Severe hypodontia – interdisciplinary planning, outcome and psychosocial impact

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Doctoral thesis for the degree of Philosophiae Doctor (Ph.D.)

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Faculty of Dentistry
University of Oslo
Norway
2016
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Series of dissertations submitted to the
Faculty of Dentistry, University of Oslo


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Cover: Hanne Baadsgaard Utigard.
Print production: Reprosentralen, University of Oslo.
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Acknowledgements

This project was financed by the Faculty of Dentistry at the University of Oslo. The research is based on a unique collection on clinical data from patients with hypodontia gathered since the inception of “Eksperttjenesten” in 1998 at the Department of Orthodontics, Faculty of dentistry, University of Oslo. This systematic collection of quality records to which I was given free access, formed the basis for my research.

I am deeply grateful to my principal supervisor Associate Professor Kari Birkeland for her scientific guidance, for sharing her great insight in orthodontics, and for her always-positive enthusiasm and commitment to this project. Her dedication and effort in always seeking the best possible solution for patients with very complex dental issues has truly inspired me. I also wish to express my sincere gratitude to my co-supervisor Professor Bjørn Øgaard who has kindly shared his extensive knowledge and experience in orthodontics. His accurate and constructive guidance, as well as his friendly and encouraging nature, have been invaluable in this process.

I would also like to thank Professor Anne N. Åstrøm at the Faculty of Dentistry, University of Bergen for her excellent guidance and scientific competence in the field of community dentistry, and Professor Arild Stenvik who has provided inspiration and great ideas for the project. Profound thanks to Professor Leiv Sandvik for his statistical support, and the way he always makes the statistical sessions memorable and interesting.

My appreciation extends to the staff at the Department of Orthodontics, always kind and helpful. I have spent three years with my seven fellow specialist candidates, and would like to thank them for exciting and eventful years in a close-knit group of unique and humorous individuals.

My faithful and patient friends have always been a big support, reminding me of what is important in life. The quality time we spend hanging out together forms my absolute favourite moments. My family and in-laws’ support, inspiration and care throughout this journey have been priceless. Thank you for your kind encouragement and always believing in me. Special thanks go to my mother and mother-in-law for taking care of my son Albert during long working sessions. Another special thank you goes to my father for interesting and challenging discussions in the field of orthodontics.
Finally, and most of all, I would like to thank my husband Tore for his eternal and patient support and care. He has spent hours proofreading my work and helping me with technical statistical computerish problems. My greatest love goes to him and our beautiful son Albert.

Oslo, November 2016

Christina L. Hvaring
List of papers

This thesis is based on original research carried out at the Department of Orthodontics, Faculty of Dentistry, University of Oslo. The thesis includes three papers listed below, which will be referred to by their Roman numerals in the text.

Paper I

Paper II

Paper III
## Abbreviations

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<th>Abbreviation</th>
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<tr>
<td>COHIP</td>
<td>Child Oral Health Impact Profile</td>
</tr>
<tr>
<td>CPQ</td>
<td>Child Perceptions Questionnaire</td>
</tr>
<tr>
<td>CS OIDP</td>
<td>Condition specific Oral Index on Daily Performances</td>
</tr>
<tr>
<td>CS</td>
<td>Condition specific</td>
</tr>
<tr>
<td>DHC</td>
<td>Dental health component</td>
</tr>
<tr>
<td>ED</td>
<td>Ectodermal dysplasia</td>
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<tr>
<td>FDP</td>
<td>Fixed dental prosthesis</td>
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<tr>
<td>ICC</td>
<td>Intraclass correlation coefficient</td>
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<tr>
<td>ICIDH</td>
<td>International Classification of Impairments, Disabilities and Handicap</td>
</tr>
<tr>
<td>IOTN</td>
<td>Index of Orthodontic Treatment Need</td>
</tr>
<tr>
<td>MIQ</td>
<td>Malocclusion Impact Questionnaire</td>
</tr>
<tr>
<td>miRNA</td>
<td>Micro-RNA</td>
</tr>
<tr>
<td>OHIP</td>
<td>Oral Health Impact Profile</td>
</tr>
<tr>
<td>OHRQoL</td>
<td>Oral health-related quality of life</td>
</tr>
<tr>
<td>OIDP</td>
<td>Oral Index on Daily Performances</td>
</tr>
<tr>
<td>OQLQ</td>
<td>Orthognathic Quality of Life Questionnaire</td>
</tr>
<tr>
<td>RPD</td>
<td>Removable partial denture</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for the Social Sciences</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom of Great Britain and Northern Ireland</td>
</tr>
<tr>
<td>USA</td>
<td>United States of America</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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Summary

The general purpose of this thesis was to increase the knowledge and understanding of treatment outcome and psychosocial status in patients with severe hypodontia.

Paper I is a retrospective study aiming at pointing out the limiting prognostic factor for the persistence of primary mandibular molars whose successors are lacking. Primary mandibular molars and their degree of infraocclusion, root resorption and restorations were assessed on panoramic radiographs in 111 subjects missing at least one second mandibular premolar. The patients had a mean age of 12.6 years and missed 8.4 teeth on average. All persisting primary mandibular molars were included in the study, as no decision had been made as to whether they should be kept or extracted. Clinically significant infraocclusion was observed in 43.6 per cent of the patients and classified as severe in 18.8 per cent. The mesial and distal root exhibited no resorption in 18.9 and 33.3 per cent, respectively (P = 0.01). Most primary molars had no restorations (78.4 per cent). A significant correlation was found between root resorption and infraocclusion. Infraocclusion was estimated to be a more critical factor for the prognosis of retained primary molars than root resorption.

Paper II is a cross-sectional survey assessing the discriminative ability of the generic and condition specific (CS) forms of the oral impact on daily performance (OIDP) inventory among adolescents with hypodontia and with a malocclusion of similar treatment need. The groups consisted of 62 patients with non-syndromic hypodontia and 101 patients with a malocclusion. The mean number of missing teeth in the hypodontia group was 6.2. Both groups reported a considerable burden of oral impacts. The prevalence of generic and CS oral impacts in the hypodontia group were 64% and 30%, respectively, and the corresponding rates in the non-hypodontia group were 62% and 10%. The CS OIDP measure discriminated most effectively between patients with and without hypodontia and was related to severity and upper anterior location of hypodontia.

Paper III is a longitudinal follow-up study of 50 patients with severe hypodontia aged 18 years or more (mean age, 25.6 years). The purpose of the study was to describe types and locations of substitutes for missing teeth in patients with severe hypodontia, and to compare the crown and soft tissue morphologies of orthodontic space closure, dental implants, and tooth-supported fixed dental prostheses replacing teeth in the anterior region. The patients were examined clinically, with panoramic radiographs and clinical photographs being taken. Dental implants, orthodontic space closure, and retaining deciduous teeth were the most commonly prescribed treatments. Persisting deciduous teeth showed a good survival rate at the follow-up examination. Dental implants in the anterior region proved to be an inadequate
treatment modality in patients with severe hypodontia because of mucosal discoloration seen for almost all fixtures in the anterior mandible and two thirds of those in the anterior maxilla.
Introduction

Hypodontia

Definitions

Hypodontia is a congenital condition of having fewer teeth than the normal number of teeth. The word originates from Greek where hypo means under and odous means tooth. The condition is the most common dental anomaly in man (2, 3), and the term hypodontia is used to describe congenitally missing teeth in general. Various synonyms have been used in the literature to describe the phenomenon: oligodontia, anodontia, aplasia of teeth, agenesis of teeth, congenitally missing teeth and lack of teeth. Agenesis of teeth is perhaps the most precise definition, referring to the failure of an organ to develop during embryonic growth. Schalk-van der Weide et al. (4) defined oligodontia as a condition in which six or more teeth, excluding third molars, are congenitally missing. The author defined two forms of oligodontia: oligodontia/I (isolated) and oligodontia/S (syndrome), as the condition can occur alone or as part of a syndrome (4). Severe hypodontia was considered by Hobkirk et al. (5) to be the same as oligodontia, and the definition is commonly used in the dental literature. Anodontia is a rare developmental dental anomaly characterized by absence of all teeth. These definitions of hypodontia, oligodontia/severe hypodontia and anodontia will be used in this thesis.

Prevalence

The reported prevalence of hypodontia varies depending on population and gender. Because of its high frequency and limited functional importance, lack of third molars is usually excluded from the definition of hypodontia, as is the case in the present thesis. Absence of at least one third molar has been reported in as much as 20-30% of the European population (6, 7). A meta-analysis by Polder et al. (8) in 2004 reviewed 31 studies of the prevalence of hypodontia published from 1936 to 2001. The same year, Mattheeuws et al. (9) performed a meta-analysis including 19 articles from 1936 to 1993 concerning a possible increase in hypodontia during the 20th century. The authors concluded that the considered period of time was too short and the available data too limited to describe a trend in the human dentition. However, hypodontia seems to have been diagnosed more often in recent studies. In 2014, Khalaf et al. (1) published an updated meta-analysis extending the two already mentioned with additional data from articles published after 2002. The authors included 93 studies, of which 39 studies were taken from the previous two systematic reviews. The overall
prevalence of hypodontia was found to be 6.4% (95% CI: 5.7-7.2). Table 1 shows the prevalence of hypodontia in schoolchildren. Fifteen of these 27 studies were from the Nordic countries. The variation in reported prevalence may be due to differences in methods of sampling, age distribution, gender and racial origin. The assessment of congenitally missing teeth in younger individuals might also be inaccurate due to the occasionally insufficient mineralisation of the mandibular second premolar (10). A study by Wisth et al. (10) found that the prevalence of hypodontia was higher when the same patient sample was examined at the age of 7 years, as compared to when it was examined at 9 years of age. The meta-analysis by Khalaf et al. (1) revealed a statistically significant difference in prevalence by continent, with the highest prevalence in Africa (13.4%) followed by Europe (7%), Asia (6.3%), Australia (6.3%), North America (5%) and Latin America and the Caribbean (4.4%). Furthermore, the prevalence among females was 1.22 times that among males. In general, hypodontia is mild (1 or 2 teeth missing) in most subjects (82%) (1), whereas oligodontia is much more rare. A Norwegian study examined 9532 subjects in two counties aged 18 years, and found 0.084% with oligodontia (11). Furthermore, two studies from Denmark and Netherlands reported a prevalence of oligodontia of 0.16% and 0.08% respectively (12, 13).
Table 1. Prevalence of hypodontia in schoolchildren from various countries according to Khalaf et al. (1)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Age</th>
<th>Sample size</th>
<th>Prevalence (%)</th>
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Characteristics

The distribution of congenitally missing teeth by tooth type is shown in Figure 1. The most commonly missing tooth, in most studies, is the mandibular second premolar, followed by the maxillary lateral incisor and the maxillary second premolar (1). However, this distribution varies between populations. In a Norwegian study, 50% of the missing teeth were mandibular premolars, 20% maxillary second premolars, 16% maxillary lateral incisors and 4% mandibular central incisors (14). In a study of Chinese schoolchildren, the most commonly affected teeth were the mandibular incisors, followed by the upper second premolars and the upper lateral incisors (15). Absence of maxillary central incisors, maxillary and mandibular first molars, and mandibular canines seems to be very rare. No clear difference in congenitally missing teeth has been found between the maxilla and mandible and between the right and the left side (16). Unilateral hypodontia is most common, with the exception of maxillary lateral incisors, where bilateral lack of teeth is most often seen (8).

Associated skeletal effects

The craniofacial structure and growth pattern of patients with hypodontia have been assessed in a number of cephalometric studies. Some studies have reported a Class I skeletal
relationship and a normal growth pattern (17-19), while others have reported a smaller and more retrognathic maxilla with a tendency towards a Class III skeletal pattern (20-23). The hypodontia patients also have a tendency towards a reduced anterior lower face height and a decrease in the mandibular plane angle (22, 24). These tendencies become more evident as the severity of the hypodontia increases (23, 24). A study by Ogaard et al. (24) compared the craniofacial morphology of hypodontia patients with a varying number of missing teeth. When more than 10 teeth were missing, the maxillary protrusion was significantly reduced and the mandible rotated anteriorly, probably as a consequence of less posterior support.

Associated dental anomalies

Hypodontia is frequently accompanied by reduction in tooth size (microdontia), short root anomaly, malformation of other teeth, impaction, maxillary canine and first premolar transposition, delayed formation or eruption of teeth, taurodontism, enamel hypoplasia and altered craniofacial growth (7). A phenotype of congenital absence of a maxillary lateral incisor on one side and a peg-shaped lateral incisor on the other side is common; these two anomalies are considered different manifestations of the same genotype (7).

Etiology

Several theories on the etiology of hypodontia have been proposed in the literature (2). Brook (25), (26) suggested a unifying aetiological explanation for anomalies of tooth number and size, and argued that hypodontia is caused by a number of complex interactions between genetic, epigenetic and environmental factors during the process of dental development. Kjaer (27) refers to embryological investigations showing the existence of neural development fields in the jaws and dentition, namely the incisor field, the canine/premolar field and the molar field. The hypothesis is that agenesis of teeth might be the result of deviations in nerve tissue proliferation in a field during embryogenesis, resulting in lack of formation of hard tissue, such as teeth. The region within a single field where innervation occurs last is more likely to manifest tooth agenesis.

Environmental factors

Hypodontia may be associated with environmental factors such as infections, trauma in the dental region, surgical procedures on the jaws or extraction of the preceding primary tooth (7). Somatic diseases such as syphilis, scarlet fever, rickets, or nutritional disturbances during pregnancy or infancy may also affect tooth development (2). Developing teeth are irreversibly
affected by multi-agent chemotherapy and radiation therapy, with the latter having the strongest adverse impact (28).

**Genetics**
The genetic basis is the most important factor in the etiology of hypodontia, and the occurrence of hypodontia among individuals related to hypodontia patients is higher than in the general population (2, 7, 16, 29). Non-syndromic hypodontia is more common than the syndromic variant, and the condition can follow autosomal dominant, autosomal recessive or X-linked patterns of inheritance, with variations in penetrance and expressivity (30). Since the condition segregates in families, strategies for gene identification can be performed. The genes PAX9, MSX1, AXIN2, EDA, EDAR, EDARADD, and WNT10A have been described as being involved in tooth development (2, 16, 30), and mutations of these may disrupt the epithelial-mesenchymal interactions necessary for tooth formation. In 2009, Shimizu et al. (30) published a review of genetic studies addressing hypodontia in humans and mouse models. The authors concluded that although recent genetic studies provide information regarding genes related to hypodontia, the causes of the most common form of hypodontia are still unknown. It is therefore likely that other hypodontia-related genes still exist and will be identified in the future (30). A high discordance rate of hypodontia sub-phenotypes has been established in a study of monozygotic twins; epigenetic influences on spatiotemporal gene regulation might be involved (31). Regulation of gene expression by miRNAs may also affect tooth development (32). Recently, a robust investigation mapping out tooth agenesis patterns and phenotype variation in a Belgian cohort of 67 families with oligodontia and 12 families with hypodontia was published (33). The authors found an extreme variation in the expressivity of the hypodontia/oligodontia between affected family members, and concluded that tooth agenesis is not a simple monogenic condition, but that a complex interaction of genetic and environmental factors comes into play.

**Syndromic hypodontia**
Congenitally missing teeth can occur as an isolated feature or as part of a syndrome. The London dysmorphology database reports 150 syndromes as being associated with hypodontia (34), indicating that the development of teeth and certain organs are under the control of the same molecular mechanisms. Commonly associated syndromes are ectodermal dysplasia, Rieger syndrome, Down syndrome (trisomy 21), Witkop syndrome, van der Woude syndrome, Brook syndrome, hemifacial microsomia and many others (16). Ectodermal dysplasia refers to a heterogeneous inherited disorder characterized by variable defects in the morphogenesis of ectodermal structures including hair, skin, nails, sweat glands, and teeth.
Oral and facial clefts are one of the most common birth anomalies: 1 in every 730 children is born with a cleft lip and/or palate (35). The anomaly is highly associated with hypodontia, with a reported frequency (outside the cleft region) between 17.5% and 31.5% (36).

**Persisting primary teeth without successor**

When a permanent successor tooth is absent, the corresponding primary tooth often remains in place beyond the time it would otherwise be shed. Once a congenitally absent successor has been diagnosed, the choice of treatment must be based on the skeletal relationship, occlusion and space requirements. Persisting primary teeth serve as space maintainers, prevent resorption of the alveolar bone, may function as a semi-permanent solution long into adulthood, and postpone the need for prosthetic replacement. Primary teeth left in situ carry a risk of developing idiopathic root resorption and infraocclusion.

Infraocclusion refers to a tooth that has failed to maintain its occlusal relationship relative to the adjacent teeth. Kurol (37) defined infraocclusion as the occlusal surface of the primary molar being more than 1 mm below the occlusal plane of fully erupted neighbouring teeth. Ankylosis is believed to be the primary pathological process in infraocclusion (38, 39). Dental ankylosis occurs when partial root resorption is followed by either cementum or bone formation, fusing the root and the alveolar bone (40). The mechanism may be due to an imbalance in the normal pattern of resorption and repair, with repair processes prevailing over resorptive ones, leading to excessive deposition of simple lamellar bone and cellular cementum (41). The epithelial cell rests of Malassez are also believed to maintain the function and regeneration of the periodontal membrane (42), and changes in the distribution of these cells have been observed in the periodontium of ankylosed deciduous molars (40). This might indicate a protective role of the epithelial rest of Malassez against root resorption. Genetic factors may also be of importance, as the incidence of ankylosis is much higher amongst siblings (37, 43). In addition, children with one infraoccluded primary molar often develop infraocclusion of additional teeth (37). There is also an association, and most likely a common genetic origin, between infraoccluded teeth and ectopic eruption of first molars, peg-shaped laterals, enamel hypoplasia, palatal displacement of maxillary canines and congenitally absent second premolars (44).

Infraocclusion occurs most commonly in the primary dentition, and the primary mandibular molars are most frequently affected (37). The prevalence of infraoccluded primary molars has been reported to vary between 8% and 14% among Swedish children (45), with an increasing prevalence when the permanent successor tooth is missing. In a retrospective study, 66% of
patients with hypodontia showed infraocclusion of primary molars (46). In a longitudinal study, infraocclusion of the primary mandibular second molar when lacking a successor was found in 52% cases when the patients were 28-29 years (47). The extent of infraocclusion is directly correlated with the rate of facial growth. If the infraocclusion is manifested before the pubertal growth spurt, it may increase to a considerable amount when the velocity of growth is at its peak (48). The ankylosed tooth will not be able to keep up with the vertical growth and simultaneous eruption of the adjacent teeth, which may lead to occlusal disturbances such as tilting of adjacent teeth and supra-eruption of antagonists. Progression of infraocclusion in adults, however, has been reported to be negligible (49). The mandibular second premolar, which is the successor of the primary mandibular second molar, is the most commonly missing tooth with a prevalence of 2.4-4.3% (47). Despite the risk of infraocclusion, the primary canines and mandibular second molars have the longest reported life span among persisting primary teeth without successors (50). As a result, these particular teeth have been the focus of the modest number of publications on the long-term survival of persisting primary teeth left in situ. In general, these studies show a favourable prognosis (47-49, 51, 52), which will be discussed further in the section “Treatment options and methods for replacing missing teeth in growing individuals”.

Other detrimental factors for the prognosis of persisting primary teeth are root resorption and the amount of restorations. Root resorption occurs regardless of whether the permanent successor is present or not, indicating that these processes are, to a great extent, governed by intrinsic factors (40). The resorptive process has been reported not to follow any particular pattern; both individual roots and teeth in the same patient can show completely different degrees of resorption (40). It has also been observed that the rate of resorption of the roots of primary teeth diminishes with age (45, 48, 51).

**Oral health-related quality of life**

**Development**

Several measures of oral health-related quality of life (OHRQoL) have been developed in the recent years in order to improve the understanding of the psychosocial consequences of oral diseases. OHRQoL was defined by Locker et al. (53) as “The impact of oral diseases and disorders on aspects of 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 perception of their life overall”. Adding a subjective dimension to the objective clinical assessment of oral conditions gives a broader insight into oral health (54). There is now a
substantial body of research documenting self-perceived oral health, and the number of indices continues to evolve (55). In general, these measures assess the frequency and/or severity of functional, psychosocial and social impacts associated with oral disorders. They have been referred to as sociodental indicators, subjective oral health status measures, patient-based outcome measures, participant-based outcome measures or OHRQoL measures (55).

The use of patient-based outcome measures, such as OHRQoL, in dentistry emerged in the early 1980s in line with the shift from a biomedical perspective to a broader biopsychosocial model of health (56, 57). OHRQoL is a multi-dimensional approach to the impact of oral disorders on an individual’s life measured from their own viewpoint, and includes subjects’ expectations and values (58). The assessment of the patient perspective offers new opportunities for the improvement of dental care may serve as a basis for the allocation of health care resources (59). OHRQoL questionnaires are used in epidemiological surveys to identify the impact of oral conditions on the quality of life, and in clinical trials to measure the effectiveness of interventions (55). The fundamental aim in all studies using these measures is to detect differences between groups, either at one point in time (e.g. patients with malocclusion or hypodontia) or over time (e.g. pre- and post-treatment) (55). Clearly defined cut-off values for classifying an individual as mildly, moderately or severely compromised on the basis of an OHRQoL measure have not been established.

**Oral Index on Daily Performance**

**Background**

One of the most commonly used OHRQoL instruments is the Oral Index on Daily Performance (OIDP). The scale was developed to measure oral impacts that seriously affect individuals’ daily activities (60), and has proven to be reliable and valid in cross-sectional population-based studies as well as in studies of patients with specific oral disorders (61, 62). The theoretical framework of OIDP is modified from the World Health Organization’s (WHO) International Classification of Impairments, Disabilities and Handicap (ICIDH), which was amended for dentistry by Locker (54). The modification is shown in Figure 2, and is constructed with different consequence variables: impairment, intermediate impacts (pain, discomfort, functional limitation and dissatisfaction with appearance) and ultimate impacts. The first level refers to the oral status or the immediate biophysical outcome of disease, which most clinical indices attempt to measure. The second level addresses the possible earliest negative impacts caused by the oral health status. The dimensions may lead to one another; functional limitation may cause pain, discomfort or dissatisfaction with appearance and vice versa. The third level represents the physical, psychological and social impacts affecting the
ability to perform daily activities, i.e., “ultimate impacts,” which correspond to WHO’s and Locker’s concept of disability and handicap (54, 63). Any of the dimensions in the first and second level can lead to the third level. The advantages of measuring only level three consequences are precise measurement while covering all dimensions, avoiding overscoring of the same impact at each of the levels, the recording of significant impacts only, and the ease of measuring behavioural impacts rather than feeling-state dimensions. Another advantage of the OIDP instrument is that it consists of only eight items: eating, speaking, cleaning teeth, smiling, sleeping, emotional balance, studying, and social contact. The OIDP inventory has been translated into Norwegian, and validated in a representative sample of the Norwegian adult population (64).

**Generic and condition specific**

The OIDP inventory is designed as a generic or condition specific (CS) measure. While the generic inventory assesses the overall impact of oral problems simultaneously, the CS form focuses on impacts attributed to a particular disease or condition. This makes the CS instrument more sensitive to small, but clinically relevant, changes in specific oral diseases (65, 66). This unique characteristic may provide insight into the consequences of an untreated oral condition, and is particularly important when assessing treatment need as well as prioritising dental health care services (67). A couple of studies have compared the generic and CS forms of the OIDP, finding the CS OIDP to discriminate better among groups with or without normative dental treatment requirements for caries, malocclusion, periodontal disease, and traumatic dental injuries (68).
Other health-related quality of life instruments in children and adolescents

Child Perceptions Questionnaire (CPQ)

The questionnaire was developed in Canada, and originally validated in children with caries, malocclusion and craniofacial anomalies. The questionnaire is one of the most widely used (69). It consists of questions divided into four domains, which encompass oral symptoms, functional limitations, emotional and social well-being. The questions assess the child’s opinions, the perceived views of peers about his/her dental appearance and behavioural problems. The CPQ originally consisted of 37 questions; however, in order to facilitate its use in clinical studies and population-based health surveys, the CPQ was shortened to 16 and 8 item versions (70). The CPQ has been translated into Norwegian, but not validated in a Norwegian population (69).

The Oral Health Impact Profile (OHIP)

The OHIP index was originally developed based on Locker’s model of oral health (54). The questionnaire was developed by asking Australians about their experience with oral diseases, and the kinds of consequences that arose from the diseases. The most commonly used experiences were reduced to 49 indicators/questions, which was the basis for the OHIP-49 (71). A shortened version of the OHIP with 14 items was developed later, and is organised into seven dimensions (functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap). The OHIP-14 and its Norwegian translation have been shown to have acceptable reliability, validity and precision (72-74).

Condition-specific measures in orthodontics

A condition-specific measure to assess quality of life in patients with hypodontia was developed in 2011 by Akram et al. (75). A series of focus groups were used to identify four issues (treatment, effect on daily activities, appearance and other peoples’ reactions) of importance for patients with hypodontia. The themes were incorporated into a questionnaire, which was later tested, and proved to be a valid and reliable tool (76). The measure was designed to illustrate how hypodontia affects a person’s quality of life, and how orthodontic treatment might improve it, and also to influence issues such as funding for patients with hypodontia.
Very recently, Patel et al. (77) developed the Malocclusion Impact Questionnaire (MIQ) to measure oral-health related quality of life of young people with malocclusion. Three themes (appearance of teeth, effect on social interactions and oral health/function) related to the impact of malocclusion emerged after semi-structured interviews of patients referred for orthodontic treatment. The themes were used to generate individual items for inclusion in the questionnaire. The items were tested, and reduced to 17 questions. Cross-sectional testing showed that the new MIQ was both valid and reliable (78); however, further evaluation is required to confirm whether the measure is generalizable and has the ability to detect change over time.

A condition-specific measure for patients with severe dentofacial deformities requesting orthognathic treatment, called the Orthognathic Quality of Life Questionnaire (OQLQ) was developed in 2000 by Cunningham et al. (79). The instrument’s content was derived through a literature review and interviews with clinicians and patients. Four clinically meaningful domains were established (social aspects of deformity, facial aesthetics, oral function and awareness of facial deformity), with 22 contributing items/statements. The OQLQ shows good evidence of reliability, validity and responsiveness, suggesting that the instrument may be useful both in clinical trials (e.g. comparing the effects of single jaw and bimaxillary surgery) and in quality assurance.

**Quality of life in patients with hypodontia**

The quality of life in patients with hypodontia has been examined to some extent. Anweigi et al. (80) investigated the impact of mild, moderate and severe hypodontia on OHRQoL in 82 patients using the OHIP-49. All patients experienced one or more impact, with impacts related to appearance being the most prevalent. The number and location of missing permanent teeth was not a good predictor of quality of life. Females reported a higher level of impacts than males. Using the CPQ, Wong et al. (81) assessed the OHRQoL in 25 patients with severe hypodontia and its association to the number of missing teeth. All participants reported OHRQoL impacts. When accounting for retained primary teeth, the number of missing teeth correlated positively with OHRQoL impacts. The drawback to these two studies is that they do not have any comparable control group.

Laing et al. (82) and Kotecha et al. (83) compared children with hypodontia to a malocclusion control group using the CPQ. Laing et al. (82) compared 62 hypodontia patients to a malocclusion group of similar normative treatment need and found no difference in quality of life. Kotecha et al. (83) compared 86 hypodontia patients to a malocclusion group of lesser normative treatment need and observed significantly higher oral impacts in the hypodontia group. Locker et al. (84) assessed the functional and psychosocial impact of oligodontia in 36
children, and compared the results to published data of other clinical groups. Slightly above three-quarters of the subjects reported one or more functional and/or psychosocial impacts. Children with oligodontia appeared to have worse OHRQoL than children with dental decay and malocclusion, but better OHRQoL than children with oro-facial conditions. A few studies have demonstrated a clear improvement in OHRQoL among patients with hypodontia after missing teeth have been replaced by either resin-bonded bridges (85) or dental implants (86).

**Therapeutic approaches in cases with severe hypodontia**

**Interdisciplinary approach**

Children and adolescents with congenitally missing teeth need thorough planning and serious consideration of different therapies, in order to optimise the outcome of treatment in a lifelong perspective (87). The treatment approach will depend on the overall dentofacial morphology, the location and the number of missing teeth, the availability of different treatment methods, and the age of the patient. Severe hypodontia is often complicated and requires an interdisciplinary approach at specialist level, both during the initial evaluation phase and when treatment is provided. The interdisciplinary team may include participation from the disciplines of orthodontics, paediatric dentistry, oral surgery, prosthodontics and oral radiology (88).

The co-operation of specialists has the advantage that each discipline contributes with their expertise to assure a satisfactory outcome. Experience from Aplasicenteret in Northern Jutland documents that treatment of severe hypodontia is complex, with numerous treatment alternatives, and that that the interventions carried out by different specialist disciplines must be coordinated (89). Furthermore, centralising the management of patients with rare diagnoses allows the team of participating specialists to accumulate knowledge and gain relevant experience with such a patient group. It also provides a unique opportunity for aggregation of research data.

**Treatment course in hypodontia patients**

Treatment usually takes place in stages. In an early stage, often at the end of the mixed dentition phase, vertical dimensions are increased if necessary; teeth are orthodontically moved to the anterior region; and primary teeth and/or small permanent teeth (peg-shaped) are reshaped in order to improve aesthetics. Eruption disturbances are treated, and primary teeth sometimes extracted to guide the eruption of the permanent teeth. The option of
autotransplantation is always kept in mind, especially in cases of asymmetric hypodontia, and primary teeth with a reasonably good prognosis are maintained. When appropriate, the patients may receive semi-permanent solutions such as resin-bonded bridges, laminates or crowns. Partial dentures may be applied as an interim phase, or, in some cases, as a definitive treatment. A further stage usually takes place when the need arises, after the cessation of growth. At this point in time, more permanent solutions are considered, such as dental implants and bridges. Orthodontic therapy is often required prior to prosthetics in order to parallel the roots, optimise the location of the teeth and, in some cases, increase the bone volume.

**Treatment options and methods for replacing missing teeth in growing individuals**

An overarching goal in growing individuals is to minimise the number of teeth to be replaced. Biological methods, such as growth-adapted measures, orthodontic treatment and autotransplantation are preferable to prosthetic replacement (88). The loss of teeth, primary or permanent, leads to a risk of reduction in the volume of the alveolar ridge by resorption. A 25% reduction of the ridge width within 3 years after extraction of a primary mandibular molar with a missing permanent successor has been reported (90). A reduction in alveolar ridge width or height is likely to influence future treatment options, and the preservation of the alveolar processes should be strived for whenever possible. Therapies that both substitute missing teeth and preserve the alveolar ridge are orthodontic or spontaneous space closure, autotransplantation and preservation of primary teeth.

**Preservation of primary teeth**

In children with a reduced number of permanent teeth, the primary teeth are of great value, and should be preserved as long as they remain functional and other treatment does not require extraction. Extraction of primary teeth with a missing successor may be contraindicated in some types of malocclusions such as low-angled cases with deep bite, patients with general spacing or patients with broad jaws and narrow teeth. The decision to preserve a primary tooth as a substitute for a missing permanent tooth depends on the prognosis of the primary tooth in terms of infraocclusion, root resorptions and the extent of restorations. Nordquist et al. (52) collected x-rays of patients with retained primary teeth. The authors concluded that the primary mandibular molars and maxillary canines had the best prognosis.
Bjerklint et al. (47) found that only 7 of 99 primary molars were lost from the age of 12-13 to adulthood. Ith-Hansen et al. (51) carried out a follow-up study spanning 15 years. Out of 26 persisting primary molars, only three had been extracted and three showed extensive root resorption. Rune et al. (48) observed 77 children with 123 retained primary molars to a mean age of 17 years. Only 5% of the teeth had been extracted, and root resorption remained unchanged in 50%. Sletten et al. (49) evaluated 20 adults with 28 persisting mandibular molars. Four teeth were lost due to caries or periodontal disease, and 86% were still in function. In 2008, Bergendal (91) reviewed the topic of when to extract deciduous teeth in young individuals and replace them with implants. There was only limited, low-level evidence concerning this question in the literature. Recommendations were mainly based on clinical experience. The review stated that there are a limited number of reports, which support that a majority of the deciduous teeth that are healthy at 20 years of age can serve for many more years, and that retaining them can be a viable and biologic treatment alternative.

Space closure

**Spontaneous space closure**

Spontaneous space closure involves extracting a primary tooth with the intention of guiding the eruption of a permanent tooth to a more favourable position. Thereby, the need for orthodontic therapy is reduced.

Lindqvist (92) reported that in subjects congenitally missing the mandibular second premolar, extraction of the second primary molar at the age of 8 to 9 – before the root development of the mandibular first premolar and the emergence of the second permanent molar – was followed by spontaneous space closure. Mamopoulou et al. (93) investigated the amount of space closure and occlusal changes in 11 patients (mean age 11.8 years) with agenesis of the mandibular second premolar after extraction of the primary molar and the maxillary second premolar on the side of the agenesis. After four years, only 1 mm and 2 mm residual space were recorded in the maxilla and in the mandible, respectively. Most of the extraction space closed during the first year. In the maxilla, the mesial and rotational movements of the first molars contributed to 70% of the closure of the extraction space, while in the mandible, the space closure occurred by mesial/rotational movements and tipping of the first molars, as well as distal movement and tipping of the first premolars. The teeth were extracted when the occlusion of the first premolars was secured, close to the peak of the pubertal growth spurt. Unilateral extraction had no influence on the maxillary midline, whereas it caused a statistically significant mandibular dental shift to the extraction side. Extraction therapy had no impact on the overjet, overbite or incisor inclination. A favourable factor for space closure according to Bjork et al. (94) is the growth in facial height, which stimulates tooth eruption.
and mesial dental drifting of the molars. Additionally, a growth pattern involving anterior rotation of the mandible influences the direction of eruption of the posterior teeth, with correlations between mandibular growth and mesial migration of the lower molars (95). In patients with severe hypodontia, extraction of primary teeth might be suitable, in order to guide the eruption of permanent teeth such as permanent molars or canines in a more mesial direction.

**Orthodontic space closure**

The obvious advantages of orthodontic space closure are the longevity of the therapeutic result, and the completion of the treatment in early adolescence (96). The movement of a tooth into an edentulous space ensures that the alveolar bone height is maintained, and that adaptive changes taking place after treatment will be in line with natural development (97). In patients with a high smile line, a normal gingival and alveolar architecture is important in order to meet the aesthetic demands (97, 98). In cases of congenitally missing lateral incisors, orthodontic space closure with canine substitution has been reported to be a viable alternative with predictable results (99-101). Interventions to improve aesthetics such as tooth reshaping, positioning and bleaching, and in some cases thin porcelain veneers or composite build-ups, might be necessary (97). According to Kokich et al. (102), there are two malocclusions that permit canine substitution. These are an Angle class II malocclusion, with no crowding in the mandibular arch, or an Angle class I malocclusion, with severe crowding in the lower arch where it is necessary to carry out extractions. Other factors to be considered are the facial profile, and the size and colour of the canine.

In patients with severe hypodontia, reaching the therapeutic goal solely by orthodontic space closure is unrealistic, and might also compromise facial aesthetics. In these severe cases, orthodontic space closure seeks to mesialise teeth into the anterior region, preparing spaces posteriorly for prosthetics. A disadvantage of orthodontic space closure is that long-term retention with directly bonded lingual retainers is often required in order to assure stability. In addition, orthodontic treatment may involve substantial tooth movements over a prolonged period of time, which increases the risk of apical root resorption (103). A long-lasting treatment is also burdensome for the patient and orthodontist.

**Autotransplantation**

Dental autotransplantation is a procedure in which a tooth is surgically moved from one site in the mouth to another in the same individual (104). An autotransplanted tooth can substitute either a congenitally missing tooth or early loss of teeth due to trauma or caries. The treatment has the potential to preserve the alveolar bone during growth, and re-establish a
normal alveolar process after traumatic bone loss (105). The missing tooth is replaced by the patient’s own tooth, which is the most biocompatible material (104).

Autotransplantation can be suitable in patients with asymmetrical agenesis, where the transplanted teeth can provide a more even distribution of teeth in the arch. The procedure has shown highly predictable results and good long-term outcomes, with reported survival rates ranging from 75.3% to 91% (104, 106). The teeth most frequently used as grafts are premolars, whose root development is favourable for transplantation in the age range 10 to 12 years on average. Autotransplantation carries a significant risk in hypodontia patients, as failure of the procedure will result in the loss of one of the patient’s already few teeth. One must therefore be confident of a good prognosis for this intervention to be recommended. In addition, the success rate depends to a great extent upon surgeon skill (106). Complications after autotransplantation include the risk of root resorption, arrested root formation and replacement resorption (ankylosis) (107). Clinical signs of ankylosis include arrested eruption within 6 to 12 months (107).

Removable dentures

Removable dentures may be indicated to restore long spans and multiple missing teeth where dental implants are not possible. In young patients where a definitive treatment is postponed, they may also function as a semi-permanent solution. The dentures can provide a predictable solution and are able to replace soft and hard tissue deficiencies without invasive surgery (108). However, they do have the potential to increase caries incidence and periodontal problems, increasing the importance of preventative measures and appropriate case selection (108).

Conventional and adhesive fixed bridgework

Conventional bridgework is generally contraindicated in young patients with relatively immature pulps, and where abutment teeth are sound (108). In cases with a narrow alveolar ridge not suitable for dental implants and where the edentulous span is relatively short, this treatment option may be indicated. This may be the case where teeth are conical, diminutive or worn, requiring only limited preparation, and there is a plan to increase the occlusal vertical dimension (108). Another indication for a conventional bridge is the presence of adjacent teeth that require rehabilitation due to caries, fractures or discolorations (96). A systematic review conducted by Sailer et al. (109) reported a 5-year survival rate of 94.4% for metal-ceramic restorations and of 88.6% for all-ceramic restorations.
The adhesive technique has the great advantage that it requires only a limited amount of tooth substance to be removed during preparation. Other advantages include the avoidance of pulpal trauma, the supragingival preparation, the simplicity of the clinical procedures and the reduced cost and chair time, in comparison with conventional fixed prostheses (96). The vertical position of the abutment teeth is a prognostic factor, as a shallow overbite reduces the excessive lateral forces on the abutments and permits sufficient tooth surface for bonding. Other concerns influencing the prognosis are the inclination, mobility and labiolingual thickness of the abutment teeth (96). Various studies have been published regarding the longevity of resin-bonded prostheses. The change in design from two retainers to a single-retainer cantilever, as well as from metal-ceramic to all-ceramic restorations with more recent cementation systems, have led to increased survival rates (96). Recent studies have shown survival rates of single-retained resin bonded fixed dental prostheses from 94.4% to 100% after 4 to 10 years of follow-up (110-113).

**Dental implants**

Modern dental implantology began more than 40 years ago with the work of Professor Brånemark from Sweden and Professor Schroeder from Switzerland. Brånemark was the first to observe that titanium had the unique property of developing a direct attachment to bone, which he termed “osseointegration” (114). The concept of osseointegration was designed and evaluated for the mature skeleton (114). Dental implants in the growing maxilla or mandible have been demonstrated, both clinically and experimentally, to behave like ankylosed teeth, becoming submerged adjacent to natural teeth, because of the continued eruption of teeth and associated growth of the alveolus (115-118). The insertion of osseointegrated dental implants should therefore, in general, be delayed until the permanent dentition is fully erupted and growth is completed. However, large variations in skeletal maturation exist among individuals.

In extreme forms of hypodontia, such as hypohidrotic ectodermal dysplasia, severe oligodontia or anodontia, early placement of dental implants may take place as early as at the age of 3 years in order to provide support for overdentures or bridge restorations (89). A consensus conference recommended that the earliest age for placement of implants in the anterior region of the growing mandible (with the absence of alveolar bone) should be 7 or 8 years of age (119). In the growing edentulous maxilla, there was insufficient clinical or experimental data to support a recommendation for the placement of implants (119). Several studies have reported the successful osseointegration of single implants replacing missing teeth, provided that there is sufficient bone volume and appropriate space between adjacent teeth (96, 120-124). The main advantage of placing a dental implant is that healthy
adjacent teeth remain untouched. The most frequently reported aesthetic complications with implants have been resorption of the facial bone wall, recession of the facial soft tissue, incomplete papilla filling, thread exposure and infraocclusion (96, 125-129). Additional biological and technical complications include fistulas, peri-implantitis, screw loosening and porcelain chipping (96, 120, 123, 125).

**Treatment outcome in patients with severe hypodontia**

Clinical studies of hypodontia patients are challenging due to the dynamic nature of the condition, where the clinical picture and treatment need are in constant change. Recently, a systematic review was published comparing the outcome of dental treatment in patients with severe hypodontia (Table 2) (130). The authors emphasised that there is currently no standard approach or favourable dental treatment option to treat this group of patients. Twenty-one studies were included; seventeen studies had a retrospective design; sixteen studies described the results of implant treatment. The results of treatment with dentures, orthodontics, fixed crowns or bridges were sparsely presented. Implant survival ranged from 35.7% to 98.7% (mean 93.7%), and was influenced by bone quantity and implant location. Most implants were lost during the first year after placement, and more implants were lost in the maxilla than in the mandible. Patients with severe hypodontia have a higher implant loss compared to healthy subjects. Deepened peri-implant sulci and radiographic crestal bone resorption were seen in severe hypodontia patients, with most bone resorption occurring the first year after placement and continuing at a relatively constant level afterwards. The review concluded that it is currently not possible to make evidence-based decisions for the treatment of patients with severe hypodontia due to the condition’s heterogenic presentation, its low prevalence and the poor quality of studies.
Table 2. Overview of studies regarding treatment outcome in patients with severe hypodontia, adapted from the systematic review by Filius et al. (130)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Treatment</th>
<th>Age range (mean in years)</th>
<th>Survival rate (mean follow-up)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Implants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Becelli et al.</td>
<td>2007</td>
<td>8 patients with 60 fixtures</td>
<td>17-19 (17.8)</td>
<td>96.7% (8.5 years)</td>
<td></td>
</tr>
<tr>
<td>Bergendal et al.</td>
<td>2008</td>
<td>5 patients with 14 fixtures</td>
<td>5-12 (7.4)</td>
<td>35.7% 3-23 years</td>
<td>All with ED</td>
</tr>
<tr>
<td>Créton et al.</td>
<td>2010</td>
<td>44 patients with 214 fixtures</td>
<td>16.6-48.5 (25.1)</td>
<td>91.6% 2.9 years</td>
<td>6 with syndromes</td>
</tr>
<tr>
<td>Dustberger et al.</td>
<td>1999</td>
<td>13 patients with 72 fixtures</td>
<td>12-33 (18.9)</td>
<td>95.8% 5 years</td>
<td></td>
</tr>
<tr>
<td>Finnema et al.</td>
<td>2005</td>
<td>13 patients with 87 fixtures</td>
<td>17-30 (20)</td>
<td>89.7% 3 years</td>
<td></td>
</tr>
<tr>
<td>Garagiola et al.</td>
<td>2007</td>
<td>33 patients with 186 fixtures</td>
<td>16-68 (3 years)</td>
<td>94.1% 13 with ED</td>
<td></td>
</tr>
<tr>
<td>Grecchi et al.</td>
<td>2010</td>
<td>8 patients with 78 fixtures</td>
<td>19-46 (1.75 years)</td>
<td>98.7% All with ED</td>
<td></td>
</tr>
<tr>
<td>Guckes et al.</td>
<td>2002</td>
<td>51 patients with 264 fixtures</td>
<td>8-68 (20.5)</td>
<td>89.8% 1.75 years</td>
<td>All with ED</td>
</tr>
<tr>
<td>Heuberer et al.</td>
<td>2011</td>
<td>6 patients with 16 fixtures</td>
<td>6-14 (1-7.1 years)</td>
<td>93.8% 5 with ED</td>
<td></td>
</tr>
<tr>
<td>Kearns et al.</td>
<td>1999</td>
<td>6 patients with 41 fixtures</td>
<td>5-7 (11.2)</td>
<td>97.6% 7.8 years</td>
<td>All with ED</td>
</tr>
<tr>
<td>Sweeney et al.</td>
<td>2005</td>
<td>14 patients with 61 fixtures</td>
<td>12-21 (3.3 years)</td>
<td>88.5% All with ED</td>
<td></td>
</tr>
<tr>
<td>Worsaae et al.</td>
<td>2007</td>
<td>46 patients with 283 fixtures</td>
<td>8-48 (20.5)</td>
<td>97.7% (2.3 years)</td>
<td></td>
</tr>
<tr>
<td>Zou et al.</td>
<td>2014</td>
<td>25 patients with 179 fixtures</td>
<td>17-28 (3 years)</td>
<td>98.3% All with ED</td>
<td></td>
</tr>
<tr>
<td>Johnson et al.</td>
<td>2002</td>
<td>Craniofacial morphology did not differ significantly between implant-treated and nontreated ED children. Treatment with intraosseous dental implants did not rescue normal craniofacial growth and development.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standford et al.</td>
<td>2008</td>
<td>Of the 109 participants with ED, 50% reported a complication of implant treatment, and 24% reported some form of failure with implant therapy. However, 91% of participants reported being either satisfied or very satisfied with dental implants.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Implant-supported and tooth-supported fixed dental prostheses

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dueled et al.</td>
<td>2008</td>
<td>Patients with tooth agenesis had a high risk of severe root resorption after orthodontic treatment. A better aesthetic outcome was obtained with implant-supported reconstructions than with tooth-supported reconstructions. However, mucosal discoloration was recorded in 57% of the patients with dental implants.</td>
</tr>
</tbody>
</table>

### Orthodontics

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levander et al.</td>
<td>1998</td>
<td>There is a high risk of apical root resorption during orthodontic treatment in patients with multiple aplasia (four or more teeth), in particular in teeth with an abnormal root form and lengthy treatment with elastics and rectangular archwires.</td>
</tr>
</tbody>
</table>

### Orthodontics and fixed dental prostheses

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anweigi et al.</td>
<td>2013</td>
<td>Hypodontia has a significant impact on OHRQoL. Provision of resin-bonded bridges has a positive impact on OHRQoL of patients with hypodontia.</td>
</tr>
</tbody>
</table>

### Removable partial dentures

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lexner et al.</td>
<td>2009</td>
<td>Ten males affected with X-linked hypohidrotic ectodermal dysplasia were treated with removable prostheses. Of those who completed treatment, 3 out of 4 (at the age of 18 years), chose to continue treatment with prostheses as adults and postpone the implant treatment.</td>
</tr>
<tr>
<td>Montanari et al.</td>
<td>2012</td>
<td>Early oral rehabilitation with removable dentures in ED patients (2-3 years of age) improves oral function, phonesis and aesthetics, reducing social impairment. The placement of a two-way expanding screw could tell if a real transversal growth occurs in the anterior mandible and could follow the transversal expansion of the anterior mandible.</td>
</tr>
<tr>
<td>Hobkirk et al.</td>
<td>1989</td>
<td>Removable partial dentures are frequently used in the treatment of severe hypodontia. Failures primarily occurred either early or late in the life of the prostheses. The dentures had a relatively short lifespan, and needed to be replaced within 3.5–4 years in the maxilla on average. Reasons for replacement were patient dissatisfaction with the appearance of the prosthesis, fracture, wear or oral changes.</td>
</tr>
</tbody>
</table>
Aims of this work

Overall aim

The overall objective of this work was to gain knowledge about the clinical course of hypodontia, treatment alternatives and their suitability in different circumstances, and how the condition affects the patients’ psychosocial wellbeing.

Specific aims

- To assess the prognosis of persisting primary mandibular molars without a successor, in terms of root resorption, infraocclusion and restorations (Paper I).

- To survey the psychosocial status of patients with hypodontia and a malocclusion of similar normative treatment need. The two groups were compared using a generic form and a condition specific form of the Oral Impact on Daily Performance (OIDP) inventory (Paper II).

- To follow up patients with severe hypodontia, comparing the resulting crown and soft-tissue morphology for orthodontic space closure, dental implants and tooth-supported fixed dental prostheses (FDPs) replacing teeth in the anterior region. Also, the treatment performed and the types and locations of substitutes for all congenitally missing teeth are assessed (Paper III).
Materials

Study groups

The basis of this thesis is a patient sample collected through the activities of an interdisciplinary team (Eksperttjenesten) at the Department of Orthodontics, University of Oslo from 1998 to 2010. During this period, 573 patients were referred by their primary dentist or dental hygienist. Of these, 212 had hypodontia and 134 suffered from severe hypodontia.

The interdisciplinary team was established in 1998, and includes specialists in orthodontics, paediatric dentistry, oral surgery and prosthodontics. The purpose of the unit is to provide advisory and therapeutic dental services for children and adolescents in need of advanced oral health care. The patients are referred to the team for a clinical examination, and a tentative treatment plan in both a short- and a long-term perspective is established. Patients residing within a practical distance to the university clinic are often offered to complete the entire treatment course there, and the remaining patients usually carry out treatment at their local dentist or specialist clinic. Seventy-seven patients received treatment at the university clinic, and 135 patients were treated at their place of residence.

In paper I, 111 of the 212 patients with hypodontia are included, as the inclusion criteria are the congenital absence of at least one mandibular second premolar.

In paper III, 71 of the 134 patients with severe hypodontia are included, as they were aged 18 or more, and could be expected to have completed the majority of the treatment course. The patients were invited by mail or telephone to participate in a follow-up study, and 50 patients (70%) accepted. Of those not attending, 5 could not be reached, 7 did not wish to participate in the study, and 9 declined for practical reasons. In 9 of the 50 cases, the patients were unable to travel to the University of Oslo, and examination was performed in cooperation with an orthodontist at the patient’s place of residence.

In paper II, patients referred to the interdisciplinary team or to the post-graduate clinic at the Department of Orthodontics between January 2012 and September 2013 were consecutively recruited. Sixty-two patients with non-syndromic hypodontia and 101 non-hypodontia patients with a malocclusion of similar normative treatment need were included.
Data collection

All records for the 212 hypodontia patients were retrieved, and the following data denoted: gender, date of birth, year of referral, referring dentist or specialist, original place of residence, diagnosis, involved teeth (number and location), persisting primary teeth (number and location), and recommended treatment plan. Treatment was categorised as orthodontic treatment, implant-supported prostheses, retaining primary teeth, composite restoration, tooth-supported fixed dental prostheses, veneer restoration, orthognathic surgery, autotransplantation, or combinations of the above.

Methodological considerations

Measurements on panoramic radiographs (paper I)

Decisions on whether or not to preserve a persisting primary molar without a successor should be based on a prediction of the tooth’s longevity. In this regard, the three parameters infraocclusion, root resorption and restorations will guide the clinical decision about the fate of the primary tooth.

For the purpose of measuring infraocclusion, linear measurements on intraoral radiographs or dental casts have been the most common method (45, 47-49, 51). With only panoramic radiographs available in the records of patients included in paper I, relative measurements were chosen, knowing that magnification is not reproducible between panoramic radiographs and even between regions in the same image. These relative measurements are not directly comparable with absolute measurements from other studies. Therefore, a threshold of clinically significant infraocclusion roughly equivalent to other authors’ definitions (37, 131) was established. Root resorption was scored subjectively on a six-point scale of severity, adapted from Bjerklin et al. (132), and restorations were recorded as no restoration, approximal restoration or occlusal restoration.

OIDP questionnaire (paper II)

The hypodontia patients and the malocclusion patients were administered a structured questionnaire, including the OIDP inventory and questions regarding their perceived oral health status. Both generic and condition specific OIDP indicators were calculated. The questionnaire was self-administered at the university clinic. All included patients were
assigned to either the hypodontia group or the malocclusion group based on available dental casts, intraoral photographs and radiographs.

Other measures of OHRQoL, such as the Child Perception Questionnaire (CPQ) (133) or the Child Oral Health Impact Profile (COHIP) (134), which, in addition to the OIDP, are the most frequently used measures for self-completion by children (69), could also have been appropriate for the study. The OIDP has already been translated into Norwegian and validated in a representative population sample; thus, a set of normative data exists (64). The OIDP is also simple in that it measures behavioural impacts only rather than feeling-state dimensions, and consists of only eight questions.

In addition to the generic OIDP measure, the inventory is also designed with a condition specific measure, assessing impacts caused by a particular disease or condition. Paper II compared the ability of the generic and condition specific OIDP measures to discriminate between patients with hypodontia and patients with a malocclusion of similar normative treatment need. A malocclusion group was chosen as controls, rather than patients with an ideal Class I occlusion that would not be comparable due to expected large differences in daily impacts. By including the condition specific measure, it is also possible to assess whether impacts experienced by hypodontia patients are directly associated to the condition, and not to a co-existing malocclusion. Impacts attributed to small teeth, gaps between teeth and missing teeth were considered to be condition specific impacts attributed to hypodontia, and only these items were scored in the condition specific analysis.

**Follow-up with clinical examination (paper III)**

After several years of operation, the interdisciplinary team at the University of Oslo had evaluated a relatively large group of hypodontia patients. The time was appropriate to gather knowledge on the patients’ outcome. Patients with severe hypodontia aged 18 or more, who would most likely have completed the majority of the planned treatment course, were invited for a follow-up examination. Mucosal discoloration, crown morphology, colour of the replacement tooth, and papilla level was compared for three different treatment modalities: orthodontic space closures, dental implant fixtures (either single or part of an implant-retained prosthesis) and FDPs (tooth-supported conventional or resin-retained prostheses) replacing one or more missing teeth in the anterior region. Neither biological (e.g. pocket depths, bleeding on probing, bacteriological sampling) nor radiographic (marginal bone level, buccal bone level, 3D imaging) measures were performed, as no prior data for comparison existed in the patients’ records. In addition, treatment had already been performed at a number of different clinics, and such parameters had not been systematically recorded.
The patients who accepted to take part in the study were invited to the university clinic. For those who accepted, but could not attend due to a long travel distance, a local orthodontist carried out the examination after being briefed by one of the investigators. The morphological variables were assessed by the author using standardised photographs and radiographs taken during the examination. This gives rise to potential errors, as a perfect standardisation of photographs is not possible due to different equipment and operators.

The treatment performed was noted and compared to the original plan. The number of persisting primary teeth without successors, and their survival, was recorded. In addition, the patients were given a questionnaire regarding their satisfaction with their dental status, the treatment process and the outcome.

### Statistical methods (Papers I-III)

All data were processed with the Statistical Package for the Social Sciences (versions 19.0—22.0; SPSS Inc., Chicago, IL, USA).

Papers I and III raised a common methodological issue, namely the unit of analysis for statistical tests. Both papers involved several measurements being performed on individual teeth. If the individual tooth is chosen as unit of analysis, measurements made on different teeth belonging to the same patient will represent a problem, as the data are not independent. A requirement for tests of statistical significance is that the data to be tested are independent. Therefore, the data in question had to be aggregated with the patient as unit of analysis. This was achieved by selecting only one data point from each patient to be included in significance testing. A consequence of this is that some information will be lost; however, we found this to be the most correct method of performing rigorous statistics on such unstructured clinical data.

Table 3 summarizes the statistical methods used in the papers; the specific statistical tests performed are described in detail in the separate papers.
Table 3. Statistical methods and tests used in Papers I-III.

<table>
<thead>
<tr>
<th>Statistical method</th>
<th>Paper I</th>
<th>Paper II</th>
<th>Paper III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraclass correlation coefficient (ICC)</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paired <em>t</em>-test</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spearman correlation coefficient</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Effect size statistics</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Chi-square statistics</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Mann-Whitney <em>U</em> test</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Cronbach’s alpha coefficient</td>
<td>+</td>
<td></td>
<td></td>
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<tr>
<td>Logistic regression</td>
<td>+</td>
<td></td>
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</tbody>
</table>

Summary of results

Paper I: The prognosis of retained primary molars without successors: infraocclusion, root resorption and restorations in 111 patients

The prognosis of the persisting primary molars without successors was estimated in terms of infraocclusion, root resorption and restoration. An infraocclusion ratio was calculated in 92 patients (49 left molars and 43 right molars); infraocclusion of clinical significance (ratio > 2, i.e. more than 20% of the neighbouring first molar’s crown height) was found in 44% of the patients. The analyses of root resorption and restorations were carried out on 111 patients (58 left molars and 53 right molars). The mesial and distal root exhibited no root resorption in 19% and 34%, respectively. Most of the patients had no restorations (78%). Infraocclusion and age were found to be weakly, but significantly correlated with root resorption.

Paper II: Discriminative ability of the generic and condition specific Oral Impact on Daily Performance (OIDP) among adolescents with and without hypodontia

Questionnaires and clinical data were obtained for 62 patients (mean age 13.6, SD 2.1) with hypodontia and 101 patients (mean age 12.5, SD 1.5) without hypodontia, but with a malocclusion of similar normative treatment need (IOTN, DHC 4 or 5). The mean number of missing teeth (absolute hypodontia) in the hypodontia group was 6.2 (1–21), and the mean number of missing teeth minus number of persisting primary teeth (relative hypodontia) was 3.1 (0–14). The prevalence of generic and CS oral impacts in the hypodontia group were 64% and 30%, respectively, and the corresponding rates in the non-hypodontia group were 62%
and 10%. The generic OIDP did not discriminate between the two groups with respect to overall scores. The CS OIDP discriminated strongly between patients with and without hypodontia regarding problems with emotional status, showing teeth, social contact, speaking and carrying out work. Compared to the non-hypodontia group, patients with hypodontia, with severe hypodontia (≥ 6 missing teeth) and upper anterior hypodontia were respectively 3.4, 2.5 and 7.0 times more likely to report any oral impact attributed to small teeth, gaps between teeth and missing teeth.

**Paper III: Tooth replacements in young adults with severe hypodontia: orthodontic space closure, dental implants and tooth-supported fixed dental prostheses. A follow-up study**

Fifty patients (mean age 25.6 years) with severe hypodontia were invited to participate in a follow-up study of treatment outcome. The most commonly prescribed treatments were dental implants, orthodontic space closure and retaining primary teeth. The persisting primary teeth showed a good survival rate at the follow-up examination. Crown and soft-tissue variables (mucosal discoloration, crown morphology, colour and papilla index) were compared for orthodontic space closure, dental implant fixtures and tooth-supported fixed dental prostheses (FDPs) replacing teeth in the anterior region. All implant fixtures in the anterior mandible and almost two thirds in the anterior maxilla had either mucosal discoloration or visible metal. The crown morphology in the anterior mandible was significantly better for FDPs than implant fixtures, but the colour score was better with an implant fixture than an FDP in the anterior maxilla. For both dental fixtures and FDPs, poor papilla indexes were observed. Orthodontic space closure resulted in superior papilla aesthetics, but had the drawback of a less optimal crown morphology in the anterior mandible.

**Additional data: Persisting primary teeth**

The persisting primary teeth that were present at the follow-up examination are presented in Table 4. Thirty patients were recommended to keep one or more primary teeth. At the follow-up examination after a mean of 12 years 28 patients still possessed primary teeth.
Table 4. Persisting primary teeth present at the follow-up examination.

<table>
<thead>
<tr>
<th>Tooth type</th>
<th>Number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>1</td>
</tr>
<tr>
<td>53</td>
<td>11</td>
</tr>
<tr>
<td>54</td>
<td>2</td>
</tr>
<tr>
<td>55</td>
<td>18</td>
</tr>
<tr>
<td>63</td>
<td>9</td>
</tr>
<tr>
<td>64</td>
<td>1</td>
</tr>
<tr>
<td>65</td>
<td>18</td>
</tr>
<tr>
<td>71</td>
<td>2</td>
</tr>
<tr>
<td>73</td>
<td>8</td>
</tr>
<tr>
<td>74</td>
<td>2</td>
</tr>
<tr>
<td>75</td>
<td>16</td>
</tr>
<tr>
<td>81</td>
<td>2</td>
</tr>
<tr>
<td>83</td>
<td>7</td>
</tr>
<tr>
<td>84</td>
<td>1</td>
</tr>
<tr>
<td>85</td>
<td>16</td>
</tr>
</tbody>
</table>

Additional data: OIDP questionnaire
The patients participating in the study published in Paper III were also asked to complete the OIDP questionnaire. These data have not yet been processed, but will form the basis of a future publication.

Additional data: Patient satisfaction
The patients participating in the study published in Paper III were asked to complete a questionnaire regarding their satisfaction with the treatment outcome (Table 5). The general level of satisfaction was very high, with 95.5% of the patients reporting satisfaction with the outcome. As the majority of the patients had received multiple replacement types (e.g. dental implants posteriorly and orthodontic space closure anteriorly or vice versa), we could not statistically discriminate between the different treatment categories, or whether the answers reflected the patients’ satisfaction with anterior or posterior treatments. For this reason, the results were not relevant to the aim of paper III, and were not included in the publication.


<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How was your experience with pain and discomfort in conjunction with the treatment?</td>
<td>No such problems, Acceptable, Uncomfortable</td>
<td>6 (13.6%)</td>
<td>20 (45.5%), 18 (40.9%)</td>
</tr>
<tr>
<td>2. Did you or your parents receive sufficient information about the treatment procedures?</td>
<td>Yes, Don’t remember, No</td>
<td>31 (70.5%)</td>
<td>7 (15.9%), 6 (13.6%)</td>
</tr>
<tr>
<td>3. Did you or your parents receive sufficient information about other treatment options?</td>
<td>Yes, Don’t remember, No</td>
<td>12 (27.3%)</td>
<td>25 (56.8%), 7 (15.9%)</td>
</tr>
<tr>
<td>4. Did you/your parents find it easy or difficult to choose a tooth replacement as a solution to your problem with missing teeth?</td>
<td>Easy, Unsure, Difficult</td>
<td>36 (81.8%)</td>
<td>6 (13.6%), 2 (4.5%)</td>
</tr>
<tr>
<td>5. Were you concerned about whether the replacements would look similar to your natural teeth?</td>
<td>Yes, Don’t remember, No</td>
<td>16 (36.4%)</td>
<td>2 (4.5%), 26 (59.1%)</td>
</tr>
<tr>
<td>6. In general, how do the replacements feel compared to your natural teeth?</td>
<td>The same or almost the same, Different, but good enough, Completely different</td>
<td>34 (77.3%)</td>
<td>4 (9.1%), 6 (13.6%)</td>
</tr>
<tr>
<td>7. What is your opinion of the replacements’ appearance?</td>
<td>Satisfied, Dissatisfied</td>
<td>42 (95.5%)</td>
<td>2 (4.5%)</td>
</tr>
<tr>
<td>8. Does the gum surrounding the replacements bleed?</td>
<td>Yes, Unsure, No</td>
<td>9 (20.9%)</td>
<td>5 (11.6%), 29 (67.4%)</td>
</tr>
<tr>
<td>9. When brushing teeth, do you need to be more meticulous around the replacements compared to your natural teeth?</td>
<td>The same, It is more demanding, It is a lot of work</td>
<td>17 (38.6%)</td>
<td>25 (56.8%), 2 (4.5%)</td>
</tr>
<tr>
<td>10. When eating, do you chew in a similar way with the replacements as with your natural teeth?</td>
<td>Yes, Unsure, No</td>
<td>39 (88.6%)</td>
<td>3 (6.8%), 2 (4.5%)</td>
</tr>
<tr>
<td>11. Do the replacements feel similar to your natural teeth?</td>
<td>Yes, Unsure, No</td>
<td>34 (77.3%)</td>
<td>4 (9.1%), 6 (13.6%)</td>
</tr>
<tr>
<td>12. Are you satisfied with the treatment outcome?</td>
<td>Satisfied</td>
<td>Dissatisfied</td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-----------</td>
<td>--------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>42 (95.5%)</td>
<td>2 (4.5%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>13. Is the result as expected?</th>
<th>Yes</th>
<th>Unsure</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>34 (77.3%)</td>
<td>8 (18.2%)</td>
<td>2 (4.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>14. Is the result worth the effort that the treatment has entailed?</th>
<th>Yes</th>
<th>Unsure</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>39 (88.6%)</td>
<td>4 (9.1%)</td>
<td>1 (2.3%)</td>
</tr>
</tbody>
</table>
Discussion

This thesis deals with different issues related to the condition of congenitally missing teeth. The studies (papers I-III) address the prognosis of persisting primary teeth, the psychosocial impact caused by missing teeth, and the treatment outcome in patients with hypodontia. The unpredictable and complex nature of the condition, the long treatment duration and the relatively small sample of patients do not allow a randomised clinical trial design for comparison of treatment alternatives. Paper I has a retrospective design, paper II is a cross-sectional survey and paper III is a longitudinal follow-up study.

Study group and inclusion criteria

The study group in paper I and III is based on 212 hypodontia patients referred to an interdisciplinary team at the University of Oslo between 1998 and 2010. For paper I, 111 patients missing one or both mandibular second premolars with a corresponding persisting primary molar and a panoramic radiograph of acceptable quality were included. Paper III was based on the same study group, and only patients missing six or more teeth and aged 18 years or more, 71 patients in total, were invited for a follow-up study. For paper II, patients referred to the Department of Orthodontics, either to the specialist clinic or to the interdisciplinary team, from January 2012 to September 2013 were consecutively recruited. Only patients with a hypodontia diagnosis or a malocclusion with a similar normative treatment need (measured by the index of orthodontic treatment need (IOTN), dental health component (DHC) of 4 or 5) were included.

Evaluation of results

Persisting primary teeth without successors

The option of retaining primary teeth when successors are lacking might be viewed as a temporary and uncertain alternative by professionals, as well as by patients and their caregivers. Paper I showed that infraocclusion was the limiting prognostic factor for the preservation of primary mandibular molars. This is particularly the case if it occurs before the pubertal growth spurt. In cases where the number of missing teeth is limited to only a few, other alternatives such as orthodontic space closure or insertion of a single implant after cessation of growth is often more suitable. However, in growing individuals with a large number of missing teeth, the primary teeth are an invaluable resource that artificial substitutes cannot match in a biological perspective. Persisting primary teeth preserve the alveolar bone
and corresponding soft tissue, and are of importance for speech and chewing. The results from the follow-up study described in paper III show that primary teeth can be a reliable long-term semi-permanent solution. Figure 3 shows a male, aged 11 at referral, missing eight teeth. Orthodontic treatment with preservation of the primary teeth was recommended, followed at a later time by dental implants if necessary. Twelve years later, he has eight persisting primary teeth that are still in good condition; further, the bone level has been maintained. Figure 4 shows a female, aged 10 years at referral, missing ten teeth. At 18 years of age, the primary and permanent canines substitute the upper lateral incisors on the right and left side, respectively. The upper first premolars substitute the canines, and all six upper anterior teeth have been reshaped with bonded veneers. In the lower jaw, teeth 73 and 83 still persist and function as lower incisors. Both primary mandibular second molars persist, but are infraoccluded below the occlusal plane, especially tooth 75. This was not the case when the patient was 10 years old; the primary molars have most likely ankylosed during the pubertal growth spurt. An optimal time for extraction of infraoccluded primary teeth without successors has not been properly established in the literature, and a definitive answer to this question may not even exist. In cases where the degree of infraocclusion increases, resulting in occlusal disturbances, extraction must be considered (135). In this particular case, had 75 been extracted at an earlier time, e.g. when the tooth showed more than 2 mm of infraocclusion, the vertical bone loss which is now evident would most likely have been smaller. A vertical bone deficiency represents a problem for future implant placement, as the probability of achieving predictable outcomes is poor when vertical bone augmentation is needed, compared to lateral bone augmentation (136, 137). In other words, when an infraoccluded tooth is kept and this leads to vertical bone loss, the prognosis for a future dental implant decreases. Consequently, extraction at an earlier stage might have been justified. On the other hand, if tooth 75 had been extracted earlier, a longstanding space-maintainer would have been required in order to prevent mesial tipping of tooth 36; further, an earlier extraction of 75 would still not have guaranteed sufficient bone conditions for implant placement after cessation of growth. As growth is now virtually completed, the infraocclusion is expected to progress very slowly (51). The tooth may now serve as an ankylosed pillar for a prosthetic solution, such as a porcelain crown or onlay. Figure 5 shows a female, aged 24 years, with thirteen teeth missing. The primary teeth in the upper jaw have been reshaped with composite restorations or veneers. Considering the substantial root resorption affecting the primary teeth in the upper jaw, their long-term prognosis is uncertain. However, the prosthetic rehabilitation was performed three years earlier, and the conditions have remained stable since. In any case, preserving and reshaping the primary teeth will improve the patient’s appearance and oral function during some important and formative years of adolescence, postponing the need for dental implants.
Figure 3. Male aged 25 years missing 15, 13, 23, 25, 33, 43, 44, 45 with persisting 55, 53, 63, 65, 85, 84, 83, 73. The primary teeth are in good condition twelve years after the initial consultation. Note that the bone level in the lower jaw (yellow lines) is equal on the right side with primary teeth and the left side with permanent teeth.
Figure 4. Female aged 18 years missing 15, 13, 12, 22, 35, 34, 31, 41, 44, 45 with persisting 55, 53, 75, 73, 83, 85. The roots of the primary teeth have shortened since first consultation ten years ago, but the teeth are in occlusion and in function, except for the ankylosed primary molars 75 and 85.
Figure 5. Female aged 24 years missing 17, 16, 15, 14, 12, 22, 24, 25, 26, 37, 34, 44, 47 with persisting 55, 54, 53, 63, 64, 65, 75. The primary teeth in the upper jaw have been reshaped with veneers or composite restorations. The upper canines substitute the upper lateral incisors and all anterior teeth are reshaped with veneers. The prosthetic rehabilitation was performed three years ago.
Mental health and social aspects related to hypodontia

Patients missing a large number of teeth not only struggle with functional problems, but might also receive negative comments about their appearance from peers, and in some cases experience bullying. Bullying has been described as a situation in which a person is exposed repeatedly and over time to negative actions by at least one other person (138). The prevalence of bullying among children and adolescents was examined in 11 European countries, with 20.6% reporting being bullied, ranging from 10.5% in Hungary to 29.6% in the United Kingdom (139). A study examining the prevalence of bullying, its effect on school attendance and the contribution of general physical and dentofacial features was performed among Jordanian schoolchildren (140). The prevalence of bullying among 11- to 12-year old schoolchildren was 47%, and more boys reported being bullied than girls. Teeth were the feature most frequently targeted, and the three most commonly reported dentofacial features targeted by bullies were spacing between teeth or missing teeth, shape or colour of the teeth, and prominent maxillary anterior teeth. A British study (141) examined 531 schoolchildren between 9 and 13 years, and found that 66% were teased about one or more characteristics. Height and weight were the commonest targets for teasing, dental features the fourth commonest, and 7% of the children reported to be teased about their teeth once per week or more. In comparison, the prevalence of peer victimization was found to be 12.8% in a group of 10-14-year-olds awaiting orthodontic treatment (142). Adolescents who are bullied because of a malocclusion or their dentofacial features experience a general impact on their OHRQoL, including more pronounced oral symptoms and functional limitations, as well as emotional and social effects (142, 143). Dentofacial appearance can affect interpersonal relationships and perceived qualities such as friendliness, social class, intelligence, and popularity, from infancy to adulthood (82). For young people with hypodontia, it is especially distressing that their malocclusion is not just a phase in the mixed dentition or early permanent dentition, which can be solved in the teenage years. Instead, the condition entails a lifelong treatment need, and can never be considered fully treated.

The findings from paper II show that a malocclusion and congenitally missing teeth have an almost equal negative impact on quality of life. The hypodontia patients reported more problems with emotional status, and patients with upper anterior hypodontia were more affected than those with a malocclusion of similar treatment need. Both groups scored significantly worse than the general Norwegian population: 64% in the hypodontia group and 62% in the malocclusion group reported oral impacts, as compared to 18% of the general population (64). Paper II also showed that the impacts reported by the hypodontia patients were directly related to the missing teeth, and not to a co-existing malocclusion, since the condition specific measure discriminated much better between the groups than the generic
measure. Gaps between teeth and small teeth might be regarded as unattractive, leading to reluctance to interact socially. In some cases, the condition may exacerbate self-consciousness and prevent young people from expressing themselves the way they would otherwise have done, e.g. by smiling, talking and laughing. As an ultimate consequence, the condition might lead to isolation and academic underachievement. This underlines the importance of remedying the issues caused by missing teeth at least in the early teens, with emphasis on making the anterior segment as attractive as possible.

The hypodontia patients examined in paper II were relatively young at the time of investigation with a mean age of 13.6 years, had little treatment experience and may not yet have understood the extent of treatment needed. The treatment of hypodontia patients is often undertaken in phases, and some procedures, such as dental implants, are usually conducted when the patients are over 20 years of age. The Norwegian public dental health service provides all services except orthodontics free of charge until the age of 18; from 19 to 20 years, the patients pay 25% of the treatment cost. Persons above the age of 20 years are no longer eligible for public dental health care, but treatment costs for certain defined conditions are partly covered by the national insurance scheme. As treatment plans for patients with severe hypodontia usually extend into adulthood, the financing situation may lead to uncertainty at the planning stage as to whether the part of the treatment plan extending after the age of 20 will actually come to execution. Experience from this work suggests that patients with severe hypodontia should be offered dental treatment free of charge conducted and coordinated by interdisciplinary teams, which continue to accumulate experience with this patient group.

**Treatment alternatives in individuals with multiple missing teeth**

Methods to replace teeth in individuals with multiple missing teeth involve dental implants, tooth-supported fixed dental prostheses, partial dentures and orthodontic space closure.

**Dental implants**

The literature on treatment outcome for patients with severe hypodontia has focused mostly on dental implant treatment (130). The systematic review by Filius et al. (130) regarding treatment outcome in patients with severe hypodontia revealed an implant survival rate from 35.7% to 98.7% (mean 94%). A systematic review by Pjetursson et al. (144) investigated survival rates for implant-supported prostheses in the general population, and compared the rates in studies published before the year 2000 to rates in studies published after year the 2000. The 5-year overall survival rate increased from 93.5% to 97.1%, and lower complication rates were reported in the more recent clinical studies. The incidence of
aesthetic, biologic, and technical complications were, however, still high. The lower implant survival rate in hypodontia patients compared to the general population may be associated with the bone quality. The jawbone density in patients with ectodermal dysplasia is higher than in healthy individuals, possibly impairing the prognosis for dental implants in this patient group (145, 146). Such an association has not been demonstrated in patients with severe hypodontia, as no radiographic difference in the structure of mandibular trabecular bone could be found between hypodontia patients without ectodermal dysplasia and healthy subjects in a study by Creton et al. (147). Other factors, such as location and amount of available bone, might explain the higher loss of implants in patients with severe hypodontia (130).

Paper III did not assess the survival of dental implants, biological variables such as pocket depth, bleeding on probing, plaque index etc., or the marginal bone level on radiographs. Part of the reason for this was that records from the time of treatment were often incomplete, and many patients were not treated at the University clinic, but by local dentists with different practices with regard to clinical documentation. Instead, the paper attempted to describe what the patients actually looked like several years after treatment. The patients were a heterogeneous group, and had undergone numerous interventions over many years; the majority expressed tiredness from treatment. Dental implants in the anterior mandible showed gingival discoloration in almost all subjects, with four different cases exemplified in Figure 6. Dueled et al. (148) had similar observations, finding discoloration surrounding dental implants in almost 60% of a group of hypodontia patients. The patients in paper III had a mean age of 25.6 years at the follow-up examination, and the prosthetic rehabilitation was performed on average 4.6 years earlier. The extent of the gingival discoloration and/or visible metal after such a short observation period indicates that the anterior mandible provides anatomical and biological limitations for implant insertion. Treatment alternatives that preserve the alveolar process, such as retaining primary teeth, orthodontic space closure or autotransplantation, are certainly preferable if the alveolar process is narrow; this is usually the case when teeth are not present. Alternatively, based on the findings from paper III, a tooth-supported fixed dental prosthesis (FDP) in the anterior mandible will probably serve as a better solution than an implant-based solution.

Fixed dental prostheses

The replacement of congenitally missing teeth by an FDP has not been thoroughly discussed in the literature. Dueled et al. (148) compared the aesthetic outcome of FDPs and dental implants in patients with tooth agenesis, and found acceptable aesthetics in 92% of the implant reconstructions and 83% of the FDPs. Replacing teeth with a conventional full-
coverage FDP is the least conservative approach, as extensive tooth reduction is usually required, leading to a risk of pulpal trauma in young patients. If the conditions are favourable, or rendered favourable by pre-prosthetic orthodontics, minimally invasive techniques using resin-bonded FDPs are preferable. The findings from paper III showed that the crown morphology was better for FDPs than for implant fixtures. A possible explanation for this might be that there are fewer biological limitations to take into account when designing an FDP, namely the bone level and corresponding soft tissue. An FDP has two pillar teeth defining its design, whereas if an implant is placed in an area of deficient or little bone, the crown morphology must be designed so that it compensates for this to some extent.

A viable alternative for the replacement of single missing teeth is a single-retained resin-bonded prosthesis. In recent literature, the reported survival rates (94.4% to 100% after 4 to 10 years of follow-up (110-113)) for these have been promising, and this option should therefore be regarded as a long-term semi-permanent or permanent alternative. Experience from patients in this work supports this view, as the aesthetics are satisfactory, the durability is good and minimal grinding of neighbouring teeth is required. Figure 7 shows a female, aged 22 years with nine teeth missing. Two single-retained resin bonded prosthesis have replaced 12 and 41 respectively, with a pleasing aesthetical and functional result.

**Removable partial dentures**

None of the 50 investigated patients in paper III had been recommended a removable partial denture (RPD) or received one as a permanent option. Some of the patients reported to have used one during an intermediate phase before receiving permanent replacements. A few studies have described the use of RPDs in patients with severe hypodontia or ectodermal dysplasia. In 1989, RPDs were frequently used in the treatment of severe hypodontia, as reported by Hobkirk et al. (149). The dentures had a relatively short lifespan, and needed to be replaced within 3.5–4 years in the maxilla on average. Reasons for replacement were dissatisfaction with the appearance of the prosthesis, fracture, wear or oral changes. Lexner et al. (150) investigated ten males affected with X-linked hypohidrotic ectodermal dysplasia who were treated with removable prostheses. In 7 out of 10, the treatment was a success according to the patient, their parents and the dentist. The prostheses had to be re-made regularly due to eruption of teeth or growth of the mandible.
Figure 6. Four different cases of visible metal after implant insertion in the anterior mandible; a) 23 year old female 5 years after implant placement, b) 25 year old female 2 years after implant placement, c) 23 year old male 3 years after implant placement, d) 30 year old female 10 years after implant placement.

Figure 7. Female aged 22 years missing 15, 14, 12, 22, 24, 25, 35, 41, 45 with persisting 55, 63, 65, 75, 85. Single-retained resin bonded prostheses are replacing 12 and 41. Teeth 11, 21 and 63 have received bonded veneer restorations.
Orthodontic treatment

Orthodontic treatment is usually unavoidable for the majority of hypodontia patients. Most patients require an increase in the vertical dimensions of the jaw, a more favourable distribution of developed teeth and, if possible, to close gaps after missing teeth. Paper III showed that out of the 571 teeth that were missing among the 50 investigated subjects, 111 were substituted by orthodontic space closure. The literature regarding orthodontic space closure in hypodontia patients has mainly focused on closing spaces due to congenitally missing maxillary lateral incisors or premolars; the success of space closure has often been compared to dental implant treatment. Space closure with canine substitution in cases of missing lateral incisors is associated with aesthetic challenges such as the large canine dimensions, the darker and more yellow colour of the canine and the gingival height (151). Other disadvantages are the tendency for relapse, usually requiring long-term retention, and the lack of a canine-protected occlusion. However, no significant difference in the prevalence of temporomandibular disorders was found between patients treated with space closure or prosthetic replacement (152). Insertion of dental implants usually involves an initial phase of orthodontic treatment to upright and parallel the adjacent teeth, and to gain sufficient space in the mesio-distal dimension (151). A few studies have shown that orthodontic space opening prior to implant insertion leads to reduction of the alveolar ridge dimension (153-155), and one author argued that space opening before the age of 13 led to the least amount of alveolar ridge reduction (155). Some negative observations have been reported for the implant technique, such as infra-position of the implant-supported crown, even when growth and dental development is complete, due to continuous eruption of the adjacent teeth (126), resulting in apical displacement of the soft-tissue margin. Mucosal recession, reduction of the buccal bone wall, thread exposure and reduction of the marginal bone level of the adjacent teeth have also been reported (96, 151). A review by Kiliaridis et al. (96) of treatment options for missing lateral incisors showed that both space closure and implants have their advantages as well as disadvantages, but that in cases where both therapeutic options are indicated, orthodontic space closure is more preferable than space opening, due to superior periodontal health and aesthetic outcome. In addition, early completion of the definitive treatment and absence of long-term biological and technical complications are aspects in favour of orthodontic space closure (96). A study by De-Marchi et al. (156) assessed smile attractiveness in patients with missing lateral incisors treated with either space opening followed by implant placement, or space closure followed by teeth recontouring, in addition to a control group with a complete dentition. Smile attractiveness was rated by laypersons, dentists and the patients themselves. The smiles of patients with maxillary lateral incisor agenesis were judged to be as attractive as those of the controls. All participants had high levels of satisfaction with their own smile; patients treated with space closure were the most
satisfied. These results indicate that both treatments are capable of achieving aesthetic results similar to an intact dentition. A very recent and similar study by Schneider et al. (157) concluded that orthodontists and dentists rank implant treatment and space closure as equally aesthetically pleasing, whereas laypersons prefer space closure.

**Treatment outcome from the patients’ perspective**

Previously unpublished data on patients’ own evaluation of treatment outcome are listed in the result section. The patients are the same as those included in paper III. The preceding discussion has mainly dealt with objective evaluations of different treatment options. However, in line with a patient-centred philosophy, self-reported satisfaction must be considered an equally important indicator as objective measures of treatment outcome. The patient is, after all, the supreme judge of whether the treatment is to be considered a success. The patients from paper III were in surprising agreement, with 95.5% reporting satisfaction with the treatment outcome. We were unable to distinguish whether there was any difference in satisfaction between the groups that had received different treatment alternatives. The reason for this was twofold: almost all patients were satisfied, and each patient had gone through many different procedures. Only a very few had undergone a single means of treatment (e.g. solely implant treatment or orthodontic space closure) to replace missing teeth. The majority of the patients, 77.3% and 88.6% respectively, reported that the replacement teeth felt similar to the natural teeth, and that chewing with the replacement teeth was similar to the natural teeth. As all patients had received several replacements, these results indicate a reasonable good acceptance of the artificial teeth as substitutes for their natural teeth. However, 61.3% found it more demanding or a lot of work to maintain hygiene around the replacement teeth.

High patient satisfaction has also been found in other studies where teeth have been replaced. In a study of treatment outcome in hypodontia patients, Dueled et al. (148) reported that 98% of the patients treated with dental implants and 84% of the patients treated with FDP were satisfied. Czochrowska et al. reported high patient satisfaction after tooth transplantation (106) and space closure of a missing maxillary central incisor (158).
Clinical implications

Standardisation, specialisation and the participation of high-volume operators have been shown to result in favourable outcomes for patients with other conditions such as cleft lip and palate (159). The development of such standards for patients with severe hypodontia would be most welcome, but still remains a challenge. These patients form a heterogeneous group, with large individual differences, and a clinical picture in constant change. There is also a lack of evidence evaluating treatment outcome. In order to optimise treatment planning in this group, early diagnosis and referral to an interdisciplinary team is crucial. Owing to the low prevalence of severe hypodontia, a single clinician will encounter patients with this condition only rarely. Interdisciplinary teams will serve to increase knowledge and experience with rare conditions. They also contribute to information and support to the patient and family, offer a thoroughly planned and co-ordinated treatment with high continuity, and the involved specialists share responsibility for treatment decisions (88). The findings from this thesis suggest that children who were referred early and recommended to preserve and take care of their primary teeth were better off than those who were referred late. Early referral leaves all treatment options available, whereas some options (e.g. autotransplantation or growth-adaptive approaches) may have become unavailable if patients are referred late. Results from this work show that tooth replacements can be made minimally invasive in growing children, for example by using resin bonded prostheses attached to either permanent or primary teeth, especially in the anterior region. This has proven to result in an aesthetically pleasing result with good durability as a semi-permanent solution. In addition, such solutions will ease the psychosocial burden for young patients. More invasive prosthetic interventions such as conventional FDPs and implants may thereby be postponed for as long as possible. The placement of dental implants in the anterior mandible, in these individuals with reduced amounts of alveolar bone, should be considered inadvisable based on the results of the follow-up study described in paper III, and all other means should be considered prior to undertaking such therapy.
Conclusions

In accordance with the proposed aims, the following conclusions can be drawn:

Prognostic factors for retaining persisting primary mandibular molars

- Critical factors for the survival of a persisting primary molar without successor are infraocclusion, root resorption and restorations. Clinically significant infraocclusion was found in 43.6% of the patients, and was the most critical factor for the prognosis of primary mandibular molars. This is particularly important for individuals who have not yet completed the pubertal growth spurt.

Generic and condition-specific impacts in patients with hypodontia or a malocclusion with similar treatment need

- Hypodontia and malocclusion patients reported a considerable burden of oral impacts. The generic inventory did not discriminate between patients with and without hypodontia, whereas the condition specific measure attributed to hypodontia discriminated with statistical significance between the groups, and was related to severity and upper anterior location of hypodontia. This indicates that the hypodontia patients have psychosocial impacts directly related to their condition, and consequently an objective need for treatment.

Tooth replacements in young adults with severe hypodontia

- Dental implants in the anterior region proved to be an inadequate treatment modality in patients with severe hypodontia, with visible metal the most notable issue. Mucosal discoloration was evident in the anterior mandible in almost all patients and, in the anterior maxilla, in two thirds of the patients. Orthodontic space closure resulted in superior papilla aesthetics, but had the drawback of a less optimal crown morphology in the anterior mandible. Dental implants, orthodontic space closure, and retaining primary teeth were the most commonly prescribed treatments. Persisting primary teeth showed a good survival rate.

In conclusion, results from this thesis show that patients with severe hypodontia require a comprehensive, interdisciplinary planning, as well as life-long treatment and follow-up. In addition to understanding of the patients’ dental issues, a more profound comprehension of their social and emotional struggles is also essential for the clinicians involved. Patient satisfaction is very high after treatment regardless of replacement type; however, professionals should be aware of biological limitations in different circumstances, and always
pursue the most appropriate and longest-lasting solutions possible for these young individuals.
References


