, communication abruptly ceased, and no explanation was provided for their withdrawal from the study. Due to these lost sites, additional sites had to be identified, and Non-Substantial Amendments were submitted for the addition of these into the study. The details of these can be found in Chapter 4, Section 4.7.

6.5.4. Loss of Consultant Workforce

In one of the sites (site 3), the PI recruited a total of 22 participants into the study. The PI was a consultant orthodontist, who then moved on to work at a different district general hospital. Unfortunately, there was no other consultant in the unit, or other members of staff, who were able to take over as PI. As such, the research governance team at the unit advised that the site could no longer participate in the study, and all the participants recruited were lost to follow-up. Additionally, the participant screening logs, and the clinical data collection sheets that had been completed for the recruited participants could not be located by the site, which led to loss of data.

6.5.5. Tendering of NHS Orthodontic Services Contracts in Primary Care

The tendering of NHS orthodontic services in primary care has been an ongoing issue in different areas of the country at different time-points. Discussions around the tendering of contracts in the Yorkshire & Humber region started in 2017/2018 and as the re-tendering process occurred, some practitioners/practices lost their NHS orthodontic contracts. As such, the ongoing care of their patients had to be transferred to an alternative provider. The process was a stressful and time-consuming process for those in possession of an NHS orthodontic contract and led to one of the sites (site 9),

withdrawing from the study and not following up any of the participants recruited at T1. As the site had recruited 116 participants into the WLCG, this was significant number of participants who were lost to follow-up at T2.

6.5.6. Impact of a Global Pandemic (COVID-19)

Without a doubt, the global consequences of the COVID-19 pandemic in 2020 were devastating across various areas. It severely affected economies, put immense pressure on healthcare systems, and resulted in a tragic loss of life. In numerous ways, the pandemic transformed how we work, interact, and engage with digital technology. Regrettably, the progress of this study was also impacted, with the effects of COVID-19 proving to be significant.

When the pandemic began in March 2020, all routine healthcare services in the UK were effectively halted, and dentistry and orthodontics were no exceptions. For several weeks, routine orthodontic treatments were suspended in both primary and secondary settings. As services gradually resumed, they did so on a limited and prioritised basis, focusing on the most urgent cases. At the time, the study was in its follow-up phase. For the OTG, the study was structured so that T2 marked the first retainer review appointment (6 to 15 weeks after the completion of active treatment), and T3 occurred at the second retainer review appointment (9 to 15 months after the end of active orthodontic treatment). In the WLCG, the follow-up corresponded to the point when the patient was about to begin their orthodontic treatment after being removed from the waiting list. The impact of the pandemic on the follow-up of participants in the OTG group was particularly significant. Routine retainer review appointments were of very low priority, and as time progressed, in many sites, retainer review appointments were carried out over the phone and patients were no longer attending these appointments in person. As such, participants in the study were no longer attending their planned follow-up time points (T2 and T3) in person.

Amendments to the study were submitted to alter the time points for T2 and T3 and change them to '6 weeks up to 9 months', and '9 months up to 18 months' respectively.

As there was a large backlog of patient appointments in various sites, the timeline for T3 was subsequently changed to '9 months up to 32 months', to enable follow-up of participants at T3. Amendments were also made to enable sites to contact participants via phone, email or post, in order to provide them with a link which could be used to complete the questionnaires. Whilst every effort was made to encourage the follow-up of participants, this became increasingly challenging, and the study closed to data collection in July 2024.

As we witnessed the impact of COVID-19 on the progression of the study, it became increasingly evident that our initial protocol, which included clinicians completing a data collection sheet to record features of the malocclusion at T2 (and T3 where relevant), so that the change in malocclusion pre- to post-orthodontic treatment, or pre- to post-placement on the orthodontic treatment waiting list could be assessed, was no longer feasible. In addition to this, whilst we had initially planned that the PI for the study (HJ) would visit sites and assess the study models of a random sample of recruited participants, to determine the inter-rater reliability of the data collection sheets, this too became unfeasible.

6.5.7. Summary of Limitations

The most significant limitation of this study was the high number of participants lost to follow-up. This issue arose due to various factors, including the loss of consultants (PIs) at recruitment sites, challenges related to the re-tendering of orthodontic contracts at some of the specialist practice locations, and the profound impact of COVID-19. Despite considerable efforts to follow up participants, 199 participants were lost to follow-up in the WLCG at T2, 363 participants in the OTG at T2, and an additional 165 in the OTG at T3. Our initial sample size calculation had indicated that 450 participants in the TG and 320 in the WLCG were needed (excluding participants lost to follow-up). However, the number of participants followed up at T2 was 222 in the OTG and 177 in the WLCG, both of which were below our intended sample size. Whilst this is invariably a large limitation of this study, it is important to note that our initial sample size calculation was based on limited OHRQoL data that was available at the time, and as further evidence has been published,

particularly with the use of the MIQ, it is becoming increasingly apparent that, perhaps, a smaller sample size may have been sufficient to detect a significant difference, should one have existed. The longitudinal study by Peter et al. (2023), exploring the change in OHRQoL before and after the completion of orthodontic treatment, using the MIQ, found the MID in their sample to be 7.7 with a Guyatt's responsiveness statistic estimated to be 1.75, indicating that far smaller sample sizes may be needed to detect the MID in clinical trials using the MIQ.

Given the large number of participants that were lost to follow-up, A post-hoc power calculation was conducted to determine whether the study was sufficiently powered to detect the observed differences OHRQoL between the OTG ($n = 212$) and the WLCG ($n = 173$), resulting in a total sample size of 385. The MIQ interval scores showed a mean difference of -10.6 points ($SE = 0.7$), with a Cohen's d of -1.6 (95% CI: -1.3 to -1.8) and this was found to be highly statistically significant ($p < 0.001$). Based on the sample sizes in each group, the observed mean differences, and standard errors, the estimated statistical power exceeded 99.9%, assuming a two-sided significance level of $\alpha = 0.05$ and approximately 383 degrees of freedom. These results indicate that the study was more than adequately powered to detect a difference in OHRQoL change between the two groups.

Regarding participants lost to follow-up, there is always concern that their characteristics might differ from those who remain in the study. However, in this study, this concern was somewhat reduced, as a significant portion of the participants lost to follow-up were due to the loss of the PI at a site, rather than participants withdrawing themselves.

Nonetheless, to thoroughly investigate any potential differences, the data in relation to socio-demographic, clinical, OHRQoL, and psychosocial characteristics of all participants lost to follow-up versus those who were followed up at T2 were presented and compared (Section 5.4). The comparison revealed no noticeable differences.

6.7: Strengths of the Study

Despite the challenges encountered, this study and its findings represent a significant contribution to the literature exploring the effect of completing orthodontic treatment on OHRQoL. Although a significant number of participants were lost to follow-up, 222 participants in the OTG and 177 participants in the WLCG were successfully followed up at T2. To date, this is the largest, longitudinal cohort study which has assessed the effect of orthodontic treatment completion on OHRQoL, and included a comparable control group. The inclusion of a WLCG was essential in ensuring that any changes observed in the OTG could be attributed directly to orthodontic treatment rather than natural variations in OHRQoL that may occur in adolescents (Benson et al., 2015a).

Another notable strength of the study was its multi-centre, recruitment strategy, based on a diverse range of settings, including teaching hospitals, district general hospitals, and specialist practices in the UK NHS healthcare system. This broad recruitment strategy ensured that the sample was representative of the varied clinical environments in which orthodontic treatment is provided within the NHS. By including participants from different types of NHS healthcare settings, the study was able to capture a wide spectrum of patient characteristics, including those from different socio-economic backgrounds, as well as patients with varying levels of orthodontic treatment need. As a result, the findings are more likely to be generalisable to the larger cohort of individuals who receive orthodontic treatment through the NHS, enhancing the external validity of the study and ensuring its relevance to real-world clinical practice.

Finally, one of the major strengths of this study was its use of the malocclusion-specific OHRQoL outcome measure, the MIQ. This study represents the largest longitudinal cohort study to date that has utilised this measure, and the results provide strong evidence for its responsiveness and longitudinal construct validity. By demonstrating these qualities, this study has significantly contributed to the further validation of the MIQ, allowing it to be used with greater confidence in future trials. The findings from this study not only support the reliability of the MIQ as an outcome measure but also enhance its credibility for assessing malocclusion-related QoL in clinical research.

Chapter 7

Recommendations & Conclusions

7.1. Introduction

The work within this thesis aimed to examine the impact of the completion of orthodontic treatment on the OHRQoL of adolescents aged 11 to 16 years. The secondary aim was to explore the characteristics that are associated with any observed changes in OHRQoL. The specific objectives were to:

- To recruit a sample of adolescents aged 11-16 years in primary and secondary orthodontic care settings, who qualify for NHS Orthodontic treatment. These must comprise a cohort of adolescents that are about to undergo orthodontic treatment, and a cohort of adolescents that are about to be placed on an orthodontic treatment waiting list (which must be a minimum of 12-months).
- To collect data for the cohort of adolescents undergoing orthodontic treatment at time-point 1 (pre-treatment), time-point 2 (6 weeks up to 9 months post-treatment), and time-point 3 (9 months up to 32 months post-treatment).
- To collect data for the cohort of adolescents being placed on an orthodontic treatment waiting list at time-point 1 (just before they are placed on the waiting list) and time-point 2 (just as they are coming off the waiting list).
- To describe the socio-demographic, clinical, psychosocial and OHRQoL levels of participants recruited.
- To determine the responsiveness and longitudinal construct validity of the MIQ.
- To analyse the OHRQoL of adolescents aged 11-16 years, before and after the completion of orthodontic treatment compared to adolescents on an orthodontic treatment waiting list.
- To examine the socio-demographic, clinical and psychosocial variables that may predict OHRQoL levels following the completion of orthodontic treatment.

The objectives were met through a multi-centre, longitudinal, cohort study. The research presented provides additional knowledge regarding the impact of orthodontic treatment completion on OHRQoL, and the identification of factors that were associated with these changes.

7.2. Recommendations

Based on the findings of this study, several recommendations can be made. These recommendations pertain to both clinical practice and future research, and they will be discussed in detail in Sections 7.1.1 and 7.1.2, respectively.

7.2.1. Recommendations for Clinical Practice

This study examined the impact of completing orthodontic treatment on the OHRQoL of adolescents aged 11 to 16 years at the start of treatment. The findings revealed significant improvements in OHRQoL following treatment, highlighting the positive effects orthodontic treatment can have on individuals' OHRQoL. Conversely, the study also found a deterioration in OHRQoL in those with untreated malocclusion, emphasizing the potential negative impact of not receiving orthodontic treatment. These findings have important implications for clinical practice, particularly in the context of discussions about the benefits of orthodontic treatment during the consent process. The results of this study, and the significant improvements in OHRQoL observed in adolescents following treatment, can serve as compelling evidence when informing patients and their families about the potential positive outcomes of orthodontic treatment. This information can support clinicians in guiding patients and parents through informed decision-making regarding orthodontic care.

The findings of this study may also have implications for other stakeholders, such as dental commissioners. Whilst the commissioning of orthodontic treatment by the NHS has come under scrutiny (Vernazza et al., 2023), the results of this study provide powerful evidence demonstrating the benefits that orthodontic treatment can provide for adolescents, and, the potential determinantal impact that lack of treatment may pose in relation to OHRQoL.

7.2.2. Recommendations for Future Research

This study has highlighted some important areas for future research. While factors such as self-esteem and life satisfaction (QoL) were identified as characteristics that may influence OHRQoL following the completion of orthodontic treatment, the complex inter-relationships between these variables, as theorized by the Wilson and Cleary model (Wilson and Cleary, 1995), could not be explored using SEM due to the impact of COVID-19 on participant follow-up, particularly at T3. Therefore, it is imperative that future studies investigating the impact of orthodontic treatment on OHRQoL recruit sufficient participants and ensure appropriate follow-up time points to enable the use of such mathematical modelling. This will help provide a more in-depth understanding of how these factors influence QoL outcomes observed after orthodontic treatment and further elucidate the mechanisms behind these relationships.

The results of this study have provided further, robust evidence to support the responsiveness and longitudinal construct validity of the MIQ. This condition-specific OHRQoL measure is an excellent tool for assessing OHRQoL levels in individuals with malocclusion or those undergoing orthodontic treatment in future research studies. The effect sizes demonstrated when comparing OHRQoL changes in those undergoing orthodontic treatment versus those on the waiting list were greater when using the MIQ, compared to the results observed with the generic COHIP SF-19 and OHIP-14. This highlights the increased sensitivity of the MIQ to detect changes in these cohorts of participants, further solidifying its value as a reliable and effective instrument for measuring OHRQoL outcomes in orthodontic research. Furthermore, the data generated in this study was used to calculate the MID for the MIQ, which can be used in future research studies to calculate appropriate sample sizes when using this measure. Future studies, aiming to measure OHRQoL in patients with malocclusion or orthodontic needs, should utilise the MIQ within their studies.

7.3. Conclusions

Orthodontic treatment provided during adolescence led to a significant improvement in OHRQoL following the completion of treatment. In contrast, a deterioration in OHRQoL was observed in participants with malocclusion who were placed on an orthodontic treatment waiting list. The difference in OHRQoL between the two groups, the OTG and the WLCG, was statistically significant and associated with a large effect size (1.6). Over the study period, life satisfaction (QoL) remained stable in both groups, while self-esteem declined in the WLCG but improved in the OTG. Further analysis revealed that participants with lower self-esteem, higher life satisfaction (QoL), and higher OHRQoL at baseline were more likely to experience improved OHRQoL following orthodontic treatment. The MIQ, a measure of OHRQoL in orthodontic patients and those with malocclusion, was found to be responsive and demonstrated good longitudinal construct validity. The MID for the MIQ was calculated to be 4.7 when aiming to detect a change in bite, and 1.9 when seeking to detect an aesthetic change. Overall, this study highlights the effectiveness of orthodontic treatment in improving OHRQoL and the effectiveness of the MIQ as a reliable tool in assessing these changes.

Chapter 8

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Chapter 9

Appendices

9.1 Appendix 1: Participant/Parent Information Leaflets



THE UNIVERSITY OF SHEFFIELD

Academic Unit of Oral Health and Development

▲ DOES ORTHODONTIC TREATMENT IMPROVE ORAL HEALTH-RELATED QUALITY OF LIFE? A LONGITUDINAL, COHORT STUDY

Young Persons' Information Sheet

You are being invited to take part in a research project. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Thank you for reading this.

What is the project's purpose?

It will help us understand why young people want to wear braces and if braces help. By answering some questions, you will help us learn more about young people's experiences.

What will I have to do?

We would like you to fill in a questionnaire before your braces are fitted and twice after your braces have been taken off – we think this will take about 20 minutes each time. It is as simple as that!

Don't worry – it is **not a test** and there are no right or wrong answers. We are just interested in how you feel. Your answers will be **private**; no one you know will see them.

Who has reviewed the study?

This study has been reviewed by XXXX Research Ethics Committee.

Do I have to take part?

No, not if you don't want to – if you do not take part that is fine, we will not ask you why.

IRAS 214707/STH19669 PIS (11-15yrs) Version No 2 16-05-2017

If you don't understand something, or want to know more, please feel free to ask anyone involved in the study or contact me:

Philip Benson

Contact Telephone Number: 0114 271 7972 / 7885

Thank you for thinking about taking part

IRAS 214707/STH19669 PIS (11-15yrs) Version No 2 16-05-2017



THE UNIVERSITY OF SHEFFIELD

Academic Unit of Oral Health and Development

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We would like you to fill in a questionnaire twice before your braces are fitted – we think this will take about 20 minutes each time. It is as simple as that!

Don't worry – it is **not a test** and there are no right or wrong answers. We are just interested in how you feel. Your answers will be **private**; no one you know will see them.

Who has reviewed the study?

This study has been reviewed by the Proportionate Review Sub-committee of the North West - Preston Research Ethics Committee Research Ethics Committee.

Do I have to take part?

No, not if you don't want to – if you do not take part that is fine, we will not ask you why.

IRAS 214707/STH19669 PIS (11-15yrs - Control) Version No 1 16-05-2017

If you don't understand something, or want to know more, please feel free to ask anyone involved in the study or contact me:

Philip Benson

Contact Telephone Number: 0114 271 7972 / 7885

Thank you for thinking about taking part

IRAS 214707/STH19669 PIS (11-15yrs - Control) Version No 1 16-05-2017



THE UNIVERSITY OF SHEFFIELD

Academic Unit of Oral Health and Development

DOES ORTHODONTIC TREATMENT IMPROVE ORAL HEALTH-RELATED QUALITY OF LIFE? A LONGITUDINAL, COHORT STUDY

Information for Young People aged 16 years

You will be given a copy of this information sheet and a signed consent form to keep.

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and, if you wish, discuss it with friends, relatives and your dentist. Ask us if there is anything that is not clear or if you would like more information.

If you want further information an organisation called NHS England is responsible for patient safety (website: www.england.nhs.uk/patientsafety/)

Telephone: 0300 311 22 33

Email: england.contactus@nhs.net

Post: NHS England, PO Box 16738, Redditch, B97 9PT

What is the purpose of this study?

This study is being done so that we will understand better why young people, like you, want braces and any benefits which braces may have. By answering the questions, you will help us learn more about young people's experiences.

The study is also being undertaken for an educational qualification and a report of the study will be produced, which will contribute to someone's training to become a specialist orthodontist.

What is involved?

We will ask you to complete a questionnaire before your brace is fitted and twice after the brace has been removed. We think this will take about 20 minutes each time. We will not be doing or asking anything unpleasant or harmful.

Who is organising and who has reviewed the study?

The study is being organised by a team from the School of Clinical Dentistry, University of Sheffield and University College London Eastman Dental Institute. The study has been reviewed by XXXX Research Ethics Committee and the sponsor is Sheffield Teaching Hospitals NHS Foundation Trust.

Do I have to take part?

No, participation is voluntary. You are entitled to decline or to withdraw from the study at any time, without having to give a reason.

IRAS 214707/STH19669 PIS (16yrs) Version No 2 16-05-2017

Are there any benefits or risks to taking part?

You will not directly benefit from taking part in the study, but as we explained earlier it will help us to understand better the effect that brace treatment has on young people. There are no specific risks to taking part either.

Will taking part in this study be kept confidential?

All information collected during the course of the research will be kept strictly confidential. The Data Protection Act will be complied with.

What will happen to the results?

The study will be published in a medical journal (details unknown at present time). Copies of a report, explaining the results of the study in lay language, will be provided upon request to the study team (details below).

What will happen to the data?

According to guidelines produced by the Medical Research Council and referenced by the Department of Health document 'Research Governance Framework for Health and Social Care', research data from clinical or public health studies should ideally be kept for 20 years following the completion of the study, to allow for review, reappraisal, and any concerns about the research to be addressed. The only personal data stored will be age, gender and home postcode and this will be retained, along with the research data itself, in case further analysis is required according to those guidelines.

Who do I contact for further information?

If you have *any* cause to complain about *any* aspect of this investigation, e.g. the way in which you have been approached or treated during the course of this study, please contact the project co-ordinator:

Professor Philip Benson at the Academic Unit of Oral Health and Development, School of Clinical Dentistry, Claremont Crescent, Sheffield. S10 2TA.

Contact Telephone Number: 0114 2717885

For complaints to the University please contact: the Registrar and Secretary, University of Sheffield, Western Bank, Sheffield, S10 2TN.

For complaints to the NHS please contact: the Patient Advice and Liaison Service (PALS) at the hospital on telephone number (0114) 2712450.

IMPORTANT

Please remember; if you prefer not to take part in the study please let us know

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Philip Benson

Contact Telephone Number: 0114 2717885

Thank you for reading this leaflet.



THE UNIVERSITY OF SHEFFIELD

Academic Unit of Oral Health and Development

DOES ORTHODONTIC TREATMENT IMPROVE ORAL HEALTH-RELATED QUALITY OF LIFE? A LONGITUDINAL, COHORT STUDY

Information for Young People aged 16 years

You will be given a copy of this information sheet and a signed consent form to keep.

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and, if you wish, discuss it with friends, relatives and your dentist. Ask us if there is anything that is not clear or if you would like more information.

If you want further information an organisation called NHS England is responsible for patient safety (website: www.england.nhs.uk/patientsafety/)

Telephone: 0300 311 22 33

Email: england.contactus@nhs.net

Post: NHS England, PO Box 16738, Redditch, B97 9PT

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What is involved?

We will ask you to complete a questionnaire twice before your brace is fitted. We think this will take about 20 minutes each time. We will not be doing or asking anything unpleasant or harmful.

Who is organising and who has reviewed the study?

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Do I have to take part?

No, participation is voluntary. You are entitled to decline or to withdraw from the study at any time, without having to give a reason.

IRAS 214707/STH19669 PIS (16yrs - Control) Version No 1 16-05-2017

Are there any benefits or risks to taking part?

You will not directly benefit from taking part in the study, but as we explained earlier it will help us to understand better the effect that brace treatment has on young people. There are no specific risks to taking part either.

Will taking part in this study be kept confidential?

All information collected during the course of the research will be kept strictly confidential. The Data Protection Act will be complied with.

What will happen to the results?

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Academic Unit of Oral Health and Development

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Do all children have to take part?

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IMPORTANT

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Philip Benson

Contact Telephone Number: 0114 2717885

Thank you for reading this leaflet.

IRAS 214707/STH19669 PIS (parents) Version No 2 16-05-2017



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Academic Unit of Oral Health and Development

DOES ORTHODONTIC TREATMENT IMPROVE ORAL HEALTH-RELATED QUALITY OF LIFE? A LONGITUDINAL, COHORT STUDY

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Do all children have to take part?

No, participation is voluntary. Either you or your child is entitled to decline or to withdraw from the study at any time, without having to give a reason.

IRAS 214707/STH19669 PIS (Parents-Control) Version No 1 16-05-2017

Are there any benefits or risks to taking part?

Neither your child nor you will directly benefit from taking part in the study, but as we explained earlier it will help us to understand better the effect that brace treatment has on young people. There are no specific risks to taking part either.

Will taking part in this study be kept confidential?

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Philip Benson

Contact Telephone Number: 0114 2717885

Thank you for reading this leaflet.

IRAS 214707/STH19669 PIS (Parents-Control) Version No 1 16-05-2017

9.2 Appendix 2: Consent/Assent forms



Does Orthodontic Treatment Improve Oral Health-Related Quality of Life? A longitudinal, Cohort Study

Project Leader: Professor Philip Benson

Co-ordinating Centre: Academic Unit of Oral Health & Development, School of Clinical Dentistry

Phone: 0114 271 7885 Fax: 0114 271 7843

ASSENT CONSENT FORM (young people aged 11 to 15 years)

Young person to circle all they agree with please:

- | | |
|--|--------|
| Have you read (or had read to you) the information about this project? | Yes/No |
| Has somebody explained this project to you? | Yes/No |
| Do you understand what this project is about? | Yes/No |
| Have you asked all the questions you want? | Yes/No |
| Have you had your questions answered in a way you understand? | Yes/No |
| Do you understand it is OK to stop taking part at any time? | Yes/No |
| Are you happy to take part? | Yes/No |

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

If you **DO** want to take part, please write your name and today's date

Your name: _____

Date _____

The dentist who explained this project to you needs to sign too:

Print Name: _____

Sign: _____

Date: _____

Thanks for your help

IRAS 214707/STH19669 Assent (11-15yrs) Version No 2 16-05-2017



The
University
Of
Sheffield.

Does Orthodontic Treatment Improve Oral Health-Related Quality of Life? A longitudinal, Cohort Study

Project Leader: Professor Philip Benson

Co-ordinating Centre: Academic Unit of Oral Health & Development, School of Clinical Dentistry

Phone: 0114 271 7885 Fax: 0114 271 7843

PARTICIPANT (AGED 16 yrs) CONSENT FORM

Patient study number.....Name of Researcher.....

Please initial the boxes

1. I confirm that I have read and understand the participant information sheet dated May 2017 (version 2) for the above study and have had the opportunity to ask questions.

☐

Any comments.....

2. I confirm that I have had sufficient time to consider whether or not to take part in the study.

☐

Any comments.....

3. I understand that my participation is voluntary and that I can withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

☐

Any comments.....

4. I understand that sections of my dental notes and data may be looked at by responsible individuals from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.

☐

Any comments.....

IRAS 214707/STH19669 Consent (16yrs) Version No 2 16-05-2017

5. I agree to take part in the above study

☐

Any comments:.....

Name of Participant

Signature

Date

Name of Researcher

Signature

Date

Name of Person taking consent
(if different from researcher)

Signature

Date

3 copies: Original to be placed in researcher's site file; 1 for participant; 1 to be kept with patient notes.



Does Orthodontic Treatment Improve Oral Health-Related Quality of Life? A longitudinal, Cohort Study

Project Leader: Professor Philip Benson

Co-ordinating Centre: Academic Unit of Oral Health & Development, School of Clinical Dentistry

Phone: 0114 271 7885 Fax: 0114 271 7843

PARENT CONSENT FORM

Patient study number Name of Researcher.....

Please initial the boxes

1. I confirm that I have read and understand the Parent Information Sheet version 2 16 May 2017 for the above study and have had the opportunity to ask questions.

☐

Any comments.....

2. I confirm that we have had sufficient time to consider whether or not my child wishes to take part in the study.

☐

Any comments.....

3. I understand that my child's participation is voluntary and that he/she can withdraw at any time, without giving any reason, without his/her medical care or legal rights being affected.

☐

Any comments.....

4. I understand that sections of my child's dental notes or data may be looked at by responsible individuals from regulatory authorities where it is relevant to his/her taking part in research. I give permission for these individuals to have access to my child's records.

☐

Any comments.....

IRAS 214707/STH19669 Consent (parents) Version No 2 16-05-2017

5. I agree that my child can take part in the above study

☐

Any comments:.....

Name of Parent

Signature

Date

Name of Researcher

Signature

Date

Name of Person taking consent
(if different from researcher)

Signature

Date

3 copies: Original to be placed in researcher's site file; 1 for participant; 1 to be kept with patient notes.

9.3 Appendix 3: Screening and Enrolment Logs

RESEARCH DEPARTMENT PARTICIPANT SCREENING LOG						
Study Nos:	IRAS 214707					
Study Title:	Orthodontic Longitudinal Cohort					
Site:						
Investigator Name:						
No.	Patient Initials	Date of Birth	Hospital/ Practice Identifier	Recruited (Yes/No)	Comments (if no give reason)	Date of Screening
1						
2						
3						
4						
5						
6						
7						
8						
9						

RESEARCH DEPARTMENT SUBJECT ENROLMENT LOG								
Please note: This must be stored in the site file in a secured location.								
Study Nos:	IRAS 214707							
Study Title:	Orthodontic Longitudinal Cohort							
Site:								
Investigator Name:								
Participant Nos	Name	DOB	Hospital or Practice Nos	Home postcode	Date of Recruitment	Date of Informed Consent (T1)	Date of T2	Final Status*
4001								
4002								
4003								
4004								
4005								
4006								
4007								
4008								
4009								
4010								
4011								

* Final Status Key: C = Completed, W = Withdrawn, L = Lost to follow up, O = Other (please specify).

IRAS 214707 Recruitment Log
1

9.4 Appendix 4: Clinical and Socio-Demographic Data Collection Sheet

Does Orthodontic Treatment Improve the Oral Health-Related Quality of Life of Young People with Malocclusion? A Longitudinal, Cohort Study.

Clinician to complete and return to folder.

Today's Date:	Patient Identifier:	D.O.B:	Gender:	Postcode:
---------------	---------------------	--------	---------	-----------

Details of participant's malocclusion

Patients main complaint	
-------------------------	--

Incisor relationship		Overjet (in mm)	Overbite (please tick as appropriate)			
I			Average	Increased	Reduced	Anterior open bite
II	Div 1					
	Div 2		Incomplete		Complete	
III					To hard tissue	To soft tissue

Spacing: <i>(Spacing between the mesial of the 4's or d's)</i>		Upper labial segment		Lower labial segment	
		Combined total	mm	Combined total	mm
		Single largest space	mm	Single largest space	mm

Dental irregularity: <i>(Contact point displacements between the mesial of the 4's or d's)</i>		Upper labial segment		Lower labial segment	
		Combined total	mm	Combined total	mm
		Single largest displacement	mm	Single largest displacement	mm

Developmentally absent teeth:	No		Details:	UR	UL
	Yes			LR	LL

Impacted teeth:	No		Details:	UR	UL
	Yes			LR	LL

IOTN DHC	
----------	--

Type of brace worn (Please tick all that apply)	Removable	Functional	Fixed appliances	Extraction(s)	Other (please specify)

9.5 Appendix 5: Screenshot of Electronic Patient Questionnaire

QuestionsResponses9Settings

End of Waiting list Questionnaire (11-17 yrs)

B *I* U

Participants Aged 11 to 17 years

Thank you very much for helping us.

We are doing this study to better understand how young people feel about their teeth and themselves.

Please read each statement carefully and choose the answer that best describes how you feel about your teeth.

There are no right or wrong answers - we want to know how you really feel.

Some things to keep in mind:

- Answer the questions as honestly as you can;
- Don't talk to anyone about the questions when you are answering them;
- Before you answer, ask yourself: Does this happen because of my teeth?

Choose the answer that best describes you.

Participant Number: *

Short-answer text

Today's Date: *

Day, month, year

Please look at the 10 pictures of teeth below. It is unlikely that any of these photographs will look exactly like your teeth, but where do you think your teeth are on this scale from picture 1, which shows quite straight teeth to picture 10, which shows very crooked teeth?

9.6 Appendix 6: Ethical and Health Research Approvals, Research Governance & Certificate of insurance.

Page 1



Health Research Authority

North West - Preston Research Ethics Committee

Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 020 71048008

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

16 March 2017

Professor Philip E. Benson
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Sheffield
S10 2TA

Dear Professor Benson

Study title: Does Orthodontic Treatment Improve the Oral Health-Related Quality of Life of Young People with Malocclusion? A longitudinal, Cohort Study
REC reference: 17/NW/0204
IRAS project ID: 214707

The Proportionate Review Sub-committee of the North West - Preston Research Ethics Committee reviewed the above application in correspondence.

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 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.

Ethical opinion

On behalf of the Committee, the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

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").

Summary of discussion at the meeting

Favourable risk benefit ratio; anticipated benefits/risks for research participants (present and future)

It was noted that the IRAS form (A13) referred to following a cohort of patients who had been seen at a new patient appointment and before they started to receive treatment. Follow up would be for a year. There was some initial concern that children might be kept waiting for an appointment due to taking part in the study. However, the protocol confirmed that this cohort would be recruited from practices whether the waiting list was routinely more than a year and the Committee was satisfied with this justification.

Informed consent process and the adequacy and completeness of research participant information

The Committee commented that the Participant Information Sheets and Consent/Assent forms were very clear.

Approved documents

The documents reviewed and approved were:

Document	Version	Date
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [University Insurance Certificate]	1	08 March 2017
IRAS Application Form [IRAS_Form_14032017]		14 March 2017
IRAS Application Form XML file [IRAS_Form_14032017]		14 March 2017
Participant consent form [Assent Young People (<16 yrs)]	1	24 February 2017
Participant consent form [Consent Young People (16 yrs)]	1	24 February 2017
Participant consent form [Consent Parents]	1	24 February 2017
Participant information sheet (PIS) [PIS Stage 1 Young People]	1	24 February 2017
Participant information sheet (PIS) [PIS Young People (16 yrs)]	1	24 February 2017
Participant information sheet (PIS) [PIS Parents]	1	24 February 2017
Referee's report or other scientific critique report [STH ISR]	v1	27 January 2017
Referee's report or other scientific critique report [Response ISR]	v1	27 January 2017
Research protocol or project proposal [Protocol]	v7	27 January 2017
Summary CV for Chief Investigator (CI) [PB Summary CV]	1	09 November 2016
Summary CV for student [Hanieh Javidi CV]	v1	26 January 2017
Summary CV for student [Keegan Gowans CV]	v1	24 January 2017
Summary CV for supervisor (student research) [PB Summary CV]	1	09 November 2016
Summary CV for supervisor (student research) [SC Summary CV]	1	09 November 2016
Validated questionnaire [Pre-treatment Questionnaire 11-16yrs]	1	24 February 2017
Validated questionnaire [Post-treatment Questionnaire 11-17yrs]	1	24 February 2017
Validated questionnaire [Post-treatment Questionnaire >18yrs]	1	24 February 2017

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Karen Rouse declared an interest.

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.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received 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/>

HRA Training

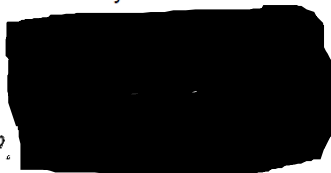
We are pleased to welcome researchers and R&D staff at our training days – see details at <http://www.hra.nhs.uk/hra-training/>

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

17/NW/0204

Please quote this number on all correspondence

Yours sincerely



Dr Rob Monks
Chair

Email: nrescommittee.northwest-preston@nhs.net

Enclosures:

List of names and professions of members who took part in the review

“After ethical review – guidance for researchers”

Copy to:

*Ms Samantha Walmsley, Sheffield Teaching Hospitals NHS Foundation
Trust*

North West - Preston Research Ethics Committee

Attendance at PRS Sub-Committee of the REC meeting March 2017

Committee Members:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Professor Carol Haigh	Professor of Nursing	Yes	
Dr Rob Monks	Principal Lecturer in Nursing, Research and Innovation Lead	Yes	
Dr Karen Rouse	Principal Postgrad Programmes	Yes	

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Mrs Carol Ebenezer	REC Manager



Health Research Authority

North West - Preston Research Ethics Committee

Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Tel: 020 71048008

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

05 June 2017 revised

Professor Philip E. Benson
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Sheffield
S10 2TA

Dear Professor Benson

Study title:	Does Orthodontic Treatment Improve the Oral Health-Related Quality of Life of Young People with Malocclusion? A longitudinal, Cohort Study
REC reference:	17/NW/0204
Amendment number:	1
Amendment date:	16 May 2017
IRAS project ID:	214707

Addition of several PIS for control group and changes to documents amending IRAS number

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

The members had no ethical issues with this amendment.

Approved documents

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Notice of Substantial Amendment (non-CTIMP)	1	16 May 2017
Other [Hanieh Javidi CV]	2	16 May 2017
Other [PB CV]		18 October 2016
Other [SJC CV]	2	16 May 2017
Other [Post-Treat Questionnaire (11-17yrs)]	2	16 May 2017
Other [Keegan Gowans CV]		24 January 2017
Other [Post-Treat Questionnaire 18yrs & Over]	2	16 May 2016
Other [Pre-Treat Questionnaire (11-16yrs)]	2	16 May 2017
Participant consent form [(16yrs)]	2	16 May 2017
Participant consent form [(parents)]	2	16 May 2017
Participant consent form [Assent 11-15 years]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (11-15yrs)]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (11-15yrs-Control)]	1	16 May 2017
Participant information sheet (PIS) [Information Sheets (16 yrs)]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (16 yrs-Control)]	1	16 May 2017
Participant information sheet (PIS) [Information Sheets (Parent)]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (Parent-Control)]	1	16 May 2017
Research protocol or project proposal	8	16 May 2017

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

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.

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

17/NW/0204:	Please quote this number on all correspondence
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Yours sincerely



Dr Rob Monks
Chair

E-mail: nrescommittee.northwest-preston@nhs.net

Enclosures: List of names and professions of members who took part in the review

Copy to: Ms Samantha Walmsley, Sheffield Teaching Hospitals NHS Foundation Trust

North West - Preston Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 05 June 2017

Committee Members:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Professor Carol Haigh	Professor of Nursing	Yes	
Dr Rob Monks	Principal Lecturer in Nursing, Research and Innovation Lead	Yes	

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Mrs Carol Ebenezer	REC Manager

Professor Philip E. Benson
Academic Unit of Oral Health and Development
School of Clinical Dentistry
Sheffield
S10 2TA

Email: hra.approval@nhs.net

19 June 2017 Reissued 05 September 2017

Dear Professor Benson,

Letter of HRA Approval

Study title:	Does Orthodontic Treatment Improve the Oral Health-Related Quality of Life of Young People with Malocclusion? A longitudinal, Cohort Study
IRAS project ID:	214707
REC reference:	17/NW/0204
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](http://www.hra.nhs.uk), 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](http://www.hra.nhs.uk).

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.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application

IRAS project ID	214707
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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/>.

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details at <http://www.hra.nhs.uk/hra-training/>

Your IRAS project ID is **214707**. Please quote this on all correspondence.

Yours sincerely

Miss Lauren Allen
Assessor

Email: hra.approval@nhs.net

*Copy to: Ms Samantha Walmsley, Sheffield Teaching Hospitals NHS Foundation Trust
(Sponsor contact and Lead NHS R&D contact)*

NIHR CRN Portfolio Applications Team

Appendix A - List of Documents

The final document set assessed and approved by HRA Approval is listed below.

<i>Document</i>	<i>Version</i>	<i>Date</i>
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [University Insurance Certificate]	1	08 March 2017
IRAS Application Form [IRAS_Form_14032017]		14 March 2017
Letter from funder		09 May 2017
Notice of Substantial Amendment (non-CTIMP)	1	16 May 2017
Other [Hanieh Javidi CV]	2	16 May 2017
Other [PB CV]		18 October 2016
Other [SJC CV]	2	16 May 2017
Other [Keegan Gowans CV]		24 January 2017
Other [post treat questionnaire 11-17 years]	2	16 May 2017
Other [post treat questionnaire 18 yrs over]	2	16 May 2017
Other [pre treat questionnaire 11-16 years]	2	16 May 2017
Participant consent form [(16yrs)]	2	16 May 2017
Participant consent form [(parents)]	2	16 May 2017
Participant consent form [Assent 11-15 years]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (11-15yrs)]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (11-15yrs-Control)]	1	16 May 2017
Participant information sheet (PIS) [Information Sheets (16 yrs)]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (16 yrs-Control)]	1	16 May 2017
Participant information sheet (PIS) [Information Sheets (Parent)]	2	16 May 2017
Participant information sheet (PIS) [Information Sheets (Parent-Control)]	1	16 May 2017
Referee's report or other scientific critique report [STH ISR]	v1	27 January 2017
Referee's report or other scientific critique report [Response ISR]	v1	27 January 2017
Research protocol or project proposal	8	16 May 2017

Appendix B - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in England, please refer to the, *participating NHS organisations, capacity and capability and Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections in this appendix.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Name: Ms Samantha Walmsley
Tel: 0114 2265932
Email: samantha.walmsley@sth.nhs.uk

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	The applicant has confirmed that the study involves questionnaires only and there will be no participant interviews. The applicant has confirmed that further sites will be added as an amendment.
2.1	Participant information/consent documents and consent process	Yes	No comment
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	An agreement will not be required as this is a non-commercial single site study where the single site is also the study sponsor.
4.2	Insurance/indemnity arrangements assessed	Yes	The applicant has confirmed that insurance/indemnity for the design of the study will be covered by the University of Sheffield. A copy of the

Section	HRA Assessment Criteria	Compliant with Standards	Comments
			insurance has been provided. Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this research study
4.3	Financial arrangements assessed	Yes	The research is funded by the Royal College of Surgeons of England
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	Data will be stored at the University of Sheffield. Members of the study team will be responsible for transferring the data securely.
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	A Substantial Amendment has been approved to add participant information sheets for the control groups and to correct the IRAS project ID.
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

There is one site type. Participants will be identified by the clinical care team. A named contact at the site will take consent and administer questionnaires.

If this study is subsequently extended to other NHS organisation(s) in England, an amendment should be submitted to the HRA, with a Statement of Activities and Schedule of Events for the newly participating NHS organisation(s) in England.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.

This is a single site study sponsored by the site. The R&D office will confirm to the CI when the study can start.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).

A Principal Investigator should be identified at the site to identify participants, take consent and administer the questionnaire.

GCP training is not a generic training expectation, in line with the [HRA statement on training expectations](#).

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken

IRAS project ID	214707
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No access arrangements will be needed for study activity conducted by staff employed by the site. External staff (e.g. University or other NHS Trust) will be expected to obtain a Letter of Access to conduct study activity at the site. Enhanced Disclosure and Barring Service and Occupational Health checks will need to be confirmed where a Letter of Access is in place.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.

- The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.



Health Research Authority

North West - Preston Research Ethics Committee

Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Tel: 02071048234

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implemented at NHS sites in England until the outcome of the HRA assessment has been confirmed.

30 October 2018

Dr Hanieh Javidi
Academic Clinical Fellow
University of Sheffield
Academic Unit of Oral Health and Development,
School of Clinical Dentistry
Sheffield
S10 2TA

Dear Dr Javidi

Study title:	Does Orthodontic Treatment Improve the Oral Health-Related Quality of Life of Young People with Malocclusion? A longitudinal, Cohort Study
REC reference:	17/NW/0204
Amendment number:	2
Amendment date:	30 August 2018
IRAS project ID:	214707

- Following patient feedback the team would like to remove the need for 7 days to think about joining the study. The protocol, consent form and PIS documents have been amended to incorporate this change and section A31 in IRAS.
- The follow-up questionnaire has been amended
- All the PIS have been amended to incorporate a statement following the introduction of the GDPR.

Participant information sheet (PIS) [Information Sheets (Parent) Control]	2	04 September 2018
Participant information sheet (PIS) [Information Sheets (Parent) treatment]	3	04 September 2018
Participant information sheet (PIS) [Information Sheets (Parent) treatment - Tracked Changes]	3	04 September 2018
Research protocol or project proposal [Sp Practice Long Cohort Protocol - Tracked Changes]	9	30 August 2018
Research protocol or project proposal [Sp Practice Long Cohort Protocol]	9	30 August 2018

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

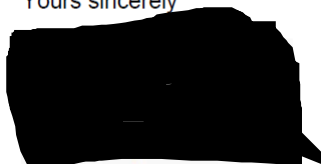
Statement of compliance

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.

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

17/NW/0204:	Please quote this number on all correspondence
--------------------	---

Yours sincerely



**On Behalf Of
Professor Carol Haigh
Chair**

E-mail: nrescommittee.northwest-preston@nhs.net

Enclosures: List of names and professions of members who took part in the review

- There has been the addition of a new site (Devon) as per the updated list of sites

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

The sub-committee did not raise any ethical issues.

Approved documents

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Non-validated questionnaire [End of waiting list Questionnaire (11-17yrs)]	1	30 August 2018
Non-validated questionnaire [End of waiting list Questionnaire (18yrs_Over)]	1	30 August 2018
Non-validated questionnaire [Post-Treat Questionnaire (11-17yrs)]	3	30 September 2018
Non-validated questionnaire [Post-Treat Questionnaire (11-17yrs) - Tracked Changes]	3	30 September 2018
Non-validated questionnaire [Post-Treat Questionnaire (18yrs_Over)]	3	30 August 2018
Non-validated questionnaire [Post-Treat Questionnaire (18yrs_Over) - Tracked Changes]	3	30 August 2018
Notice of Substantial Amendment (non-CTIMP) [Amendment Form]	2	30 August 2018
Other [List of Sites]	4.0	26 September 2018
Participant consent form [Consent (16yrs)]	3	04 September 2018
Participant consent form [Consent (16yrs) - Tracked Changes]	3	04 September 2018
Participant consent form [Consent (Parents)]	3	04 September 2018
Participant consent form [Consent (Parents) - Tracked Changes]	3	04 September 2018
Participant consent form [Assent (11-15yrs)]	3	04 September 2018
Participant consent form [Assent (11-15yrs) - Tracked Changes]	3	04 September 2018
Participant information sheet (PIS) [Information Sheets (11-15yrs) Control]	2	04 September 2018
Participant information sheet (PIS) [Information Sheets (11-15yrs) Control - Tracked Changes]	2	04 September 2018
Participant information sheet (PIS) [Information Sheets (11-15yrs) Treatment]	3	04 September 2018
Participant information sheet (PIS) [Information Sheets (11-15yrs) Treatment - Tracked Changes]	3	04 September 2018
Participant information sheet (PIS) [Information Sheets (16 yrs) Control]	2	04 September 2018
Participant information sheet (PIS) [Information Sheets (16 yrs) Control - Tracked Changes]	2	04 September 2018
Participant information sheet (PIS) [Information Sheets (16 yrs) Treatment]	3	04 September 2018
Participant information sheet (PIS) [Information Sheets (16 yrs) Treatment - Tracked Changes]	3	04 September 2018
Participant information sheet (PIS) [Information Sheets (Parent) Control - Tracked Changes]	2	04 September 2018

North West - Preston Research Ethics Committee

Attendance at Sub-Committee of the REC meeting on 26 October 2018

Committee Members:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Professor Carol Haigh	Professor of Nursing	Yes	
Professor Karen Wright	Professor of Nursing	Yes	

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Miss Nafeesa Khanam	REC Assistant

From: hra.amendments@nhs.net [mailto:noreply@harp.org.uk]
Sent: 08 January 2019 09:06
To: Benson, P (Sheffield University); Walmsley, Samantha (Research)
Cc: Patel, Dipak (Research)
Subject: IRAS Project ID 214707. HRA Approval for the Amendment

Dear Professor Benson,

IRAS Project ID:	214707
Short Study Title:	Orthodontic Longitudinal Cohort
Amendment No./Sponsor Ref:	2
Amendment Date:	30 August 2018
Amendment Type:	Substantial Non-CTIMP

I am pleased to confirm **HRA and HCRW Approval** for the above referenced amendment.

You should implement this amendment at NHS organisations in England and Wales, in line with the conditions outlined in your categorisation email.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received 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/>.

Please contact hra.amendments@nhs.net for any queries relating to the assessment of this amendment.

Kind regards

Steph Blacklock

Health Research Authority

Ground Floor | Skipton House | 80 London Road | London | SE1 6LH

E: hra.amendments@nhs.net

W: www.hra.nhs.uk

Thank you for submitting an amendment to add one or more new sites to your project

If you have listed new sites in any other UK nations we will forward the information to the national coordinating function(s) for nations where the new site(s) are being added. In Northern Ireland, Scotland and Wales, NHS/HSC R&D offices will be informed.

What Happens Next?

Please set up the new site(s) as per the guidance found within IRAS. **Please note** that processes change from time to time so please use the most up to date guidance about site set up.

If your study is supported by a research network, please contact the network as early as possible to help support set up of the new site(s).

IRAS Project ID:	214707
Short Study Title:	Orthodontic Longitudinal Cohort
Date complete amendment submission received:	18/08/2017
Sponsor Amendment Reference Number:	NonSub1
Sponsor Amendment Date:	16/08/2017
Amendment Type	Non-substantial
For new sites in Northern Ireland, Scotland and/or Wales only:	Please start to set up your new sites. Sites may not open until NHS management permission is in place.
For new sites in England only:	For studies which already have HRA Approval: This email also constitutes HRA Approval for the amendment, and you should not expect anything further from the HRA. Please start to set up your new sites. Sites may not open until the site has confirmed capacity and capability (where applicable). For studies which do not yet have HRA Approval: HRA Approval is pending and you will receive confirmation of HRA Approval. You can start the process of setting up the new site but cannot open the study at the site until HRA Approval is in place and the site has confirmed capacity and capability (where applicable).

If you have any questions relating to setting up sites in England, please direct these to hra.approval@nhs.net.

If you have any questions relating to setting up sites in Northern Ireland, Scotland or Wales, please direct these to the relevant national coordinating function.

Note: you may only implement changes described in the amendment notice.

Please do not hesitate to contact me if you require further information.

Kind regards

New Site Amendment: Implementation Information

Dear Hanieh Javidi,

IRAS Project ID:	214707
Short Study Title:	Orthodontic Longitudinal Cohort
Date complete amendment submission received:	02/04/2018
Sponsor Amendment Reference Number:	NSA 2 - addition of 2 new NHS sites to the study - The Orthodontic Practice, Mansfield Nottingham and The Orthodontic Clinic, Sheffield
Sponsor Amendment Date:	02 April 2018
Amendment Type:	Non-substantial
For new sites in Northern Ireland, Scotland and/or Wales only:	Please start to set up your new sites. Sites may not open until NHS management permission is in place.
For new sites in England only:	For studies which already have HRA Approval. This email also constitutes HRA Approval for the amendment, and you should not expect anything further from the HRA. Please start to set up your new sites. Sites may not open until the site has confirmed capacity and capability (where applicable).

Thank you for submitting an amendment to add one or more new sites to your project. This amendment relates solely to the addition of **new sites**.

What should I do next?

Please set up the new site(s) as per the guidance found within IRAS. **Please note** that processes change from time to time so please use the most up to date guidance about site set up.

If your study is supported by a research network, please contact the network as early as possible to help support set up of the new site(s).

If you have listed new sites in any other UK nations we will forward the information to the national coordinating function(s) for nations where the new site(s) are being added. In Northern Ireland, Scotland and Wales, NHS/HSC R&D offices will be informed by the national coordinating function.

Note: you may only implement changes described in the amendment notice.

Who should I contact if I have further questions about this amendment?

If you have any questions about this amendment please contact the relevant national coordinating centre for advice:

- England – hra.amendments@nhs.net
- Northern Ireland – research.gateway@hscni.net
- Scotland – nhsq.NRSPCC@nhs.net
- Wales – research.permissions@wales.nhs.uk

Additional information on the management of amendments can be found in the [IRAS guidance](#).

User Feedback

We are continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the amendment procedure. If you wish to make your views known please use the feedback form available at: <http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>.

Please do not hesitate to contact me if you require further information.

Kind regards

Dear Professor Benson,

IRAS Project ID:	214707
Short Study Title:	Orthodontic Longitudinal Cohort
Date complete amendment submission received:	25 May 2018
Amendment No./ Sponsor Ref:	NonSub3
Amendment Date:	25 May 2018
Amendment Type:	Non-substantial
Outcome of HRA and HCRW Assessment	This email also constitutes HRA and HCRW Approval for the amendment , and you should not expect anything further.
Implementation date in NHS organisations in England and/or Wales	35 days from date amendment information together with this email, is supplied to participating organisations (providing conditions are met) .
For NHS/HSC R&D Office information	
Amendment Category	B

Thank you for submitting an amendment to your project. We have now categorised your amendment and please find this, as well as other relevant information, in the table above.

What should I do next?

Please read the information in [IRAS](#), which provides you with information on how and when you can implement your amendment at NHS/HSC sites in each nation, and [what actions you should take now](#)

If you have participating NHS/HSC organisations in any other UK nations please note that **we will** forward the amendment submission to the relevant national coordinating function(s).

If not already provided, please email to us any regulatory approvals (where applicable) once available.

When can I implement this amendment?

You may implement this amendment in line with the information in [IRAS](#). Please note that you may only implement changes described in the amendment notice.

Information relating to the addition of new sites

This amendment also adds new participating NHS/HSC organisations to the study. The 35 day implementation date does not apply to the new sites. Please set up new sites as detailed below (as processes change from time to time, we recommend that you refer to the most up to date guidance about site set up, found within [IRAS](#)).

If your study is supported by a research network, please contact the network as early as possible to help support set up of the new site(s).

For new sites in Northern Ireland and/or Scotland:	Please start to set up your new sites. Sites may not open until NHS/HSC management permission is in place.
For new sites in England and/or Wales:	<u>For studies which already have HRA and HCRW Approval:</u> This email also constitutes HRA and HCRW Approval for the amendment, and you should not expect anything further. Please start to set up your new sites. Sites may not open until the site has confirmed capacity and capability (where applicable). <u>For studies which do not yet have HRA and HCRW Approval:</u> HRA and HCRW Approval for the initial application is pending. You can start the process of setting up the new site but cannot open the study at the site until HRA and HCRW Approval is in place and the site has confirmed capacity and capability (where applicable). <u>For studies with HRA Approval adding Welsh NHS organisations for the first time:</u> Please take this email to confirm your original HRA Approval letter is now extended to cover NHS organisations in Wales. You now have HRA and HCRW Approval. Please start to set up your new sites. Sites may not open until the site has confirmed capacity and capability (where applicable).

Amendment Categorisation and Implementation Information

Dear Professor Benson,

IRAS Project ID:	214707
Short Study Title:	Orthodontic Longitudinal Cohort
Date complete amendment submission received:	20 April 2020
Amendment No./ Sponsor Ref:	NonSub4
Amendment Date:	03 March 2020
Amendment Type:	Non-substantial
Outcome of HRA and HCRW Assessment	This email also constitutes HRA and HCRW Approval for the amendment , and you should not expect anything further.
Implementation date in NHS organisations in England and Wales	35 days from date amendment information together with this email, is supplied to participating organisations (providing conditions are met)
Implementation date in NHS/HSC organisations in Northern Ireland and/or Scotland (remove row if no sites in NI or Scotland)	INSERT DATE (providing conditions are met)
For NHS/HSC R&D Office information	
Amendment Category	A

Thank you for submitting an amendment to your project. We have now categorised your amendment and please find this, as well as other relevant information, in the table above.

What should I do next?

Please read the information in [IRAS](#), which provides you with information on how and when you can implement your amendment at NHS/HSC sites in each nation, and what actions you should take now.

If you have participating NHS/HSC organisations in any other UK nations please note that **we will** forward the amendment submission to the relevant national coordinating function(s).

If not already provided, please email to us any regulatory approvals (where applicable) once available.

When can I implement this amendment?

You may implement this amendment in line with the information in [IRAS](#). Please note that you may only implement changes described in the amendment notice.

Who should I contact if I have further questions about this amendment?

If you have any questions about this amendment please contact the relevant national coordinating centre for advice:

- England – amendments@hra.nhs.uk
- Northern Ireland – research.gateway@hscni.net
- Scotland – nhsg.NRSPCC@nhs.net
- Wales – HCRW.amendments@wales.nhs.uk

Additional information on the management of amendments can be found in the [IRAS guidance](#).

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received 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/>.

Please do not hesitate to contact me if you require further information.

Kind regards

----- Forwarded message -----

From: **New IRAS Dev** <no-reply-iras@hra.nhs.uk>

Date: Fri, 18 Mar 2022 at 12:23

Subject: IRAS 214707. Amendment

To: <h.javidi@sheffield.ac.uk>

IRAS Project ID: 214707

Sponsor amendment reference: Non-substantial amendment 06

Thank you for submitting your study amendment. In accordance with the outcome of your completed amendment tool, this amendment requires no further regulatory review. Please now share this amendment with your UK research sites, in accordance with the instructions in your completed amendment tool.

For studies with more than one UK research site, your amendment will now be automatically shared with the R&D offices of any NHS/HSC research sites in Scotland and Northern Ireland, but you should share the amendment by email directly with those Research team/s.

For all NHS research sites in England and Wales, please now share this amendment by email directly with those sites, including both the R&D offices and research teams.

Do not reply to this email as this is an unmonitored address and replies to this email cannot be responded to or read.

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Trueman House
Capitol Park
Leeds
LS27 0TS

Tel 0113 393 6300

To Whom It May Concern

Date: 28th September 2020
Our Ref: 17827891

EVIDENCE OF INSURANCE - The University of Sheffield and Subsidiary Companies

We are writing to confirm that we act as Insurance Brokers to the above client and that we have arranged liability insurance on their behalf as detailed below:

CLINICAL TRIALS

Legal liability in respect of accidental injury of any research subject arising out of a Clinical Trial carried out in the course of University activities.

INSURER	:	Lloyds of London Newline Underwriting Management Ltd, Syndicate 1218 Suite 5 / 4, The London Underwriting Centre, 3 Minster Court, Mincing Lane, London EC3R 7DD
POLICY NUMBER	:	WIBCLT16227
PERIOD OF INSURANCE	:	29 th September 2020 – 28 th September 2021
LIMIT OF INDEMNITY	:	£10,000,000 any one event and in the annual aggregate
SITUATION	:	Clinical Trials held in the United Kingdom

All policies are subject to the terms, conditions and exceptions of the policies themselves. The information provided is based on the insurance arrangements at the time of writing. Alterations may be made during the period of cover. We have no obligation to advise you of any changes which may be made to the policies or advise you of their cancellation or termination.

Please do not hesitate to contact us if you have any queries.

Yours faithfully,



Gail Schofield | Senior Broker
T: 0113 393 6338 E: gail.schofield@aon.co.uk

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To Whom It May Concern

Our ref: TK/IND

25 September, 2019

Zurich Municipal Customer: University of Sheffield and Subsidiary Companies

This is to confirm that University of Sheffield and Subsidiary Companies has in force with this Company until the policy expiry on 28 September 2020 Insurance incorporating the following essential features:

Policy Number: NHE-03CA06-0013

Limit of Indemnity:

Public Liability: £ 30,000,000

Products Liability: £ 30,000,000

Pollution:

any one event
for all claims in the
aggregate during
any one period of
insurance

Employers' Liability: £ 30,000,000

any one event
inclusive of costs

Excess:

Public Liability/Products Liability/Pollution:

Nil any one
event

Employers' Liability:

Nil any one
claim

Indemnity to Principals:

Covers include a standard Indemnity to Principals Clause in respect of contractual obligations.

Full Policy:

The policy documents should be referred to for details of full cover.

Yours faithfully



Underwriting Services
Zurich Municipal

Zurich Municipal
Zurich House
1 Gladiator Way
Farnborough
Hampshire
GU14 6GB

Telephone: 0800 335500
E-mail:
paul.3.green@uk.zurich.com

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name Zurich Insurance plc
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Registration No. 13460

Registered Office: Zurich House,
Ballsbridge Park, Dublin 4,
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UK Branch registered in England
and Wales Registration No.
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UK Branch Head Office: The
Zurich Centre, 3000 Parkway,
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Our FCA Firm Reference Number
is 203093.

MSTDNA01

Sent on behalf of Prof Simon Heller, Director of R&D, Sheffield Teaching Hospitals NHS FT

Dear Philip

STH ref:	19669
IRAS Number:	214707
Study Title:	Does Orthodontic Treatment Improve the Oral Health-Related Quality of Life of Young People with Malocclusion? A longitudinal, Cohort Study
Principal Investigator:	Professor Philip Benson, University of Sheffield
NIHR Target FFPV recruitment Date:	28Aug2017

The Research Department has received the required documentation as listed below:

1.	Clinical Trial Agreement Material Transfer Agreement Statement of Activities Sponsor Monitoring Arrangements	N/A N/A N/A N/A
2.	Local ARSAC certificate/IRMER assessment	N/A
3.	Evidence of local Capacity and Capability - STH Principal Investigator - Clinical Director - General Manager - Research Finance - Data Protection Officer	P. Benson, 01Sep2017 A. Loescher, 29Jul2017 K. Allred, 21Jul2017 L. Fraser, 08Sep2017 P. Wilson, 31Aug2017
4.	Honorary Contract/Letter of Access	N/A
5.	Protocol	V8.0, 16May2017
6.	Additional Approvals noted: NHS REC approval letter HRA Approval	North West – Preston REC 16Mar2017 (FO) 05June2017 (SA01) 19June2017 27June2017 (SA01) 26Aug2017 (NSA01)

This email confirms that Sheffield Teaching Hospitals NHS Foundation Trust has the capacity and capability to deliver the above referenced study. Please find attached our Conditions of Confirmation of Capacity and Capability. We agree to start this study on 01Oct2017, as previously discussed. This will effectively be the date of **Sponsor Green Light**. If you wish to discuss further, please do not hesitate to contact me.

Kind regards

Sam

9.7 Appendix 7: Histograms Illustrating the Change in Response of the GOH2-5 in the Orthodontic Treatment Group and the Waiting List Control Group using the Wilcoxon Signed Rank Test

