DOCTORAL DISSERTATION IN ODONTOLOGY

JENNY KALLUNKI

EARLY TREATMENT OF CLASS II MALOCCLUSION WITH EXCESSIVE OVERJET

Evaluating oral health-related quality of life, randomised controlled trials on headgear activator treatment and costs

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Department of Orthodontics
Faculty of Odontology, Malmö University, Sweden
Center of Orthodontics and Pediatric Dentistry
Region Östergötland
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To Kristoffer and Lovisa

I could not help laughing at the ease with which he explained his process of deduction.
"When I hear you give your reasons," I remarked, "the thing always appears to me to be so ridiculously simple that I could easily do it myself, though at each successive instance of your reasoning I am baffled until you explain your process. And yet I believe that my eyes are as good as yours."
"Quite so," he answered, lightning a cigarette, and throwing himself down into an armchair. "You see, but you do not observe. The distinction is clear. For example, you have frequently seen the steps which lead up from the hall to this room."
"Frequently."
"How often?"
"Well, some hundreds of times."
"Then how many are there?"
"How many? I don´t know."
"Quite so! You have not observed. And yet you have seen. That´s just my point."

A Scandal in Bohemia
– Sir Arthur Conan Doyle, 1891

CONTENTS

PREFACE

This thesis is based on the following four papers, which are referred to by the Roman numerals I–IV.

I. Kallunki J., Bondemark L. and Paulsson L. (2018) Outcomes of Early Class II Malocclusion Treatment – a Systematic Review. Journal of Dentistry: Oral Health Cosmesis, 2: 009 DOI: 10.24966/DOHC-6783/100009.

II. Kallunki J., Sollenius O., Paulsson L., Petrén S., Dimberg L., and Bondemark L. (2019) Oral health-related quality of life among children with excessive overjet or unilateral posterior crossbite with functional shift compared to children with no or mild orthodontic treatment need. European Journal of Orthodontics, 41, 111–116.

III. Kallunki J., Bondemark L. and Paulsson L. (2020) Early headgear activator treatment of Class II malocclusion with excessive overjet: a randomized controlled trial.
European Journal of Orthodontics, cjaa073. doi: 10.1093/ejo/cjaa073. [Online ahead of print]

IV. Kallunki J., Bondemark L. and Paulsson L. (2021) Comparisons of costs and treatment effects – an RCT on headgear activator treatment of excessive overjet in the mixed and late mixed dentition.
European Journal of Orthodontics, cjab026. doi: 10.1093/ejo/cjab026. [Online ahead of print]

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THESIS AT A GLANCE

Paper	Aim	Study design	Sample	Primary outcome measure	Main findings
I	To review the evidence supporting early treatment (before the age of 10) of Class II malocclusion.	Systematic review	297 studies retrieved from four databases between January 1960 and October 2017.	Short and long-term effects regarding correction of overjet, dental and intermaxillary relationships, soft tissue profile, associations to temporo-mandibular disorders, quality of life, incidence of trauma and cost-effectiveness.	Treatment with functional appliances reduces overjet and improves antero-posterior skeletal relationship (High level of evidence). Headgear reduces overjet and restrains forward growth of the maxilla (Moderate level of evidence). Insufficient evidence regarding effects on soft tissue profile, quality of life, incidence of trauma or costs. Lack of knowledge regarding long-term outcome and stability of early treatment.
II	To register and compare oral health-related quality of life (OHRQoL) among 9-year-old children with excessive overjet (EO) to children with unilateral posterior crossbite with functional shift (UPC) and children with normal occlusion (NO).	Clinical controlled trial	The patients sourced from 19 Public Dental Service Clinics in Sweden. The EO group comprised 71 children, the UPC group 93 children, and the NO group 65 children.	OHRQoL registered by the Child Perceptions Questionnaire (CPQ8-10). Corrected for the possible confounders of gender, caries, trauma, enamel defects, and headache.	Young children with EO reported significantly lower self-perceived OHRQoL compared to peers with UPC or normal occlusion. However, despite the presence of malocclusions, the children generally reported low CPQ scores, which imply an overall fairly good self-perceived OHRQoL.
III	To evaluate the effects of early headgear activator treatment of Class II malocclusion with excessive overjet when compared to an untreated control group.	Randomised controlled trial	Sixty patients randomised to either early treatment with headgear activator (starting at 9 years of age) or to an untreated control group.	Effects on reduction of overjet and overbite as well as effects regarding OHRQoL, lip closure, incidence of trauma, and skeletal changes. Intention-to-treat strategy was applied.	Treatment with headgear activator was successful in terms of reducing overjet for those patients who completed treatment. The effects were mainly dentoalveolar. No other significant treatment effects were found.
IV	To evaluate and compare the costs and treatment effects of headgear activator treatment of Class II malocclusion with excessive overjet between treatments started in the mixed dentition, at 9 years of age, or late mixed dentition, at 11 years of age.	Randomised controlled trial	Fifty-one children randomised to treatment with headgear activator either in the mixed dentition (9 years old, n = 30), or late mixed dentition (11 years old, n = 21).	Cost analysis including societal costs, direct and indirect costs. Registrations of overjet and overbite as well as effects regarding OHRQoL, lip closure, incidence of trauma, and skeletal changes. Intention-to-treat strategy was applied.	Costs and treatment effects were equal regardless of whether headgear activator treatment was performed in mixed or late mixed dentition.

ABBREVIATIONS

CPQ	the Child Perceptions Questionnaire
EO	Excessive overjet (Paper II)
EW	Emotional well-being (Domain in CPQ)
FL	Functional limitations (Domain in CPQ)
LMD	Late mixed dentition (Paper IV)
MD	Mixed dentition (Paper IV)
NO	Normal occlusion (Paper II)
OHRQoL	Oral health-related quality of life
OS	Oral Symptoms (Domain in CPQ)
SW	Social well-being (Domain in CPQ)
TG	Treated group (Paper III)
UG	Untreated group (Paper III)
UPC	Unilateral posterior crossbite (Paper II)

ABSTRACT

Class II malocclusion with excessive overjet is one of the most common malocclusions among children and adolescents. In addition to increasing the risk for dental trauma, the malocclusion can also be related to bullying due to the prominent maxillary incisors. The treatment for a Class II malocclusion can be initiated at different ages and with different treatment strategies, but the treatment timing has often been, and still is, discussed within the orthodontic profession and literature. Research reports that an early treatment approach, initiated in mixed dentition and often including an additional phase of treatment in permanent dentition, reduces the incidence of dental trauma. Otherwise, no differences in treatment effects have yet been seen between treatment that is started early in mixed dentition or treatment initiated later in permanent dentition.

During the last decades, there has been an increased focus on patient-reported outcomes within orthodontic research. The patient perspective and economic evaluations of performed treatment are areas where knowledge gaps can be found in the available research.

This thesis is based on four studies. The studies were designed with high level of methodology and validity as a priority and with the objective to identify and address knowledge gaps related to the impact of Class II malocclusion with excessive overjet and a subsequent early treatment with headgear activator. Firstly, a systematic review addressing treatment effects was performed. This was followed by the implementation of a randomised controlled trial (RCT) with the aim to evaluate treatment effects and self-perceived oral health-related quality of life (OHRQoL) as well as the cost associated with treatment. In addition, a clinical controlled

trial was performed to assess the self-perceived OHRQoL for children with Class II malocclusion with excessive overjet, and compare to children with unilateral posterior crossbite or normal occlusion with no or mild orthodontic treatment need.

The papers referred to in this thesis:

Paper I. A systematic literature review performed to evaluate the evidence supporting early treatment (before the age of 10) of Class II malocclusion. The search included four data bases and spanned from January 1960 to October 2017.

Paper II. A clinical controlled multicenter trial with the objective to investigate the OHRQoL among 9-year-old children in mixed dentition and to compare the self-perceived OHRQoL by the use of the Child Perceptions Questionnaire (CPQ). Evaluation and comparisons were made for children with Class II malocclusion with excessive overjet (EO), children with unilateral posterior crossbite (UPC), and children with normal occlusion (NO) presenting with no or mild orthodontic treatment need. The sample consisted of 229 children, sourced from 19 Public Dental Service Clinics in Sweden and covering a range of demographic areas.

A single centre RCT designed to evaluate the effects of headgear activator treatment and the associated costs forms the basis of the final two papers:

Paper III. The effects of early headgear activator treatment was compared to an untreated control group. The sample consisted of 60 children presenting with a Class II malocclusion with excessive overjet. Primary outcome was the reduction of overjet and overbite as well as effects regarding oral health-related quality of life, lip closure, incidence of trauma, and skeletal changes.

Paper IV. The costs and treatment effects of headgear activator treatment started in the mixed or late mixed dentition was registered and compared. The sample consisted of 51 children starting treatment at 9 or 11 years of age. The primary outcome measure was comparison of the treatment costs between the two groups. Secondary outcomes were comparisons of oral health-related quality of life, dental and skeletal treatment effects, lip closure, and trauma incidence.

The following conclusions were drawn:

- There is moderate to high level of evidence, depending on treatment appliance, that early treatment reduces overjet and improves antero-posterior skeletal relationship, but currently, insufficient evidence is available regarding the effects of early treatment on OHRQoL, incidence of trauma, soft tissue profile, or treatment-related costs. There is a knowledge gap with respect to long-term outcome and the stability of early treatment.

- Children with Class II malocclusion with excessive overjet report significantly lower self-perceived OHRQoL compared to children with unilateral posterior crossbite or normal occlusion, with the domains of social and emotional well-being being most affected. The children in all three groups reported generally low CPQ scores, which implies an overall fairly good self-perceived OHRQoL.

- Early treatment with headgear activator was successful in reducing overjet and correcting molar relationship. Early treatment did not result in any significant difference regarding self-reported OHRQoL, lip closure, or incidence of trauma when compared to the untreated control group.

- The costs associated with headgear activator treatment, as well as the treatment effects, were equivalent regardless of whether treatment was started at 9 or 11 years of age. The most pronounced treatment effects were reduction of overjet and correction of molar relationship, whereas the treatment effects regarding OHRQoL, lip closure, and trauma incidence were found to be modest.

- With costs and treatment effects being equivalent, an early treatment approach can be advocated to enhance trauma prevention.

The results will be beneficial for the patients, as the added knowledge will enhance the possibility to improve the care and provide the most appropriate treatment. Furthermore, the structured evaluation of treatment effects and cost analysis is important for orthodontists when planning care and deciding on a treatment strategy as well as for dental care when addressing the allocation of resources.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Postnormalt bett med förstorad horisontell överbitning benämns ofta helt enkelt som ”förstorat överbett”. Det är en av de vanligaste bettavvikelserna och förekommer hos cirka 20 procent av alla barn och ungdomar. Ett förstorat överbett är ofta förenat med utstående framtänder i överkäken, vilket är kopplat till en ökad risk att drabbas av tandskador, framförallt om läpparna inte sluts om överkäksframtänderna (ofullständig läppslutning). Risken att drabbas av tandolyckor är störst för barn innan tio års ålder. Barn och ungdomar med förstorat överbett riskerar också en negativ psykosocial påverkan då bettavvikelser i framtandsområdet har visat sig ha en försämrande effekt på den munhälsorelaterade livskvalitén och barn med utstående framtänder rapporterar en ökad förekomst av mobbning.

Tandregleringsbehandling av förstorat överbett kan inledas tidigt då mjölktänder tappas och de permanenta tänderna växer fram (växelbettet). Behandling genomförs då ofta med en avtagbar tandställning för att normalisera och korrigera det förstorade överbettet. Det finns olika varianter av avtagbara tandställningar för att korrigera det förstorade överbettet och en av de vanligaste i Sverige är aktivator med inbyggt extra oralt drag (EOD). En annan strategi är att avvakta tills barnet har fått alla sina permanenta tänder och då behandla med enbart en fastsittande tandställning. En tidig behandlingsstart förefaller minska risken för tandolyckor.

I avhandlingens första delarbete utfördes en systematisk litteraturöversikt för att undersöka det vetenskapliga underlaget, och identifiera eventuella kunskapsluckor, gällande behandlingseffekter vid tidig behandling av postnormalt bett med förstorad horisontell överbitning. I det andra delarbetet genomfördes en kontrollerad multicenterstudie för att kartlägga den inverkan ett förstorat överbett har på barns munhälsorelaterade livskvalitet. För att få ett starkt vetenskapligt underlag användes randomiserad kontrollerad studiedesign i delarbete tre och fyra för att undersöka behandlingseffekterna på förstorat överbett av aktivator med extra oralt drag då behandling inleddes vid 9 år eller 11 års ålder. Utöver analys av behandlingseffekterna på bettet registrerades också de kostnader som var förenade med behandlingarna liksom behandlingarnas inverkan på barnens munhälsorelaterade livskvalitet och om tandolyckor kunde förebyggas.

Avhandlingens slutsatser:

- Det finns medelhög till hög evidens för att tidig behandling är effektiv för att normalisera förstorat överbett och förbättra käkarnas relation, men det finns kunskapsluckor om hur tidig behandling påverkar barnens munhälsorelaterade livskvalité. Vidare finns även kunskapsluckor om behandlingskostnader (hälsoekonomiska analyser) vid tidig behandling av förstorat överbett liksom för hur stabila behandlingsresultaten är flera år efter genomförd behandling.

- Redan vid 9 års ålder rapporterar barn med förstorat överbett en försämrad munhälsorelaterad livskvalitet jämfört med barn med korsbett eller normalbett. Försämringen är tydligast beträffande socialt och känslomässigt välmående. Däremot hade samtliga barn, med eller utan bettavvikelser, en förhållandevis god generell munhälsorelaterad livskvalitet.

- Tidig behandling (vid 9 års ålder) med aktivator och extraoralt drag är effektiv för att normalisera det förstorade överbettet. Jämfört med en obehandlad kontrollgrupp hade behandlingen inte några tydliga effekter på munhälsorelaterad livskvalitet, förebyggande av tandolyckor eller förbättring av läppslut.

- Kostnaderna för behandling av förstorat överbett är likvärdiga oavsett om behandling startar vid 9 eller 11 års ålder. Vidare är påbörjad behandling vid 9 eller 11 år lika effektivt för att normalisera det förstorade överbettet. Behandlingseffekterna på munhälsorelaterad livskvalitet, förebyggande av tandolyckor samt förbättring av läppslut är ringa oavsett om behandling startar vid 9 eller 11 års ålder.

Klinisk betydelse

Postnormalt bett med förstorad horisontell överbitning berör många barn, och de negativa effekterna av bettavvikelsen kan påverka barnen både psykosocialt och funktionellt. Eftersom kostnader och behandlingseffekter är likvärdiga oavsett om behandlingen påbörjas vid 9 eller 11 års ålder kan en tidig behandlingsstart vid 9 års ålder förespråkas för att redan i tidig ålder minska eventuella negativa effekter på munhälsorelaterad livskvalitet och verka förebyggande av tandolyckor.

INTRODUCTION

The classification of normal occlusion and subsequent classifications of malocclusions by Edward H. Angle in the late 19th century is based on the mesiodistal relation of teeth and depends primarily on the relation between the mandibular and maxillary first molars. A Class II malocclusion is defined by the distal positioned mandibular molar to the extent of more than one-half the width of one cusp on each side.[1]

The Class II malocclusion is thereafter divided into two divisions, with Class II Division 1 including proclined maxillary incisors and associated increased overjet and Class II Division 2 with retroclined maxillary central incisors and proclined lateral incisors, as seen in Figure 1a,b.

Figure 1a. A child with a Class II Division 1 malocclusion.

Figure 1b. A child with a Class II Division 2 malocclusion.

Aetiology

Both hereditary and environmental factors interact in the development of a malocclusion. The process is often complex and only rarely can the aetiology of a specific malocclusion be derived from one single factor. In addition, a higher heritability for skeletal features than for dental variables has been reported.[2,3]

Various combinations of dental and skeletal features constitute the Class II malocclusion. Mandibular retrusion and deviations in both vertical and sagittal mandibular development are the most common denominators for Class II patients, whereas maxillary protrusion is a rare finding.[4]

Non-nutritive sucking behaviour presents various risks of developing malocclusions. In the primary dentition, the use of pacifiers increases the risk for a Class II canine relationship, whereas digit sucking is associated with an increased overjet when compared to the use of pacifier.[5] A higher prevalence of Class II malocclusion has been seen for children with sleep-disordered breathing[6], further indicating the significance of environmental factors. However, when left untreated, a Class II Division 1 malocclusion does not seem to deteriorate with age.[7]

Prevalence

A Class II malocclusion is one of the most prevalent malocclusions in children and adolescents. Division 1 dominates and is almost nine times more frequent than Division 2.[8] In Swedish 7- to 13-year-old children and young adolescents, the reported prevalence of Class II malocclusion varies from 14% up to 49%.[8-10] Registrations from the United Kingdom report a prevalence of 25% in 12-year-old children.[11] When measuring overjet exceeding 5 millimetres as an indication for Class II malocclusion, the reported prevalence in the United States is 22% for 8- to 11-year-old children, thereafter, decreasing to 15% for 12- to 17-year-olds.[12] The varying reported prevalence is presumably due to a difference in methodology and definition.

Treatment need

Malocclusions are deviations from what is considered and accepted as a normal occlusion. However, a diagnosed malocclusion does not necessarily imply a treatment need. Each individual needs to be evaluated as to how the

malocclusion, in both the short- and long-term perspective, can influence growth, function and psychosocial well-being.[13] The advocated treatment needs for Class II malocclusion with excessive overjet include both functional and psychosocial needs.

An overjet exceeding 6 mm can more than double the risk of dental trauma.[14] Furthermore, the presence of an incomplete lip closure (Figure 2) increases the risk of dental trauma,[15] up to threefold if combined with an overjet exceeding 4 mm.[9] Early treatment of Class II malocclusion has been shown to reduce the incidence of new incisal trauma when compared to patients where treatment was initiated in adolescence.[11]

Figure 2. Three different children with incomplete lip closure.

The presence of malocclusion can impair the individual from a psychosocial point of view. Malocclusions in the anterior zone, including increased overjet, have been shown to have a negative impact on oral health-related quality of life (OHRQoL). The negative effects predominately affect social and emotional well-being.[16] Examples of the negative impact can be illustrated by the findings that enlarged overjet and incomplete lip closure are rated as less attractive features by both children and adults[17] and that children with Class II Division 1 malocclusion report a higher incidence of being bullied mainly relating to the proclined incisors.[18, 19] There is a complex correlation between malocclusion, self-esteem and OHRQoL, but treatment of Class II malocclusion has been reported to have positive effect on self-concept as well as reducing negative social experiences such as bullying.[20, 21] However, there is no evidence that early treatment of Class II malocclusion renders any significant difference in self-concept score.[11]

Orthodontic priority indices are often used to define treatment need and establish the priority of the patients in need of treatment. Evaluating and deciding on treatment need is important for the allocation and effective use of resources – a necessity, as all publicly funded care presents with limited resources. There are many indices available which consider, and aim to grade, both functional and psychosocial impairments due to the presence of a malocclusion. Although widely used, the evaluated evidence of the validity of these indices is insufficient. Even though individual indices present with limitations to cover the full spectrum of occlusal traits, and especially the subjective treatment need, they are currently the best instruments available.[15] Orthodontic priority indices emphasise the treatment need of Class II Division I malocclusion. [22,23] Excessive overjet of more than 6 mm implies a moderate objective treatment need, and if surpassing 9 mm, a severe treatment need.[22]

Treatment timing and strategies

Treatment of Class II malocclusion with excessive overjet can be initiated at various ages and with different treatment strategies. Treatment in the primary dentition is rarely indicated, as a chance of spontaneous correction exists, but the relation of any sucking habits as a contributor to excessive overjet should be observed.[24] Treatment in mixed dentition offers a variety of removable appliances with the aim of correcting molar relationship and reducing overjet. The focus can be put on the maxilla by the use of headgear or to the mandible by the use of functional appliances. Regardless of approach, treatment in the mixed dentition usually aims at improving dental and skeletal relations. If postponed to permanent dentition, treatment is mainly performed with fixed appliance, and the treatment strategy is highly dependent on the individual skeletal and dental features. After teeth alignment with fixed appliance, the molar relation and overjet can be corrected by the use of Class II intermaxillary elastics or by fixed functional appliance. The achieved effects by Class II intermaxillary elastics are primarily the result of moving the mandibular teeth forward rather than the maxillary teeth backwards. If it is considered more desirable to retract the maxillary incisors, upper premolar extraction is an alternative, resulting in a Class I canin relationship and a Class II molar relationship. This is often referred to as camouflage treatment which assumes the lack of pronounced skeletal discrepancy as a requisite for success. For patients presenting with mild or moderate skeletal Class II relation, camouflage

treatment by tooth movements alone can achieve both good occlusion and facial appearance. If the skeletal Class II relation is severe, the sole correction of the occlusion might present with a high tendency for relapse as well as a compromised facial aesthetics. For these patients, a combined surgical and orthodontic treatment is more appropriate.[25]

Treatment philosophy

With deviations in mandibular development, both sagittally and vertically, treatment of Class II malocclusion would ideally focus on stimulating mandibular forward growth.[4] The general thought of mandibular growth modification can be divided into two different possible effects: a final size of the mandible that is larger than the size that would have been the result without treatment, or the occurrence of an accelerated mandibular growth during treatment than otherwise would have been expected but does not affect the final size of the skeleton.[25]

The use of functional appliances in orthodontic treatments has a very long history, with the introduction of the activator by Andresen in the early 20th century as somewhat of a milestone.[26] The purpose of a functional appliance is to sagittally and vertically alter the position of the mandible.[27] With the mandible moved forward, the Class II dental relation is corrected and the bite opened. The changed position of the mandible generates an activity and stretch of the orofacial muscles and soft tissue when the muscles attempt to return the mandible to its original position. The intention of the functional appliance is therefore, through the altered muscular activity, to induce orthodontic forces directed at the teeth and orthopaedic forces directed at the jaws. The muscular activity generates an anteriorly directed force on the mandible and an opposite distally directed force on the maxilla that is transmitted through the functional appliance to the dentition and onto the jaws, which results in tooth movement and growth modification.[28,29]

Functional appliances provide a limited ability to individual tooth movement compared to fixed orthodontic appliances. A treatment with removable functional appliance can therefore be followed by a second phase with fixed appliances[30] if there is a need to produce individual tooth movements and improve occlusion.

Functional appliances

Functional appliances can be divided into removable and fixed. The start of removable functional appliance therapy was seen with the 'bite-jumping' appliance introduced by Kingsley in the late 19th century. However, the first appliance to gain widespread use and clinical acceptance was the activator developed by Andresen in the 1920s, forming the basis of the 'Norwegian system'.[31] With the objective to further enhance functional adaption of the orofacial muscles, the Fränkel functional regulator was developed in the mid-20th century.[32] Other removable appliances designed to correct a Class II malocclusion include the less bulky Bionator developed by Balters,[33] the Bass appliance,[34] and with the modification introduced by Clark,[35] the Twin-block appliance was developed for full-time use.

Geographical differences can be seen regarding preferred appliance. In Sweden, treatment with removable functional appliances is often undertaken by the general dentist after consultation, or in collaboration, with an orthodontist, and for Class II malocclusion treatment, the most recommended removable appliance is the headgear activator.[36] The Twin-block has been the preferred appliance among British orthodontists,[37] whereas the Bionator is more prevalent than the activator among American orthodontists.[38]

Fixed functional appliances can be sub-grouped into rigid and flexible. The Herbst appliance, being a leading fixed functional appliance, was developed in the beginning of the 20th century, but it is from the extensive work later performed by Pancherz that the appliance has been evaluated.[31] The Herbst appliance consists of bilateral arms with telescope mechanism attached to maxillary molar bands and mandibular premolar bands or a cantilever, holding the mandible in an anterior position full time.[39] It is rigid and restricts lateral movement of the mandible and may therefore complicate for patients regarding chewing and oral hygiene. The Jasper Jumper[40] and Forsus[41] are used in conjunction with fixed orthodontic appliance and operate by the same methodology as the Herbst appliances but adds an amount of flexibility. The main difference between removable and fixed functional appliances is the aspect of compliance with the removable variants, whereas full-time wear is guaranteed with the fixed design. However, a fixed design is correlated to more emergency visits due to breakage or debonding.[42]

Treatment effect and stability

The maxillary and mandibular dental and skeletal treatment effects by functional appliances have been the subject of debate and research for a long time. Dental movement caused by the altered muscular activity induced by functional appliances includes retroclination of the maxillary incisors and proclination of the mandibular incisors. The distal directed force on the maxillary dentition transmitters to the underlying skeleton and can cause a growth strain effect on the maxilla, and the sequent anterior directed force affects the mandible.[28,43-47] The remodelling and stimulation of condylar growth,[48-51] and to some extent, advancement of the glenoid fossa[27,44,52,53] have been attributed to the skeletal changes on the mandible by functional treatment.

An accelerated anterior and vertically directed mandibular growth during treatment ceases, however, indicating that any growth modification effect is temporary.[54,55] Therefore, the main treatment effect achieved by functional appliances mainly derives from tooth movement, and altered skeletal growth has less significance.[47,56] There is a lack of RCT studies reporting long-term follow-up of early Class II malocclusion treatments.

Headgear activator

Headgear

To apply extraoral pressure on the maxilla by the use of headgear with the intention to modify skeletal growth has a long history. Edward Angle reasoned that the use of intermaxillary elastics would effect mandibular growth, and under his strong influence, the use of headgear decreased in favour of the use of Class II intraoral elastics. As cephalometric evaluations later revealed that intraoral elastics corrected Class II malocclusion mainly by displacing the mandibular teeth forward, headgear also became classified as merely a tooth-moving appliance.[25] The thought of headgear as having solely dentoalveolar effects was rejected by Wieslander,[57] and the restraint of maxillary growth exerted by headgear has thereafter been shown.[46,58]

Activator

The activator introduced by Andresen[26] was initially made out of rubber and was loose fitting, requiring patients to actively keep the appliance in place. Later, the activators started to be made out of acrylic.[29] A labial

bow is in contact with the maxillary incisors, and the passive, tooth-borne activator is customised to advance the mandible sagittally and vertically in order to correct the Class II malocclusion. In its original design, eruption planes for the posterior teeth were incorporated to guide the mandibular segments to erupt mesially and vertically, whereas the maxillary lateral segments were guided distally and buccally.[26]

Present activators are usually some type of modification of the original appliance. The vertical dimension of the construction bite can be altered, and the treatment effects with various bite opening have been addressed.[43,44,49,56]

Prefabricated functional appliances (PFA) made from elastomeric material were introduced in the 1980s.[59] Besides aiming at reducing sagittal and vertical dental discrepancies, prefabricated functional appliances also intend to align the incisors. With no need to customise the appliance, the accessibility can be stated as one major advantage. The outcomes of Class II malocclusion treatment with prefabricated functional appliances have been described, and the effects are mainly dento-alveolar.[60-62]

Headgear activator

The simultaneous use of headgear and activator was introduced by Pfeiffer and Grobety in the 1970s, when headgear with cervical traction to banded maxillary first molars were combined with the use of an activator.[63] The authors stated that the simultaneous use of these was highly effective, as the appliances seemed to favour each other when the activator, in addition to its own properties, also eliminated occlusal interferences and the headgear (apart from delivering orthodontic and orthopaedic force) could enhance retention of the activator. The concept was further developed when the headgear was incorporated into the activator and provided with a high-pull headgear.[64] By incorporating the headgear, the appliance affected the maxillary dentition as a whole, and by elevating the direction of the headgear, the extraoral force was applied closer to centre of resistance of the maxilla. It has been claimed that headgear activator enhances maxillary restraint and reduces proclination of the mandibular incisors when compared to the sole use of activator.[65,66] The headgear activator has gained widespread use and is the most frequently recommended functional appliance for Class II malocclusion treatment in Sweden.[36]

Compliance

Successful treatment with removable appliances is highly dependent on the compliance and the actual wear-time.[30,67] Suboptimal compliance is however a frequent finding when evaluating patient adherence to given recommendations. Registrations of wear-time can be made subjectively by patient or parental reports or by objective measuring with a microsensor incorporated in the appliance.[68] Objective measures indicate that the patients' actual wear-time is about five hours less per day than prescribed by the orthodontist, regardless of which type of appliance used. Patients and parents tend to over report wear-time to a similar extent.[69-71] Younger children have been shown to have higher compliance than adolescents,[68,71] but contradictory reports exist.[69]

Compliance is influenced by many factors. Younger children have less internal motivation for treatment and require their parents support in order to comply with treatment. If parental involvement and control is lacking, it is usually a better idea to postpone treatment until the child is older.[72] The influence of family relationships on compliance is further illustrated with the higher wear-time registered in patients with private health insurance.[68] Internal motivation for treatment increases with age, and compliance is further enhanced by external support and continuous feedback from the orthodontist regarding treatment progress.[72,73]

Oral health-related quality of life (OHRQoL)

Good oral health is recognised as essential to both general health and quality of life. The condition implies being free from diseases and disorders that could limit the capacity in biting, chewing, smiling, speaking, or negatively affect psychosocial well-being.[74] To fully evaluate the efforts made by health care and the achieved results, the need to register patient reported outcome measures, such as quality of life, is emphasised. Adding patient reported outcome measures to the evaluation enables continuous improvement of the care given.[75] Even though the need to register patients' reported outcome measures has been stressed, it has also been recognised that orthodontic research tends to overlook these outcomes and do not reflect the patients' perspective enough.[76]

Patient reported outcome measures, such as OHRQoL, is usually registered by the use of questionnaires. The number of questionnaires

specifically developed to register children's self-reported OHRQoL are few, with the Child Oral Health Impact Profile (COHIP), Child Perceptions Questionnaire, and Early Childhood Oral Health Impact Scale being the most commonly used instruments.[77]

The Child Perceptions Questionnaire

The Child Perceptions Questionnaire (CPQ) is one of few instruments available in dental research that is specifically developed to register OHRQoL in children and young adolescents. Children's self-concept is dependent on their cognitive, emotional, social, and language development. Therefore, the CPQ is designed in two age-specific versions. CPQ 8-10[78] is constructed for children from eight to ten years of age and CPQ 11-14[79] for eleven to fourteen years old. The two age-specific versions differ in the number of items to be answered, wording, and recall period in order to be age-adapted. The Child Perceptions Questionnaire encompasses four domains: oral symptoms, functional limitations, emotional well-being, and social well-being, enabling the evaluation of subscale scores and the overall score. The CPQ has gained widespread use and is translated and validated in several languages and cultural contexts[80-83] making it one of the most applied instruments when registering OHRQoL in children and young adolescents.

Economic health evaluations

All medical treatments are associated with effects and costs, and the choice of one action over another will presumably render a difference in effect, cost, or both. Economic evaluations are defined by Drummond[84] as 'the comparative analysis of alternative courses of action in terms of both their costs and consequences'. Given that resources are limited within healthcare in terms of personnel, equipment, time, and money, knowledge regarding treatment effects and economic evaluation is essential in order to make well-grounded decisions regarding the most appropriate treatment. An economic evaluation needs also to have a broad perspective to identify costs and consequences that have to do with other actors than healthcare, such as patients and their families.[84] Health economic evaluations are highly dependent on local factors, such as insurance systems, salaries, and costs for equipment, and therefore, the monetary result cannot be directly applied to other settings.

Dental healthcare is free of charge until the age of 23 in Sweden. Provided an objective treatment need according to indices, this also includes orthodontic treatment.[85] Approximately 30 percent of Swedish children receive some form of orthodontic treatment during childhood or adolescence.[15] Nevertheless, economic evaluations of orthodontic treatments are scarce. Few recent studies report clinical and economic outcomes,[86-88] but there are advocates for further research given that the assembled evidence regarding the health economics of orthodontic treatment is low.[89]

There is an overall limited number of studies reporting on the costs associated with Class II malocclusion treatment, and none specifically targeting an early treatment approach. It has been presented that treatment with prefabricated functional appliance is associated with reduced costs when compared to Andresen activator treatment and therefore should be preferred, as both appliances showed equivalent treatment results.[86] The costs related to dental trauma in children with Class II malocclusion have been evaluated, and it has been suggested that treatment would have to be initiated soon after incisor eruption in order to be trauma-preventing and subsequently reduce the costs associated with dental trauma.[90,91]

Within health economic evaluations, four main analyses can be carried out. Cost-minimization analysis (CMA) evaluate treatments where the consequences are broadly equivalent, which reduces the difference between treatments to a comparison of costs. A cost-effectiveness analysis (CEA) compares the costs related to one common outcome that might differ in magnitude between the evaluated treatments and can be reported as the incremental cost per unit of effect. A cost-utility analysis (CUA) is a form of CEA in which a generic measure of health gain, often expressed as QALY (quality-adjusted life year) is used. This approach enables comparisons between different areas within healthcare, provided that the effects can be converted into the generic measure. Lastly, a cost-benefit analysis (CBA) introduces the aspect of willingness to pay, which is of interest in the possible situation of expanding a budget.[84]

Adopting a societal perspective when performing health economic evaluations is preferred. This broad perspective attempts to include all costs associated with an intervention, direct as well as indirect (patient-borne) costs. Direct costs refer to those costs associated with the care

and treatment provided by the resources of healthcare, such as cost for personnel and equipment. The indirect cost refers primarily to loss of production for the patient (or family) but can also include out-of-pocket expenses.[84]

Evidence-based health evaluations

A prerequisite for good healthcare is an evidence-based approach in order to assure the patient of the most effective and least risky treatment. The concepts also include making the best use of available resources and to avoid treatment methods with dubious benefits.

A systematic review is a compilation of all available research within a defined research area and reviewed according to a specific predetermined methodology. The conclusions of a systematic review are therefore based on the best scientific evidence available at the time, making the information easily accessible for clinicians and decision makers. Systematic reviews can also identify knowledge gaps and the need for further research. When assessing research studies and rating their quality of evidence, the risk of potential bias has to be evaluated.[92]

Randomised controlled trials (RCT) has long been considered a golden standard when conducting clinical research. With patients randomly allocated to different treatments, the distribution of potential bias and confounding factors is presumptively evenly distributed in the involved groups, provided there is a sufficient number of participants. To further reduce bias, an Intention-to-treat (ITT) approach should be applied. To analyse all included patients according to the group they were originally assigned, regardless of what treatment they received or if the treatment was discontinued, provides valid conclusions regarding the effectiveness of an intervention.

Why the studies in this thesis were conducted

The conclusion of limited or low evidence for a treatment does not imply lack of effect. On the contrary, inconclusive or low evidence based on a few number of relevant studies illustrates the need for further well-designed studies regarding early treatment of Class II malocclusion with excessive overjet.

The studies in this thesis have been designed with an evidence-based approach with the aim to evaluate the impact a Class II malocclusion with excessive overjet imposes on OHRQoL in children, and the effectiveness and associated costs of early treatment with headgear activator. The results will add to the body of knowledge and level of evidence, enabling caregivers to provide the most effective treatment to patients, from a patient and societal perspective.

AIMS AND HYPOTHESES

The overall aim of this thesis was to evaluate the impact of a Class II malocclusion with excessive overjet and the effects of treatment with headgear activator when treatment is initiated at 9 or 11 years of age. A randomised controlled trial generated three papers (Papers II-IV), in which one presents as a clinical controlled multicenter trial (Paper II). In addition, a systematic review (Paper I) was performed to evaluate the scientific evidence regarding the early treatment of Class II malocclusion.

The specific aim and hypothesis for each paper are as follows:

Paper I
Paper I undertakes a systematic literature review of published studies regarding early treatment (before the age of 10) of Class II malocclusion, assessing the evidence from studies presenting short- and long-term treatment outcomes. The paper's hypothesis is that even though treatment of Class II malocclusion has been extensively investigated, the evidence regarding an early treatment approach (before 10 years of age) is limited.

Paper II
Paper II investigates the OHRQoL of 9-year-old children with Class II malocclusion and excessive overjet (EO) and compare this to peers with forced unilateral posterior crossbite (UPC) and to children with normal occlusion (NO) presenting little or no orthodontic treatment need. The paper's hypothesis is that children with Class II malocclusion with excessive overjet present lower OHRQoL than children with unilateral posterior crossbite with functional shift or children with no or mild orthodontic treatment need due to the excessive overjet being a malocclusion in the aesthetic zone.

Paper III

Paper III evaluate early treatment, at 9 years of age, of Class II malocclusion with excessive overjet with headgear activator in terms of the primary outcomes of overjet and overbite, in addition to the effects regarding OHRQoL, lip closure, incidence of trauma, and skeletal changes, and compare this with an untreated control group. The paper's hypothesis is that early treatment with headgear activator treatment is successful in improving overjet and overbite and has a positive effect regarding OHRQoL, lip closure, and incidence of trauma.

Paper IV

Paper IV compares the costs associated with headgear activator treatment of Class II malocclusion with excessive overjet when treatment is started early in mixed dentition at 9 years of age or in late mixed dentition at 11 years of age. In addition, it analyses and compares OHRQoL, dental and skeletal treatment effects, lip closure, and incidence of trauma between the groups. The paper's hypothesis is that treatment started at 9 years of age or at 11 years of age is equal regarding costs and the treatment effects regarding OHRQoL, skeletal and dental changes, lip closure, and trauma incidence.

MATERIALS AND METHODS

Subjects

This thesis is mainly based on the patients included in an ongoing randomised controlled trial regarding Class II malocclusion with excessive overjet. The characteristics and evaluation of the orthodontic patients and orthodontic treatments are presented in Papers II–IV.

The patients were sourced from nine Public Dental Service Clinics in Östergötland, Sweden, between 2013 and 2019. After referral from the General Dental Clinic, the patients were screened and consecutively recruited to the trial at the Specialist Orthodontic Clinic, Public Dental Service, in Norrköping.

The inclusion criteria were set to:

- 8 to 10 years of age at the start of the trial
- Mixed dentition
- Excessive overjet (≥6 mm) and first maxillary permanent molars in Class II malocclusion (bilaterally, ≥½ cusp)
- No sucking habits or ceased sucking habits should have been evident at least 1 year before the trial was started

The exclusion criteria were craniofacial syndromes, any previous orthodontic treatment, or severe crowding of teeth, as in, making the extraction of teeth necessary.

If eligible for the trial, patient and parents were provided with oral and written information about the trial and invited to participate.

Ethical approval

The Regional Ethical Review Boards in Linköping and Lund follow the Declaration of Helsinki. The trial protocol and informed consent form were approved (Dnr: 2012/302–31) by The Regional Ethical Review Board in Linköping, Sweden (Papers II–IV). The ethics committee of Lund University, in Lund, Sweden, (Dnr: 2012/650) approved the consent form and protocol for subjects in Paper II. This trial was registered at ClinicalTrials.gov, registration number: NCT04508322 (Paper III, IV).

Randomisation

If eligible after screening, the patient and parent were provided with oral and written information about the trial and invited to participate. After consent to enter the trial, the patient was randomised to one of three groups: either early treatment with headgear activator in the mixed dentition starting at nine years of age or postponed treatment with headgear activator initiated in the late mixed dentition at 11 years of age or treatment in permanent dentition with fixed appliance starting at 13 years of age, as illustrated in Figure 3. Focusing on early treatment, the group treated in permanent dentition is not reported in this thesis.

Randomisation was performed by staff not involved in the trial and undertaken in an office space away from patient, parents and operator. To ensure an equivalent distribution to the groups, concealed envelopes containing folded notes (10 notes for each group) were used. A note from the envelope was extracted, and the patient was allocated to one of the groups. When all notes had been taken, a second envelope was opened, and new notes were extracted as the patients were recruited to the trial. This procedure was then repeated.

Clinical examination and registrations

Following enrolment and randomisation, a clinical examination and medical history were performed. The following registrations were made at baseline and follow-up:

- Study casts
- Intra- and extraoral photographs
- Lateral head radiographs
- Child Perceptions Questionnaire (CPQ8-10 or CPQ11-14)

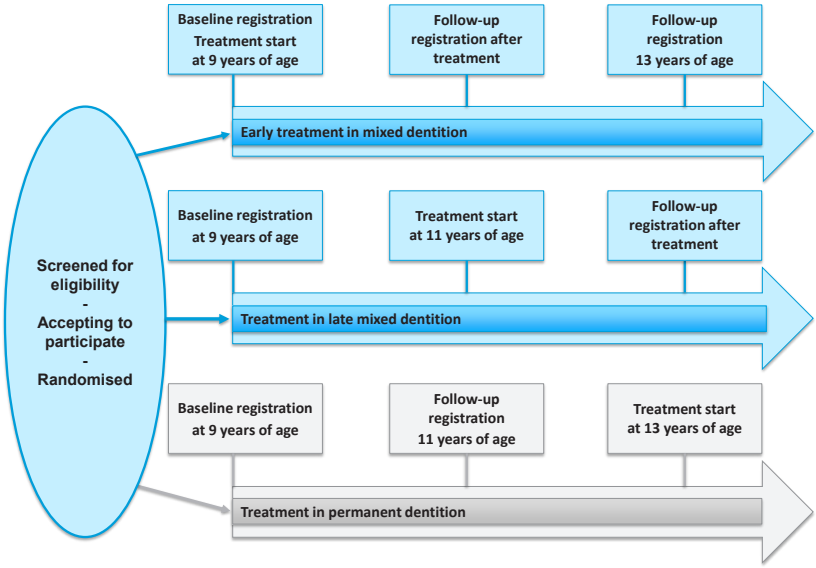

Figure 3. RCT Flowchart. Children randomised to early treatment in mixed dentition or treatment in late mixed dentition (blue arrows) are reported in the thesis. Children randomised to single-phase treatment in permanent dentition (grey arrow) are not reported.

Appliance and treatment

Treatment for Class II malocclusion with excessive overjet was provided with a headgear activator with a labial bow, illustrated in Figure 4, 5. The treatment goals were set to improve overjet and overbite, enable lip closure, and to obtain a Class I molar relationship bilaterally. Construction bite was taken in edge-to-edge position. To allow bite opening by vertical molar eruption, the mandibular lateral segments of the activator were reduced. Tubes were incorporated into the acrylic, close to the maxillary first molars, to make it possible to attach a high-pull headgear to the activator.

All appliances were manufactured in the orthodontic dental laboratory at the specialist clinic by the same dental technician.

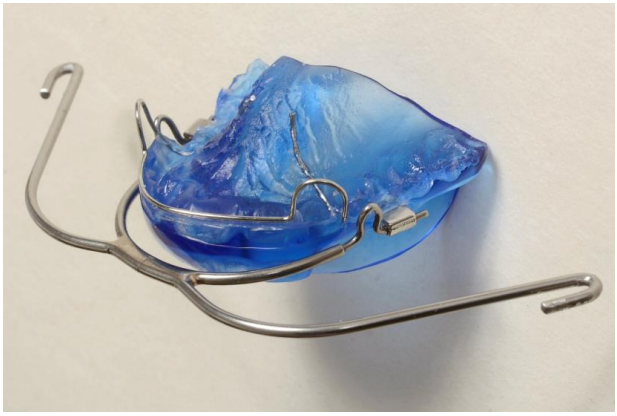

Figure 4. Headgear activator used in this RCT.

When first handed the headgear activator, thorough instructions were given to patient and parents to use the appliance at the evening and night, totalling 10–12 hours per day. One to two weeks after receiving the appliance, a first check-up was scheduled with the patient to control adaption and cooperation. Thereafter, the treatment progress was evaluated regularly with 8-week intervals when overjet, overbite, and molar relation were measured and registered. In addition, the headgear was controlled at visits to ensure that approximately 400 g of force per side were delivered. Adjustments of the appliance for erupting teeth or force delivery from headgear were made at these check-ups if needed.

Figure 5. Headgear activator.

When the treatment goals were obtained, the patients continued to wear the headgear activator as a retainer at night for an additional period of 6 months. Treatment was considered unsuccessful if the treatment goals were not achieved or if the intervention was discontinued or lack of cooperation was evident.

ITT

An intention-to-treat (ITT) strategy was applied for Papers III and IV. With ITT, all patients, whether successful or not, and any potential dropouts are included in the final analysis. This is usually described as 'once randomised, always analysed', and as such, the ITT strategy reduces the risk of false-positive treatment results.

Papers I–IV

Paper I

A systematic review was conducted according to the Goodman model.[93] The aim was to answer the beforehand formulated research question: 'How effective is early treatment of Class II malocclusion in terms of the following outcomes: correction of overjet, dental relationship, improvement in intermaxillary relationship, soft tissue profile, associations to TMD, quality of life, incidence of trauma and cost effectiveness?' To identify all relevant studies, the appropriate search strategy, including deciding appropriate Medical Subject Headings (MeSH) terms and selecting relevant databases, was designed in consultation with a senior librarian at the University library in Linköping, Sweden. Four databases – MEDLINE via PubMed, Web of Science, Cochrane Library and CINAHL – were searched to find all relevant articles published between January 1960 and October 2017.

The search strategy comprised five different search syntaxes: first, Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term) was applied; second, Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term) and Costs and Cost Analysis (MeSH term); third, Tooth injuries (MeSH term) and/or Tooth fractures (MeSH term) and Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term); and fourth, Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term)

and Temporomandibular Joint Dysfunction Syndrome (MeSH term). The fifth and final search syntax used was Quality of Life (MeSH term) and/or Self Concept (MeSH term) and/or Patient Satisfaction (MeSH term) and Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term).

Inclusion criteria were set to randomised controlled trials or prospective controlled trials of treatment of Class II malocclusion in the early mixed dentition. Treatment start before the age of 10 years was required to ensure an early treatment approach. No limitations were made concerning language.

The titles and abstracts of potentially relevant articles were assessed by three reviewers independently. The full-text version of an article was ordered if at least one of the reviewers considered it to be potentially relevant or if the title/abstract was ambiguous or lacking information, and thus the full-text version would provide more details. Reference lists from articles deemed eligible were hand-searched for any supplementary studies. Reviewing was undertaken independently, and the quality of the articles was assessed using a pre-prepared, calibrated protocol. The quality of each separate study was classified as high, moderate or low,[92] and the strength of the scientific evidence was assessed according to the GRADE system.[94] Cases of disagreement between reviewers was discussed until consensus was reached. According to the GRADE system, the quality of each study was graded as low, moderate or high. The presence of at least one of the following shortcomings rendered the assessment of low quality: only reporting successful treatments, historical control-groups, unclear inclusion criteria, insufficient material or unclear methodological approach.

Paper II

The study sample was sourced from 19 Public Dental Service Clinics in Sweden and originated from two different ongoing trials, the above mentioned of treatment of Class II malocclusion with excessive overjet (EO) and one regarding unilateral posterior crossbite with functional shift (UPC).[95] A control group of peers with normal occlusion with no or mild orthodontic treatment need (NO) was included and derive from the same trials.

Inclusion criteria for the UPC group were children 8 to 10 years of age in mixed dentition with unilateral posterior crossbite with functional shift of more than 1 mm (including the first permanent molars and a Class I occlusion). In addition, no sucking habits or ceased sucking habits should have been evident at least 1 year before the trial start.

Inclusion criteria for the NO group were children between the ages of 8 to 10 years in mixed dentition with normal occlusion and with no or mild orthodontic treatment need, as in, Index of Orthodontic Treatment Need – Dental Health Component (IOTN-DHC) of 1 or 2.[22]

The exclusion criteria were craniofacial syndromes, children who had previously undergone orthodontic treatment, or severe crowding of teeth (extraction of teeth necessary).

The EO group comprised 71 children (36 boys and 35 girls), the UPC group 93 children (45 boys and 48 girls) and the NO group 65 children (32 boys, 33 girls).

The study comprised baseline characteristics and evaluation of OHRQoL, thus the clinical examination was performed together with completion of the Child Perceptions Questionnaire (CPQ8-10)[78] in order to evaluate OHRQoL.

Paper III

Paper III evaluated early headgear activator treatment of Class II malocclusion with excessive overjet, starting at the age of 9 and where the treatment group (TG) was compared to an untreated control group (UG). The patients were sourced from the RCT regarding Class II malocclusion.

Paper IV

In Paper IV, early headgear activator treatment in mixed dentition, starting at the age of 9 (MD), was evaluated and compared to headgear activator treatment in late mixed dentition, starting at the age of 11 (LMD). Patients were part of the RCT regarding Class II malocclusion.

Child Perceptions Questionnaire (CPQ)

To evaluate the OHRQoL, the CPQ was used. The instrument is available in two age-specific versions, CPQ8-10[78] validated for children 8 to10 years

of age and CPQ11-14[79] validated for 11 to 14 year-olds. The questionnaires start with two global self-rating questions: one concerning oral health using a four-point scale ranging from 'excellent' to 'poor' and one aimed at overall well-being using a four-point scale ranging from 'not affected at all' to 'very much affected'. The questionnaires thereafter comprise questions grouped into four domains: oral symptoms (OS), functional limitations (FL), emotional well-being (EW), and finally social well-being (SW). Each question has five answer possibilities: 'never' (scoring 0), 'once or twice' (scoring 1), 'sometimes' (scoring 2), 'often' (scoring 3), and 'every day or almost every day' (scoring 4). The domains are added in order to produce a total score. For CPQ8-10, the total score ranges between 0 and 100, with a subscale score range of each domain from 0 to 20 (OS, FL, EW) or 40 (SW). The CPQ11-14 comprises an additional 12 questions: one additional question for OS, four each for FL and EW, and three for SW, giving a total of 37 questions. Due to the additional questions, the total score for CPQ11-14 ranges from 0 to 148. Within the domains, the scores are extended to 0 to 24 (OS), 0 to 36 (FL, EW), and 0 to 52 (SW).

The questionnaire was filled out in conjunction with the clinical examination. The children were instructed to answer the questions without any support from their parents. However, all children had the opportunity to ask questions about the questionnaires, and if needed, could receive support with reading the questions by clinical staff personnel.
The longitudinal design of the trial brought CPQ8-10 to be administrated at baseline registrations, whereas CPQ11-14 were to be administrated at follow-up registrations.

Cost analysis

Paper IV evaluates the costs associated with headgear activator treatment. Both groups received a headgear activator with the intention to correct a Class II malocclusion with excessive overjet. With results and consequences of the group's treatments, presumably broadly equivalent to each other, the difference between the groups was reduced to a comparison of costs.

Direct costs refer to those cost that are a result of the care and treatment provided. The direct costs mainly consist of the consumption of the healthcare resources, for example personnel, facilities, and equipment. The calculations were based on the costs per hour for a specialist dentist; 2700 SEK (€267), according to the 2020 price list for specialist dentistry

in the Public Dental Service in Östergötland. The headgear activator's material costs were derived by the dental technician costs; 1700 SEK (€168), according to the prices for 2020.

Indirect costs aim to cover production losses; in this paper, this refers to time absent from work for parents accompanying their children to the dentist. The total time, as in, chair time and travel time, for the visits were registered. It was assumed that the parents of a 9 to 11-year-old patient were between 35 and 44 years old. As reported by the Swedish National Bureau of Statistics (www.scb.se), the mean income per year for a 35- to 44-year-old in Sweden was 444 000 SEK/year (€43 960/year) in 2019. The average income per hour was calculated by dividing the mean income per year with 1980 working hours and then adding social security costs by a factor of 0.4. All costs were expressed in Euros (€), 100 SEK= €10.1 at a mean currency value (www.xe.com). Societal costs refer to the sum of direct and indirect costs.

The following evaluations were made:

1. The mean societal costs of successful cases only on completion of treatment in the two groups:

   (a) The mean societal costs for all successful treatments in the MD group divided by the number of successful patients, i.e., societal costs for 22 treatments divided by 22 patients.

   (b) The mean societal costs for all successful treatments in the LMD group divided by the number of successful patients, i.e., societal costs for 15 treatments divided by 15 patients.

2. The mean societal costs of the successful and unsuccessful cases (cases that would have to retreat, as no correction was achieved) on completion of treatment in the two groups:

   (a) The mean societal costs for all successful treatments and unsuccessful treatments in the MD group divided by the number of successful patients, i.e., 30 treatments divided by 22 patients, thus eight unsuccessful treatments and an increase in costs.

   (b) The mean societal costs for all successful treatments and unsuccessful treatments in the LMD group divided by the number of successful patients, i.e., 21 treatments divided by 15 patients, thus six unsuccessful treatments and an increase in costs.

Blinding

Due to the character of the randomised controlled trial, and the evaluated appliance, blinding to treatment allocation was not feasible for children, parents or trial staff. However, blinding was implemented when assessing outcomes. Consequently, the operators were not involved in the project and unaware of group allocation and whether the data corresponded to pre- or post-treatment when assessing the outcomes.

Sample size calculations

Paper II

The sample size calculation was based on detecting a difference in proportions of 25%. The difference of 25% was selected as the smallest difference in the sense that any smaller difference would not be of clinical or substantive significance. It was also assumed that this effect size was reasonable in the sense that an effect of this magnitude could be anticipated within this field of research. To attain a significance level of $P < 0.05$ and a power of 81.6%, the proposed sample size was 60 patients in each group. The test was two-tailed, which means that an effect in either direction was interpreted.

Paper III

With no RCTs having compared the actual used activator type to an untreated control group, the clinically significant difference of 1.5 mm in overjet reduction was chosen as the basis for sample size calculation. The calculation showed a necessity for at least 21 patients to obtain a power of 90% and a significance level of $P < 0.05$ with a standard deviation of 1.5 mm.

Paper IV

The primary outcome was cost comparison. No RCTs have assessed treatment with headgear activator, when treatment is initiated at different ages, regarding costs. Therefore, a clinically relevant and realistic difference in cost of 1000 SEK/€99 (SD 1000/99) was used as a base for the sample size analysis. At least 21 patients per group were needed to obtain a power of 90% and a significance level of $P < 0.05$.

Statistical analysis

Paper II

The data were statistically analysed using SPSS software (version 24, SPSS, Chicago, Illinois, USA). Means between groups were compared using ANOVA. Chi-square analysis and Fisher's exact test were used to determine difference between groups regarding categorical data. General linear model in combination with Tukey's test were performed when corrections were made for the following background/confounding variables: gender, caries, enamel defects, headache, and trauma. Differences with probabilities of less than 5% ($P < 0.05$) were considered to be statistically significant.

Papers III–IV

The data were statistically analysed using SPSS software (version 25 and 27, SPSS, Chicago, Illinois, USA). Descriptive data were presented as means, standard deviations (SD), and confidence intervals. The effect in either direction was interpreted as the tests were two-tailed. Changes within the groups were calculated using a paired samples t-test, and the means between the groups were compared using an independent t-test. Chi-square analysis and Fisher's exact test were used to determine difference between groups regarding categorical data.

Method error analysis

In Papers III and IV, orthodontists not involved in the trial assessed photos, study casts, and lateral head radiographs. Extraoral photos were evaluated regarding lip closure separately by two orthodontists and re-evaluated after a period of at least two weeks. The assessors showed concordance in 93% of the assessments. Cases of disagreement were resolved by discussion to reach consensus. With kappa value 0.72-0.93, internal consistency was substantial to almost perfect.

Study casts and lateral head radiographs in Papers III and IV were assessed by two other orthodontists. Fifteen randomly selected lateral head radiographs, and study casts were measured at two separate times by the same assessor and with an interval of at least three weeks. No significant differences between the records were found using t-test. Therefore, no random errors could be found. The method error size was less than 0.3 mm for linear measurements. For angular measurements, NL/NSL and ANB

showed the greatest error, with a variation of 0.7 and 0.4 degrees (Paper III) and 1.0 and 0.3 degrees (Paper IV), respectively.[96]

Complementary new study

An update of the systematic review (Paper I) was carried out on the basis that the editor of the *Journal of the World Federation of Orthodontics* kindly and urgently requested it from our research group. Consequently, repeated searches using the search syntaxes and databases described in Materials and Methods were conducted, with the extended time-scope of January 1960 to April 2019. Reference lists in the retrieved articles were hand-searched for additional studies. Inclusion criteria, search syntaxes, databases, data extraction and analysis followed the same methodology as described in Paper I.

RESULTS

Paper I – Systematic review

The search method identified 297 studies of interest. The removal of one duplicate and one animal study generated 295 papers screened for eligibility. Applying inclusion and exclusion criteria resulted in the exclusion of 240 articles, in which the most prevalent causes were not following the objective of the review (160), review articles (12), case reports (34), case series (19), discussion papers (8) and method descriptions (7). Additional findings after reviewing reference lists yielded a total of 74 full-text studies remained to be reviewed and evaluated.

After assessing the full-text articles, another 51 were excluded due to not following the objective of the review (32), retrospective study design (13), case reports (4), and method descriptions (2).

For the final 23 studies that fulfilled the eligibility criteria, 15 were graded as low quality and not included in the final analysis, as illustrated in Figure 6. Hence, the level of evidence was based on eight studies.[17,20,46,47,58,90,91,97] The final studies were all RCTs, and conducted in Sweden,[58] the United Kingdom,[17,20,47] and in the United States.[46,90,91,97]

All medium and high-quality studies were generated from four study populations. Activator and headgear treatment as well as controls were evaluated in one study.[58] Two studies reported about treatment with Headgear/biteplane or Bionator to untreated controls.[91,97] Twin-block was compared to untreated controls in three articles,[17,20,47] and two studies examined treatment with either Bionator or headgear to untreated controls.[46,90]

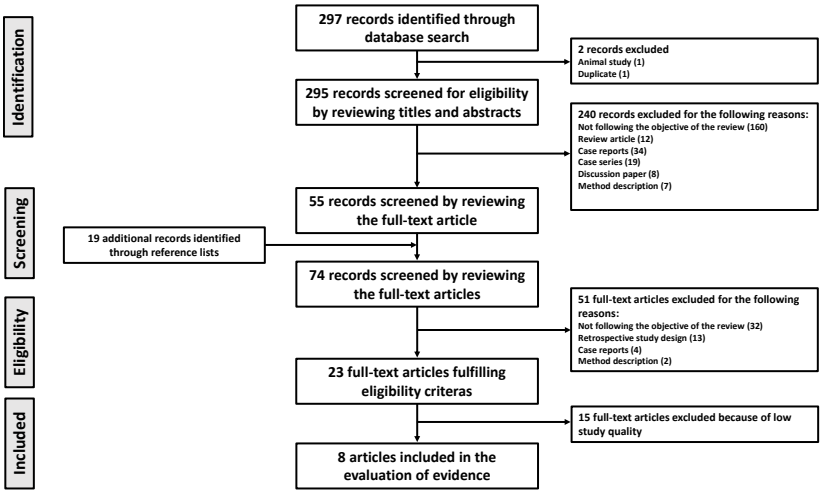

Figure 6. Flow of information through the different phases of the systematic review.

Grading of quality and evaluation of evidence

The level of evidence was based on three studies graded as moderate quality[58,91,97] and five graded as high quality.[17,20,46,47,90] The results are presented in Table 1.

All studies reported effects shortly after treatment, and the lack of long-term follow-up was evident. Based on the results of two studies of high quality and two of moderate, there was a high level of evidence that overjet was reduced and basal skeletal relationships improved by treatment with functional appliances. Based on the results of one study of high quality and one of moderate quality, it was concluded that early treatment with headgear reduced overjet and restrained forward growth of the maxilla (moderate level of evidence).

Conclusions concerning level of evidence regarding early treatment and its effects regarding soft tissue profile, quality of life, incidence of trauma, or whether early treatment was cost-effective could not be drawn due to lack of studies, few studies or contradictory results.

Table 1. Studies included in the evaluation of evidence

Author, year	Study design	Study population	Outcome measures	Results	Study quality/Comments
Chen et al. 2011[91]	RCT	93 Headgear/biteplane 9.7 years 87 Bionator 9.7 years 81 Controls 9.5 years	Modified Ellis injury classification	A significant number of children (25%) had already experienced incisor trauma before treatment were initiated. No correlation was found between initial overjet and the prevalence of trauma. Early orthodontic treatment did not significantly affect the incidence of trauma. Most injuries before and after treatment were minor, consisting of enamel fractures.	**Moderate** + Randomised study design + Blinding when analysing - Attrition >20% - Pretreatment performed in treatment (approx. 50%) and control (approx. 10%) groups, unclear method - No adjustment for confounders (lip closure, socio-economics, leisure activities)
O´Brien et al. 2009[17]	RCT	20 Twin-block 8-10 years 20 Controls 8-10 years Randomly selected from O´Brien et al. 2003	Attractiveness graded by 5-point Likert scale	After Twin-block treatment, the profile was rated as more attractive when compared to untreated controls. Visible front teeth and large overjet had negative impact on profile perception.	**High** + Randomised study design + Multicenter + Sample-size calculations + Blinding when analysing + Method error analysis
O´Brien et al. 2003[20]	RCT	89 Twin-block 9.7±0.98 years 87 Controls 9.8±0.94 years	Piers-Harris Children´s Self-Concept Scale Childhood Experience Questionnaire Perceptions of the Benefits of Orthodontic Treatment Scale (modified version)	At onset and at 15 months follow-up, both groups reported medium- to high self-esteem. Twin-block treatment resulted in an increased self-concept and a reduction in negative social experiences.	**High** + Randomised study design + Multicenter + Sample-size calculations + Intention-to-treat approach + Blinding when analysing - Attrition > 20% (28% for Twin-block, 22% for controls)

O´Brien et al. 2003[47]	RCT	89 Twin-block 9.7±0.98 years 85 Controls 9.8±0.94 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relationships: Overjet, incisor and molar positioning PAR-score	Twin-block treatment resulted in a reduction of overjet with 70% of the correction due to dentoalveolar changes. Skeletal improvement after early treatment with Twin-block was on average 2mm, the result of a similar degree of growth modification in the maxilla and the mandible. PAR-score was reduced by 42% in the treated group whereas in the controls PAR-score was increased by 9%.	**High** + Randomised study design + Multicenter + Control of confounders (age, gender, treatment) + Attrition <20% + Sample size calculations + Intention-to-treat approach + Blinding when analysing + Method error analysis
Koroluk et al. 2003[90]	RCT	52 Bionator 9.4±1.0 years 50 Headgear 9.4±1.0 years 61 Controls 9.4±1.2 years	Incidence of trauma Estimations regarding: Extent of trauma Required trauma treatment Costs	Trauma to maxillary incisors was found in all groups. Most injuries were minor and related costs were estimated as low. Treatment with Bionator might reduce the incidence of trauma, but should be initiated soon after eruption of maxillary incisors in order to be effective. It was estimated that the expected cost of trauma per child was less for patients who had early growth modification treatment than for patients whose treatment was delayed until their permanent dentition. However, early 2-phase orthodontic treatment is usually more expensive than a single-phase treatment approach.	**High** + Randomised study design + Sample size calculations + Intention-to-treat approach + Attrition <20%
Keeling et al. 1998[97]	RCT	90 Headgear/biteplane 9.7 years 78 Bionator 9.7 years 81 Controls 9.5 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relationships: Overjet, incisor and molar positioning Significance of retention Relapse	Bionator and Headgear groups showed significantly more skeletal Class II correction than untreated controls. Early treatment with Headgear resulted in significant dental Class II correction, affecting maxillary incisors and molars. Treatment with Bionator or Headgear/ biteplane showed no effect on maxillary growth but both appliances enhanced mandibular anterior growth. Skeletal	**Moderate** + Randomised study design + Blinding when analysing - Attrition >20% - Pretreatment performed in treatment (approx. 50%) and control (approx. 10%) groups, unclear method

				changes were stable one year after treatment but relapse was evident for dental changes.	
Tulloch et al. 1997[46]	RCT	53 Bionator 9.4±1.0 years 52 Headgear 9.4±1.0 years 61 Controls 9.4±1.2 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relations: Overjet, overbite Mandibular length	Overall, early treatment showed a reduction in overjet and a 75% chance for improving the jaw relationship. Basal improvement was achieved through different mechanisms. Headgear resulted in maxillary restraint and Bionator in forward positioning and increased length of the mandible. Great individual response to treatment and difference in growth were registered in both the treatment and control groups.	**High** + Randomised study design + Sample size calculations + Intention-to-treat approach + Attrition <20% + Method error analysis
Jakobsson 1967[58]	RCT	20 Headgear 8.5 years 20 Activator 8.5 years 20 Controls 8.5 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relations: Overjet, overbite Mandibular length	Early treatment reduced overjet. Activator and Headgear treatment appeared to affect positioning of the maxilla, most pronounced by Headgear treatment. Both treatments significantly increased facial height. Activator treatment had an effect within the dento-alveolar area of the mandible, but no support for an orthopedic effect was found.	**Moderate** + Randomised study design + Method error analysis + Attrition <20% - No sample-size calculations - No blinding when analysing - No Intention-to-treat Approach

Supplementary search

An updated search performed in 2019 extended the search period from 1960 to April 2019 using the same search syntaxes and databases as described for Paper I. This yielded an additional three articles, totalling the number of identified studies to 300. All three additional findings were excluded after screening, as they did not follow the objective of the review. Hence, the conclusions and level of evidence remained unaltered compared to the initial systematic review in Paper I.[98]

Paper II – OHRQoL

A total of 229 children were included in the study. All children with excessive overjet (n=71) had a Class II molar relation and significantly enlarged overjet when compared to the children in the UPC group (n=93) and NO group (n=65), who all showed a Class I molar relation and overjet within normal range. The treatment need for children in the EO group was severe to extreme due to the extent of overjet, and in the UPC group, moderate to severe due to forced guidance of the mandible. Children in the NO group showed no or mild orthodontic treatment need (IOTN).[22] The groups showed low prevalence regarding trauma, enamel defects, headache and with no intergroup differences.

Oral health-related quality of life

With all questionnaires filled in, there were no dropouts in this study. The mean CPQ scores was 7.4 for the EO group, 5.1 for the UPC group, and 4.4 for the NO group (Table 2). The total CPQ score was significantly higher for the EO group when compared to the UPC group ($P = 0.048$) and NO group ($P = 0.012$). No difference was found between the UPC and NO group ($P = 0.385$). There were no gender differences.

Domain scores

No significant differences could be detected between the groups regarding the domains oral symptoms and functional limitations. The children in the EO group reported a significantly higher score for the domain emotional well-being when compared to children in the UPC group ($P = 0.039$) and for the domain social well-being when compared to the NO group ($P = 0.012$). These differences prevailed after correction for potential confounders: gender, caries, trauma, enamel defects, and headache. Headache was the only variable correlated to OHRQoL, showing a significant negative impact in the domain oral symptoms ($P < 0.05$).

Table 2. CPQ8-10 scores for the three groups; Excessive overjet (EO), Unilateral posterior crossbite (UPC), and Normal occlusion (NO)

	CPQ total		Oral symptoms (OS)		Functional limitations (FL)		Emotional well-being (EW)		Social well-being (SW)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
EO (n=71)	7.4	8.2	3.9	2.7	1.2	1.8	1.2	2.4	1.2	3.2
UPC (n=93)	5.1	5.1	3.3	2.7	0.9	1.6	0.5	1.2	0.5	0.8
NO (n=65)	4.4	5.2	3.0	2.7	0.7	1.3	0.5	1.8	0.2	0.8
P-level when adjusted for possible confounders (caries, MIH, trauma, headache)[a]	EO vs UPC *P*= 0.048[b] EO vs NO *P*= 0.012[b]						EO vs UPC *P*= 0.039[b]		EO vs NO *P*= 0.012[b]	

[a]General linear model [b]Tukey´s test

Paper III – Early treatment compared to untreated controls

Patient flow

As illustrated in Figure 7, 60 patients joined the trial and were randomised. There were no dropouts since all patients fulfilled the trial.

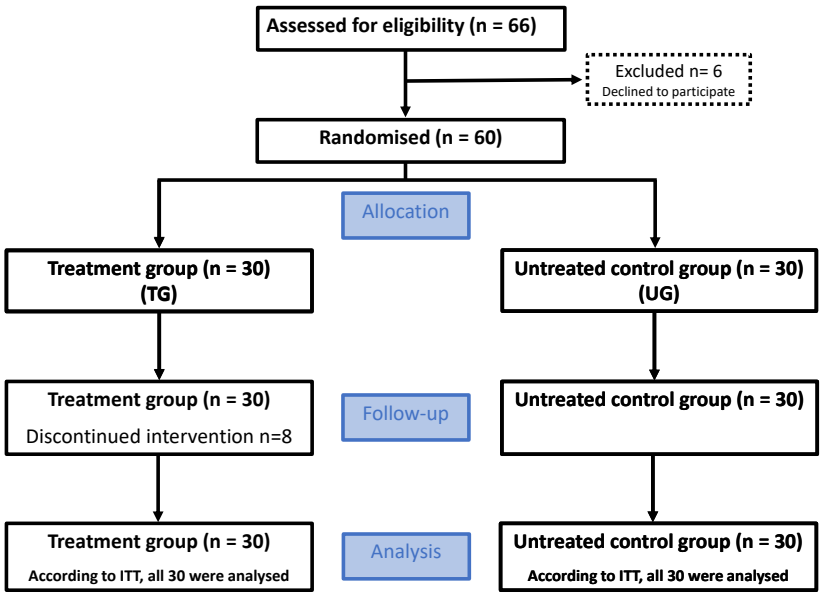

Figure 7. CONSORT Flow diagram

Age at baseline for the patients in both groups were 9.4 years (SD 0.4). The treatment group (TG) consisted of 17 girls and 13 boys, the untreated group (UG) of 12 girls and 18 boys. The mean active treatment time with headgear activator was 1.1 years. Eight children (27%) discontinued the treatment by either refusing to wear the appliance or lack of cooperation.

Dental effects

Apart from a small difference in overjet whereby the TG showed one additional mean millimetre in overjet, the groups were equal at baseline (Table 3). Treatment significantly decreased overjet ($P \leq 0.001$), whereas it remained unchanged in the UG. After treatment, the children in the TG showed significantly smaller overjet compared to the UG ($P \leq 0.001$). If treatment was discontinued, the overjet remained unaltered. Figure 8a,b illustrate different treatment outcomes.

Overbite remained stable in the TG, whereas an increase was found in the UG ($P = 0.012$). Treatment improved molar relation significantly, and 73% of the patients in the TG displayed a normal relation after treatment ($P \leq 0.001$). No spontaneous change in molar relation was registered in the UG.

Figure 8a. An example of a successful treatment with normalisation of the occlusion, overjet and overbite. Top row before treatment, bottom row after treatment.

Figure 8b. An example of a discontinued treatment. Top row before treatment, bottom row at follow-up.

Table 3. Dental and skeletal changes from baseline (T0) to follow up (T1) for the two groups; early treatment with headgear activator (TG) versus untreated control group (UG).

	Within-group TG				Within-group UG				Between groups		
	Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)	Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)	*P* (T0)	*P* (T1)	*P* (T0-T1)
Overjet [mm]											
T0	9.0 (1.5)				8.0 (1.0)						
T1	5.5 (2.5)	-3.5	-4.6 to -2.5	<0.001	8.0 (1.5)	0.1	-0.3 to 0.5	0.583	0.029	<0.001	<0.001
Overbite [mm]											
T0	3.5 (1.0)				3.5 (1.5)						
T1	3.5 (1.0)	-0.3	-0.7 to 0.2	0.260	4.0 (1.5)	0.7	0.3 to 1.1	0.001	0.612	0.012	0.002
SNA [°]											
T0	81.9 (3.6)				81.3 (3.3)						
T1	80.7 (3.3)	-1.2	-1.8 to -0.7	<0.001	81.8 (3.3)	0.5	0.0 to 1.0	0.038	0.502	0.175	<0.001
SNB [°]											
T0	76.0 (3.5)				75.6 (2.7)						
T1	76.3 (3.7)	0.3	-0.2 to 0.9	0.187	76.6 (2.5)	1.0	0.5 to 1.5	<0.001	0.657	0.737	0.088
ANB [°]											
T0	6.0 (1.8)				5.8 (1.7)						
T1	4.4 (2.2)	-1.6	-2.2 to 1.1	<0.001	5.3 (1.9)	-0.5	-0.9 to 0.0	0.035	0.601	0.095	0.001
NL/NSL [°]											
T0	6.3 (3.3)				6.6 (2.6)						
T1	7.2 (3.7)	0.9	0.3 to 1.4	0.003	7.1 (3.2)	0.5	0.0 to 1.1	0.056	0.704	0.950	0.363
ML/NSL [°]											
T0	33.1 (4.1)				32.2 (3.5)						
T1	33.4 (4.4)	0.3	-0.5 to 1.2	0.466	31.3 (3.5)	-0.9	-1.7 to -0.2	0.012	0.367	0.042	0.026
ML/NL [°]											
T0	26.8 (4.5)				25.6 (3.2)						
T1	26.3 (4.7)	-0.5	-1.6 to 0.4	0.228	24.2 (3.7)	-1.4	-2.3 to -0.6	0.002	0.236	0.063	0.174
ILs/NL [°]											
T0	117.3 (7.3)				116.9 (7.5)						
T1	112.7 (8.2)	-4.6	-7.7 to -1.5	0.005	116.3 (8.2)	-0.6	-2.1 to 1.0	0.456	0.813	0.095	0.023
ILi/ML [°]											
T0	95.3 (7.2)				97.3 (6.0)						
T1	94.1 (6.4)	-1.2	-3.3 to 0.9	0.255	96.5 (5.4)	-0.8	-1.9 to 0.4	0.169	0.249	0.121	0.730

Cephalometric analysis

All variables are presented in Table 3. Skeletal characteristics were equivalent for the two groups at baseline. Treatment with headgear activator restrained the maxilla ($P \leq 0.001$) and retroclined the maxillary incisors ($P = 0.005$). In the UG, the maxilla and mandible grew forward ($P = 0.038$ and $P \leq 0.001$) and the mandible rotated anteriorly ($P = 0.012$). When comparing children where treatment was successful to untreated children, a reduction in ANB ($P = 0.02$) and difference in ML/NL ($P = 0.03$) was registered for the treated children.

Oral health-related quality of life

Total CPQ mean for the groups were equivalent at baseline, 7.1 for the TG and 7.2 for the UG ($P = 0.975$). The equivalence remained after treatment, where the mean score was 6.9 in the TG and 9.1 in the UG ($P = 0.263$). No significant differences could be registered between the groups for the separate domains, nor any intra-group changes between baseline and follow up. (Table 4) The lack of differences prevailed when comparing the UG group to children where treatment was considered successful.

Evaluation of lip closure

At baseline, 67% of the children in the TG and 60% in the UG displayed an incomplete lip closure. After treatment, the incomplete lip closure was reduced to 27% in the TG while incomplete lip closure was registered in 37% of the UG-children at follow-up ($P = 0.350$). However, no significant difference in improved lip closure could be registered between the children where treatment was completed when comparing to the untreated children.

Dental trauma

The prevalence of dental trauma was 18% at baseline (5 boys, 6 girls). One maxillary incisor had been exarticulated and successfully replanted two years before the patient was enrolled in the trial. In addition, one enamel-dentin fracture, two enamel fractures and seven teeth with infractions were registered. After treatment and at follow up, four additional dental traumas were registered in the UG and one in the TG ($P = 0.353$), all consisting of infractions. The additional traumas affected four boys and one girl.

Table 4. CPQ scores (0–100) at baseline (T0) and when adjusted for the number of questions at T1.
CPQ scores unadjusted at T1 (0-148)

	Within-group TG				Within-group UG				Between groups		
	Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)	Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)	Mean	CI (95%)	*P*
CPQ total											
T0 (8-10)	7.1 (7.4)				7.2 (9.1)				-0.1	-4.4 to 4.2	0.975
T1 (11-14)	5.5 (5.6)	-1.6	-4.3 to 1.0	0.206	6.7 (6.5)	-0.5	-3.1 to 4.0	0.792	-1.2	-1.3 to 1.6	0.421
T1 (0-148)	6.9 (6.9)				9.1 (8.1)				-2.2	-6.1 to 1.7	0.263
CPQ OS											
T0 (8-10)	3.8 (2.8)				3.7 (2.5)				0.1	-1.3 to 1.5	0.884
T1 (11-14)	3.5 (2.8)	-0.3	-1.6 to 1.1	0.683	3.7 (2.7)	0.0	-0.9 to 0.9	1.00	-0.2	-1.6 to 1.3	0.816
T1 (0-148)	3.8 (3.4)				4.1 (3.5)				-0.3	-2.1 to 1.4	0.707
CPQ FL											
T0 (8-10)	1.0 (1.5)				1.3 (2.1)				-0.3	-1.2 to 0.7	0.574
T1 (11-14)	0.7 (1.3)	-0.3	-1.0 to 0.4	0.411	1.1 (1.6)	-0.2	-0.8 to 1.1	0.715	-0.4	-1.1 to 0.3	0.284
T1 (0-148)	1.7 (2.3)				2.8 (2.7)				-1.1	-2.4 to 0.2	0.091
CPQ EW											
T0 (8-10)	1.5 (2.9)				1.0 (2.0)				0.5	-0.8 to 1.8	0.474
T1 (11-14)	0.4 (1.0)	-1.1	-2.2 to 0.1	0.07	1.3 (2.2)	0.3	-1.3 to 0.8	0.654	-0.9	-1.7 to 0.1	0.067
T1 (0-148)	0.5 (1.1)				1.5 (2.6)				-1.0	-2.0 to 0.0	0.061
CPQ SW											
T0 (8-10)	0.8 (1.7)				1.2 (4.3)				-0.4	-2.0 to 1.3	0.664
T1 (11-14)	0.8 (1.8)	0.0	-0.7 to 0.6	0.917	0.7 (1.6)	-0.5	-1.1 to 2.2	0.507	0.1	-0.7 to 1.0	0.759
T1 (0-148)	0.9 (1.9)				0.7 (1.6)				0.2	-0.7 to 1.1	0.607

Paper IV – Treatment at 9 or 11 years of age

Patient flow

The flow of the participants in the study is illustrated in Figure 9. There were no dropouts, with all 51 entering patients completing the trial.

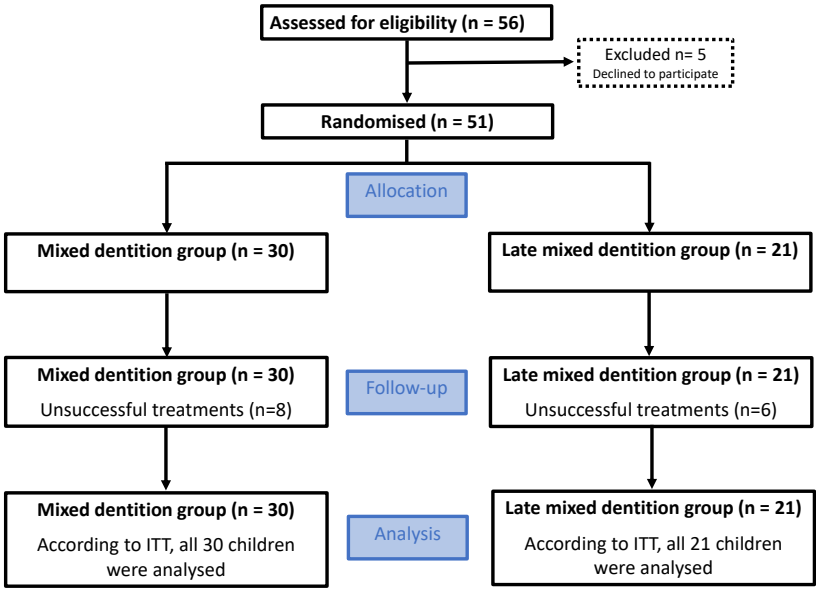

Figure 9. CONSORT Flow diagram

The mixed dentition group (MD) consisted of 17 girls and 13 boys, with the mean age of 9.4 years (SD 0.40). The late mixed dentition group (LMD) included 9 girls and 12 boys ($P = 0.400$), and the mean age was 11.1 years (SD 0.20). Dental stages[99] were DS2M1 (83%) and DS3M1 (17%) in the MD group and DS2M1 (5%), DS3M1 (81%), DS4M2 (14%) in the LMD group ($P = 0.001$).

Treatment

The mean active treatment time was 1.1 years (SD 0.27) for the children in the MD group. Treatment in MD was discontinued for 8 children (27%), and therefore, 22 children were successfully treated. The mean active treatment time for the LMD group was 1.2 years (SD 0.31). Within this group, treatment was discontinued for 6 children (29%), and therefore, 15 children were successfully treated. Reasons for discontinuing treatment

were refusal to wear the appliance or lack of cooperation. No difference could be detected between the groups regarding treatment time ($P = 0.392$) or unsuccessful treatments ($P = 1.000$). A total of four activators (13%) in the MD group and three (14%) in the LMD group were repaired or replaced due to loss, breakage or inadequate fit.

Number of appointments

For successful treatments, the mean number of appointments, including the retention period, was 10.2 (SD 1.94) in the MD group and 10.3 (SD 2.12) for the LMD group ($P = 0.901$). The number of average emergency visits was 0.7 (SD 0.94) in the MD group versus 1.1 (SD 1.03) in the LMD group ($P = 0.306$). Also, the total chair time was 247 minutes (SD 56) in the MD group and 250 (SD 60) in the LMD group ($P = 0.892$).

Cost evaluation

Costs for successful treatments

There was no difference between the groups regarding the costs associated with treatment, as shown in Table 5. The mean societal costs (i.e. direct and indirect costs) for successful treatments were €1634 (SD 338) for the MD group, whereas a successful treatment in late mixed dentition costed €1667 (SD 363) ($P = 0.778$).

Costs including unsuccessful treatments

When costs for unsuccessful treatments were added and included, no difference in cost was found between the groups. Therefore, the mean societal costs (i.e. direct and indirect costs) for successful treatments including unsuccessful treatments increased to € 2053 (SD 662) for the MD group and € 2160 (SD 842) for the LMD group ($P = 0.668$).

Dental effects

Headgear activator treatment was successful in reducing overjet ($P \leq 0.001$) and improving molar relation in both groups ($P = \leq 0.001$) for the children who had completed treatment. Figure 10a,b illustrates different treatment outcomes. After treatment, 73% of the patients in the MD group and 71% in the LMD group presented a Class I molar relation ($P = 1.000$). A minor difference regarding overbite could be detected between the groups before the start of treatment, with the LMD group displaying a more pronounced overbite ($P = 0.046$). Even after treatment, this difference prevailed for the LMD group ($P = 0.028$). As shown in Table 6, no other differences could be found.

Table 5. Mean societal, direct, and indirect costs (€) for treatment with headgear activator in MD and LMD group.

	MD group		LMD group		Group differences
	Mean (SD)	**CI (95%)**	**Mean (SD)**	**CI (95%)**	***P***
Successful treatments alone					
Societal costs	1634 (338)	1484 – 1784	1667 (363)	1466 – 1868	0.778
Direct costs	1292 (269)	1173 – 1411	1303 (283)	1146 – 1460	0.904
Material costs	191 (59)	165 – 218	191 (59)	158 – 224	0.980
Treatment costs	1101 (248)	991 – 1211	1112 (267)	964 – 1260	0.892
Indirect costs	342 (112)	292 – 392	364 (108)	304 – 424	0.556
Successful treatments including the cost for unsuccessful treatments					
Societal costs	2053 (662)	1759 – 2347	2160 (842)	1694 – 2627	0.668
Direct costs	1638 (551)	1394 – 1883	1690 (671)	1319 – 2062	0.797
Material costs	260 (100)	216 – 305	269 (106)	210 – 328	0.791
Treatment costs	378 (479)	1166 – 1590	1421 (586)	1097 – 1746	0.807
Indirect costs	415 (149)	349 – 481	470 (190)	364 – 575	0.332

Table 6. Dental and skeletal changes from before treatment (T0) to completed treatment (T1) with headgear activator in the MD and LMD group.

	Within-group MD				Within-group LMD				Between groups		
	Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)	Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)	*P* (T0)	*P* (T1)	*P* (T0-T1)
Overjet [mm]											
T0	9.0 (1.5)				8.3 (1.8)						
T1	5.5 (2.5)	-3.5	-4.6 to -2.5	<0.001	5.5 (2.3)	-2.8	-3.7 to -1.8	<0.001	0.180	0.830	0.261
Overbite [mm]											
T0	3.5 (1.0)				4.2 (1.3)						
T1	3.2 (1.0)	-0.3	-0.7 to 0.2	0.260	4.0 (1.3)	-0.2	-0.6 to 0.2	0.303	0.046	0.028	0.873
SNA [°]											
T0	81.9 (3.6)				82.0 (3.7)						
T1	80.7 (3.3)	-1.2	-1.8 to -0.7	<0.001	81.8 (3.7)	-0.2	-0.9 to 0.6	0.657	0.960	0.243	0.012
SNB [°]											
T0	76.0 (3.5)				76.7 (2.6)						
T1	76.3 (3.7)	0.3	-0.2 to 0.9	0.187	77.5 (2.4)	0.8	0.4 to 1.2	<0.001	0.439	0.211	0.200
ANB [°]											
T0	6.0 (1.8)				5.3 (2.2)						
T1	4.4 (2.2)	-1.6	-2.2 to 1.1	<0.001	4.4 (2.1)	-0.9	-1.5 to -0.3	0.004	0.257	0.984	0.110
NL/NSL [°]											
T0	6.3 (3.3)				7.1 (3.3)						
T1	7.2 (3.7)	0.9	0.3 to 1.4	0.003	7.9 (3.2)	0.8	-0.1 to 1.7	0.069	0.408	0.470	0.913
ML/NSL [°]											
T0	33.1 (4.1)				31.1 (3.9)						
T1	33.4 (4.4)	0.3	-0.5 to 1.2	0.466	30.5 (3.8)	-0.6	-1.5 to 0.2	0.142	0.084	0.017	0.129
ML/NL [°]											
T0	26.8 (4.5)				24.1 (4.0)						
T1	26.3 (4.7)	-0.5	-1.6 to 0.4	0.228	22.6 (3.9)	-1.5	-2.6 to -0.4	0.011	0.028	0.005	0.223
ILs/NL [°]											
T0	117.3 (7.3)				116.1 (8.7)						
T1	112.7 (8.2)	-4.6	-7.7 to -1.5	0.005	113.8 (9.9)	-2.3	-4.5 to -0.1	0.046	0.586	0.658	0.250
ILi/ML [°]											
T0	95.3 (7.2)				96.9 (5.8)						
T1	94.1 (6.4)	-1.2	-3.3 to 0.9	0.255	96.9 (6.1)	0.0	-1.5 to 1.5	0.985	0.382	0.117	0.352

Figure 10a. An example of a successful treatment with normalisation of the occlusion, overjet and overbite. Top row before treatment, bottom row after treatment.

Figure 10b. An example of a discontinued treatment. Top row before treatment, bottom row at follow-up.

Cephalometric analysis

Treatment reduced ANB and retroclined the maxillary incisors in both groups (Table 6). Within each group, small significant changes could be registered for different variables; however, these did not result in any statistical intergroup differences except for ML/NSL and ML/NL. Before treatment and when compared to the MD group, the LMD group showed a reduced intermaxillary relation ($P = 0.028$). This finding remained after treatment ($P = 0.005$). Furthermore, the LMD group presented a more anteriorly rotated mandible after treatment compared to the MD group ($P = 0.017$).

Table 7. CPQ scores before treatment (T0) and after completed treatment (T1) using CPQ8–10 and CPQ11–14. CPQ11–14 scores unadjusted (0–148).

	Within-MD group					Within-LMD group				Group differences		
	Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)		Mean (SD)	Mean T0-T1	CI (95%)	*P* (T0-T1)	Mean	CI (95%)	*P*
CPQ total					**CPQ total**							
T0 (8-10)	7.1 (7.4)				**T0 (11-14)**	6.4 (7.3)				0.7	-3.4 to 4.9	0.720
T1 (11-14)	5.5 (5.6)	-1.6	-4.3 to 1.0	0.206	**T0 (0-148)**	8.5 (8.9)	-0.2	-4.4 to 4.9	0.915			
T1 (0-148)	6.9 (6.9)				**T1 (0-148)**	8.3 (7.3)				-1.4	-5.4 to 2.7	0.505
CPQ OS					**CPQ OS**							
T0 (8-10)	3.8 (2.8)				**T0 (11-14)**	3.0 (2.9)				0.8	-0.8 to 2.5	0.297
T1 (11-14)	3.5 (2.8)	-0.3	-1.6 to 1.1	0.683	**T0 (0-148)**	3.8 (3.8)	-0.5	-1.1 to 2.1	0.547			
T1 (0-148)	3.8 (3.4)				**T1 (0-148)**	3.3 (1.7)				0.5	-0.9 to 2.0	0.481
CPQ FL					**CPQ FL**							
T0 (8-10)	1.0 (1.5)				**T0 (11-14)**	1.5 (1.8)				-0.5	-1.4 to 0.5	0.319
T1 (11-14)	0.7 (1.3)	-0.3	-1.0 to 0.4	0.411	**T0 (0-148)**	2.3 (2.7)	-0.2	-1.7 to 2.1	0.796			
T1 (0-148)	1.7 (2.3)				**T1 (0-148)**	2.1 (3.4)				-0.4	-2.0 to 1.2	0.620
CPQ EW					**CPQ EW**							
T0 (8-10)	1.5 (2.9)				**T0 (11-14)**	1.4 (2.4)				0.1	-1.4 to 1.7	0.877
T1 (11-14)	0.4 (1.0)	-1.1	-2.2 to 0.1	0.07	**T0 (0-148)**	1.8 (2.9)	0.3	-2.0 to 1.4	0.724			
T1 (0-148)	0.5 (1.1)				**T1 (0-148)**	2.1 (2.9)				-1.6	-2.9 to -0.2	0.026
CPQ SW					**CPQ SW**							
T0 (8-10)	0.8 (1.7)				**T0 (11-14)**	0.6 (1.7)				0.2	-0.7 to 1.2	0.593
T1 (11-14)	0.8 (1.8)	0.0	-0.7 to 0.6	0.917	**T0 (0-148)**	0.6 (1.7)	0.2	-0.9 to 0.5	0.489			
T1 (0-148)	0.9 (1.9)				**T1 (0-148)**	0.8 (1.3)				0.1	-0.9 to 1.1	0.850

Oral health-related quality of life

The groups were equivalent before treatment start, as shown in Table 7, with a mean total CPQ score of 7.1 in the MD group and 8.5 in the LMD group ($P = 0.720$). After treatment, the mean total CPQ score was 6.9 in the MD group and 8.3 in the LMD group ($P = 0.505$). No significant differences could be registered regarding intra-group changes during treatment, nor could any significant between-group differences be registered before or after treatment for the separate domains, except for the domain emotional well-being where children in the LMD group reported a higher score after completed treatment ($P = 0.026$).

Evaluation of lip closure

Before treatment, incomplete lip closure was registered in 67% of the MD and 43% of the LMD children ($P = 0.150$). After treatment, the incomplete lip closure was reduced to 27% in the MD and 10% in the LMD group ($P = 0.167$).

Dental trauma

A total of fourteen children, six in the MD group (20%) and eight in the LMD group (38%), had experienced dental trauma before treatment ($P = 0.207$). One maxillary incisor had been exarticulated and successfully replanted two years before the patient was enrolled in the trial. In addition, one enamel-dentin fracture, two enamel fractures and ten teeth with infractions were registered before treatment. After treatment, three more traumas were registered. One child in the MD group and two children in the LMD group were affected ($P = 0.561$), with the additional traumas consisting of one enamel dentin facture and two infractions.

DISCUSSION

The objective of this thesis was to analyse the consequences of a Class II malocclusion with excessive overjet on oral health-related quality of life and to systematically evaluate the effects of early headgear activator treatment (i.e. with treatment start at 9 or 11 years of age).

The strength of evidence was a high priority, and the studies were designed to provide as high a level of evidence as possible. Consequently, this thesis was started with a systematic review to evaluate the evidence supporting early treatment of Class II malocclusion and to determine what knowledge gaps exist regarding the early treatment of Class II malocclusion with excessive overjet. Thereafter, a controlled study was performed to investigate the self-reported OHRQoL of children with Class II malocclusion with excessive overjet and then compare to peers with unilateral posterior cross-bite or normal occlusion with no to mild orthodontic treatment need. Finally, an RCT was performed analysing the treatment effects of early treatment and evaluating the costs and treatment effects associated with treatment started at 9 or 11 years of age.

The systematic review (Paper I) concluded that a high level of evidence backs up the claim that early treatment with functional appliance was successful in reducing overjet and improving the antero-posterior skeletal relationship. In addition, a moderate level of evidence was found to back up the claim that early treatment with headgear reduced overjet and restrained forward growth of the maxilla. However, there was insufficient evidence in regard to early treatment and the effects regarding dental trauma, OHRQoL and treatment-related costs. One important conclusion of the systemic review was the identification of the knowledge gap regarding long-term

outcome and the stability of early treatment of Class II malocclusion. A later update of the systematic review identified few new studies; however, this did not in any way alter the conclusions presented in Paper I.[98]

The main finding of Paper II was that young children with Class II malocclusion with excessive overjet report significantly lower self-perceived OHRQoL compared to peers with unilateral posterior crossbite or children with normal occlusion that present no or mild orthodontic treatment need. The Child Perceptions Questionnaire was used, and the domains of social well-being and emotional well-being were the ones most affected by the Class II malocclusion. Nevertheless, with all three groups reporting generally low scores, the overall self-perceived OHRQoL was considered fairly high among all the children.

When evaluating early headgear activator treatment effects (Paper III), it was concluded that early treatment was successful in reducing overjet and correcting the molar relation. Treatment effects regarding self-reported OHRQoL and growth were insignificant compared to untreated controls. Finally, Paper IV showed that treatments effects, treatment success, and treatment related costs were the same regardless of whether treatment was initiated at the age of 9 or 11 years of age.

Methodological considerations

Paper I

Goodman's model[93] was applied for the systematic review presented in Paper I. The structured method enabled the identification of all relevant studies evaluating early treatment of Class II malocclusions. Furthermore, using Goodman's model ensured repeatability and reduced the risk of inconsistent or arbitrary conclusions. The pre-set reviewing protocol enabled evaluation of coherence for the reviewers. The quality of retrieved studies[92] and the rating of the level of evidence[94] was conducted according to the GRADE guidelines, further ensuring a systematic approach.

When conducting a systematic review, the literature search is designed to reduce the risk of missing or disregarding relevant articles. A usual finding with this approach is that an initial high retrieval of studies is significantly reduced as studies are excluded during the reviewing process. The most common reason for exclusion in Paper I was that the study did not follow

the objective of the review. The evaluated studies in the review displayed a variance in reported outcome measure, primarily regarding cephalometric analysis. The difference in reported variables could only enable general conclusions regarding skeletal treatment effects. To enhance comparisons and additional analyses, increased coherence in cephalometric outcome measures is desirable. The identified knowledge gaps in Paper I reflect that there is an urgent need to carry out the trials described in Paper II-IV.

Paper II

The Child Perceptions Questionnaire is one of the most frequently used instruments for registering OHRQoL among children and adolescents. With its global distribution, its use enables comparisons within research. For evaluation of self-perceived OHRQoL, it is important to account for potential confounders. It was concluded from Paper II that children with Class II malocclusion with excessive overjet report an overall lower OHRQoL compared to peers, with the psycho-social domains primarily affected. This finding prevailed after taking the possible confounding factors of caries, trauma, gender, and headache into account. Headache was the only variable that showed significant negative impact on the OHRQoL, not surprisingly in the domain of oral symptoms. Dental fear has shown a strong correlation with reduced OHRQoL in children.[100] Even though dental fear was not evaluated within this trial, it should be noted that the children in the trial had voluntarily accepted to participate in the study. Participation entailed additional clinical examinations as well as taking impressions. This voluntary participation by patients and parents indicates that the prevalence of dental fear presumably was low among the participating children.

All the children in the study, regardless of the presence of malocclusion or not, reported generally low CPQ scores. This finding implies that the participants in this controlled trial consider themselves to have a fairly good OHRQoL. One possible reason for the fairly good self-perceived OHRQoL in the trial may be the negative impact caries poses regarding OHRQoL. Caries experience has been shown to have a greater negative effect on OHRQoL than the presence of malocclusions or the experience of dental trauma.[101] The low prevalence of caries among Swedish schoolchildren might account for the findings in Paper II, further highlighting the advocated need for evaluation of children's OHRQoL

in different cultural and societal settings.[16] Finally, the young age of the children participating might also contribute to the results, as the self-perceived need for orthodontic treatment has been reported to increase during the age of eight to eleven years of age[102] and the internal motivation to undergo orthodontic treatment for Class II malocclusion has also been shown to increase with age.[72]

Papers III and IV

All patients were treated in a specialist clinic and by the same operator. It has been stated that single-centre trials tend to overestimate treatment effects.[103] By designing a single-centre trial at a specialist clinic, one might argue that the results in this thesis reflect treatment efficiency rather than treatment effectiveness. Furthermore, with all the treatments performed by one operator, operator-related error may have affected the results. However, with a single-centre trial, the awareness of the ongoing RCT and knowledge of the treatment protocol was high, which perhaps can explain the absence of dropouts in the studies.

Randomised controlled trials

Within evidence-based health evaluations, the randomised controlled trial has been advocated as the golden standard when assessing clinical research. The GRADE guidelines categorise the randomised controlled trial design as providing high quality evidence. The assessed quality can thereafter be graded down if there are deficiencies in conduct, resulting in different biases which increases the risk of misleading results.[92] If randomisation is carefully performed, the distribution of known and unknown confounding factors are evenly distributed between the groups, providing that the sample is large enough. The methodology increases the chance that the provided treatment is the only significant difference between the groups investigated. The suitability for RCTs within orthodontic research has been debated[104]; however, given the underreporting of patient-centred outcomes[76] and cost evaluations of established treatment strategies[89], the requisite for RCTs is evident.

Intention-to-treat (ITT)

With an ITT approach, each patient is evaluated according to the group allocation, regardless of whether treatment was completed or discontinued, successful or unsuccessful, all according to the principle ‘once randomised,

always analysed'. When applying ITT, the risk for over-reporting treatment effects or over-estimating treatment results is reduced, which means significant false positive results are avoided. In this thesis, there were no dropouts. Children in which treatment was discontinued were categorised as unsuccessful, but the children were still evaluated and included in the final analysis. However, results related to the successful treatments alone were also presented in order to illustrate treatment efficiency.

The Hawthorne effect

The Hawthorne effect can be categorised as an observational bias, where there is a change in the behaviour of patients or caregivers due to participating in a research trial. The behavioural change may be attributed to an increased interest in the treatment or the knowledge of being observed and therefore wanting to do better. The Hawthorne effect may result in an overestimation regarding treatment results, but this has been seldom discussed within orthodontic research.[105] It cannot be ruled out that the results in this trial were unaffected by the Hawthorne effect, given that patient compliance and full cooperation is a key factor when working with a removable functional appliance. However, time appears to be of importance, as the Hawthorne effect has been reported to decrease after six months.[106] Treatment time with headgear activator exceeded six months by margin, arguing for a minimised overestimation regarding treatment results due to the Hawthorne effect.

Blinding

To reduce the risk of overestimating treatment effect, all operators evaluating study cast, lateral head radiographs, and photos were blinded to treatment allocation and whether the data corresponded to pre- or post-treatment. Blinding of patient and clinical operator was not possible due to the character of the trial.

Treatment effects

Dental and skeletal effects

The main treatment effects with headgear activator were attributed to dentoalveolar changes. This agrees with the effects achieved by early treatment with the Twin-block appliance.[47] The skeletal change when treating with removable functional appliances has been concluded to be of minimal clinical importance, and the predominately dentoalveolar effect

attained by treatment is highly related to the retroclination of the maxillary incisors.[107] Furthermore, the treatment with headgear activator, regardless of the age when initiated, showed to be successful in inhibiting proclination of the lower incisors – a finding also consistent with previous research.[65,66]

The cephalometric analysis in Paper III was unable to detect any major significant differences between the children receiving early treatment and the untreated controls. However, this finding could be due to the ITT approach, as a difference was registered when focusing solely on the children in which treatment was completed. Even though the children who completed treatment showed a reduction in skeletal Class II relationship compared to untreated controls, it must be noted that the individual variance and unpredictability regarding skeletal growth is high. Tulloch et al. reported that one fifth of the children treated with functional appliance experienced less mandibular growth than children not receiving treatment, and even though the study result showed a 75% chance of improving the jaw relationship with early treatment, there was considerable variation in growth during the period, both with and without treatment.[46]

Oral health-related quality of life

Class II malocclusion with excessive overjet has been rated as a less attractive feature and is connected with bullying and reported to have negative impact on OHRQoL,[16-20] as verified in Paper II. However, the children in this trial showed a fairly good self-perceived OHRQoL, and it is noteworthy that treatment initiated at 9 or 11 years of age did not show any significant effect in further improving OHRQoL for these children. This can be put in relation to the findings by O´Brien et al., where children with Class II malocclusion reported self-concept scores that exceeded population norms.[20]

Regarding OHRQoL, the negative impact that malocclusion may have appears to increase during childhood, as adolescents with severe levels of malocclusion are those who are most affected.[108] To ensure an early treatment of Class II malocclusion in this trial, the inclusion criteria regarding age was narrow. The early mixed dentition entails a large variance in dental appearance regardless of the presence of malocclusion with orthodontic treatment need or not. Therefore, young children with excessive overjet might not yet have observed any deviance concerning

their teeth. It may be reasonable to assume that low prevalence of caries and the young age in the children participating in this trial contributed to the overall low CPQ scores. In an RCT conducted by O´Brien et al., young children with Class II malocclusion reported self-concept scores that were higher than reported population norms, reflecting medium to high self-esteem for the group. Early treatment with the Twin-block appliance further increased the self-concept score; however, how this affected OHRQoL or translated into different behaviours or experiences, was unclear. [20] Good psychological well-being and high self-esteem have been found to act as protective factors for OHRQoL regarding the negative impact induced by malocclusion and orthodontic treatment,[109-111] findings that illustrate the complexity when evaluating OHRQoL.

Evaluation of lip closure

The frequency of incomplete lip closure decreased after treatment with headgear activator, but a reduction was also seen in the group of untreated children in Paper III. As incomplete lip closure increases the risk for dental trauma,[9] the finding of occasional spontaneous improvement in the group that did not start treatment until 11 years of age can be seen as somewhat reassuring. As an improvement in lip closure also has been shown for children where treatment with functional appliances has been categorised as unsuccessful regarding dental effects,[62] the question as to how the overjet influences lip seal is raised. As lip seal can improve even though the overjet is unaltered, the awareness and behaviour of the patient as well as normal growth, may play an important role. Lip seal is often categorised as a dichotomous variable, the individual appearance may however present on a descending scale. Well-defined criteria and the calibration of assessors carried out in Paper III and IV increase the validity of the assessment, and clinical examination or evaluation of photographs should be preferred, as cephalometric radiographs do not show the patients at rest.

Dental trauma

This trial could not identify any statistically significant difference in dental trauma for children starting treatment early, at the age of 9, or later at 11 years of age. Although no statistical difference was found, all additional dental trauma registered in Paper III affected children in the untreated control group or children in which treatment was discontinued, advocating the need for larger samples when evaluating dental trauma. The observation

in Paper III coincides with the finding that an early treatment approach with functional appliance is more effective in preventing dental trauma for children with excessive overjet.[11]

Early treatment with functional appliance has been found to reduce the incidence of new incisal trauma by 11 percentage points and the risk by 35% when compared to treatment initiated in adolescence.[11] The results from The Cochrane report[11] indicates that nine children need to receive an early treatment with functional appliance in order to prevent one dental trauma. A significant number of the traumas affecting the children reported in this thesis had occurred before enrolment in the study. This finding coincides with earlier studies that further suggest that orthodontic treatment aimed at reducing trauma should be initiated soon after the eruption of the maxillary incisors in order to be effective.[90] An additional common finding for the results presented in Papers III and IV and earlier research was that even though a significant number of children experienced dental trauma, the majority of injuries were minor.[90,91]

Economic evaluations and costs

Paper IV is the first study to evaluate the costs associated with headgear activator treatment when started at different ages. It was demonstrated that the costs associated with treatment were equal regardless of whether treatment started at 9 years of age or at 11 years of age. There was no significant difference regarding treatment effect between the two groups. Therefore, the hypothesis that cost-effectiveness was equivalent for treatment started early, at the age of 9 years or later at the age of 11 years, could not be rejected.

To include the costs related to dental trauma when evaluating headgear activator treatment could add an additional dimension to a cost analysis. Koroluk et al. report that the expected cost of trauma per child is less for the patients that receive an early growth modification treatment than for patients receiving one-phase treatment in the permanent dentition. The reasoning continues that these costs need to be put in relation to the relatively minor traumas registered that presumably are treated at low cost and with good prognosis to the usually larger cost of a two-phase early treatment start.[90]

Economic evaluations within dentistry are highly influenced by local factors, such as insurance systems, costs for salaries and equipment, availability and so on, making extrapolation to other settings inappropriate. The comparability of cost-analyses could be improved by not only reporting the registered costs, but also including the general outcomes, such as treatment time and number of visits. Thereafter, the local economic prerequisites would define the actual costs. It can also be noted that, in Paper IV, the indirect costs might be higher than the corresponding indirect costs associated with treatments performed in general practice dentistry. This because the specialist clinics are fewer in number and generally located further away from the patients than the general practice clinics, thus implying a longer travel duration for children and their parents. Therefore, a slight increase in indirect costs could be expected when treatment is performed at the specialist clinic. On the other hand, it is interesting that the costs presented in Paper IV are within the same range as the costs for Andresen activator treatment, as presented by Čirgić et al., who, in a Swedish study performed in general dentistry, evaluated and compared treatment between an Andresen activator and a prefabricated functional appliance.[86]

Treatment with removable functional appliances may be associated with treatment discontinuation caused by insufficient compliance.[112] Treatments performed by general dentists have been shown to have lower success rates[62,113,114] than the treatments carried out and evaluated in this thesis. It can be assumed that there is a variance in clinical experience and orthodontic skills among general dentists. Consequently, the differences in success rate among general dentists indicate a possible potential for increase in treatment success in general dentistry, and thereby, an improved cost-effectiveness for treatment with removable functional appliances.

Ethical considerations

Recognising the significance of patient-reported outcome measures within dental research is of the utmost importance in order to improve and ensure the best possible care for the patient. Within orthodontic care, the majority of patients are children and young adolescents – a patient group in which dental research predominately has been conducted *on*, rather than *with*, but whose perspective is gaining increased attention.[115] Practice has shifted, and children's perceptions and opinions, experiences, and desires are now

being both requested and valued. When conducting research involving patients, the trial protocol requires approval from Swedish Ethical Review Authority. Moreover, when including children under the age of 15, Swedish law requires informed consent from both patients and parents. If the child opposes participation even though the parents have consented, the child's will takes precedence. The children's voluntary participation and intention to cooperate with treatment was a fundamental requirement for the implementation of all the trials in this thesis.

The postponement of treatment for children starting treatment at 11 years of age could raise doubts and be questioned, but nevertheless, treatment with removable functional appliance can certainly and with good reason be started at various ages. One prevailing approach has been to try and coincide treatment start with the prepubertal growth spurt, normally between 9 and 12 years of age. Therefore, starting treatment at 9 years of age or else postponing treatment until 11 years of age is appropriate, and from an ethical viewpoint, unproblematic.

Environmental considerations

Further implementation of intraoral 3D scanning will presumptively reduce some of the adverse environmental effects that may result from treatment with removable functional appliances. In order to customise the appliance, impressions of the teeth using alginate or silicon materials is required. These materials, and the subsequent plaster study models burdens chemically, and the study models require room for storage. Handling plaster is associated with some spreading of dust, thus affecting the working environment for the dental technician but is avoided if working with intraoral scanning. Given that intraoral 3D scanning is sent digitally, the need for transportation and delivery is diminished. It must however be recognised that the manufacturing of an appliance requires a 3D printed model in plastic. Another advantage with intraoral scanning is the ease of producing new study or working models if, for example, a removable appliance is broken or lost, thus making the need for additional travel to the clinic, impressions and associated materials unnecessary.

Strengths and generalisability of this thesis

The results in this thesis are based on a well-defined study population with well-described baseline characteristics. The strict inclusion and exclusion criteria ensured the evaluation of Class II malocclusion with excessive

overjet exclusively. This was of particular interest regarding patient-reported outcome measures. Moreover, sample size estimation (power analysis) was performed for each evaluated primary outcome.

A randomised controlled trial design was undertaken in order to eliminate bias in treatment assignment – specifically, selection bias (without therapists' or patients' preferences), and most importantly, confounding variables (hidden or variables out of control) were of equal value or equally distributed in the groups. Furthermore, the treatment protocol corresponded to the everyday treatment procedure performed at the clinic and the prospective design and protocol ensured that treatment and progress was thoroughly monitored and registered. In addition, with no dropouts in the trial, attrition bias was insignificant. The results presented in Paper II derives from a clinical multicenter study, representing children from a wide range of demographic areas, and potential confounders were accounted for. Paper III present results where children with Class II malocclusion with excessive overjet is compared to untreated controls and paper IV presents results derived from treatment at different ages and different dental stages. Accordingly, the conclusions drawn from this thesis may be considered to be generalisable for children between 9 to 11 years of age, presenting with a Class II malocclusion with excessive overjet and treated with headgear activator.

The evaluated treatment made blinding impossible for patients and clinical operator. However, blinding was always applied when evaluating the data. Hence, operators not involved in the clinical trial were blinded to treatment allocation, to whether the data was collected before or after treatment, or to which group the data belonged. Furthermore, over-optimistic estimates of the effectiveness of treatment were avoided by applying an intention-to-treat (ITT) strategy.

Overall limitations

The clinical studies in Paper III and IV are based on a single-centre randomised controlled trial, and the treatments were performed by one operator, at a specialist clinic. The trial can therefore be affected by both operator-related error and single-centre bias. It should also be emphasised that the results are applicable under Swedish conditions, given that both health economic evaluations and studies regarding OHRQoL are contextually dependent.

The monetary results presented in the cost analysis are difficult to extrapolate or apply to other settings, as local factors such as insurance systems, demographics, and staff salaries, to mention but a few, are highly influential in economic evaluations.

In addition, cultural and demographic differences may play a role regarding OHRQoL, as can be seen when children from different countries report differently regarding CPQ scores. Nevertheless, the results from this thesis can still form a basis for discussion, and enable comparisons and evaluations to other settings.

Final remarks and recommendations

Treatment with headgear activator is effective in reducing overjet and normalising molar relation. As the treatment effects and associated costs were similar regardless of whether treatment was started at 9 or 11 years of age, an early treatment approach at 9 years of age can be advocated in order to maximise the trauma-preventive effect.

Self-perceived OHRQoL was fairly high among the children at these ages, regardless of the presence of a Class II malocclusion with excessive overjet, and treatment does not appear to render any further improvement. The incentives to undergo treatment might thus not be apparent for the child them self; therefore, it is important to involve both the child and their parents in order to enhance cooperation. This applies specifically if the child is at risk for dental trauma due to the excessive overjet or if the child has been teased or bullied because of the prominent incisors.

As the success rate of treatment with removable functional appliances varies considerably, measures to increase treatment effectiveness, and hence, also cost-effectiveness are desirable.

Therefore, if the child has a history or lifestyle that predisposes them for dental trauma or is being harmed due to bullying and the child, together with the parents, is eager for and positive to headgear activator treatment, then - an early treatment start is the most beneficial.

As the available cost analyses regarding early treatment of Class II malocclusion and the results concerning dental trauma and OHRQoL are based on a limited number of studies, further well-designed studies are likely to add knowledge to the subjects. Furthermore, the long-term effects

of early treatment of excessive overjet are important to evaluate, as there is a knowledge gap with respect to the long-term outcome and stability of early treatment.

Future research

With the ambition to generate an overall picture of treatment of Class II malocclusion with excessive overjet the randomised controlled trial includes a third group, monitored during mixed dentition and treated with fixed appliance in permanent dentition. This, together with a plausible second phase of treatment with fixed appliance for the children presented in this thesis, enables a thorough evaluation of Class II malocclusion treatment. Comparisons as to how OHRQoL is affected by the malocclusion and the treatment effects of early treatment is therefore made possible. Furthermore, the design illustrates treatment-related costs and enables the inclusion of costs associated with dental trauma related to the costs of an early intervention. Finally, a stated goal for the trial is to report long-term follow-up regarding treatment effects and stability of treatment.

CONCLUSIONS

From the systematic review (Paper I), the following conclusions were made regarding the short-term effects of early treatment of Class II malocclusion:

- There is high level of evidence that treatment with functional appliances reduces overjet and improves antero-posterior skeletal relationship and moderate evidence that treatment with headgear reduces overjet and restrains forward growth of the maxilla.
- There is currently knowledge gaps or insufficient evidence available regarding the effect on soft tissue profile, oral health-related quality of life, incidence of trauma, treatment-related costs as well as to long-term outcome and stability of early treatment.

In the controlled trial (Paper II), which presented oral health-related quality of life (OHRQoL) for children with Class II malocclusion with excessive overjet when compared to children with unilateral posterior crossbite or normal occlusion, it was concluded that:

- Children with Class II malocclusion with excessive overjet reported significantly lower self-perceived OHRQoL compared to children with unilateral posterior crossbite or normal occlusion. The domains of social and emotional well-being were those most affected.
- No significant difference in self-perceived OHRQoL could be registered between the children with unilateral posterior crossbite and normal occlusion.
- Children in all three groups reported generally low CPQ scores which implies an overall fairly good self-perceived OHRQoL, despite the presence of a malocclusion.

The RCT on the treatment effects of early treatment with headgear activator (Paper III) concluded that:

- Early treatment with headgear activator was successful in reducing overjet and correcting molar relationship.
- No significant difference could be registered after treatment regarding self-reported OHRQoL, lip closure, or incidence of trauma when compared to the untreated control group.

In the RCT on cost analysis of treatment with headgear activator when treatment was started at 9 or 11 years of age (Paper IV), it was concluded that:

- The costs associated with headgear activator treatment, as well as the treatment effects, were equivalent regardless of whether treatment was started at 9 or 11 years of age.
- The most pronounced treatment effects were reduction of overjet and correction of molar relationship, whereas the treatment effects regarding OHRQoL, lip closure, and trauma incidence were found to be modest.
- With costs and treatment effects being equivalent, an early treatment approach can be advocated to enhance trauma prevention.

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APPENDIX

Child Perceptions Questionnaire 8-10 (Swedish)

Folktandvården
Region Östergötland
pernilla.larsson.gran@regionostergotland.se

Tandvårdshögskolan
Malmö Högskola
gunilla.klingberg@mah.se

ENKÄT OM BARNS MUNHÄLSA

8-10 år

FOLKTANDVÅRDEN
Östergötland

Hej på dig!

Tack för att du vill hjälpa oss med vår undersökning.
Vi gör den här undersökningen för att förstå bättre hur barn påverkas av sin mun och tänderna.

Kom ihåg:

- Du ska inte skriva ditt namn på frågeformuläret
- Det är inget prov och det finns inga rätta eller felaktiga svar
- Prata inte med någon om frågorna när du svarar på dem
- Läs varje fråga noggrant och tänk på det som hänt den senaste månaden
- Innan du svarar, fråga dig själv:
  händer det här mig på grund av mina tänder eller min mun.

Sätt ett kryss ☒ i rutan för det svar som stämmer bäst för dig.

Försök att svara med det som bäst beskriver hur du upplever och känner.
Om du inte kan svara på frågan, sätt ett kryss ☒ i rutan för Aldrig.

Exempel:
Hur ofta har du svårt att koncentrera dig i skolan?

Om du har haft svårt att koncentrera dig i skolan på grund av problem med munnen eller tänderna väljer du det svar som passar bäst.
Om det beror på något annat, sätt ett kryss ☒ i rutan för Aldrig.

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Först några frågor om dig

Dagens datum:_____

1. Är du en pojke eller en flicka?

   ☐ pojke
   ☐ flicka

2. När är du född? _____ Ålder:_____
   År Månad Dag

3. När du tänker på dina tänder eller din mun, hur tycker du att tänderna och munnen mår?

   ☐ Mycket bra
   ☐ Bra
   ☐ Okej
   ☐ Dåligt

4. Hur mycket bryr du dig om dina tänder och din mun en vanlig dag?

   ☐ Inte alls
   ☐ Mycket lite
   ☐ Lite
   ☐ Mycket

Här är några frågor om dina tänder och din mun. Hur ofta har du haft:

5. Ont i dina tänder eller mun den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

6. Ont från sår i munnen den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

7. Ont från tänderna när du ätit eller druckit något som är varmt eller kallt den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

8. Mat som fastnat mellan tänderna den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

9. Dålig andedräkt den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Här är några fler frågor om dina tänder och din mun. Hur ofta har du haft:

10. Behövt längre tid än andra för att äta en måltid på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

11. Svårt att bita av eller tugga mat som äpple, morot eller kött på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

12. Haft svårt att äta mat du velat ha på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

13. Haft svårt att uttala något ord på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

14. Haft problem att sova på natten på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

Några frågor om hur du känner.
Hur ofta har du:

15. Varit upprörd på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

16. Känt dig arg och frustrerad på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

17. Varit blyg eller generad på grund av dina tänder den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

18. Oroat dig över vad andra personer tycker om dig på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

19. Oroat dig över att du inte ser lika bra ut som andra på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

Och nu frågor om skolan.
Hur ofta har du:

20. Varit borta från skolan på grund av dina tänder eller mun den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

21. Haft svårt att göra dina läxor på grund av dina tänder eller mun den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

22. Haft svårt att koncentrera dig i skolan på grund av dina tänder eller mun den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

23. Inte velat tala eller läsa högt inför klassen på grund av dina tänder eller mun den senaste månaden?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Frågor om när du är med andra.
Hur ofta har du:

24. Inte skrattat eller velat le tillsammans med andra på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

25. Inte velat prata med andra barn på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

26. Inte velat vara med andra barn på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

27. Inte varit med på fritidsaktiviteter efter skolan på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

Hur ofta har:

28. Andra barn retat dig eller kallat dig för dumma saker på grund av dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

29. Andra barn frågat dig om dina tänder eller mun den senaste månaden?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

Nu är det slut på frågorna. Tack för din hjälp!

Child Perceptions Questionnaire 11-14 (Swedish)

Folktandvården
Region Östergötland
pernilla.larsson.gran@regionostergotland.se

Tandvårdshögskolan
Malmö Högskola
gunilla.klingberg@mah.se

ENKÄT OM BARN OCH UNGDOMARS MUNHÄLSA

11-14 år

Hej på dig!

Tack för att du ställer upp och hjälper oss med vår undersökning. Den här undersökningen görs för att man ska förstå mer om problem som barn kan ha på grund av sina tänder, mun, läppar och käkar. Genom att svara på de här frågorna hjälper du oss att lära oss mer om ungas upplevelser.

Kom ihåg:

- Du ska inte skriva ditt namn på frågeformuläret
- Det är inget prov och det finns inga rätta eller felaktiga svar
- Prata inte med någon om frågorna när du svarar på dem. Dina svar är hemliga och ingen du känner kommer att se dem.
- Läs varje fråga noggrant och tänk på det som hänt de senaste 3 månaderna när du svarar på frågorna
- Innan du svarar, fråga dig själv:
  händer det här mig på grund av min munhälsa (tänder, läppar, mun eller käkar).
- Med munhälsa menar vi allt som rör tänder, läppar, mun eller käkar.

Sätt ett kryss ☒ i rutan för det svar som stämmer bäst för dig.

Försök att svara med det som bäst beskriver det du upplever. Om du inte kan svara på frågan, sätt ett kryss ☒ i rutan för Aldrig.

Exempel:
Hur ofta har du svårt att koncentrera dig i skolan?

Om du har haft svårt att koncentrera dig i skolan på grund av problem med munnen eller tänderna väljer du det svar som passar bäst.
Om det beror på något annat, sätt ett kryss ☒ i rutan för Aldrig.

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Först några frågor om dig

Dagens datum:_____

1. Är du en pojke eller en flicka?

   ☐ pojke
   ☐ flicka

2. När är du född? _____ Ålder:_____
   År Månad Dag

3. Hur skulle du säga att din munhälsa är?
   (Med munhälsa menar vi allt som rör dina tänder, läppar, käkar eller mun.)

   ☐ Mycket bra
   ☐ Bra
   ☐ Sådär
   ☐ Dåligt

4. Hur mycket påverkar munhälsan ditt dagliga liv?

   ☐ Inte alls
   ☐ Mycket lite
   ☐ Något
   ☐ Väldigt mycket

Frågor om problem från munnen.

Under de senaste **3 månaderna**, hur ofta har du haft:

5. Ont i dina tänder, läppar, käkar eller mun?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

6. Blödande tandkött?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

7. Sår i munnen?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

8. Dålig andedräkt?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

9. Mat som fastnat i eller mellan dina tänder?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

10. Mat som fastnat i gommen?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

För de kommande frågorna…
Har detta hänt på grund av din munhälsa?

Under de senaste **3 månaderna**, hur ofta har du:

11. Andats genom munnen?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

12. Behövt längre tid än andra för att äta en måltid?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

13. Haft svårt att sova?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

14. Haft svårt att bita av eller tugga mat som äpple, morot eller kött?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

15. Haft svårt att gapa stort?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Några fler frågor om din munhälsa.

Under de senaste **3 månaderna**, hur ofta har du haft:

16. Svårt att uttala något ord?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

17. Svårt att äta mat som du skulle vilja äta?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

18. Svårt att dricka med sugrör?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

19. Svårt att dricka eller äta varm eller kall dryck eller mat?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Några frågor om känslor.
Har du känt så här pga av din munhälsa?
Om du känt så här pga något annat ska du sätta kryss i rutan Aldrig

Under de senaste **3 månaderna**, pga din munhälsa -hur ofta har du:

20. Känt dig irriterad eller frustrerad?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

21. Känt dig osäker på dig själv?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

22. Känt dig blyg eller generad?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

23. Oroat dig för vad andra tycker om dina tänder, läppar, mun eller käkar?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Några fler frågor om känslor i samband med din munhälsa.

Under de senaste **3 månaderna**, pga av din munhälsa -hur ofta har du:

24. Oroat dig för att du inte ser lika bra ut som andra?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

25. Varit upprörd?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

26. Känt dig nervös eller rädd?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

27. Oroat dig för att inte vara lika frisk som andra?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

28. Oroat dig för att du är olik andra barn och ungdomar?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Några frågor om skolan.
Har du varit med om att detta hänt pga din munhälsa?

Om det hänt på grund av något annat ska du svara Aldrig

Under de senaste **3 månaderna**, pga av din munhälsa
-hur ofta har du:

29. Varit borta från skolan på grund av munnen eller tänderna eller tandbehandling?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

30. Haft svårt att koncentrera dig i skolan?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

31. Haft svårt att göra dina läxor?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

32. Inte velat tala eller läsa högt inför klassen?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Frågor om dina fritidsaktiviteter och när du är med andra personer.

Har du varit med om att detta hänt på grund av din munhälsa?

Om det hänt på grund av något annat ska du svara Aldrig

Under de senaste **3 månaderna**, pga din munhälsa
- hur ofta har du:

33. Undvikit att delta i fritidsaktiviteter efter skolan?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

34. Inte velat tala med andra barn och ungdomar

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

35. Undvikit att le eller skratta när du varit med andra barn och ungdomar?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

36. Haft svårt att spela musikinstrument som blockflöjt, flöjt, klarinett, trumpet?

☐ Aldrig ☐ Någon enstaka gång ☐ Ibland ☐ Ofta ☐ Varje eller nästan varje dag ☐ Vet inte

Fler frågor om dina fritidsaktiviteter och när du är med andra.

Har du varit med om att detta hänt på grund av din munhälsa?

Om det hänt på grund av något annat ska du svara Aldrig

Under de senaste **3 månaderna**, hur ofta har (du):

37. Inte velat vara med andra barn och ungdomar?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

38. Varit osams med andra barn eller din familj?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

39. Andra barn och ungdomar retat dig eller kallat dig för dumma saker?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

40. Andra barn lämnat dig utanför?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

41. Andra barn och ungdomar frågat dig om dina tänder, läppar, käkar eller mun?

☐	☐	☐	☐	☐	☐
Aldrig	Någon enstaka gång	Ibland	Ofta	Varje eller nästan varje dag	Vet inte

Så där, nu är det klart.
Tack för att du hjälper oss.

Papers I-IV

I

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HSOA Journal of Dentistry: Oral Health & Cosmesis

Review Article

Outcomes of Early Class II Malocclusion Treatment - A Systematic Review

Jenny Kallunki[1], Lars Bondemark[2*] and Liselotte Paulsson[2]

[1]*The Center for Orthodontics and Paedodontics, County Council of Östergötland, Linköping, Sweden*

[2]*Department of Orthodontics, Malmö University, Malmö, Sweden*

Abstract

Aim

To undertake a systematic review of the evidence supporting early treatment (before the age of 10) of Class II malocclusion, with special reference to short and long-term outcomes: correction of overjet, dental relationships, improvement in intermaxillary relationships, soft tissue profile, associations to Temporomandibular Disorders (TMD), quality of life, incidence of trauma and cost-effectiveness.

Material and methods

Four databases were searched, from January 1960 to October 2017. Inclusion criteria were randomized controlled or controlled trials reporting short or long-term effects on dental or basal relationships, soft tissue profile, associations to TMD, quality of life, incidence of trauma, or costs. The quality of evidence was scored according to GRADE.

Results

297 studies were identified and 23 satisfied the inclusion criteria for full evaluation. The quality of evidence was high in 5 studies, moderate in 3, and low in 15. There is lack of data on long-term outcomes and stability, thus all evidence is based on short-term results. There is high level of evidence that early treatment of Class II malocclusion with functional appliances reduces overjet and improves skeletal relationships, moderate evidence that headgear reduces overjet and restrains forward growth of the maxilla, but insufficient evidence to determine how early treatment influences soft tissue profile, TMD, quality of life, incidence of trauma or treatment-related costs.

Conclusion

There is moderate to high evidence that in the short term, early treatment of Class II malocclusion division 1 reduces overjet and improves skeletal relationships.

Keywords: Class II malocclusion; Early treatment; Orthodontic appliance; Systematic review; Treatment outcomes

***Corresponding author:** Lars Bondemark, Department of Orthodontics, Malmö University, Malmö, Sweden, Tel: +46 406658473; E-mail: lars.bondemark@mau.se

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Introduction

Class II malocclusion is one of the more common malocclusions in children. The reported prevalence ranges from 14 to about 25% depending on the age of the children observed [1,2].

Various dental and basal deviations may result in a Class II malocclusion. Mandibular retrusion is common finding [3], as are pronounced overjet and prominent maxillary incisors with incomplete lip closure. Pronounced overjet and incomplete lip closure has been shown to increase the risk for dental trauma [4]. Recent Cochrane review reported that early treatment with a functional appliance achieved a statistically significant reduction in the incidence of incisal trauma [2]. This finding has however been further discussed due to a high degree of uncertainty [5]. Also Temporomandibular Disorders (TMD) has claimed to be associated with Class II malocclusions [6] but the effect treatment of Class II malocclusions may have on development of TMD is insufficient [7].

Early versus late orthodontic treatment has been debated. Proponents of early intervention have claimed that treatment is easy to perform, there is better use of growth potential, the extent of treatment in the permanent dentition is reduced and there should be less damage to teeth and tissues [8]. Furthermore, early treatment of Class II malocclusion has also claimed to have positive influence on self-esteem [9].

Comparison of one and two-phase treatment of Class II malocclusion showed no difference with respect to final overjet, basal relationship or the overall treatment success as scored by Peer-Assessment-Rating (PAR) [10]. Additionally, systematic reviews have concluded that compared to one-phase treatment, two-phase treatment offers no advantage, except for the reduction in the incidence of incisor trauma. Most of the available research is based on study populations that start their treatment from the age of ten and up to early teens [2].

Treatment recommendations, whether formulated as public policies or for the individual patient, should be based on the best available research evidence. A Randomized Controlled Trial (RCT) is often the preferred study design for evaluating treatment, because it reduces bias. By assessing the overall quality of the research and exposing potential knowledge gaps, a systematic review of research into a specific question is a valuable aid to the clinician [11].

A broad approach is of interest to evaluate the full effects of a treatment. A focus on patient centred outcomes, such as quality of life and dental trauma should be put in relation to dental and basal effects as well as a socio-economic aspect. Therefore, the aim of the present

study was to undertake a systematic review of the evidence supporting early treatment (before the age of 10) of Class II malocclusion, with special reference to short and long-term outcomes: correction of overjet, dental relationships, improvement in intermaxillary relationships, soft tissue profile, associations to TMD, quality of life, incidence of trauma and cost-effectiveness.

Material and Methods

The review was structured according to the Goodman guidelines [12], starting with definition of the research question, followed by formulation of a plan for the literature search, then the search itself and retrieval of publications. Finally, data were interpreted to assess the overall evidence.

Definition of the research question

The following research question was defined: "How effective is early treatment of Class II malocclusion, in terms of the following outcomes: correction of overjet, dental relationship, improvement in intermaxillary relationship, soft tissue profile, associations to TMD, quality of life, incidence of trauma and cost effectiveness?"

Plan for literature search

An appropriate search strategy was designed in consultation with a senior librarian, including choosing appropriate Medical Subject Headings (MeSH) terms, selecting relevant databases and assisting in the computerized search. The search covered the period from January 1960 to October 2017. The databases MEDLINE via PubMed, Web of Science, Cochrane and CINAHL were selected.

Five different search syntaxes were used. The first and basic search strategy comprised Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term), supplemented by a second: Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term) and Costs and Cost Analysis (MeSH term), third: Tooth injuries (MeSH term) and/or Tooth fractures (MeSH term) and Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term) and fourth search: Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term) and Temporomandibular Joint Dysfunction Syndrome (MeSH).The final search syntax used was Quality of Life (MeSH term) and/or Self Concept (MeSH term) and/or Patient Satisfaction (MeSH term) and Malocclusion, Angle Class II (MeSH term) and Orthodontic appliances (MeSH term) and Dentition, Mixed (MeSH term).

Literature search and retrieval of publications

Using PICO-criteria (Table 1), the inclusion criteria were set to select RCTs or prospective controlled studies of treatment of Class II malocclusion in the early mixed dentition. To ensure an early approach, treatment start before the age of 10 years was required. No limitations were made concerning language.

The retrieved titles and abstracts of potentially relevant articles were assessed independently by three reviewers (J.K, L.B, and L.P). An article was ordered in full-text version if at least one of the reviewers considered it to be of potential relevance, or if the title and abstract were ambiguous, or did not provide sufficient information.

Participants	Children starting orthodontic treatment for Class II malocclusion before the age of 10 years.
Interventions and comparators	Any intervention provided to treat Class II malocclusion in the early mixed dentition.Two-phase orthodontic treatments for Class II malocclusion when short-term outcomes are specifically reported after completing first phase of treatment.Controls are comparable non-treated children or children receiving another intervention.
Outcomes	Short and long-term effects measured as: success in correction of overjet, dental relationship, improvement in intermaxillary relationship, soft tissue profile, incidence of trauma, quality of life and cost-effectiveness.
Study design	RCT or prospective controlled trials

Table 1: PICO inclusion critera.

Data extraction, quality assessment, interpretation and evaluation of evidence

A data extraction protocol was prepared for assessing the quality of the articles. The protocol was calibrated by joint review of three articles, followed by minor revision to reach consensus. Reviewing was undertaken independently by the three reviewers. In cases of disagreement the article was reread and discussed until consensus was reached.

The quality of each separate study was classified as high, moderate or low [13]. The strength of the scientific evidence was assessed according to the GRADE system [14].

To qualify as high or moderate quality, the study required sufficient material, relevant controls and attrition no greater than 30%. Quality could be downgraded if shortcomings were apparent in study design, if there was lack of adjustment for potential confounders (selected material or reporting only successful treatment results), inconsistency of results, historic controls or if other limitations were apparent.

The reference lists from articles deemed eligible were hand searched for additional studies and any supplementary studies were evaluated by following the same procedure as described above.

Results

The search strategy identified 297 studies, of which 74 were fully assessed. The selection process is illustrated, according to the PRISMA statement [15], (Figure 1) in which the most prevalent reasons for exclusions are reported. Inter-reviewer consistency in evaluation and grading of the full-text articles was 95 per cent. Twenty-three studies satisfied the inclusion criteria and were analysed for study quality. Fifteen studies were graded as low quality [16-30], as presented in Table 2. Thus, eight studies were finally assessed: 5 were graded as high quality [9,31-34] and three as moderate [35-37] (Table 3). All eight studies were RCTs, four conducted in USA [31,34,35,37], three in United Kingdom [9,32-33] and one in Sweden [36].

The three studies from United Kingdom [9,32-33] originated from one and the same study population. In these studies, twin-block appliance therapy was compared with untreated controls. The American studies [31,34,35,37] were based on two different study populations. Two of them compared bionator and headgear treatment with untreated control subjects [31,34]. The other two studies compared bionator or headgear/bite plane treatments to untreated controls [35,37]. In the Swedish study [36] headgear and activator appliances were compared with untreated controls.

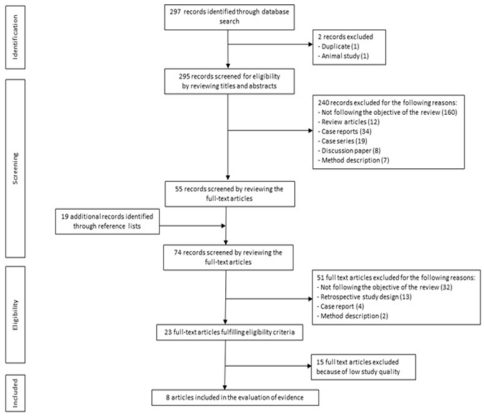

Figure 1: Flow of information through the different phases of the systematic review.

Author	Year
Stamenković et al. [27]	2015
Landázuri et al. [22]	2013
Silvestrini-Biavati et al. [26]	2012
de Almeida et al.* [19]	2008
Quintão et al. [25]	2006
de Almeida et al.* [18]	2005
Janson et al. [21]	2003
de Almeida et al. [17]	2002
Mills and McCulloch** [24]	2000
Mills and McCulloch** [23]	1998
Dann et al. [16]	1995
Wieslander [30]	1993
Wieslander*** [28]	1984
Wieslander *** [29]	1984
Harvold and Vargenvik [20]	1971

Table 2: Studies classified as low level of quality. Downgraded to low quality because at least one of the following shortcomings was apparent: successful treatments only reported, historical controls, unclear inclusion criteria, insufficient material or unclear methodological approach.

* Patient material in de Almeida et al., [19] and de Almeida et al., [18] is the same.

** Patient material in Mills and McCulloch [23] and Mills and McCulloch [24] is the same.

*** Patient material in Wieslander [28] and Wieslander [29] is the same.

Dental changes

Early treatment with twin-block showed a reduction in overjet and a correction of molar relationship in comparison with untreated controls [32]. Three studies [34,36-37] reported that early treatment with bionator, activator or headgear also reduced overjet.

Skeletal changes

Skeletal improvement after early treatment with twin-block was on average 2 mm, the result of a similar degree of growth modification in the maxilla and mandible. Although statistically significant, the improvement was not regarded as clinically important [32]. Tulloch et al., [34] showed that treatment with bionator or headgear reduced the basal Class II malocclusion in comparison with untreated controls. The headgear primarily restrained the forward growth of the maxilla while the bionator enhanced the forward positioning of the mandible. It was pointed out, however, that within all three study groups there were large individual variations in growth. Keeling et al., [37] concluded that an overall apical base correction was found in both bionator and headgear/bite plane treatment groups when compared to untreated controls. The effect was due to mandibular enhancement, not restricted maxillary growth.

Jacobson [36] found that both headgear and activator treatment restrained the forward growth of the maxilla. No support for enhanced condylar growth or forward positioning of the mandible could be found.

Soft tissue profile

The perceptions of facial profiles were favoured by early treatment with twin-block. When judged by other children and teaching staff, treatment enhanced the profile, mainly due to the reduction in overjet and reduced visibility of teeth [33].

Temporomandibular Disorders (TMD): No studies evaluating early Class II treatment and effects regarding TMD was identified.

Quality of life related effects: Early treatment with twin-block improved self-concept and reduced negative social experiences, but the effects on social behaviour were unclear [9].

Author, Year	Study Design	Study Population	Outcome Measures	Results	Study Quality/Comments
Chen et al., 2011 [32]	RCT	93 Headgear/biteplane 9.7 years 87 bionator 9.7 years 81 controls 9.5 years	Modified Ellis injury classification	A significant number of children (25%) had already experienced incisor trauma before treatment were initiated. No correlation was found between initial overjet and the prevalence of trauma. Early orthodontic treatment did not significantly affect the incidence of trauma. Most injuries before and after treatment were minor, consisting of enamel fractures.	Moderate + Randomized study design + Blinding when analysing - Attrition >20% - Pretreatment performed in treatment (approx. 50%) and control (approx. 10%) groups,unclear method - No adjustment for confounders (lip closure, socio-economics, leisure activities)
O´Brien et al., 2009 [29]	RCT	20 twin-block 8-10 years 20 controls 8-10 years Randomly selected from O´Brien et al. 2003	Attractiveness graded by Likert-scale	After twin-block treatment, the profile was rated as more attractive when compared to untreated controls. Visible front teeth and large overjet had negative impact on profile perception.	High + Randomized study design + Multicenter + Sample-size calculations + Blinding when analysing + Method error analysis
O´Brien et al., 2003 [6]	RCT	89 twin-block 9.7±0.98 years 87 controls 9.8±0.94 years	Piers-harris children´s self-concept scale. Childhood experience questionnaire. Perceptions of the benefits of orthodontic treatment scale	At onset and at 15 months follow-up, both groups reported medium- to high self-esteem. Twin-block treatment resulted in an increased self-concept and a reduction in negative social experience.	High + Randomized study design + Multicenter + Sample-size calculations + Intention-to-treat approach + Blinding when analysing - Attrition > 20% (28% for twin-block, 22% for controls)
O´Brien et al., 2003 [30]	RCT	89 twin-block 9.7±0.98 years 85 controls 9.8±0.94 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relationships: Overjet, incisor and molar positioning PAR-score	Twin-block treatment resulted in a reduction of overjet, 70% of the correction due to dentoalveolar changes. Skeletal improvement after early treatment with Twin-block was on average 2mm, the result of a similar degree of growth modification in the maxilla and the mandible. PAR-score was reduced by 42% in the treated group whereas in the controls PAR-score was increased by 9%.	High + Randomized study design + Multicenter + Control of confounders (age, gender, treatment) + Attrition <20% + Sample size calculations + Intention-to-treat approach + Blinding when analysing + Method error analysis
Koroluk et al., 2003 [28]	RCT	52 bionator 9.4±1.0 years 50 headgear 9.4±1.0 years 61 controls 9.4±1,2 years	Incidence of trauma Estimations regarding: Extent of trauma Required trauma treatment Costs	Trauma to maxillary incisors was found in all groups. Most injuries were minor and related costs were estimated as low. Treatment with Bionator might reduce the incidence of trauma, but should be initiated soon after eruption of maxillary incisors in order to be effective. It was estimated that the expected cost of trauma per child was less for patients who had early growth modification treatment than for patients whose treatment was delayed until their permanent dentition. However, early 2-phase orthodontic treatment is usually more expensive than a single-phase treatment approach.	High + Randomized study design + Sample size calculations + Intention-to-treat approach + Attrition <20%
Keeling et al., 1998 [34]	RCT	90 headgear/biteplane 9.7 years 78 bionator 9.7 years 81 controls 9.5 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relationships: Overjet, incisor and molar positioning Significance of retention Relapse	Bionator and headgear groups showed significantly more skeletal Class II correction than untreated controls. Early treatment with headgear resulted in significant dental Class II correction, affecting maxillary incisors and molars. Treatment with bionator or headgear/biteplane showed no effect on maxillary growth but both appliances enhanced mandibular anterior growth. Skeletal changes were stable after one year.	Moderate + Randomized study design + Blinding when analysing - Attrition >20% - Pretreatment performed in treatment (approx. 50%) and control (approx. 10%) groups, unclear method
Tulloch et al., 1997 [31]	RCT	53 bionator 53 bionator 9.4±1,0 years 52 headgear 9.4±1,0 years 61 controls 9.4±1.2 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relations: Overjet, overbite Mandibular length	Overall, early treatment showed a reduction in overjet and a 75% chance for improving the jaw relationship. Basal improvement was achieved through different mechanisms. Headgear resulted in maxillary restraint and Bionator in forward positioning and increased length of the mandible. Great individual response to treatment and difference in growth were registered in both the treatment and control groups.	High + Randomized study design + Sample size calculations + Intention-to-treat approach + Attrition <20% + Method error analysis
Jakobsson, 1967 [33]	RCT	20 headgear 8.5 years 20 activator 8.5 years 20 controls 8.5 years	Cephalometrics: Antero-posterior skeletal discrepancies Dental relations: Overjet, overbite Mandibular length	Early treatment reduced overjet. Activator and Headgear treatment appeared to affect positioning of the maxilla, most pronounced by Headgear treatment. Both treatments significantly increased facial height. Activator treatment had an effect within the dento-alveolar area of the mandible, but no support for an orthopaedic effect was found.	Moderate + Randomized study design + Method error analysis + Attrition <20% - No sample-size calculations - No blinding when analysing - No Intention-to-treat approach

Table 3: Studies included in the evaluation of evidence.

Incidence of trauma: A significant number of children had already experienced incisor trauma before treatment were initiated [35]. Most of the acquired injuries, before and during treatment, were minor [31,35]. One study showed that early treatment with bionator might reduce the incidence of trauma [31], whereas one was unable to find such a correlation [35].

Cost-effectiveness: Koroluk et al., [31] evaluated the incidence of dental trauma and the related costs. The conclusions were that dental trauma, although less extensive, was a frequent finding within all three groups. Early treatment with bionator could have some influence on reducing the incidence of trauma and thereby related costs, a finding that Koroluk et al., [31] assessed in the context of the expected higher cost of two-phase treatment.

Evaluation of evidence: The level of evidence refers only to short-term changes, as there was a lack of long-term follow-up.

Based on the results of two studies of high quality and two of moderate, there was a high level of evidence that early treatment of Class II malocclusion with functional appliances reduced overjet [32,34,36-37]. The basal relationships were also improved by treatment, mainly by enhancing the forward positioning of the mandible [32,34,37].

Based on the results of one study of high quality [34] and one of moderate quality [36] there was a moderate level of evidence that headgear reduces overjet and also reduces the severity of the skeletal Class II malocclusion by restraining the forward growth of the maxilla.

Because too few studies or contradictory results, evidence was insufficient as to the effect of early treatment on the influence on soft tissue profile [33], quality of life [9], incidence of trauma [31,35] or whether early treatment is cost-effective [31].

Discussion

The main finding for this systematic review was a high level of evidence that early treatment of Class II malocclusion and specifically Class II division 1, using a functional appliance reduces overjet and improves antero-posterior basal relationships in the short-term. There is a moderate level of evidence, also in the short-term, that headgear reduces overjet and restrains forward growth of the maxilla. Evidence was insufficient with respect to the effect of early treatment of Class II malocclusion on soft tissue profile, quality of life, incidence of trauma or treatment related costs. Though insufficient evidence found in this review, current research points to Class II treatment not being a risk factor for TMD development [7], further well-designed studies may add knowledge to this question. Finally, no conclusions with respect to long-term outcome and stability of early treatment could be drawn.

Under the GRADE system for scoring evidence, study quality is denoted as high or moderate. Because there were few studies of adequate quality covering the same outcome, no evidence base emerged with respect to the effects of early treatment of Class II malocclusion on soft tissue profile, quality of life related measures or cost-effectiveness. However, when few relevant high quality studies are identified, it is important to bear in mind that insufficient or limited evidence does not imply lack of effect. Although it must be noted that every single case must be planned individually, with special consideration on patient's needs and desires which also implies that a large proportion of patients with Class II malocclusion might not benefit from two-phase treatment [2], it is still important to identify the variables which characterize children in whom an early treatment approach would be advantageous [38]. Therefore, in order to evaluate existing results and to fill potential knowledge gaps in this field, there is still a need for further methodologically well-designed studies.

It was notable that three [9,32,33] of the five high quality studies were based on the same study population and that the other two [31,34] also originated from one and the same population. This could be considered problematic because the weighted result is based on a rather small number of study populations. The difference in outcome measures for the high quality studies as well as differences in methodology made it difficult to compare treatment results. Therefore, only a general conclusion regarding antero-posterior basal relationships could be drawn.

From the initial 297 articles generated by the literature search, only 23 studies satisfied the eligibility criteria and were included in the final evaluation. This is not uncommon in a systematic review, as the purpose of the search strategy is to identify all relevant studies related to the research question. Furthermore, in order to avoid subjectivity in the assessments, independent observers evaluated the quality of separate studies and the overall level of evidence. Consistency among the observers was high (95%); any conflicting assessments were resolved by discussion to reach consensus. Moreover, using Goodman's model [12] fulfilled the criterion of repeatability and minimized the risk that chance or arbitrariness would affect the conclusions.

With reference to methodology, one of the most common reasons for exclusion was retrospective study design. Furthermore, because the objective was to evaluate early treatment, the composition of the study population was of great importance. A frequent reason for exclusion was the wide age range of the children who constituted the study group. This made it impossible to ensure an early treatment approach. One aspect which should be addressed is the fact that chronological age and dental age do not necessarily correlate. However, studies reporting dental age were seldom identified and an age span of several years was a common finding. An inclusion criterion limiting chronological age was considered appropriate in order to meet the definition of early treatment.

An important determinant of success with removable appliance therapy is patient compliance, yet this factor was inadequately addressed in basically all studies. At best, there were statements describing how the patients were instructed to use the different appliances. Reports as to if, or how, this was controlled were lacking. To fully assess treatment outcome, the results should be considered in relation to patient cooperation and compliance.

Finally, the findings of this systematic review are in accordance with a recent meta-analysis of cephalometric assessment of the treatment results for removable functional appliance therapy in the mixed dentition [39]. With a broader focus, the aim of this systematic review was to evaluate treatment effects on dental and basal relationships as well as cost-effectiveness, incidence of trauma and impact on quality of life.

It has been concluded that a two-phase treatment approach offers no final advantage compared to one-phase when looking at dental and basal variables [2]. Whether early treatment can be justified from a psychosocial, socioeconomic or trauma preventive aspect is not yet validated scientifically. Therefore, further research is needed.

Conclusion

- There is a high level of evidence that in the short term, early treatment of Class II malocclusion and specifically Class II division 1, with functional appliances reduces overjet and improves antero-posterior skeletal relationships, i.e., enhances forward positioning of the mandible
- There is a moderate level of evidence that in the short term, headgear reduces overjet and restrains forward growth of the maxilla
- There is insufficient evidence with respect to the effect of early treatment of Class II malocclusion on soft tissue profile, quality of life, incidence of trauma or treatment- related costs
- There is a knowledge gap with respect to long-term outcome and stability of early treatment

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Original article

Oral health-related quality of life among children with excessive overjet or unilateral posterior crossbite with functional shift compared to children with no or mild orthodontic treatment need

Jenny Kallunki[1], Ola Sollenius[2], Liselotte Paulsson[3], Sofia Petrén[3], Lillemor Dimberg[4] and Lars Bondemark[5]

[1]The Center for Orthodontics and Pedodontics, County Council Östergötland, Linköping, Sweden, [2]Department of Orthodontics, County Council Halland, Halmstad, Sweden, [3]Department of Orthodontics, Faculty of Odontology, Malmö University, Sweden, [4]Orthodontic Department, Eastman institute, County Council Stockholm, Sweden and [5]Department of Orthodontics, Faculty of Odontology, Malmö University, Sweden

Correspondence to: Jenny Kallunki, The Center for Orthodontics and Pedodontics, S-601 82 Norrköping, Sweden. E-mail: jenny.kallunki@regionostergotland.se

Summary

Objectives: To compare Oral health-related quality of life (OHRQoL) among 9-year-old children with excessive overjet (EO) to children with unilateral posterior crossbite (UPC) and children with normal occlusion (NO).

Materials and methods: The study sample sourced from 19 Public Dental Service Clinics in Sweden. Reported are baseline data originating from two controlled trials, one regarding UPC and the other focusing on EO. The NO children derive from the same trials. The UPC group comprised 93 children (45 boys and 48 girls), the EO group 71 children (36 boys and 35 girls), and the NO group 65 children (32 boys and 33 girls). In conjunction to a clinical examination, all children completed the Child Perceptions Questionnaire ($CPQ_{8\text{-}10}$) for evaluation of OHRQoL. The $CPQ_{8\text{-}10}$ comprises 25 questions grouped into four domains: oral symptoms, functional limitations, emotional, and social well-being. Validated questions about pain in the jaws and face were also included.

Results: The total mean CPQ score was 5.1 for the UPC, 7.4 for the EO, and 4.4 for the NO group, showing a significant difference between the UPC and EO ($P = 0.048$) and between EO and NO group ($P = 0.012$). These differences remained when adjusted for the confounders' caries, trauma, enamel defects, and headache. No difference between UPC and NO was found. The EO children also reported significantly higher scores in the domains emotional and social well-being ($P = 0.039$ and $P = 0.012$).

Limitations: The study would be strengthened if a longitudinal design had been performed.

Conclusion: Children with EO reported significantly lower OHRQoL compared to children with UPC or NO. The children generally reported low CPQ scores that imply an overall fairly good OHRQoL.

Introduction

The World Health Organization (WHO) states that oral health is essential to both general health and quality of life. Good oral health implies being free from diseases and disorders that could limit a person's capacity in biting, chewing, smiling, speaking, or negatively affect psychosocial well-being (1). One of the most frequent oral conditions is malocclusions and frequency ranges between 39 and 93%, whereas some of the most common specific malocclusions are excessive overjet (EO) with Class II malocclusion and unilateral posterior crossbite (UPC) (2–5).

Several indices exist to assess orthodontic treatment need in terms of the severity of a malocclusion. However, a person's self-perception of the malocclusion may not always be related to malocclusion severity, and outcomes related to patients' values or perceptions of malocclusions are often lacking. A recent systematic review confirmed that orthodontic research seems to have overlooked patient values among children while there have been many studies measuring morphological differences (6). Therefore, to include the patient's perspective is as important as clinical registrations when making decisions regarding treatments or performing research (6,7). Consequently, to incorporate patient's perspectives enables a wider evaluation of treatment need, and furthermore, treatment success (8).

The term used when evaluating patient's perceptions of psychosocial well-being and oral health is oral health-related quality of life (OHRQoL). Self-report questionnaires are commonly used to register and evaluate patients' perspective. A common instrument used in child populations is the Child Perceptions Questionnaire (CPQ) (9), and this instrument enables assessment of the OHRQoL of children in order to provide additional information when making clinical decisions or evaluating the success of treatments or interventions.

In a recent systematic review (10), it was found that malocclusions have negative effects on children's and adolescent's OHRQoL, and especially if the malocclusions were present in the aesthetic zone. However, a majority of the high-quality studies originated from Brazil, and an additional finding was the lack of OHRQoL studies with European origin. It is known that OHRQoL may differ between countries and societies, since a self-perceived measure can be dependent upon the context of the child (11, 12). Furthermore, there are no studies that explicitly investigate how the specific malocclusions UPC with functional shift and EO may affect the OHRQoL in young children. It has been reported that if UPC with functional shift, i.e. a forced guidance of the mandible where the mandible deviates to the crossbite side, is left untreated adverse effects on the temporomandibular joints, pain in the masticatory system, and altered facial growth including facial asymmetry can occur (13–15). In addition, EO, especially without complete lip seal, has greater risk of dental trauma (5, 16) and can also be associated with bullying (17). Since pain, abnormal facial appearance, and bullying are related to specific malocclusions, it is important to investigate what influence specific different malocclusions may have on the OHRQoL in children. Likewise, it is important in this context to include children with normal occlusion (NO) and with no or mild orthodontic treatment need as controls in the evaluations. Therefore, the aim of this study was to investigate the OHRQoL among 9-year-old children in mixed dentition and compare the OHRQoL of children with UPC to children with EO as well as with children with NO with no or mild orthodontic treatment need. The hypothesis was that children with EO have lower OHRQoL than children with UPC with functional shift or children with no or mild orthodontic treatment need since EO occur in the aesthetic zone.

Subjects and methods

The study sample of the children was sourced from 19 Public Dental Service Clinics in Sweden. The sample was comprised of baseline data from children that origin from two different controlled trials, one regarding UPC with functional shift and the other focusing on EO combined with Class II malocclusion. Both trials also include children with NO and with no or mild orthodontic treatment need. To ensure the representativeness of the sample, all children were selected from clinics located in different socioeconomically areas, and the clinics were located in communities ranging from 10 000 up to 140 000 inhabitants.

The inclusion criteria considering the UPC group were consecutive children, boys and girls, in the mixed dentition (between 8 and 10 years of age), with UPC with functional shift of more than 1 mm, including the first permanent molars and a Class I occlusion. In addition, no sucking habits or ceased sucking habits should have been evident at least 1 year before the trial was started.

The inclusion criteria for the group of patients with EO were consecutive children, boys, and girls, in the mixed dentition (between 8 and 10 years of age), with EO (≥6 mm) and first permanent molars in Class II malocclusion. Furthermore, no sucking habits or ceased sucking habits should have been evident at least 1 year before the trial was started.

The inclusion criteria for the normal group were consecutive children, boys and girls, in the mixed dentition (between 8 and 10 years of age), with NO and with no or mild orthodontic treatment need, i.e. Index of Orthodontic Treatment Need – Dental health Component (IOTN-DHC) (18) of 1 or 2.

The exclusion criteria were craniofacial syndromes, children who had previously undergone orthodontic treatment, or severe crowding of teeth (extraction of teeth necessary).

All children and their parents were invited to attend and were asked to give their informed consent before entering the trial. The trial protocol and informed consent form were approved by the Regional Ethical Review Board in Lund (Dno: 2012/650) and Linköping (Dno: 2012/302–31), Sweden. Data collection took place from December 2013 to April 2017.

$CPQ_{8\text{-}10}$ questionnaire

To evaluate the OHRQoL among the children in the three groups, the $CPQ_{8\text{-}10}$ (19), which is validated for children 8–10 years of age, was used. The $CPQ_{8\text{-}10}$, comprise 25 questions grouped into four domains: oral symptoms (OS), functional limitations (FL), emotional well-being (EW), and finally social well-being (SW). Each question has five answering possibilities, i.e. 'never' (scoring 0), 'once or twice' (scoring 1), 'sometimes' (scoring 2), 'often' (scoring 3), and 'every day or almost every day' (scoring 4). The domains were added in order to produce a total score. The questionnaire also contained two global self-ratings of oral health using a four-point scale ranging from 'excellent' to 'poor' and overall well-being using a four-point scale ranging from 'not affected at all' to 'very much affected'.

The total score ranged between 0 and 100, with subscale scores range of each domain from 0 to 20 (OS, FL, EW) or 40 (SW). If answer alternatives were not applicable for the child, the question was given the median input of the total score. The higher scores corresponded to poorer quality of life status.

Finally, the children also answered validated questions about pain in the jaws and face (20).

The questionnaire was filled out in conjunction to the clinical examination and the children were instructed to answer the questions without any support from their parents. However, all children had the

opportunity to ask questions about the questionnaires, and if needed, to get support with reading the questions by clinical staff personnel.

Clinical and dental record measures

The clinical measures and the determinations were performed by two experienced orthodontists (JK, OS) following a prespecified protocol that was used to collect data about malocclusions, orthodontic treatment need, caries, enamel defects, incisors with or without lip closure, and if any trauma had occurred. Alginate impressions were taken of each child who participated in the trial and study casts were made and trimmed after index in central occlusion. Study casts were evaluated according to the method of Bjoerk *et al.* (21) in order to determine malocclusions in sagittal, vertical, and transversal relations as well as determination of crowding, spacing, tooth rotations, overjet, and overbite.

Measurements of overjet and overbite were made with a stainless-steel ruler while crowding and spacing was determined by a digital sliding calipers (Digital 6, 8M007906, Mauser-Messzeug GmBH, Oberndorf/Neckar, Germany). All measurements were made to the nearest 0.5 mm.

The dental health component of the index of orthodontic treatment need (IOTN-DHC) was used to rank the treatment need (18). This index classifies the treatment need into five grades: no need 1; mild/little need 2; moderate/borderline need 3; severe need 4; and extreme need 5.

In combination with the clinical examination, dental records of the patients were used to support the determination of caries of the anterior teeth (the aesthetic zone, i.e. canine to canine in both arches). A caries lesion was characterized as caries identified by probing.

Enamel defects were registered for permanent teeth and in the evaluation dichotomized into the presence of quantitative decay of enamel (hypoplasia) or qualitative alteration in the transparence (opacity) of the enamel, and no enamel defect.

Reporting of perceived trauma was affirmed by the dental records and in the investigations dichotomized into trauma or not.

Calibration of operators

Before diagnostics and study cast evaluations in this trial, 20 study casts from patients not included in this study were separately examined by the observers. Ten patients with UPC and 10 patients with EO were evaluated. In each patient, 26 decisions had to be performed according to a pre-set protocol regarding diagnostic parameters, malocclusion traits, measurements of overjet, and overbite as well as determination of treatment need according to IOTN-DHC. The two independent observers (JK, OS), made 26 decisions in each of the 20 study casts. Consequently, each observer had to carry out 520 decisions, and concordance between the observers was reached in 97.1% of the decisions. The inter-examiner disagreements of 2.9% were resolved by discussions to reach consensus. Most of the disagreements dealt with determination of treatment need according to IOTN-DHC.

Sample size estimation and statistical analysis

The criterion for significance (alpha) was set at 0.05. The test was two-tailed, which means that an effect in either direction was interpreted. With a proposed sample size of 60 in each group, the trial had a power of 81.6 % (1 – beta) to yield a statistically significant result. This computation assumed that the difference in proportions was 0.25 (25 % difference of quality of life between the groups). The difference of 25% was selected as the smallest difference in the sense that any smaller difference would not be of clinical or substantive significance. It was also assumed that this effect size was reasonable in the sense that an effect of this magnitude could be anticipated in this field of research.

The data were statistically analyzed by using the IBM SPSS Statistics version 24. Means between groups were compared using ANOVA. Chi-square analysis and Fisher's exact test were used to determine difference between groups regarding categorical data. General linear model in combination with Tukey's test were performed when corrections were made for the following background/confounding variables: gender, caries, enamel defects, headache, and trauma. Differences with probabilities of less than 5% ($P < 0.05$) were considered to be statistically significant.

Results

Sample characteristics

In the UPC group, there were 93 children, 45 boys and 48 girls, with a mean age of 9.1 years (SD 1.02) whereas in the EO group 71 children, 36 boys and 35 girls, with a mean age of 9.5 years (SD 0.53) participated. The NO group consisted of 65 children, 32 boys and 33 girls, with a mean age of 9.4 years (SD 1.01).

Thus, the gender distribution between the groups was similar but a small albeit significant difference between the UPC and EO groups regarding age was found ($P = 0.025$).

All children in the UPC and NO group had Class I molar relation while all in the EO group showed Class II division 1 malocclusion. A significant larger overjet ($P < 0.001$) and overbite ($P < 0.001$) was found in the EO group compared to the UPC group, 8.2 (SD 1.50) and 3.7 mm (SD 1.40) versus 3.1 (SD 1.29) and 2.3 mm (SD 1.43). The overjet and overbite were 3.2 mm (SD 1.11) and 3.0 mm (SD 1.12) in the NO group. There was also a significant larger overjet ($P < 0.001$) in the EO compared to the NO group. Consequently, significantly more children without lip closure ($P < 0.001$) were found in the EO group (Table 1). No significant differences were revealed in overjet and overbite between the UPC and NO group.

The prevalence of trauma, enamel defects, and headache were low in all three groups, and without any significant inter-group differences (Table 1).

All children in the UPC group had moderate to severe treatment need indicating that the crossbite was of functional disturbing nature, i.e. a forced guidance of the mandible deviating the midline of the mandible to the crossbite side. In the EO group, all children had severe to extreme treatment need due to the EO, while in the NO group the children showed no or mild orthodontic treatment need (IOTN-DHC 1 or 2), Table 1. Furthermore, in each group there were few children with mild to moderate crowding or spacing in the aesthetic zone and with no inter-group differences.

Oral health-related quality of life (OHRQoL)

There were no dropouts, all questionnaires were completely filled in, and none had to be excluded due to missed data.

The total CPQ mean score was 5.1 for the UPC group, 7.4 for the EO group, and 4.4 for the NO group. The EO group had significant higher total CPQ mean score than the UPC group ($P = 0.048$) and the EO group also had significantly higher total CPQ mean score than the normal group ($P = 0.012$), see Table 2 and Figure 1. No gender differences were found.

For the UPC group, the mean subscale score was 3.3 for OSs, 0.9 for FLs, and 0.5 for emotional and 0.5 for SW (Table 2). The corresponding data for the EO group was 3.9, 1.2, 1.2, 1.2, and for the NO group 3.0, 0.7, 0.5, and 0.2. The children with EO reported significantly higher scores in the domains EW compared to UPC-group

Table 1. Descriptive data for the three groups of children: excessive overjet (EO), unilateral posterior crossbite (UPC), and normal occlusion (NO).

	EO N = 71		UPC N = 93		NO N = 65		
	N	%	*N*	%	*N*	%	Group differences
Gender							
Boys	36	50.7	45	48.4	32	49.2	No group differences
Girls	35	49.3	48	51.6	33	50.8	$P = 0.985$ (C)
IOTN							
5	15	21.1					EO versus UPC $P < 0.001$ (F)
4	56	78.9	18	19.4			EO versus NO $P < 0.001$ (F)
3			75	80.6			UPC versus NO $P < 0.001$ (F)
2					7	10.8	
1					58	89.2	
Lips							EO versus UPC $P < 0.001$ (F)
With closure	50	70.4	92	99	65	100	EO versus NO $P < 0.001$ (F)
Without closure	21	29.6	1	1	0	0	UPC versus NO $P = 1.00$ (F)
Caries	0	0	0	0	1	1.5	No group differences $P = 0.284$ (F)
Trauma	5	7	3	3.2	2	3.1	No group differences $P = 0.504$ (F)
Enamel defects	5	7	1	1.1	2	3.1	No group differences $P = 0.143$ (F)
Headache	3	4.2	8	8.6	4	6.2	No group differences $P = 0.558$ (F)

C: Chi-squared test; F: Fisher's exact test.

Table 2. CPQ8-10 scores for the three groups; excessive overjet (EO), unilateral posterior crossbite (UPC), and normal occlusion (NO).

	CPQ total		Oral symptoms (OS)		Functional limitations (FL)		Emotional well-being (EW)		Social well-being (SW)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
EO ($N = 71$)	7.4	8.2	3.9	2.7	1.2	1.8	1.2	2.4	1.2	3.2
UPC ($N = 93$)	5.1	5.1	3.3	2.7	0.9	1.6	0.5	1.2	0.5	0.8
NO ($N = 65$)	4.4	5.2	3.0	2.7	0.7	1.3	0.5	1.8	0.2	0.8
p-level when adjusted for possible confounders (caries, trauma, MIH, headache)[a]	EO versus UPC $P = 0.048$[b] EO versus NO $P = 0.012$[b]						EO versus UPC $P = 0.039$[b]		EO versus NO $P = 0.012$[b]	

[a]General linear model.
[b]Tukey's test.

($P = 0.039$) and SW compared to NO-group ($P = 0.012$) (Table 2). For the domains OS and FL, no significant differences were detected between the groups.

When corrections were made for the background variables/possible confounders; gender, caries, trauma, enamel defects, and headache, the significant difference between the groups still remained (Table 2). Headache was the only variable that showed significant negative impact on the OHRQoL and that in the domain OS ($P < 0.05$).

Discussion

This study analyzed the impact a UPC with functional shift or an EO may have on young children's OHRQoL and comparisons were also made to children with no or mild orthodontic treatment need. The main finding was that children with EO reported a lower self-perceived OHRQoL when compared with children with unilateral posterior cross-bite or children with no or mild orthodontic treatment need. In addition, no difference in OHRQoL could be detected between children with UPC and children with no or mild orthodontic treatment need. These findings support our hypothesis and are accordance with earlier research stating that malocclusions in the aesthetic zone have a negative impact on OHRQoL (10). The negative impact was evident in the domains of SW and EW. Perhaps not an unexpected finding, but an important finding seen in the context of the young age of the patients.

A somewhat surprising result was that children with UPC did not show reduced OHRQoL compared to children with no or mild

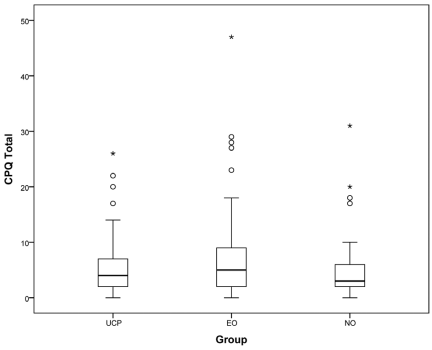

Figure 1. CPQ8-10 total score for children with unilateral posterior crossbite (UPC), excessive overjet (EO), and normal occlusion (NO). A significant difference (P = 0.048) in mean total CPQ score between EO and UPC was found, there was also a difference between EO and NO (P = 0.012) but not for UPC and NO.

orthodontic treatment need. The explanation may be that children with crossbite are not yet aware of their malocclusion, or that the functional disturbance associated has not yet caused any problems that have reflected in reduced OHRQoL among the children with UPC.

Although the primary aim of this study was to compare children with EO and children with UPC as well as with children with NO, the children in the EO group also had significant increased overbite which may influence the OHRQoL. In addition, few children in each group without any inter-group differences showed small amount of crowding and spacing, having no influence on OHRQoL.

Assessing OHRQoL, by the use of $CPQ_{8\text{-}10}$, revealed generally low scores for the children participating in this study. This indicates that the children, even though the presence of malocclusions with severe to moderate orthodontic treatment need, perceive themselves of having an overall fairly good OHRQoL. It can also be underlined that there is no clear correlation or pattern between high IOTN scores and low OHRQoL (22).

One possible explanation for the generally low CPQ scores found in this study is the low prevalence of caries among the children. Children with caries are more likely to show a reduced OHRQoL and when compared with dental trauma or malocclusions, caries may have as much as twice the negative impact on OHRQoL (23). A target has been set by WHO, namely by year 2020, the average amount of caries measured as decade filled teeth in European 12-year-olds should not exceed 1.5. This ambition has already been achieved in Sweden since the year 1995 (24). Accordingly, no caries was found in the aesthetic zone in any of the children participating in this study.

Other important confounders that may impair OHRQoL are dental fear and dental pain (12). Age presents a negative correlation, as the risk for dental fear and potential behaviour management problems increases as the child's age decreases (25). In this study, all young children had together with their parents voluntarily accepted to participate in an additional clinical examination including impressions for study casts and all children fulfilled the examinations and impressions without any problems. Thus, although not objectively verified, the children in this study did not show any signs of dental fear.

As shown in Figure 1, one child in the EO group and one in the normal group reported obvious high CPQ scores. To prevent misinterpretations of the results, the statistical analyses were repeated without these outliers. The result prevailed, implying that the group with EO still without the outlier presented significantly higher total CPQ score and higher scores in the domains of emotional and functional well-being when compared with the other groups.

There were rather few children reporting headache and there was no difference between the groups regarding the prevalence of headache. However, the only confounder in this study that exhibit to have a significant negative impact was headache. Hence, headache reduced OHRQoL, and especially for the domain OS. The impact of headache on OHRQoL is in accordance with other studies using the CPQ, however performed with older children (22). Migraine and tension-type headache are the most common types of headache in children, and can have a profound effect on the child, nevertheless the aetiology is usually medical or psychosocial (26).

Self-perceived orthodontic treatment need differs for children from different cultures (27). OHRQoL might also be affected by confounders that may be dependent upon cultural or social context (11, 12). The need for studies from different countries has been advocated since most available research regarding children and their self-perceived OHRQoL has been conducted in Brazil (10). A potential demographic impact is displayed when the children in this study scored lower on the CPQ, i.e. reported better OHRQoL than Brazilian peers with no need for orthodontic treatment (28). Whether this is due to differences regarding confounders is unclear.

The strengths of this study were the number of children participating and the well-defined groups including a NO group with no or mild orthodontic treatment need. Moreover, there were no drop-outs in this study, and clinical routines ensured that the children were able to respond to the questionnaire without the involvement of parents. In addition, the children were recruited from several clinics located in different communities to ensure an appropriate socioeconomic scope. Finally, the examiners were calibrated before evaluating clinical data and the influence of possible confounders was low.

The study would further be strengthened if psychological characteristics such as psychological well-being and self-esteem were incorporated. These dimensions have been shown to influence the OHRQoL for adolescents (29). Finally, a longitudinal study design would also strengthen the study. However, evaluating changes over time would mean postponing interventions for children with severe orthodontic treatment need.

Conclusions

Young children with EO reported significantly lower self-perceived OHRQoL compared to children with UPC with functional shift or children with NO and with no or mild orthodontic treatment need. No difference regarding self-perceived OHRQoL could be detected between children with UPC with functional shift when compared with children with NO and with no or mild orthodontic treatment need. However, despite the presence of malocclusions, the children generally reported low CPQ scores which imply an overall fairly good self-perceived OHRQoL.

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Conflict of interest

None to declare.

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III

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Randomized Controlled Trial

Randomized Controlled Trial

Early headgear activator treatment of Class II malocclusion with excessive overjet: a randomized controlled trial

Jenny Kallunki[1], Lars Bondemark[2] and Liselotte Paulsson[2]

[1]The Center for Orthodontics and Pedodontics, County Council Östergötland, Norrköping, Sweden, [2]Department of Orthodontics, Faculty of Odontology, Malmö University, Malmö, Sweden

Correspondence to: Jenny Kallunki, The Center for Orthodontics and Pedodontics, Magasinsgatan 2, S-601 82 Norrköping, Sweden. E-mail: jenny.kallunki@regionostergotland.se

Summary

Objectives: To compare early headgear activator treatment of Class II malocclusion with excessive overjet with untreated control subjects in terms of the primary outcomes overjet and overbite as well as the effect regarding oral-health-related quality of life (OHRQoL), lip closure, incidence of trauma, and skeletal changes.
Trial design: Two-arm parallel group single-centre randomized controlled trial.
Material and methods: A total of 60 children (mean age 9.5 years) presenting a Class II malocclusion with excessive overjet were recruited. The trial was designed as intention-to-treat and the participants randomized by an independent person not involved in the trial to either early treatment with headgear activator or to an untreated control group (UG). Dental and skeletal variables as well as registrations of OHRQoL, lip closure, and incidence of trauma were recorded. For the treatment group, data were registered at baseline before treatment and when treatment was finished, corresponding to approximately 2 years. For the UG, registrations were made at baseline and at 11 years of age. Observers were blinded to treatment allocation when assessing outcomes.
Results: Early treatment with headgear activator significantly decreased overjet and improved molar relationship when compared with untreated controls. The effects were primarily due to dentoalveolar changes. Early treatment had no evident effect regarding OHRQoL, lip closure, or incidence of trauma. Lack of cooperation resulted in unsuccessful treatments for 27% of the patients.
Limitations: The trial was a single-centre trial and can thus be less generalizable.
Conclusions: The main treatment effect of early headgear activator treatment of Class II malocclusion with excessive overjet is reduction of overjet.
Trial registration: NCT04508322.

Introduction

A Class II malocclusion with excessive overjet induces a greater risk of being subjected to dental trauma, especially if combined with an incomplete lip closure (1, 2). The highest incidence of dental trauma is before the age of 10, and the incidence of complicated injuries to permanent teeth is highest between 7 and 12 years of age (3). A recent Cochrane review reported that early treatment for prominent maxillary teeth is effective in reducing the incidence of incisal trauma (4). Furthermore, children with large overjet and visible teeth are rated as less attractive by peers and, in being a malocclusion in the aesthetic zone, a Class II malocclusion with excessive overjet can negatively affect children's oral-health-related quality of life

(OHRQoL) (5, 6). The negative impact on OHRQoL is most dominant in the areas of emotional (EW) and social well-being (SW) and has been registered as early as the age of nine (7). When treating Class II malocclusions, increased self-concept as well as reduction of negative social experiences have been reported (8).

Due to its frequency and different treatment approaches, the effects and efficiency of Class II malocclusion treatments are important to evaluate (4). The reported prevalence of the malocclusion varies from 14% to around 25% depending on the age of the children observed, increasing up to 45% if focussing solely on a Class II molar relation (4, 9–11).

Treatment of Class II malocclusions in the mixed dentition is usually performed with removable appliances (4). The most important indications for this early treatment approach are to prevent trauma and to protect children from a negative impact on their OHRQoL (4, 7).

There are many variants of removable functional appliances such as activator, twin-block, or bionator. The simultaneous use of activator and headgear has been advocated to enhance treatment effects (12). The headgear activator has been shown to restrict forward growth of the maxilla and reducing vertical and sagittal maxillary displacement, achieving autorotation (13, 14). Furthermore, when compared with the sole use of an activator, the headgear activator reduces the proclination of the lower incisors (15, 16). To the best of our knowledge and from an evidence-based perspective, there are no studies in the literature that have explicitly evaluated headgear activator treatment with an early treatment approach regarding the primary patient-related treatment outcomes such as overjet, overbite, oral health-related quality of life (OHRQoL), lip closure, and incidence of trauma.

Therefore, a randomized controlled trial (RCT) was conducted with the aim of comparing early headgear activator treatment of Class II malocclusion with excessive overjet with untreated control subjects in terms of the primary outcomes' overjet and overbite as well as the effect regarding OHRQoL, lip closure, incidence of trauma, and skeletal changes. It was hypothesized that early headgear activator treatment would be successful in improving overjet and overbite as well as having a positive effect regarding OHRQoL, lip closure, and incidence of trauma.

Materials and methods

A total of 60 patients that fulfilled the below stated criteria were consecutively recruited to a RCT, with an intention-to-treat (ITT) approach. Recruitment took place at the Public Dental Health Service, Östergötland County Council, Sweden, between 2013 and 2019.

The inclusion criteria were set to:

- 8–10 years of age at the start of the trial
- mixed dentition
- excessive overjet (≥6 mm) and first maxillary permanent molars in Class II malocclusion (bilaterally, ≥½ cusp)
- no sucking habits or ceased sucking habits should have been evident at least 1 year before the trial was started.

The exclusion criteria were craniofacial syndromes, any previous orthodontic treatment, or severe crowding of teeth, that is, making the extraction of teeth necessary.

One orthodontist provided all eligible patients, and their parents, with oral and written information about the trial and invited them to participate. The trial protocol and informed consent form were approved by the Regional Ethical Review Board in Linköping, Sweden (Dno: 2012/302–31). After acceptance, the children were randomized into one of two groups: early treatment with headgear activator (TG) or an untreated control group (UG) where the treatment of the Class II malocclusion with excessive overjet was postponed for 2 years.

Randomization was undertaken by staff not involved in the trial. To ensure an equivalent distribution to the groups, concealed envelopes containing folded notes (10 notes for each group) were used. When a patient and parents accepted randomization, a note from the envelope was extracted and the patient was allocated to one of the groups. When all notes had been taken, a second envelope was opened, and new notes were extracted as the patients were recruited to the trial. This procedure was then repeated.

After enrolment and randomization were completed, a clinical examination and medical history were performed as well as the following registrations:

- Study casts
- Child Perceptions Questionnaire (CPQ 8–10, CPQ 11–14) (17, 18)
- Intra- and extraoral photographs
- Lateral head radiographs.

The patients were treated in one specialist Orthodontic Clinic at the Public Dental Health Service, Region Östergötland, Sweden and by one orthodontist. The treatment goals were to improve overjet and overbite, enable lip closure, and to obtain a Class I molar relationship bilaterally. If patients refused to wear the appliance or lack of cooperation was evident the treatment was considered unsuccessful and the intervention discontinued. With an ITT design, all patients, whether successful or not as well as dropouts, were included in the final analysis.

In the treatment group (TG), registrations and data collections were performed before treatment (baseline T0) and at 11 years of age (T1), corresponding to a follow-up period of approximately 2 years. The untreated group were registered after randomization (baseline T0) and at 11 years of age (T1).

Sample size calculation

No RCTs have compared early treatment with the actual used activator type to an UG. Thus based upon a clinically significant difference of 1.5 mm in overjet reduction between the study groups, the power sample calculation showed a necessity for at least 21 patients in order to obtain a power of 90% and a significance level of $P < 0.05$ with a standard deviation of 1.5 mm.

Treatment

The treatment was provided using a modified headgear activator. All appliances were manufactured in the same orthodontic dental laboratory and by one dental technician. Construction bite was taken in edge-to-edge position. The mandibular lateral segments of the activator were reduced to allow bite opening by vertical molar eruption. Bilaterally and buccally, close to the maxillary first molars, tubes were incorporated into the acrylic to make it possible to attach a high-pull headgear to the activator. The headgear was adjusted at each appointment to deliver approximately 400 g of force per side.

The orthodontist thoroughly instructed the patient to use the appliances at the evening and night, totalling 10–12 h per day. One to two weeks after receiving the appliance, a first check-up was

scheduled with the patient to control adaption and cooperation. Thereafter, the treatment progress was evaluated regularly with 8-week intervals when overjet, overbite, and molar relation were measured and registered. When the treatment goals were obtained, the patients continued to wear the headgear activator as a retainer during night-time for an additional period of 6 months.

Study cast analysis

The study cast analyses were performed by one orthodontist not involved in the trial. The casts were primarily analysed to determine overjet and overbite and secondly sagittal molar relation, vertical, and transversal relations as well as registration of crowding, spacing, and tooth rotations (19). All measurements were made to the nearest 0.5 mm. The Class II malocclusion was defined as bilaterally ≥½ cusp Class II molar relation, and thus, if there were cases with only flush terminal plane these were not included.

OHRQoL analysis

To evaluate the children's OHRQoL, the CPQ was used. The CPQ is available in two age-specific versions: 8–10 years and 11–14 years. Since our trial covered the two periods, both versions of the questionnaire were used. Consequently, the CPQ for children 8–10 years of age (CPQ 8–10) was used at baseline (T0) in the trial (17). At T1, when the children were 11 years of age, the CPQ 11–14 was administered (18).

The CPQ 8–10 comprises 25 questions grouped into 4 domains: oral symptoms (OS), functional limitations (FL), emotional well-being (EW), and social well-being (SW). Each question has five answering possibilities, that is, 'never' (scoring 0), 'once or twice' (scoring 1), 'sometimes' (scoring 2), 'often' (scoring 3), and 'every day or almost every day' (scoring 4). The domains are added to produce a total score. In addition, the questionnaire contains two global self-rating questions, one regarding oral health using a four-point scale ranging from 'excellent' to 'poor' and one regarding overall well-being using a four-point scale ranging from 'not affected at all' to 'very much affected'.

The CPQ 11–14 includes the two global self-rating questions and is constructed by the same domains and answering possibilities as the CPQ 8–10. Furthermore, the instrument comprises an additional 12 questions: 2 additional questions for OS, 3 each for FL and SW, and 4 for EW, giving a total of 37 questions.

The questionnaire was filled out in conjunction with the clinical examination and the children were instructed to answer the questions without any support from their parents. However, all children had the opportunity to ask questions about the questionnaires, and, if needed, to get support with reading the questions by clinical staff personnel. If answer alternatives were not applicable for the child, the question was given the median input of the total score. A higher score corresponded to a poorer quality of life status.

The total score for the CPQ 8–10 ranges between 0 and 100, with the scores of each domain ranging from 0 to 20 (OS, FL, EW) or 40 (SW). For CPQ 11–14, the total score ranges from 0 to 148 due to the additional questions. Scores within the domains vary from 0 to 28 (OS), 0 to 32 (FL), 0 to 36 (EW), and 0 to 52 (SW).

Due to the longitudinal study design, the CPQ 8–10 was distributed at T0 and the CPQ 11–14 at T1. At T1, the total score and domain scores were calculated, as well as the total and domain scores when the additional questions were not included. This was done to enable a comparison between the two CPQs and within the groups.

Evaluation of lip closure

Three extraoral photographs: one frontal facial view with lips at rest, one frontal facial view smiling, and one profile view with lips at rest were taken at T0 and T1 in both groups. All three photos from T0 and T1 were intermixed and randomly evaluated, with lip closure graded as complete or incomplete. The photos were viewed by two orthodontists with an individual work experience of over 30 years.

Trauma

Dental trauma to permanent teeth was registered by clinical investigation, assessing intraoral photographs from the registrations (T0, T1) as well as reviewing dental records. Dental trauma was classified according to the injury groups supplied by the Dental Trauma Guide where trauma to permanent teeth is categorized into eight diagnoses ranging from infraction to avulsion (20).

Cephalometric analysis

The lateral head radiographs from T0 and T1 in the two groups were taken with an Orthophos XG5 Sirona OPG, Germany, and the radiographs were corrected for magnification and analysed by another orthodontist not involved in the trial, using the computer program Facad® (Ilexis AB, Linkoping, Sweden). Reported cephalometric data were based on the definitions described by Björk and Thilander (21, 22).

Blinding

Trial staff or patients could not be blinded due to the character of the trial and treatment. However, blinding was used for assessing the outcomes. Thus, analyses of OHRQoL questionnaires, lip closure from photographs, study casts, and lateral head radiographs were carried out by assessors who were not involved in the trial and unaware of group allocation and whether the data registrations were from T0 or T1.

Statistics

The data were statistically analysed using SPSS software (version 25, SPSS, Chicago, Illinois, USA). Descriptive data were presented as means, standard deviations (SD), and confidence intervals. Changes within the groups were calculated using a paired samples t-test and means between groups were compared using an independent *t*-test. Chi-square analysis and Fisher's exact test were used to determine difference between groups regarding categorical data. The test was two-tailed, which means that an effect in either direction was interpreted.

Method error analysis

When evaluating lip closure, the photos were re-evaluated after a period of at least 2 weeks and the assessors showed concordance in 93% of the assessments. The cases of disagreement were resolved by discussion to reach consensus. Internal consistency was good, with kappa value 0.72–0.93.

Fifteen randomly selected lateral head radiographs and study casts were measured at two separate times by the same assessor and with an interval of at least 3 weeks. No significant differences between the records were found using *t*-test, thus no systematic errors could be found. The error according to Dahlberg´s formula (23) was less than 0.2 mm for linear measurements. For angular measurements, NL/NSL and ANB showed the greatest error, with a variation of 0.7 and 0.4 degrees, respectively.

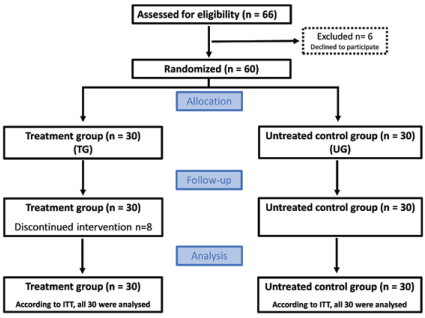

Figure 1. CONSORT flow diagram.

Results

Sample characteristics

A total of 66 patients matched the inclusion criteria and were invited to participate in the trial, but six patients declined to participate. Thus, 60 patients entered the trial and were randomized (Figure 1). The baseline demographic characteristics are presented in Table 1. No dropouts occurred since all patients fulfilled the trial.

The mean active treatment time was 1.1 years. In the TG, 27% of the children discontinued the treatment by refusing to wear the appliance or lack of full cooperation. However, since an ITT approach was used all these children were still included in the trial.

Overjet, overbite, and molar relation

At baseline (T0), a small, albeit significant, difference in overjet was registered in the TG, displaying an additional millimetre in overjet. No other differences were found (Table 2).

The overjet decreased significantly in the TG ($P \leq 0.001$), while it remained unchanged in the UG (Table 2). At T1, the TG had significantly smaller overjet compared with the UG ($P \leq 0.001$; Table 2). For the children that discontinued the treatment, no change in overjet was evident (Figure 2).

The overbite remained unchanged in the TG whereas an increase was found in the UG ($P = 0.012$; Table 2).

The molar relation was significantly improved in the TG, where 73% of the patients displayed a normal relation at T1 while no change was registered in the UG ($P \leq 0.001$).

Oral-health-related quality of life

All questionnaires were filled in and none needed to be excluded due to missing data. At T0, the total CPQ mean score was 7.1 for the TG and 7.2 for the UG ($P = 0.975$). Scores for the separate domains are presented in Table 3.

At T1, the total CPQ mean score was 6.9 in the TG and 9.1 in the UG ($P = 0.263$). No significant between-group differences for the separate domains were found nor any intra-group changes between T0 and T1 (Table 3). The lack of differences remained unaltered when comparing the UG to children where treatment was completed.

Evaluation of lip closure

At T0, an incomplete lip closure was registered in 67% of the children in TG, and 60% in the UG. At T1, incomplete lip closure was

Table 1. Baseline and follow-up demographic data; early treatment with headgear activator versus untreated control group.

	Number T0			Age (Years)		Number T1			Age (Years)	
	Total	Girls	Boys	Mean	SD	Total	Girls	Boys	Mean	SD
TG	$n = 30$	$n = 17$	$n = 13$	9.4	0.4	$n = 30$	$n = 17$	$n = 13$	11.2	0.2
UG	$n = 30$	$n = 12$	$n = 18$	9.4	0.4	$n = 30$	$n = 12$	$n = 18$	11.1	0.2

No significant differences.

Table 2. Dental and skeletal changes from baseline (T0) to follow up (T1) for the two groups; early treatment with headgear activator versus untreated control group.

	Within-group TG				Within-group UG				Between groups		
	Mean (SD)	Mean T0–T1	CI (95%)	*P* (T0-T1)	Mean (SD)	Mean T0–T1	CI (95%)	*P* (T0-T1)	*P* (T0)	*P* (T1)	*P* (T0–T1)
Overjet [mm]											
T0	9.0 (1.5)	−3.5	−4.6 to2.5	<0.001	8.0 (1.0)	0.1	−0.3 to 0.5	0.583	0.029	<0.001	<0.001
T1	5.5 (2.5)				8.0 (1.5)						
Overbite [mm]											
T0	3.5 (1.0)	−0.3	−0.7 to 0.2	0.260	3.5 (1.5)	0.7	0.3 to 1.1	0.001	0.612	0.012	0.002
T1	3.5 (1.0)				4.0 (1.5)						
SNA [°]											
T0	81.9 (3.6)	−1.2	−1.8 to −0.7	<0.001	81.3 (3.3)	0.5	0.0 to 1.0	0.038	0.502	0.175	<0.001
T1	80.7 (3.3)				81.8 (3.3)						
SNB [°]											
T0	76.0 (3.5)	0.3	−0.2 to 0.9	0.187	75.6 (2.7)	1.0	0.5 to 1.5	<0.001	0.657	0.737	0.088
T1	76.3 (3.7)				76.6 (2.5)						
ANB [°]											
T0	6.0 (1.8)	−1.6	−2.2 to 1.1	<0.001	5.8 (1.7)	−0.5	−0.9 to 0.0	0.035	0.601	0.095	0.001
T1	4.4 (2.2)				5.3 (1.9)						
NL/NSL [°]											
T0	6.3 (3.3)	0.9	0.3 to 1.4	0.003	6.6 (2.6)	0.5	0.0 to 1.1	0.056	0.704	0.950	0.363
T1	7.2 (3.7)				7.1 (3.2)						
ML/NSL [°]											
T0	33.1 (4.1)	0.3	−0.5 to 1.2	0.466	32.2 (3.5)	−0.9	−1.7 to −0.2	0.012	0.367	0.042	0.026
T1	33.4 (4.4)				31.3 (3.5)						
ML/NL [°]											
T0	26.8 (4.5)	−0.5	−1.6 to 0.4	0.228	25.6 (3.2)	−1.4	−2.3 to −0.6	0.002	0.236	0.063	0.174
T1	26.3 (4.7)				24.2 (3.7)						
ILs/NL [°]											
T0	117.3 (7.3)	−4.6	−7.7 to −1.5	0.005	116.9 (7.5)	−0.6	−2.1 to 1.0	0.456	0.813	0.095	0.023
T1	112.7 (8.2)				116.3 (8.2)						
ILi/ML [°]											
T0	95.3 (7.2)	−1.2	−3.3 to 0.9	0.255	97.3 (6.0)	−0.8	−1.9 to 0.4	0.169	0.249	0.121	0.730
T1	94.1 (6.4)				96.5 (5.4)						

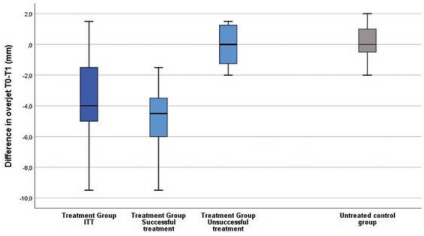

Figure 2. Change in overjet for the treatment group (intention-to-treat), as well as for successful and unsuccessful treatment, shows that no reduction could be registered if treatment was discontinued when compared to the untreated control group.

reduced to 27% in the TG and 37% in the UG ($P = 0.350$). Neither could any difference be registered between the children where treatment was completed when comparing to the untreated children.

Experience of dental trauma

A total of 11 children, 5 boys and 6 girls, had already experienced dental trauma at T0. At T1, four additional dental traumas were registered in the UG and one in the TG ($P = 0.353$). The additional traumas affected four boys and one girl.

Cephalometric analysis

No statistical differences between the groups regarding cephalometric variables could be detected at T0 (Table 2). At T1, small changes were found, that is, in the TG, the maxilla was restricted ($P \leq 0.001$) and the maxillary incisors were retroclined ($P = 0.005$; Table 2). In the UG, the maxilla and mandible moved forward ($P = 0.038$ and $P \leq 0.001$) and the mandible rotated forwards ($P = 0.012$; Table 2). When comparing children where treatment was completed to UG, a reduction in ANB ($P = 0.02$) and ML/NL ($P = 0.03$) was found.

Harm

No harm was observed in any subjects of the included groups. However, four dental traumas during the study were observed in the UG and one in the TG when treatment was discontinued. All additional dental traumas were considered minor.

Discussion

Main findings

The main finding of this study was that early headgear activator treatment of Class II malocclusion with excessive overjet was successful in reducing overjet and improving molar relation. This finding confirmed our hypothesis and is in line with earlier studies (4). Small skeletal changes within and between the groups were registered, indicating that the treatment effects were primarily due to dentoalveolar changes, which is in line with an earlier study (24). Regarding the other patient-centred outcomes no significant difference was found considering OHRQoL, lip closure, or incidence of trauma. Although not statistically significant, a clinical effect was evident with lip closure being more improved for the children receiving early treatment with headgear activator. Thus, the overall benefits of early treatment of Class II malocclusion with excessive overjet appear to be modest.

Interpretations

As anticipated in an RCT, all the children in the trial presented essentially equivalent characteristics when entering the trial. An exception was seen regarding overjet, where the children who were to receive early treatment with a headgear activator showed a slightly enlarged overjet of 1 mm. This is an unexpected finding that we cannot explain. In any event, at follow-up, the difference between the treated children and their untreated controls regarding overjet was pronounced, making the effectiveness of the treatment in terms of reducing overjet evident.

It should be noted that the children in the control group had a larger mandibular change at follow-up compared with the headgear activator group, however, without any intergroup difference. Functional appliance delivers a mandibular response and headgear renders maxillary restriction but variations are registered. This, together with the substantial variation in growth for children with Class II malocclusion, whether treated or not, could be a contributing factor to this finding (25).

The reported effects of early Class II treatment mainly consist of dental and skeletal changes. A Cochrane review has summarized the overall evidence as 'low for most comparisons and outcomes, therefore further research is needed and may change the findings' (4). With added focus on patient reported outcome measure OHRQoL, trauma, and lip closure, this trial may complement the existing research regarding early Class II treatment.

It can be pointed out that OHRQoL is of the utmost importance when evaluating treatment effects (26), but from this trial it can be stated that early treatment with headgear activator did not improve the OHRQoL. The reported CPQ scores were generally low, implying a fairly good self-perceived OHRQoL. One contributing factor for the generally low CPQ scores found in this trial could be related to the low prevalence of caries among Swedish children. A Class II malocclusion with excessive overjet primarily affects SW and EW (7), whereas dental caries has a negative impact on all aspects of OHRQoL (27). When compared with dental trauma or malocclusions, caries may have as much as double the negative impact on OHRQoL (28).

At baseline, 18% of all the children had experienced dental trauma. Incomplete lip closure was found in almost half the cases (45%). Except for one severe trauma (an exarticulated incisor), the majority of the trauma was less severe, consisting of infractions or enamel fractures. The reported prevalence of traumatic dental injuries for 12-year-old children in the European region is 13.5% (29). This prevalence was surpassed by the children in this trial, who showed a prevalence of dental trauma of 18% at 9.5 years of age. Most traumas occurred before the children entered the trial, implying that in order to prevent dental trauma, treatment of Class II malocclusions should be initiated even earlier than 9 years of age. It can, however, be noted that even though no significant differences were detected, all additional trauma during the trial affected children in the untreated group or children where treatment had been discontinued due to lack of cooperation. This tendency coincides with previous reports that early treatment may reduce the incidence of dental trauma (4). On the other hand, treatment with removable appliances requires cooperation and this aspect must be taken into consideration when discussing even earlier start of treatment in order to prevent trauma. So, if all subjects in the TG had full cooperation, the difference between the treatment and untreated group would probably have been even greater.

In this trial, 27% of the children in the TG discontinued treatment with unsuccessful results, which is in line with previous research that

Table 3. CPQ scores (0–100) at baseline (T0) and when adjusted for the number of questions at T1.

	Within-group TG				Within-group UG				Between groups		
	Mean (SD)	Mean T0–T1	CI (95%)	*P*(T0–T1)	Mean (SD)	Mean T0–T1	CI (95%)	*P*(T0–T1)	Mean	CI (95%)	*P*
CPQ total											
T0 (8–10)	7.1 (7.4)	−1.6	−4.3 to 1.0	0.206	7.2 (9.1)	−0.5	−3.1 to 4.0	0.792	−0.1	−4.4 to 4.2	0.975
T1 (11–14)	5.5 (5.6)				6.7 (6.5)				−1.2	−1.3 to 1.6	0.421
T1 (0–148)	6.9 (6.9)				9.1 (8.1)				−2.2	−6.1 to 1.7	0.263
CPQ OS											
T0 (8–10)	3.8 (2.8)	−0.3	−1.6 to 1.1	0.683	3.7 (2.5)	0.0	−0.9 to 0.9	1.00	0.1	−1.3 to 1.5	0.884
T1 (11–14)	3.5 (2.8)				3.7 (2.7)				−0.2	−1.6 to 1.3	0.816
T1 (0–148)	3.8 (3.4)				4.1 (3.5)				−0.3	−2.1 to 1.4	0.707
CPQ FL											
T0 (8–10)	1 (1.5)	−0.3	−1.0 to 0.4	0.411	1.3 (2.1)	−0.2	−0.8 to 1.1	0.715	−0.3	−1.2 to 0.7	0.574
T1 (11–14)	0.7 (1.3)				1.1 (1.6)				−0.4	−1.1 to 0.3	0.284
T1 (0–148)	1.7 (2.3)				2.8 (2.7)				−1.1	−2.4 to 0.2	0.091
CPQ EW											
T0 (8–10)	1.5 (2.9)	−1.1	−2.2 to 0.1	0.07	1.0 (2.0)	0.3	−1.3 to 0.8	0.654	0.5	−0.8 to 1.8	0.474
T1 (11–14)	0.4 (1.0)				1.3 (2.2)				−0.9	−1.7 to 0.1	0.067
T1 (0–148)	0.5 (1.1)				1.5 (2.6)				−1.0	−2.0 to 0.0	0.061
CPQ SW											
T0 (8–10)	0.8 (1.7)	0.0	−0.7 to 0.6	0.917	1.2 (4.3)	−0.5	−1.1 to 2.2	0.507	−0.4	−2.0 to 1.3	0.664
T1 (11–14)	0.8 (1.8)				0.7 (1.6)				0.1	−0.7 to 1.0	0.759
T1 (0–148)	0.9 (1.9)				0.7 (1.6)				0.2	−0.7 to 1.1	0.607

CPQ scores unadjusted at T1 (0–148); early treatment with headgear activator versus untreated control group.

report unsuccessful results due to lack of cooperation in 16–60% of the treatments (24, 30). With an ITT approach, all children whether completing treatment or not, were included in the results of this trial. However, questions may arise regarding the treatment effect for the patients who did cooperate, and therefore, those results were also included. The children where treatment was completed presented a small, but significant, reduction in ANB when compared with untreated controls.

Patients who did not complete treatment showed no change in overjet, and did not differ regarding overjet from the untreated group at T1. This suggests that if a lack of cooperation is evident, the treatment should be interrupted promptly since tedious treatment without effect increases burden of treatment for the patient and severely decreases cost-effectiveness. While our study did not include any health economic evaluation, Chen *et al*. have discussed the cost–benefit ratio of early treatment for Class II malocclusions and reason that the cost of the functional appliance treatment in order to prevent trauma should be put in relation to the costs of the predominant part of less severe trauma (31). Adding unsuccessful treatments and the majority of less severe dental traumas to the discourse further highlights the risk of reduced cost-effectiveness. All these aspects, as well as OHRQoL, must be taken into consideration when deciding upon treatment approach.

Strengths

The main strength was the use of RCT design, predominately by the allocation process, which presumptively distributes confounding factors evenly between the involved groups (32). Additionally, there were no dropouts in the trial. To further reduce bias, an ITT approach was applied, making the results applicable to overall treatments and not just the successful ones. Blinding to treatment allocation was performed when registering all outcomes and performed by orthodontists not involved in the trial.

Limitations and generalizability

The results from this single-centre RCT were from one specialist clinic, and this might reduce the applicability to other clinical settings. Nonetheless, the appliance and treatment protocol have been widely used and well established.

To reduce bias regarding the assessments of lip closure, two experienced orthodontists/investigators not involved in the trial were used. The lip closure was assessed according to a given protocol and evaluations of the assessors' intra and inter reliability were also performed to check and control their reliability. The results of the assessments of lip closure turned out to be good with kappa values between 0.72 and 0.93.

This trial did not have as its main purposes to analyse gender differences or growth and maturation effects of early headgear activator treatment. Likewise, it can be stated that factors such as growth and maturity will be equally distributed and effect the two groups through the randomization procedure.

Cooperation could be influenced by the fact of participating in a research study, and, therefore, this trial runs the risk of the Hawthorne effect (positive bias) in the treated group (33). Thus, the success rate of treatments in the treated group will conceivably be lower in everyday practice.

Further research

To fully investigate the effects of an early treatment approach, longitudinal studies must address patient-reported outcome measures, evaluate treatment stability, and any need for further treatment. These comparisons should be undertaken with untreated peers as well as with children receiving a one-phase treatment with fixed appliance. The evaluations should also focus on areas where further research is implicated such as OHRQoL and health economics. The fairly high frequency of unsuccessful treatments and modest results regarding patient-centred outcomes imply a need for future research aiming to identify those individuals who will benefit most from early treatment.

Conclusions

Early treatment with headgear activator is successful in terms of reducing overjet for those patients who complete treatment. Regarding the other patient-centred outcomes no significant difference was found considering OHRQoL, lip closure, or incidence of trauma. Anyhow, lip closure improved in both groups and to a larger extent for the children who received early treatment with headgear activator.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Conflict of interest

None to declare.

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IV

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Randomized Controlled Trial

Randomized Controlled Trial

Comparisons of costs and treatment effects—an RCT on headgear activator treatment of excessive overjet in the mixed and late mixed dentition

Jenny Kallunki[1], Lars Bondemark[2] and Liselotte Paulsson[2]

[1]The Center for Orthodontics and Pedodontics, County Council Östergötland, Norrköping, Sweden
[2]Department of Orthodontics, Faculty of Odontology, Malmö University, Malmö, Sweden

Correspondence to: Jenny Kallunki, The Center for Orthodontics and Pedodontics, Magasinsgatan 2, S-601 82 Norrköping, Sweden. E-mail: Jenny.Kallunki@regionostergotland.se

Summary

Objectives: To compare the costs and treatment effects of headgear activator treatment of Class II malocclusion with excessive overjet between treatments started in the mixed (MD) and late mixed dentition (LMD).
Trial design: Two-arm parallel-group single-centre randomized controlled trial (RCT).
Material and methods: A total of 56 children presenting Class II malocclusion with excessive overjet were assessed and invited to an RCT designed as intention-to-treat. The children were randomized, by an independent person not involved in the trial into two groups, treatment with headgear activator in the MD starting at the age of 9 or to treatment with a headgear activator in LMD, starting at the age of 11. The primary outcome measure was to compare the treatment costs between the two groups. Societal costs (the sum of direct and indirect costs) were calculated for successful treatments only and when unsuccessful treatments were included. Secondary outcomes were comparisons of oral health-related quality of life (OHRQoL), dental and skeletal treatment effects, lip closure, and trauma incidence. Data collections were performed before and after treatment, corresponding to a treatment period of 2 years. Blinding was accomplished when assessing outcomes.
Results: No group differences in costs were found of successful treatments or when unsuccessful treatments were included. The most pronounced treatment effects in both groups were the reduction of overjet and improved molar relation. Treatment started in MD or in LMD were equal and without significant differences regarding effects on OHRQoL, skeletal effects, lip closure, and incidence of trauma.
Harms: No harm was observed, but 8 of 30 children (27%) in the MD and 6 of 21 children (29%) in the LMD group showed unsuccessful results.
Limitations: Costs depend on local factors and can thereby not be directly transferred to other settings. It was a single-centre trial and can thus be less generalizable.
Conclusions: Regarding costs and treatment effects, there is no difference if headgear activator treatment of excessive overjet starts in the MD or LMD.
Clinical trial registration: NCT04508322.

Introduction

Treatment timing for Class II malocclusion with excessive overjet has often been and still is discussed in the orthodontic profession and literature. Recent research points to that early treatment, that is, treatment started in the mixed dentition (MD), decreases overjet, and reduces trauma incidence (1, 2). On the other hand, if functional appliance treatment is initiated in the late mixed dentition (LMD) to try and coincide the treatment start slightly before the pubertal growth peak, treatments have been shown to render improved skeletal response (3–5). Early treatment, usually with a removable functional appliance, is sometimes followed by subsequent and complementary treatment with fixed appliance to obtain final optimal occlusion, overjet, and overbite.

Many factors influence the result of orthodontic treatment with removable appliances, with compliance being a key factor. If patients fail to cooperate and do not use their removable appliance as stipulated, lack of effect is evident. It has been discussed at what age children are most cooperative with their removable appliances. Weiss and Eiser (6) argued that younger children are more cooperative and that activator and headgear treatment should be started sometime after age 6 and soon enough to be completed before the onset of puberty. On the other hand, Trulsson *et al.* (7) emphasizes the importance of parental involvement for younger children's compliance. If treatment compliance cannot be ensured through parents' wholehearted involvement and control, it seems to be better to delay treatment until the child is older (7).

Over the past decades, increased focus has been placed in healthcare to perform health economic evaluations (8). The primary reason is that resources within the health sector (personnel, time, facilities, and equipment) are restricted (9). Also, orthodontic treatments have gained focus from an economic perspective, but it has been reported and concluded that orthodontic research rarely presents both clinical and economic outcomes (10). With resources within dental care being limited, knowledge upon effects and associated costs are important when making treatment decisions. Furthermore, orthodontic research more often reports morphological changes attained by treatment rather than outcomes reflecting patients' perspectives (11).

To the best of our knowledge, no studies have yet explicitly evaluated headgear activator treatment of Class II malocclusion with excessive overjet when treatment is started in the MD and made comparisons to corresponding treatment started in the LMD.

Consequently, a randomized controlled trial (RCT) was carried out to compare headgear activator treatment of Class II malocclusion with excessive overjet between treatments started in the MD (at the age of 9) and in the LMD (at the age of 11). The primary outcome measure was to evaluate and compare the costs between the treatments, and secondary outcome measures were the analysis and group comparison of oral health-related quality of life (OHRQoL), dental and skeletal treatment effects, lip closure, and incidence of trauma. It was hypothesized that treatment started in MD and in LMD is equal regarding costs and effects on OHRQoL, skeletal and dental effects, lip closure, and trauma incidence.

Material and methods

Participants

The sample consisted of 56 children assessed according to inclusion criteria and asked for participation, consecutively recruited between 2013 and 2019 at the Public Dental Health Service, Region Östergötland, Sweden.

The inclusion criteria were set to:

1. children of 9 (±1) years of age at the start of the trial,
2. mixed dentition,
3. excessive overjet (≥6 mm) and first maxillary permanent molars in Class II malocclusion (bilaterally at least a half cusp Class II molar relation), and
4. no sucking habits or ceased sucking habits should have been evident at least one year before the trial was started.

The exclusion criteria were craniofacial syndromes, previous orthodontic treatment, or crowding of teeth, that is, making extractions of teeth necessary.

One orthodontist provided verbal and written information about the trial and invitation to participate to all eligible patients and their parents. The Regional Ethical Review Board in Linköping, Sweden (Dno: 2012/302–31) approved the trial protocol and informed consent form. After consent, randomization was undertaken by staff not involved in the trial. Outside the clinical setting, a note from a concealed envelope was extracted, revealing group allocation. To ensure an equivalent distribution to the groups, concealed envelopes containing folded notes (10 notes for each group) were used. When a patient and parents accepted randomization, a note from the envelope was extracted and the patient was allocated to one of the groups. When all notes had been taken, a second envelope was opened, and new notes were extracted as the patients were recruited to the trial. This procedure was then repeated. The children were randomized into treatment with headgear activator in the MD starting at 9 years of age (Group MD), or treatment postponed for 2 years. After that, treatment started in the LMD at 11 years of age (Group LMD). Postponement of treatment in the LMD group resulted in an imbalance in the number of patients between the two groups. Thus, because the treatment started and ended earlier in the MD group, and evaluation of the results in this trial started as soon as the LMD group met the sample size requirement there were different numbers of children in the two groups.

Sample size calculation

No RCTs have assessed any economic evaluation regarding headgear activator treatment when treatment is initiated at different ages. Therefore, a clinically relevant and realistic difference in cost of 1000 SEK/€99 (SD 1000/99) was used as a base for our sample size analysis. At least 21 patients per group were needed in this trial to obtain a power of 90% and $\alpha = 0.05$.

Blinding

Because of the character of the trial, and the evaluated appliance, children and trial staff could not be blinded to treatment allocation. However, blinding was used when assessing the outcomes. Consequently, the assessor was unaware of the group to which the child was allocated or whether the data corresponded to before or after treatment.

Clinical procedure and treatment

One orthodontist treated all patients in one specialist Orthodontic Clinic at the Public Dental Health Service, Region Östergötland, Sweden.

Successful treatment was set to reduce overjet and overbite and obtain a Class I molar relationship bilaterally. Treatment was considered unsuccessful if the criteria were not met or if the intervention was discontinued or lack of cooperation was evident. With an intention-to-treat (ITT) design, all patients, whether successful or not, as well as potential dropouts, were to be included in the final analysis.

Following enrolment and randomization, a clinical examination and medical history were performed together with the following registrations before treatment start and after treatment was completed, including the additional retention period of 6 months:

1. total number and time of each visit, including emergency visits,
2. time absent from school and work, time to travel to the clinic and means of transportation,
3. Child Perceptions Questionnaire (CPQ8–10, CPQ 11–14) (12, 13),
4. intra- and extraoral photographs,
5. study casts, and
6. lateral head radiographs.

Treatment

In both groups, treatment was provided using a modified headgear activator. All appliances were manufactured in the same orthodontic dental laboratory and by one dental technician. Construction bite was taken in edge-to-edge position. The mandibular lateral segments of the activator were reduced to allow bite opening by the vertical molar eruption. Bilaterally and buccally, close to the maxillary first molars, tubes were incorporated into the acrylic to make it possible to attach a high-pull headgear to the activator. The headgear was adjusted at each appointment to deliver approximately 400 g of force per side.

The children were instructed to use the appliance at the evening and night, totalling 10–12 hours per day. A first check-up was scheduled 1–2 weeks after receiving the appliance to control adaption and cooperation. After that, appointments were held regularly with an approximately 8-week interval where treatment progress was registered, and the appliances adjusted, if necessary. When the treatment goals were obtained, the patients continued to wear the headgear activator as a retainer during night-time for an additional period of 6 months.

Primary outcomes

Cost evaluation

The primary outcomes were the cost comparisons, and thus, a form was filled out at each appointment by patients and parents. Registrations were made regarding time absent from school and work, travel time to the clinic, and transportation. Orthodontic staff registered the chair time and whether the appointment was planned or an emergency visit.

The direct costs such as costs for personnel, facilities, and equipment were calculated based on the costs per hour for a specialist dentist (2700 SEK/€267) according to the price list of 2020 for specialist dentistry in the Public Dental Service in Östergötland. Based on the prices for the year 2020, the headgear activator's material costs were derived by the dental technician costs (1700 SEK/€168) plus any eventual costs for repairs of the appliance.

The indirect costs, that is, parents' loss of production and income when accompanying their child to the dental clinic, were calculated for the total time, that is, travelling to and from the clinic and chair time. It was assumed that the parents of a 9–11-year-old patient were between 35 and 44 years old. In 2019, the mean income per year for a 35–44-year-old in Sweden was 444 000 SEK/year (€43 960/year). The average income per hour, 314 SEK/hour (€31.1/hour) was calculated by dividing the mean income per year with 1980 working hours, then adding social security costs by a factor of 0.4. The data were sourced from the Swedish National Bureau of Statistics (www.scb.se). All costs were expressed in Euros (€), SEK 100 = €10.1 at a mean currency value (www.xe.com).

Cost analysis

With results and consequences of each group's treatments presumably being equivalent to each other, that is, both groups had treatment with a headgear activator that intended to correct Class II malocclusion with excessive overjet, the difference between the groups was reduced to a comparison of costs.

Societal costs

The sum of direct and indirect costs was defined as 'societal costs', and the cost was calculated as follows:

1. The mean societal costs of successful cases only on completion of treatment in the two groups:
   (a) the mean societal costs for all successful treatments in the MD group divided by the number of successful patients, that is, societal costs for 22 treatments divided by 22 patients.
   (b) the mean societal costs for all successful treatments in the LMD group divided by the number of successful patients, that is, societal costs for 15 treatments divided by 15 patients.
2. The mean societal costs of the successful and unsuccessful cases (cases that would need retreatment since no correction was achieved) on completion of treatment in the two groups:
   (a) the mean societal costs for all successful treatments and unsuccessful treatments in the MD group divided by the number of successful patients, that is, 30 treatments divided by 22 patients, thus 8 re-treatments and an increase in costs.
   (b) the mean societal costs for all successful treatments and unsuccessful treatments in the LMD group divided by the number of successful patients, that is, 21 treatments divided by 15 patients, thus 6 re-treatments and an increase in costs.

Secondary outcomes

The secondary outcome measures were analysis and group comparisons before treatment start and when treatment was completed regarding OHRQoL, dental and skeletal treatment effects, lip closure, and trauma incidence.

OHRQoL analysis

The CPQ was used to evaluate the children's OHRQoL. The CPQ is available in two age-specific versions: 8–10 and 11–14 years. Since the trial covered the children at various ages, both versions of the questionnaire had to be used. Consequently, the CPQ for children 8–10 years of age (CPQ8–10) was used before treatment start in the MD group (12), while the CPQ11–14 (13) was administered before treatment start in the LMD group. CPQ11–14 was administered in both groups upon completed treatment. Because of the expanded scope and additional questions in CPQ11–14, the total score for the CPQ11–14 range between 0 and 148 compared to 0 and 100 for the CPQ8–10. Accordingly, the additional questions in CPQ11–14 had to be excluded to be compared to CPQ8–10, that is, before treatment start when the MD and LMD group was compared and when comparison before treatment start and after completed treatment in the MD group.

All questionnaires were filled out in conjunction with the clinical registration. The children were instructed to answer the questions without any support from their parents. However, if needed, the children could ask questions about the questionnaires and get support

with reading the questions by clinical staff personnel. If answer alternatives were not applicable for the child, the question was given the total score's median input. A higher score in both CPQ8–10 and CPQ11–14 corresponded to a poorer quality of life status.

Evaluation of lip closure

Three extraoral photographs; one frontal facial view with lips at rest, one frontal facial view smiling, and one profile view with lips at rest were taken before treatment start and after treatment was completed in both groups. All three photos from before treatment start and after treatment was completed were intermixed and randomly evaluated, with lip seal graded as complete or incomplete. Two orthodontists not involved in the trial viewed the photos and with an individual work experience of over 30 years.

Trauma

Dental trauma was registered by the clinical investigation, reviewing dental records and assessment of intraoral photographs before treatment start and upon completed treatment. Dental trauma was classified according to the Dental Trauma Guide's injury groups categorizing trauma to permanent teeth into eight diagnoses, ranging from an infraction to avulsion (14).

Study cast analysis

The study cast analyses were performed by one orthodontist not involved in the trial. The casts were analysed to determine overjet, overbite, and sagittal molar relation. Furthermore, vertical and transversal relations and registration of crowding, spacing and tooth rotations were made (15). All measurements were made to the nearest 0.5 mm. The Class II malocclusion was defined as bilaterally and at least half a cusp Class II molar relation. Cases with only flush terminal plane were not included.

Cephalometric analysis

All lateral head radiographs were taken with an Orthophos XG5 Sirona OPG, Germany and the radiographs were corrected for magnification. Another orthodontist not involved in the trial made the cephalometric analysis (16, 17) at treatment start and after completed treatment using the computer program Facad® (Ilexis AB, Linkoping, Sweden).

Statistics

Data were statistically analysed using SPSS software (version 27, SPSS, Chicago, Illinois, USA). Descriptive data were presented as means, standard deviations (SD), and confidence intervals. Changes within groups were compared using a paired samples *t*-test and means between groups were compared by independent *t*-test. Categorical data were compared by chi-square analysis and Fisher's exact test. The effect in either direction was interpreted as the tests were two-tailed.

Method error analysis

Extraoral photos were re-evaluated regarding lip closure after at least 2 weeks. The assessors showed concordance in 93% of the assessments. Cases of disagreement were resolved by discussion to reach consensus. With kappa value 0.72–0.93, internal consistency was substantial to almost perfect.

A total of 15 randomly selected lateral head radiographs, and study casts were measured at two separate times by the same assessor and with an interval of at least 3 weeks. No significant differences between the records were found using *t*-test. Thus, no random errors could be found. The method error size was less than 0.3 mm for linear measurements. For angular measurements, NL/NSL and ANB showed the greatest error, with a variation of 1.0 and 0.3 degrees, respectively (18).

Results

A total of 56 children matched the inclusion criteria and were invited to participate. With five children declining to participate, the study groups consisted of totally 51 children. Figure 1 illustrates the number of children allocated to each group and the flow of children throughout the trial. All patients were registered before the start of treatment and when treatment was completed. There were no dropouts in the study. In the MD group, there was 17 girls and 13 boys, whereas the LMD group consisted of 9 girls and 12 boys ($P = 0.400$). At the start of treatment, the mean age in the MD group was 9.4 years (SD 0.40) and 11.1 (SD 0.20) in the LMD group.

In the MD group, the mean active treatment time was 1.1 years (SD 0.27). Treatment was discontinued for 8 of the 30 children (27%) by either refusing to wear the appliance or lack of cooperation and thus 22 children were successfully treated. In the LMD group, the average treatment time was 1.2 years (SD 0.31). Within this group, 6 out of 21 (29%) discontinued treatment and consequently, 15 of the 21 children were successfully treated. No significant difference between the groups was found regarding treatment time ($P = 0.392$) or unsuccessful treatments ($P = 1.000$).

Number of appointments

The mean number of appointments during successful treatments, including the retention period was 10.2 (SD 1.94) for the MD group and 10.3 (SD 2.12) for the LMD group ($P = 0.901$). In the MD group, the number of emergency visits was 0.7 (SD 0.94) versus 1.1 (SD 1.03) in the LMD group ($P = 0.306$). The total chair time was 247 minutes (SD 56) in the MD group and 250 (SD 60) in the LMD group ($P = 0.892$).

Harms and complications

No harm was observed but four activators (13%) in the MD group, and three (14%) in the LMD group, had to be replaced during the study because of loss, breakage, or inadequate fit. These additional costs for material in each group were added to the direct costs.

Cost evaluations

Costs for successful treatments

The mean societal costs, direct and indirect costs are shown in Table 1. No differences in costs were found between the MD and LMD group.

Costs for successful treatments and unsuccessful treatments

The mean societal costs, direct and indirect costs are shown in Table 1, and the costs, of course, increased in both groups when costs for unsuccessful treatments were included (Table 1). Similar to the costs for successful treatments alone, there were no differences between the groups regarding costs that included unsuccessful treatments (Table 1).

Oral health-related quality of life

The total CPQ mean score before treatment start was 7.1 in the MD group and 8.5 in the LMD group. When comparing the two groups, there were no difference in total CPQ mean score before treatment ($P = 0.720$). When treatment was completed, the total

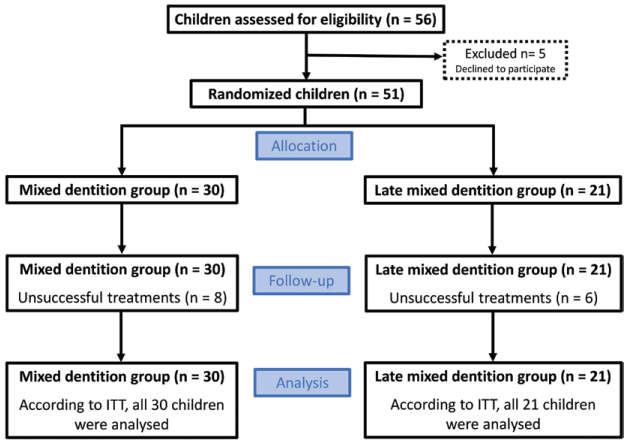

Figure 1. Consort flow diagram.

Table 1. Mean societal, direct, and indirect costs (€) for treatment with headgear activator in MD and LMD group

	MD group		LMD group		Group differences
	Mean (SD)	CI (95%)	Mean (SD)	CI (95%)	*P*
Successful treatments alone					
Societal costs	1634 (338)	1484–1784	1667 (363)	1466–1868	0.778
Direct costs	1292 (269)	1173–1411	1303 (283)	1146–1460	0.904
Material costs	191 (59)	165–218	191 (59)	158–224	0.980
Treatment costs	1101 (248)	991–1211	1112 (267)	964–1260	0.892
Indirect costs	342 (112)	292–392	364 (108)	304–424	0.556
Successful treatments including the costs for unsuccessful treatments					
Societal costs	2053 (662)	1759–2347	2160 (842)	1694–2627	0.668
Direct costs	1638 (551)	1394–1883	1690 (671)	1319–2062	0.797
Material costs	260 (100)	216–305	269 (106)	210–328	0.791
Treatment costs	1378 (479)	1166–1590	1421 (586)	1097–1746	0.807
Indirect costs	415 (149)	349–481	470 (190)	364–575	0.332

Mean costs for successful treatments, that is, costs for 22 treatments divided by 22 patients in MD group and 15 treatments divided by 15 patients in LMD group. Mean costs for successful treatments including costs for unsuccessful treatments, that is, 30 treatments divided by 22 patients in MD group and 21 treatments divided by 15 patients in LMD group.

CPQ mean score was 6.9 in the MD group and 8.3 in the LMD group (P = 0.505; Table 2). There were no significant intra-group changes before and after completed treatment nor any significant between-group differences for the separate domains except for the domain emotional well-being after completed treatment (Table 2).

Overjet, overbite, and molar relation

Treatment was successful in reducing overjet ($P \leq 0.001$) and improving molar relation in both groups ($P \leq 0.001$). After treatment, 73% of the MD group patients presented a Class I molar relation compared to 71% in the LMD group (P = 1.000). A minor difference in overbite between the groups was registered before the start of treatment, with the LMD group displaying a more pronounced overbite (P = 0.046). Overbite remained somewhat larger also after treatment for the LMD group (P = 0.028). No other differences were found between the groups before treatment (Table 3).

Cephalometric analysis

Retroclination of maxillary incisors and a reduction of ANB was registered in both groups after treatment (Table 3). Small significant changes within the groups were seen, however not resulting in any statistical intergroup differences except for ML/NSL and ML/NL (Table 3). Before treatment and compared to the MD group, the LMD group displayed a reduced intermaxillary relation (P = 0.028) that also prevailed after treatment (P = 0.005). In addition, a more anteriorly rotated mandible was found after treatment in the LMD group (P = 0.017) when compared to the MD group (Table 3).

Table 2. Treatment with headgear activator in the MD and LMD group

Within-MD group					Within-LMD group					Group differences		
	Mean (SD)	Mean T0–T1	CI (95%)	*P*(T0–T1)		Mean (SD)	Mean T0–T1	CI (95%)	*P*(T0–T1)	Mean	CI (95%)	*P*
CPQ total					CPQ total							
T0 (8–10)	7.1 (7.4)				T0 (11–14)	6.4 (7.3)				0.7	−3.4 to 4.9	0.720
T1 (11–14)	5.5 (5.6)	−1.6	−4.3 to 1.0	0.206	T0 (0–148)	8.5 (8.9)	−0.2	−4.4 to 4.9	0.915			
T1 (0–148)	6.9 (6.9)				T1 (0–148)	8.3 (7.3)				−1.4	−5.4 to 2.7	0.505
Oral symptoms					Oral symptoms							
T0 (8–10)	3.8 (2.8)				T0 (11–14)	3.0 (2.9)				0.8	−0.8 to 2.5	0.297
T1 (11–14)	3.5 (2.8)	−0.3	−1.6 to 1.1	0.683	T0 (0–148)	3.8 (3.8)	−0.5	−1.1 to 2.1	0.547			
T1 (0–148)	3.8 (3.4)				T1 (0–148)	3.3 (1.7)				0.5	−0.9 to 2.0	0.481
Functional limitations					Functional limitations							
T0 (8–10)	1.0 (1.5)				T0 (11–14)	1.5 (1.8)				−0.5	−1.4 to 0.5	0.319
T1 (11–14)	0.7 (1.3)	−0.3	−1.0 to 0.4	0.411	T0 (0–148)	2.3 (2.7)	−0.2	−1.7 to 2.1	0.796			
T1 (0–148)	1.7 (2.3)				T1 (0–148)	2.1 (3.4)				−0.4	−2.0 to 1.2	0.620
Emotional well-being					Emotional well-being							
T0 (8–10)	1.5 (2.9)				T0 (11–14)	1.4 (2.4)				0.1	−1.4 to 1.7	0.877
T1 (11–14)	0.4 (1.0)	−1.1	−2.2 to 0.1	0.07	T0 (0–148)	1.8 (2.9)	0.3	−2.0 to 1.4	0.724			
T1 (0–148)	0.5 (1.1)				T1 (0–148)	2.1 (2.9)				−1.6	−2.9 to −0.2	0.026
Social well-being					Social well-being							
T0 (8–10)	0.8 (1.7)				T0 (11–14)	0.6 (1.7)				0.2	−0.7 to 1.2	0.593
T1 (11–14)	0.8 (1.8)	0.0	−0.7 to 0.6	0.917	T0 (0–148)	0.6 (1.7)	0.2	−0.9 to 0.5	0.489			
T1 (0–148)	0.9 (1.9)				T1 (0–148)	0.8 (1.3)				0.1	−0.9 to 1.1	0.850

CPQ scores before treatment (T0) and after completed treatment (T1) using CPQ8–10 and CPQ11–14. CPQ11–14 scores unadjusted (0–148).

Table 3. Dental and skeletal changes from before treatment (T0) to completed treatment (T1) with headgear activator in the MD and LMD group

	Within-MD group				Within-LMD group				Group differences		
	Mean (SD)	Mean T0–T1	CI (95%)	*P*(T0–T1)	Mean (SD)	Mean T0–T1	CI (95%)	*P*(T0–T1)	*P*(T0)	*P*(T1)	*P*(T0–T1)
Overjet [mm]											
T0	9.0 (1.5)				8.3 (1.8)						
T1	5.5 (2.5)	−3.5	−4.6 to −2.5	<0.001	5.5 (2.3)	−2.8	−3.7 to −1.8	<0.001	0.180	0.830	0.261
Overbite [mm]											
T0	3.5 (1.0)				4.2 (1.3)						
T1	3.2 (1.0)	−0.3	−0.7 to 0.2	0.260	4.0 (1.3)	−0.2	−0.6 to 0.2	0.303	0.046	0.028	0.873
SNA [°]											
T0	81.9 (3.6)				82.0 (3.7)						
T1	80.7 (3.3)	−1.2	−1.8 to −0.7	<0.001	81.8 (3.7)	−0.2	−0.9 to 0.6	0.657	0.960	0.243	0.012
SNB [°]											
T0	76.0 (3.5)				76.7 (2.6)						
T1	76.3 (3.7)	0.3	−0.2 to 0.9	0.187	77.5 (2.4)	0.8	0.4 to 1.2	<0.001	0.439	0.211	0.200
ANB [°]											
T0	6.0 (1.8)				5.3 (2.2)						
T1	4.4 (2.2)	−1.6	−2.2 to 1.1	<0.001	4.4 (2.1)	−0.9	−1.5 to −0.3	0.004	0.257	0.984	0.110
NL/NSL [°]											
T0	6.3 (3.3)				7.1 (3.3)						
T1	7.2 (3.7)	0.9	0.3 to 1.4	0.003	7.9 (3.2)	0.8	−0.1 to 1.7	0.069	0.408	0.470	0.913
ML/NSL [°]											
T0	33.1 (4.1)				31.1 (3.9)						
T1	33.4 (4.4)	0.3	−0.5 to 1.2	0.466	30.5 (3.8)	−0.6	−1.5 to 0.2	0.142	0.084	0.017	0.129
ML/NL [°]											
T0	26.8 (4.5)				24.1 (4.0)						
T1	26.3 (4.7)	−0.5	−1.6 to 0.4	0.228	22.6 (3.9)	−1.5	−2.6 to −0.4	0.011	0.028	0.005	0.223
ILs/NL [°]											
T0	117.3 (7.3)				116.1 (8.7)						
T1	112.7 (8.2)	−4.6	−7.7 to −1.5	0.005	113.8 (9.9)	−2.3	−4.5 to −0.1	0.046	0.586	0.658	0.250
ILi/ML [°]											
T0	95.3 (7.2)				96.9 (5.8)						
T1	94.1 (6.4)	−1.2	−3.3 to 0.9	0.255	96.9 (6.1)	0.0	−1.5 to 1.5	0.985	0.382	0.117	0.352

Evaluation of lip closure

Before treatment starts, incomplete lip closure was registered in 67% of the MD and 43% of the LMD children ($P = 0.150$). After treatment, the incomplete lip closure was reduced to 27% in the MD and 10% in the LMD group ($P = 0.167$).

Experience of dental trauma

A total of 14 children, 6 in the MD (20%) and 8 in the LMD group (38%), had experienced dental trauma before treatment ($P = 0.207$). After treatment, one additional dental trauma was registered in the MD group, whereas two occurred in the LMD group ($P = 0.561$).

Discussion

Main findings

This trial found that the costs and treatment effects associated with headgear activator treatment were equivalent regardless of whether treatment was started in the MD or LMD. Thus, age or dental stadium at the start of treatment did not influence the treatment time, the number of appointments, treatment success, OHRQoL, lip closure, or trauma experience. The most pronounced effects of headgear activator treatment in both groups were reduced overjet and improved molar relation. These findings coincide with our hypothesis that treatment started in MD or in LMD are equal regarding costs and effects regarding OHRQoL, skeletal and dental effects, lip closure, and incidence of trauma.

Interpretations

Overall, the treatment effects are in line with previous research (1, 2). Specifically, treatment with headgear activator reduced the overjet and improved molar relation for most children in both groups (71–73%). Thus, the treatment effects were mainly dentoalveolar, and similar findings have been previously presented regarding Twin-block treatments (19).

Early treatment is claimed to be effective in reducing the incidence of incisal trauma (1), and with Class II malocclusion with increased overjet also being an occlusal trait strongly connected to bullying (20) incentives for early treatment would be trauma prevention or psychosocial aspects. In this trial, dental trauma before treatment was registered in 20% of the children in the MD group, while 38% in the LMD group. These numbers should be compared to 13.5% which is the reported prevalence of traumatic dental injuries for 12-year-old children in the European region (21), reinforcing the evidence that excessive overjet, especially if combined with an incomplete lip closure increases the risk for dental trauma (22). Although not statistically significant, the trauma prevalence was lower in the MD group, consistent with previous research stating that the earlier treatment of excessive overjet is carried out the better the trauma prevention will be (1). Reducing the costs associated with dental trauma will influence the overall costs. This could be added to the context of treatment-related costs associated with treatment for Class II malocclusion with excessive overjet.

It has been shown that 9-year-old children with excessive overjet report significantly lower OHRQoL than peers with posterior crossbite or peers with no orthodontic treatment need, especially in the domains of social and emotional well-being (23). Even so, this trial showed a very modest impact on OHRQoL upon completion of treatment in both groups. However, it has to be noted that the overall low CPQ scores in this trial implied a good self-perceived OHRQoL for both 9-year-old and 11-year-old children before the start of treatment. Consequently, with the success rate and effects on OHRQoL being similar for the two groups it cannot be stated from a psychosocial perspective or in terms of compliance that one age is preferable than the other when initiating treatment.

Parental support has been found to be a key factor for compliance in both younger (7) and older patients (24) when treating Class II malocclusion with removable appliances. Furthermore, interviews with older patients reveal that providing feedback regarding treatment progress and continually measuring overjet renders motivation and adds external support for compliance (24). With compliance being a prerequisite with removable appliances, our finding of similar success rate independent of age at the start of treatment was interesting. This result suggests that equal compliance and cooperation can be attained regardless of age.

Strengths

The main strength of this trial was the use of RCT design which reduced the risk of selection bias and confounding variables were avoided by ensuring that both known and unknown determinants of outcome were uniformly allocated between the two groups. In addition, the randomization was performed by persons not involved in the trial and outcomes were assessed by orthodontists not involved in the trial and blinded to treatment allocation. Furthermore, there were no dropouts in the trial. An ITT approach was also applied, and consequently, the risk of false-positive treatment results was minimal in this trial.

Limitations and generalizability

It must be noted that costs are highly dependent on local factors and can thereby not be extrapolated or directly transferred to other locations. National insurance system, staff salaries, the cost for rent and material, and so on reduce the applicability for the financial results. Furthermore, the applicability to other clinical settings might be reduced because this is a single-centre RCT conducted at a specialist clinic. The objective of this study was to evaluate and compare costs and treatment effects when initiating treatment at different ages. The appliance is widely used, and the treatment protocol well-established. The result of equivalent effects and matching costs should provide a basis for discussion when reasoning regarding treatment starts regardless of clinical settings.

Conclusions

Regardless of whether headgear activator treatment of excessive overjet was performed in MD or LMD, the costs and treatment effects were equal. The most pronounced effects of treatment were the reduction of overjet and improved molar relation, while a modest improvement effect was found on OHRQoL, lip closure, and trauma incidences. If an early treatment approach is considered, it may be advocated to start treatment as early as possible, that is, in the MD to enhance trauma prevention.

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Conflict of interest

None to declare.

Data availability

The data underlying this article will be shared on a reasonable request to the corresponding author.

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MALMÖ UNIVERSITY
205 06 MALMÖ, SWEDEN
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