UNIVERSITY OF LIVERPOOL

Orthodontic Treatment for Prominent Lower Front Teeth (Class III Incisors) in Children: A Cochrane Systematic Review

Thesis submitted in accordance

with the requirements of the

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Doctorate of Dental Science

By

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Structured Abstract

Objectives: To assess the effects of orthodontic treatment for Class III incisors in children and adolescents.

Design: A Cochrane systematic review.

Method: The following databases were searched up to 7th January 2013: Cochrane Oral Health Group Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via OVID, EMBASE via OVID.

Selection criteria: All randomised controlled trials of orthodontic treatments to correct Class III incisors. Trials were eligible for inclusion in the review if they recruited children and/or adolescents (aged 16 or less) receiving orthodontic treatment to correct Class III incisors. Trials including patients with a cleft lip and/or palate or other cranio-facial deformity/syndrome were excluded as were trials that had recruited less than 80% children or adolescents or patients who had previously received surgical orthognathic treatment. Active interventions included: orthodontic braces, chin cups, facemasks, reverse headgear, bone-anchored appliances or any other intra or extra-oral appliance aiming to correct Class III incisors. Controls included: No treatment, delayed treatment, other active intervention.

Types of Outcome Measures - Primary: Prominence of the lower front teeth (measured in mm or by any index of malocclusion). Secondary: Relationship between upper and lower jaw; psychosocial measures; patient satisfaction; jaw joint problems. Adverse effects: Health of the gums; damage to the teeth e.g. tooth decay. Outcomes were recorded at all ages reported. The results were reported according to the most common endpoints. Adverse effects were recorded and the results reported in descriptive terms.

Data collection and analysis: The titles and abstracts of the search results were examined to exclude obviously irrelevant reports. Full text reports of potentially eligible studies were examined for compliance with the eligibility criteria. Screening of references, data extraction and assessment of the risk of bias of included studies, was performed independently and in duplicate by two review authors. The mean differences, with 95% confidence intervals, were calculated for continuous data. Meta-analysis was only used when studies of similar comparisons were reporting comparable outcome measures. A fixed-effect model was used. I^2 statistics were used as measures of statistical heterogeneity.

Results: Seven randomised controlled trials were included in this review. Of these, four reported on the use of a facemask, two on the chin cup, one on the tandem traction bow appliance and one on mandibular headgear. One study reported on both the chin cup and mandibular headgear appliances. Three trials (n=155) reported ANB differences immediately after treatment with a facemask when compared to an untreated control. The pooled data, for ANB difference, showed a statistically significant mean difference of 3.93 degrees (95%CI 3.46 to 4.39; P<0.0001) in favour of the facemask. There was significant heterogeneity between these studies (I^2=82%). One well designed trial, with a low risk of bias, reported outcomes of the use of the facemask compared to an untreated control at 3 years' follow-up. This showed that improvements in overjet and ANB were still present at 3 years. However, there was no evidence of improved self-concept. The remaining trials each evaluated a different comparison and reported different outcomes so no meta-analysis was possible.

Conclusions: There is some evidence that the use of a facemask, to correct prominent lower front teeth in children, is effective when compared to no treatment on a short term basis. However, in view of the general poor quality of the included trials, these results should be interpreted with caution. Further randomised controlled trials, with long follow-up, are required.

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Abstract

Background

Prominent lower front teeth (reverse bite; under bite; Class III incisors) may be due to a combination of the jaw and/or tooth positions. The upper jaw (maxilla) can be too far back and/or the lower jaw (mandible) too far forward. Class III incisors can also occur if the upper front teeth are tipped back and/or the lower front teeth are tipped forwards. Different treatment approaches have been described to correct Class III incisors in children and adolescents.

Objectives

To assess the effects of orthodontic treatment for Class III incisors in children and adolescents.

Search methods

The following databases were searched: Cochrane Oral Health Group Trials Register (to 7th January 2013), Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, 2012, Issue 12), MEDLINE via OVID (1946 to 7th January 2013), EMBASE via OVID (1980 to 7th January 2013). Handsearching done as part of the Cochrane Worldwide Handsearching Programme and uploaded to CENTRAL was included.

Selection criteria

Types of Studies - Randomised controlled trials of orthodontic treatments to correct Class III incisors.

Types of Participants - Trials were eligible for inclusion in the review if they recruited children and/or adolescents (aged 16 or less) receiving orthodontic treatment to correct Class III incisors.

Trials including patients with a cleft lip and/or palate or other cranio-facial deformity/syndrome were excluded as were trials that had recruited less than 80% children or adolescents or patients who had previously received surgical treatment for their Class III malocclusion.

Types of Interventions - Active interventions included: orthodontic braces (removable, fixed, and functional), chin cups, facemasks, reverse headgear, bone-anchored appliances or any other intra or extra-oral appliance aiming to correct Class III incisors.

Controls included: No treatment, delayed treatment, other active intervention.

Types of Outcome Measures - Primary: Prominence of the lower front teeth (measured as the overjet in mm or by any index of malocclusion).

Secondary: Relationship between the upper and lower jaw; psychosocial measures; patient satisfaction; jaw joint problems.

Adverse effects: Health of the gums; damage to the teeth e.g. tooth decay.

Outcomes were recorded at all ages reported. The results were reported according to the most common endpoints. Adverse effects were recorded and the results reported in descriptive terms.

Data collection and analysis

The titles and abstracts of the search results were screened to exclude obviously irrelevant reports, being generally over inclusive at this stage. Full text reports of potentially eligible studies were examined for compliance with the eligibility criteria. Screening of titles and abstracts, data extraction and assessment of the risk of bias of included studies, was performed independently and in duplicate by two review authors. The mean differences, with 95% confidence intervals, were calculated for continuous data. Meta-analysis was only used when studies of similar comparisons were reporting comparable outcome measures. A fixed-effect model was used. I^2 statistics were used as measures of statistical heterogeneity.

Results

Seven randomised controlled trials were included in this review. Of these, four reported on the use of a facemask, two on the chin cup, one on the tandem traction bow appliance and one on mandibular headgear. One trial reported on both the chin cup and mandibular headgear appliances.

Three trials (n=155) reported ANB (an angular measurement relating the positions of the top and bottom jaws) differences immediately after treatment with a facemask when compared to an untreated control. The pooled data showed a statistically significant mean difference in ANB of 3.93 degrees (95%CI 3.46 to 4.39; P<0.0001) in favour of the facemask. There was significant heterogeneity between these studies (I^2=82%). This is likely to have been caused by the different populations studied and of different ages at time of treatment.

One well designed trial, with a low risk of bias, reported outcomes of the use of the facemask compared to an untreated control at 3 years' follow-up. This showed that improvements in overjet and ANB were still present at 3 years', however there was no evidence of improved self-concept.

The remaining trials each evaluated a different comparison and reported different outcomes so no meta-analysis was possible.

Authors' conclusions

There is some evidence that the use of a facemask, to correct Class III incisors in children, is effective when compared to no treatment on a short term basis. However, in view of the general poor quality of the included trials, these results should be interpreted with caution. Further randomised controlled trials, with long follow-up, are required.

Chapter 1: Introduction

People with prominent lower teeth may also be described as having a reverse bite, underbite or, within the dental profession, as possessing a Class III incisor relationship. This is often associated with a Class III skeletal discrepancy. This malocclusion may be considered disadvantageous due to appearance, problems with eating, problems with speech and a possibility it may lead to jaw joint problems.[1-3] Whilst relatively uncommon in Caucasians, it is far more common in Oriental populations.[4-8]

Orthodontics is the branch of dentistry concerned with the growth of the jaws and face, development of the teeth and the way the teeth and jaws bite together.[9] Orthodontic treatment

involves the use of a variety of appliances, some fixed and some removable, to correct discrepancies in the alignment of the teeth and in the way in which the teeth meet together.

Orthodontic treatment for a Class III malocclusion, if required, happens either early, during childhood, with the use of orthodontic appliances alone, or once growth has ceased when it may be combined with a surgical procedure, to correct not only the occlusion but also the underlying skeletal discrepancy. Many different appliances have been tried, at many different stages of development, to correct a Class III malocclusion.

The aim of this research is to report the outcome of interventions to correct Class III incisors in children and adolescents. The review will assess the relative effectiveness of these interventions when compared with each other and when compared with no treatment. It will aim to summarise the available literature and also to appraise critically the methodology used in the included journal articles. In addition to this, if previous research is found to be deficient in any areas then this review will aim to suggest possible areas for future research. Suggestions will be made for how future research should be carried out in order to maximise its value.

Chapter 2: Literature Review

2.1 Systematic Reviews

Over two million journal articles are published every year in the biomedical literature.[10] It is impossible for the majority of healthcare professionals to read every article published in their area of interest, speciality or expertise due to the sheer bulk of research and the amount of time available to read it. Health care providers, researchers, and policy makers are inundated with unmanageable amounts of information and they need a way to integrate existing information efficiently and provide data for rational decision making.[10] Therefore, this has led to a relatively new form of publication type which identifies all the research about a particular subject or question, analyses it and then reports the overall findings with suggestions for future research: the systematic review.[11] Chalmers has defined the systematic review as a review, which has been prepared using a systematic approach to minimising biases and random errors, with the different components of the process being documented in the methods section.[10] It has been stated that without the systematic review there would be a serious risk that "tens of billions of dollars, already spent on hundreds of thousands of

controlled trials, would be wasted due to the inaccessibility of the data."[12] A systematic review attempts to collate all empirical evidence, meeting pre-specified eligibility criteria, in order to answer a specific research question. It uses explicit, systematic methods, selected with a view to minimising bias, therefore providing more reliable results from which valid conclusions can be drawn and decisions made.[13] In addition, a greater level of generalisability of scientific findings can be established in systematic reviews. The diversity of multiple reviewed studies provides an interpretive context not available in any one study. This is because studies addressing similar questions often use different eligibility criteria for participants, different definitions of disease, different methods of measuring or defining exposure, different variations of a treatment, and different study designs.[10] A further advantage of the systematic review is the ability to combine the data from multiple studies into a single meta-analysis. This leads to an increased level of statistical power and therefore increases the chances of finding a true result.

The systematic nature of the methodology ensures that the risk of not including all available research, in that particular area of research, is minimised. By placing all of this research into a single journal article, it offers an easily accessible and reliable source for guiding clinicians as well as policy makers and potential researchers.

There has been an exponential increase in the popularity of systematic reviews over the past 30 years. Prior to 1982 there was roughly one systematic review published a year. By 1992, the number had risen to 500 a year and by 2007 this number was up to 2,500.[11, 14] Clinicians like systematic reviews because they efficiently integrate existing information and provide data for rational decision making.[10] They give a clinician a realistic chance of being able to keep up to date with current research and its results, in many different research areas. Systematic reviews are increasingly gaining acceptance as a starting point in the development of evidence-based clinical practice guidelines and to help design primary research and ensure

it is ethically justified.[14] Prior to starting a piece of research, systematic reviews should be sought to ensure that the research to be carried out is not answering a question already answered and is targeted to avoid wasting valuable resources. One of the main reasons for the substantial increase in systematic reviews has been the success of the Cochrane Collaboration.[15]

2.2 The Cochrane Collaboration

The Cochrane Centre, established in 1993, evolved in response to Archie Cochrane's criticism of health professions for not having organised, systematic, periodically updated reviews of all relevant randomised controlled trials.[11, 13] The Cochrane Collaboration's primary aim is to help people, including clinicians, patients, funding organisations and researchers alike, make informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews and the evidence that underpins them.[13] The work of the Cochrane Collaboration is underpinned by ten key principles (Box 1).

A Cochrane systematic review must adhere to strict guidelines and methodology. Green states that "the advances in methodology have led to improvements in the internal validity of systematic reviews and trials", for example highlighting the importance of allocation concealment and blinding, also influencing broader issues of research conduct.[12] More recently, a greater emphasis has been placed on the importance of sample size calculations to ensure that a study has sufficient power to detect a difference if one exists. This may help prevent the failure of studies to find a true positive and therefore waste time, effort and resources.[13]

A Cochrane systematic review is very strict about the types of research that are included. In order to give the most reliable and valid conclusion only the greatest level of research is

encouraged for inclusion: the randomised controlled trial. If there are no randomised controlled trials available then the use of other study designs is permitted.[13]

The risk of bias tool has been developed in order to allow every article, that is included in a review, to be assessed for potential bias that may have influenced the results of the trial. This is useful in two ways. Firstly, it allows a reviewer to assess the methodology being used in a piece of research accurately. Secondly, it can be used by potential researchers to ensure that their research methodology is designed in a way in which bias will be minimised.[13]

1. Collaboration, by internally and externally fostering good communications, open decision-making and teamwork.
2. Building on the enthusiasm of individuals, by involving and supporting people of different skills and backgrounds.
3. Avoiding duplication by good management and co-ordination, maximising economy and effort.
4. Minimising bias, thorough scientific rigour, broad participation, avoiding conflicts of interest.
5. Keeping up to date, by a commitment to ensure that Cochrane reviews are maintained through identification and incorporation of new evidence.
6. Striving for relevance, promoting the assessment of healthcare interventions using outcomes that matter to people making choices in health care.
7. Promoting access, by wide dissemination of the outputs of the Collaboration, taking advantage of strategic alliances, and by promoting appropriate prices, content and media to meet the needs of users worldwide.
8. Ensuring quality, by being open and responsive to criticism, applying advances in methodology, and developing systems for quality improvement.
9. Continuity, by ensuring that responsibility for reviews, editorial processes and key functions is maintained and renewed.
10. Enabling wide participation in the work of the Collaboration by reducing barriers to contributing and by encouraging diversity.

Box 1: The principles of the Cochrane Collaboration.[13]

2.3 Definition and Prevalence of Class III Incisors

In layman's terms, Class III incisors occur when the bottom teeth meet in front of the top teeth and the individual may be said to have prominent lower front teeth. The British Standards Institute describes the Class III incisal relationship as existing when the lower incisor tips occlude or lie anterior to the cingulum plateau of the upper incisors.[16] Class III incisors often occur as part of a Class III malocclusion. Angle described the Class III malocclusion as occurring when the mesiobuccal cusp of the permanent maxillary first molar occludes distal to the buccal groove of the permanent mandibular first molar.[17] In the Caucasian population, the prevalence of a Class III malocclusion ranges from 0.48 to 4%.[6, 7] In the Japanese population, it is in the region of 10%.[8] However, in the Chinese population it has been found to be considerably higher, between 14 to 21%.[4, 5] This relative prevalence has influenced the research with much of the work into a Class III malocclusion and its treatment, being undertaken in China and Japan.

2.4 Aetiology of a Class III Malocclusion

Until the 1970s, the terms Class III malocclusion and mandibular prognathism were virtually synonymous.[18] Since then, cephalometric work has shown that the cause of a Class III malocclusion is in fact multifactorial.[18-21] Every component of the craniofacial skeleton has, at one time, been implicated as the causative factor.[19] Sanborn separated the causes into 4 groups:

- Group A: Mandibular prognathism with a normal maxillary position (45%)

- Group B: Maxillary retrognathia with normal mandibular position (33%)

- Group C: Normal maxillary and mandibular positions (9.5%)

- Group D: Maxillary retrognathia and mandibular prognathia (9.5%).[21]

Jacobson et al. found similar results,[18] whilst Ellis and McNamara[19] found a greater percentage of Class III malocclusions could be attributed to maxillary retrusion. In addition to noting the role of solely the dentition and not their skeletal bases, they also added that excessive lower facial height was a frequent contributor. They suggested a possible 10 combinations of skeletodental components of a Class III malocclusion (Table 1).

	No. (%)	Max Skel	Max Dent	Mand Dent	Mand Skel	Vert Comp
Group I	37 (12.3)	Ret	Prot	Ret	Prot	Long
Group II	27 (8.9)	Neut	Prot	Ret	Prot	Long
Group III	23 (7.6)	Ret	Prot	Ret	Neut	Long
Group IV	13 (4.3)	Prot	Prot	Ret	Prot	Long
Group V	12 (4.0)	Ret	Prot	Ret	Prot	Short
Group VI	11 (3.6)	Ret	Prot	Ret	Ret	Long
Group VII	11 (3.6)	Ret	Ret	Ret	Neut	Long
Group VIII	10 (3.3)	Ret	Prot	Ret	Prot	Neut
Group IX	9 (3.0)	Ret	Neut	Ret	Prot	Long
Group X	8 (2.6)	Ret	Neut	Ret	Neut	Long

Table 1: Combinations of skeletodental combinations occurring in a Class III malocclusion and their relative frequency.[19]

In addition to the roles of the relative maxillary and mandibular protrusion, a role has also been implicated for the natural head position and posture as well as the cranial base angle. Cole suggested that cranial base orientation should be added to the list of theoretical causes of prognathism.[22] In the case of a Class III skeletal relationship, the cranial base angle may be reduced leading to relative protrusion of the mandible in relation to the maxilla. This in turn will result in a Class III incisal relationship.

In some cases, a Class III incisal relationship may be attributed to a functional forward displacement of the mandible as a result of retroclined maxillary incisors, often referred to as

a pseudo-Class III relationship.[23] This can be of significance when assessing a patient, because when the patient bites into maximum intercuspation the relationship between the mandible and maxilla may appear worse than is actually the case.

Due to the difficulty in treating patients with a Class III malocclusion, emphasis has been placed on early diagnosis and prediction. Jacobson et al. found that while 60% of children with a Class III malocclusion had mandibular and maxillary measurements within normal limits, only 14% of adults did.[18] This is strongly suggestive that with growth, there is a worsening of maxillomandibular disharmony. Guyer et al. found that, even in children, a Class III malocclusion does not indicate a typical facial skeletal pattern but a combination of aberrations in the craniofacial complex.[20] Williams et al. agreed, stating no one single factor could distinguish a Class III group from a Class I group and therefore act as a key to prediction.[24] Later, Chang et al. looked at 80 children who went on to have either Class I or III malocclusions. The most significant differences, in the primary dentition, were found in the anteroposterior intermaxillary skeletal relationships with a reduction in ANB, angle of convexity, Wits appraisal and AF-BF distance.[25] Therefore, although no single indicator can be determined, a tendency for a morphological difference between the maxilla and mandible in a Class III individual and a Class I individual exists and this difference occurs early.[20] More recently this has been supported on a Korean population where Choi et al. found that some of the cephalometric values are highly reliable for use to diagnose skeletal Class III malocclusion in the deciduous dentition.[26]

More recent work has focused on the role of genetics in the development of a Class III malocclusion. It has been suggested that the cartilage of the mandibular condyle is responsive to biophysical environmental change and it is likely that a Class III malocclusion might be precipitated under these biomechanical conditions by the inheritance of genes predisposing to a Class III phenotype.[27] Cruz et al. looked at 2562 individuals from 55 families. The majority

of pedigrees suggested an autosomal dominant inheritance. Heritability of mandibular prognathism was estimated to be 0.316 therefore suggesting a major gene influencing the expression of mandibular prognathism with clear signs of Mendelian inheritance.[28] A study of 13 European noble families has also shown that mandibular prognathism may be determined by a single autosomal dominant gene.[29] It appears likely, however, that this major gene is influenced by other genes as well as environmental factors.[27, 28] When looking at specific genes, a number of reports document the influence of genes involved in the regulation of mandibular morphogenesis. Genes including IHH, PTHLH, IGF-1, and VEGF, and variations in their levels of expression play an important role in the aetiology of Class III malocclusion.[27] A link between genetic polymorphisms in EPB41 gene and mandibular prognathism has been shown.[30] Certain growth hormone receptor gene polymorphisms are related to mandibular height and RUNX2 is one of many biological factors influencing the development and growth of condylar cartilage in humans.[31, 32]

Currently, genetics is yet to allow prediction of growth. It must also be noted that much of the research into Class III genetics focuses solely on mandibular prognathism and as discussed earlier, much of the cause of a Class III malocclusion is attributable to maxillary retrusion. However, it is likely that in the future use of these genes will allow early diagnosis, early treatment planning, prediction of growth and possibly alternative treatment modalities.

2.5 Treatment of Class III Malocclusions

In orthodontics, Class III malocclusions are considered amongst the most difficult to treat.[33] The main focus of concern for a Class III patient, presenting with a concave facial profile, retrusive nasomaxillary area and protrusive lower face is often their profile, not their occlusion.[1, 34] Studying the reasons for seeking treatment to correct a Class III malocclusion,

Zhou et al. found that by far the greatest reason was that of appearance, followed by problems with chewing, speaking and rarely breathing.[3] Problems with the temporomandibular joint have also been reported, although evidence for a link is weak.[2, 35] Treatment of a Class III malocclusion is either orthopaedic treatment of a growing patient, delayed intervention in the form of corrective surgery at the end of active growth or, if maxillomandibular disharmony is mild, camouflage, is also possible.[36, 37] Camouflage is particularly successful in the pseudo-Class III malocclusion cases.[23] If camouflage is not possible, early orthopaedic treatment is often indicated, because if left untreated they will ultimately comprise a significant percentage of the patients seeking orthognathic treatment as adults.[1]

Orthognathic surgery is a relatively safe procedure however it is not without risk.[38, 39] Peri-operatively risks include major blood loss requiring transfusion, necessity for a tracheostomy, deep vein thrombosis and even death.[38, 39] The most common post-operative complication is damage to the inferior alveolar nerve of which the reported incidence ranges from 0-85%.[40] Long-term damage to the infraorbital and facial nerves, whilst rare, is also of concern.[41, 42] If surgery could be avoided, through early correction, these potential complications could be avoided.

As surgical options are carried out once growth has ended, they are not applicable to this study. In the quest to find appropriate treatment regimens to correct a Class III malocclusion early, many options have been tried including:

- Functional appliance treatment

- Chin cup therapy

- Mandibular cervical headgear

- Facemask

- Other methods of maxillary protraction

- Camouflage

2.5.1 Functional Appliance Therapy

Functional Jaw Orthopaedics has been in use since the late nineteenth century. In 1902, Robin introduced the monobloc for bimaxillary expansion. Andreasen furthered this work creating an appliance that fit loosely in the mouth and transmitted the forces generated from the muscles of mastication to the teeth and jaws bringing about the correction of malocclusions.[43]

2.5.1.1 The Functional Regulator Appliance

Frankel suggested that, by inserting his appliance, the development of the dentoalveolar structures could be influenced up to the apical base. Expanding the soft tissue encapsulating the dentition, so restricting the forces of the perioral bands, would allow the dentoalveolar processes to be further developed. This would, in turn, allow a Class I jaw and tooth relationship to develop.[44] One of Frankel's appliances was designed for a Class III malocclusion, the functional regulator 3 (FR-3).
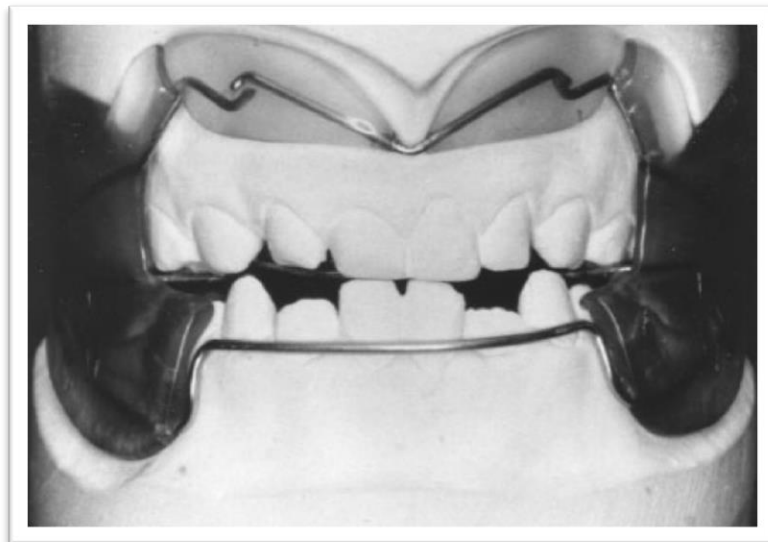
Figure 1: The Functional Regulator 3 (FR-3).[45]

The buccal shields of the FR-3 appliance provoke tension of the soft tissues in the vestibular fold achieving expansion and remodelling of the dentoalveolar arch and apical base as well as

relieving unwanted pressure and applying traction. Therefore, in the upper arch the permanent teeth erupt more buccally with expansion of the dentoalveolar arch, so correcting a Class III tendency.[46]

The results of investigations into the effects of the FR-3 are variable. The appliance has been shown to induce increased overjet, reduce SNB angle, increase ANB angle and improve soft tissue outcome.[47, 48] It has been postulated that much of this improvement is due to principally dentoalveolar changes,[49] however, Miethke et al. found that the appliance did stimulate development of the maxilla.[45] This was supported cephalometrically by Kilic et al. who found the maxilla and surrounding soft tissues showed significant anterior movement whilst mandibular growth was restricted.[50] It must be noted that all of this research was retrospective and used either no control group or an inappropriate control.

2.5.1.2 The Removable Mandibular Retractor

Tollaro et al. have suggested the use of the Removable Mandibular Retractor (RMR).[51] This consists of a resin plate attached to the maxillary teeth with Adams clasps and a labial bow extending to the cervical margin of the mandibular incisors. The labial arch is activated so to be placed 2mm anterior to these teeth when the mandible is forced into maximum retrusion, therefore acting as a stop for sagittal movement of the mandible. Expansion screws and springs are used for the proclination of the upper incisors, if indicated.[52]

Used in the deciduous dentition this appliance has been shown to produce a significant anterior morphogenic rotation of the mandible due to a more upward and forward direction of condylar growth and a reduced mandibular length.[52] Whilst the research into the RMR has used an appropriate Class III control group it must again be criticised for being retrospective in nature.
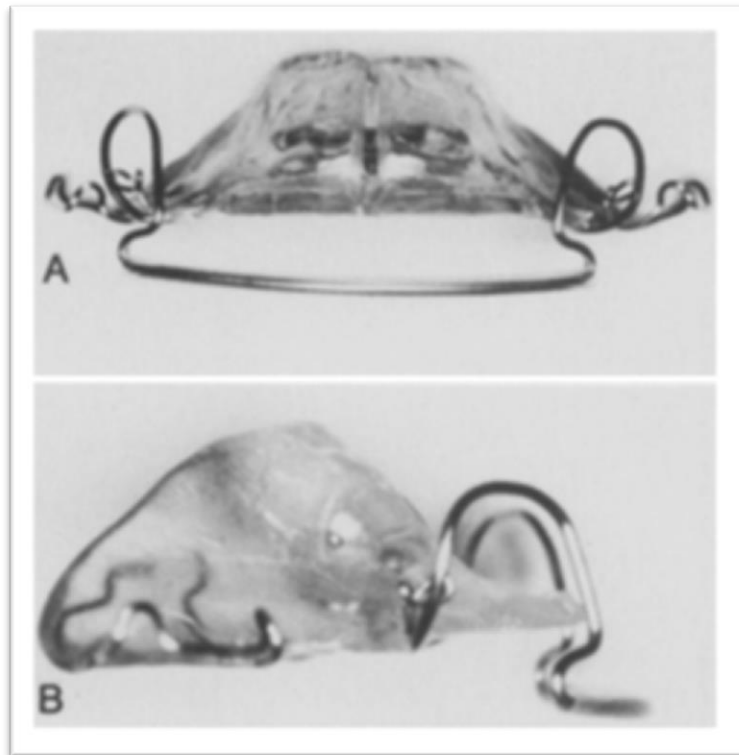
Figure 2: The Removable Mandibular Retractor (RMR).[51]

Other functional appliances found in the literature include the Bionator III and Class III Twin-block.[53, 54]

2.5.2 Chin cup Therapy

Chin cup therapy, sometimes referred to as chin cap therapy, has been used since the nineteenth century for the treatment of mandibular prognathism.[55] The chin cup apparatus involves the use of an acrylic or metal prosthesis which sits on the patients chin with force applied to the occipital region of the skull (Figure 3).

Figure 3: An example of a patient wearing the chin cup appliance.[56]

Forces used have ranged from 200-900g per side with most using between 200-250g.[33, 57, 58] The results from the literature vary widely. Whilst some research showed no effects,[55] the majority found good initial results from the chin cup when used as an early intervention.[33, 56, 59-62]

The suggested mechanisms for success of this appliance have been:

- Backward rotation or distal displacement of the mandible.

- Retardation of mandibular growth.

- Redirection of mandibular growth vertically.

- Remodelling of the mandible through closure of the gonial angle.

- Retardation of downward growth and reinforcement of forward maxillary growth.

- Alteration in the condylar growth pattern. [56, 59, 60, 62, 63]

There is further controversy with respect to the long term success. Deguchi et al. found long term success was possible with the chin cup.[56] However, Sugawara et al. showed that whilst soft tissue profile was greatly improved during the initial stages of therapy, such changes were often not maintained.[61] This is more recently supported by the work of Barrett et al. who showed that 2.6 years post-treatment, there were no significant skeletal changes in the mandible in either the vertical or horizontal direction and fewer than 50% had a favourable clinical outcome.[58]

2.5.3 Mandibular Cervical Headgear

Mandibular Cervical Headgear (MCH) uses bands on the lower first permanent molars and a connecting neck strap thus placing force through the centre of resistance of these teeth.[64] Used in cases of mandibular prognathism, the use of this headgear approach has been shown to lead to significant improvements in Wits appraisal, overjet and molar relationship.[64, 65] The mechanism of improvement with this appliance is predominantly mandibular retrusion combined with dentoalveolar changes.[64]

2.5.4 Facemask

In 1944, Oppenheim published an article suggesting the possibility of treatment to result in maxillary protraction. However, it was not until 1971 that the modern facemask was reintroduced by Delaire.[66] This design consisted of a forehead support, a chincup, a prelabial arch, and a metal frame (Figure 4).[67]
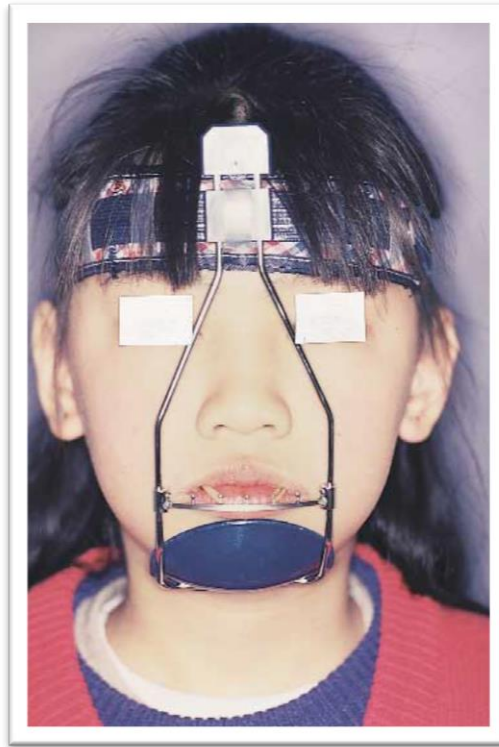
Figure 4: A Delaire Facemask.[68]

Multiple authors have modified the facemask in order to alter the angle or amount of force slightly but all rely on a similar mechanism of using the chin and forehead as a stable base against which to protract the maxilla using elastics.[67, 69-71]

Several authors have found the success for early correction of a Class III malocclusion with a facemask lies in the region of 70-75%.[72, 73] The facemask has been shown to produce maxillary and mandibular changes reliably, including:

- anterior displacement of the maxilla

- posterior rotation of the mandible

- backward movement of the mandible

- proclination of the maxillary incisors

- retroclination of the mandibular incisors

- increase in the mandibular plane angle

- increase in the anterior face height

- increase in the skeletal profile convexity

- improvement of the sagittal lip relationship

- decrease in the soft tissue facial angle and convexity.[34, 72, 74-79]

Therefore, recent work focuses on finding the conditions for producing the best long-term results. The cases that are suitable for facemask treatment tend to be those with a hypoplastic maxilla. In many of these cases, the use of some form of maxillary expander is often required. Midfacial orthopaedic expansion has been recommended for use in conjunction with protraction forces on the maxilla as it is thought to disrupt the circum-maxillary sutural system, initiate cellular responses within the sutures and, therefore, facilitate the orthopaedic effects of the facemask.[75, 80] However, research has shown that facemask treatment is equally effective without rapid maxillary expansion and therefore cannot be recommended unless clinically indicated.[80, 81] This would suggest that unless the patient requires expansion for other orthodontic reasons, no phase of pre-facemask expansion should be carried out.

Conflicting results can be found in the literature regarding the ideal age for intervention with a facemask. Much of the research advocates intervention in the early mixed dentition.[74, 75, 82, 83] Saadia and Torres recommend intervention as young as a diagnosis is made, as young as 3.[84] However, Sung and Baik and Yuksel et al. noted no significant difference between the young and adolescent groups in their studies.[85, 86]

2.5.5 Other Methods of Maxillary Protraction

2.5.5.1 Tandem Traction Bow Appliance

The tandem traction bow appliance (TTBA) comprises of upper and lower splints covering the teeth, activator tubes embedded in the splints, a conventional headgear facebow used as a traction bow and elastics connecting the upper splint to the traction bow (Figure 5).[87] The original appliance used 400-500g force per side at 20°, however, this has been modified to 35°.[87]
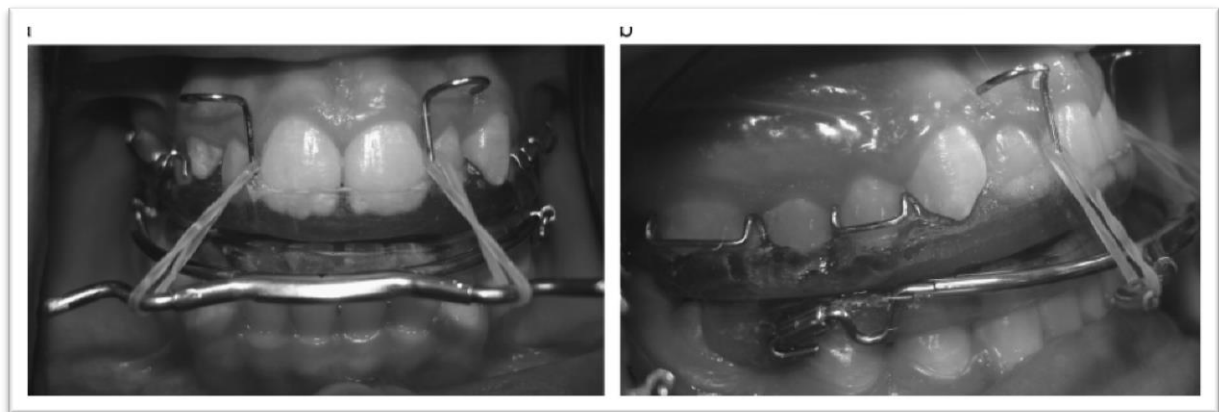
Figure 5: The modified tandem traction bow appliance (TTBA).[87]

This appliance has also been shown to produce maxillary protrusion and mandibular retrusion.[87]

2.5.5.2 Mini Maxillary Protractor

The mini maxillary protractor has a maxillary expander, hooks embedded buccally within the acrylic in the molar and premolar regions, a mandibular plate, a chincup and a lower facebow attached to the chincup applying maxillary protraction with elastics (Figures 6, 7).[88]
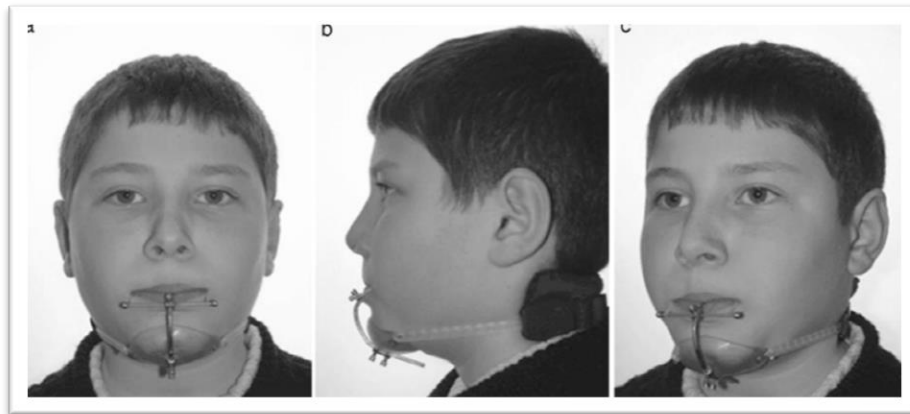
Figure 6: The mini maxillary protractor. Extra-oral views.[88]
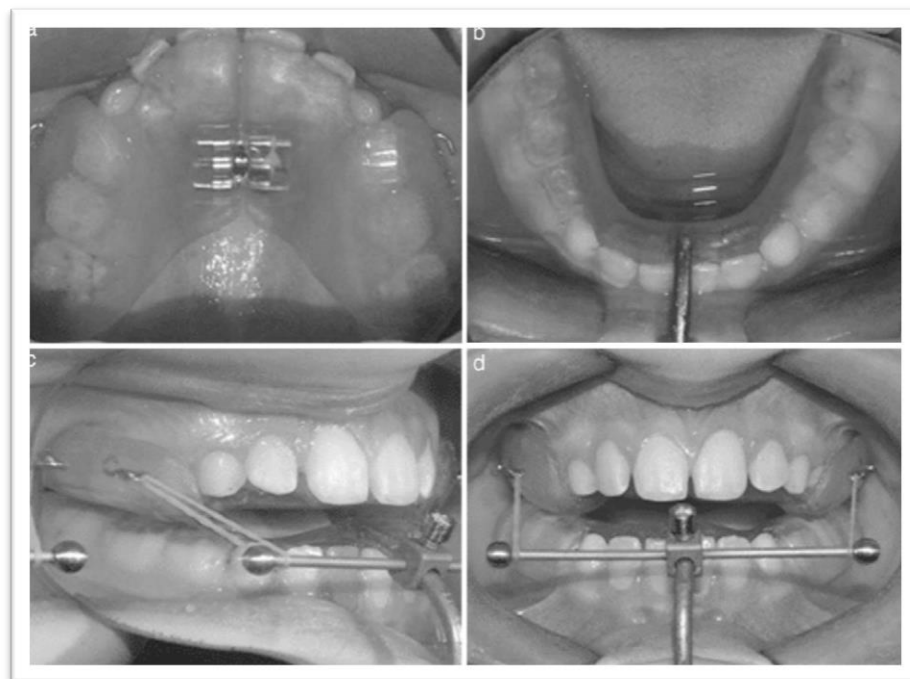
Figure 7: The mini maxillary protractor. Intra-oral views.[88]

This appliance has been shown to elicit forward maxillary movement, backward mandibular movement, protrusion of the upper incisors, retrusion of the lower incisors and opening of the mandibular plane angle.[88]

2.5.5.2 Modified Protraction Bow Appliance

The modified protraction bow appliance (MPBA) uses bands on the molars connected with a palatal button, a chin pad on an acrylic facebow and elastics to connect and apply the required force.[89] When used in the deciduous dentition this appliance has been shown to produce effective maxillary displacement.[90]

2.5.5.3 Occipitomental Anchorage

Lin et al. have carried out research into occipitomental anchorage for maxillary protraction (OMA), using buccal hooks on the upper first permanent molars and elastics to horns on a chin cap.[91]
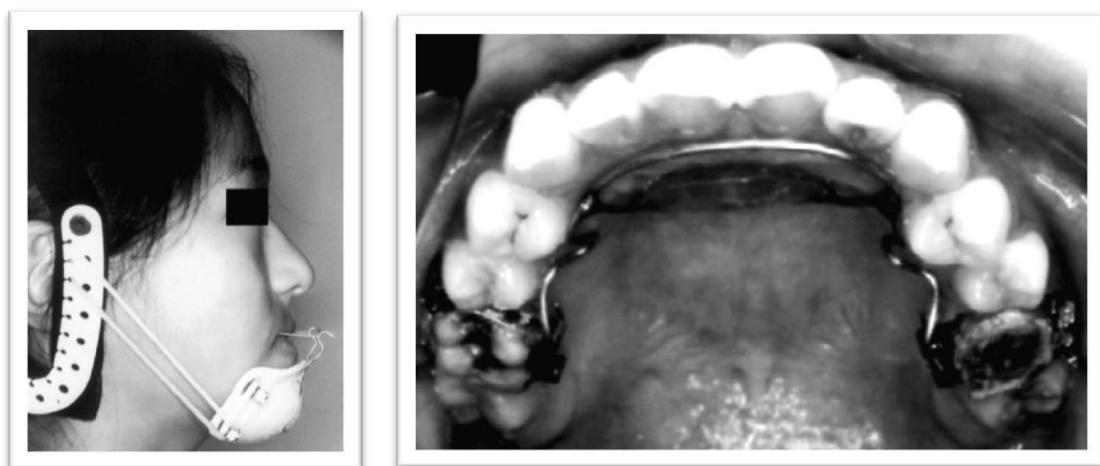
Figure 8: The Occipitomental anchorage (OMA) appliance.[91]

OMA has been shown to cause backward mandibular rotation, forward maxillary movement and considerable dentoalveolar movement leading to effective anterior crossbite correction.[91]

2.5.5.4 Bone-Anchored Maxillary Protraction

De Clerck et al. have introduced an innovative bone-anchored maxillary protraction (BAMP) protocol, removing any extra-oral component. Using 4 surgically placed miniplates, 2 in the infrazygomatic crest of the maxillary buttress and 2 between the mandibular lateral incisors

and canines, elastics are used to connect them. A removable biteplane can be used to remove occlusal interferences.[92]

Figure 9: Bone-Anchored Maxillary Protraction (BAMP).[92]

Early indications are that this may be effective at producing maxillary advancement and posteriorly relocating the mandibular condyle leading to a marked improvement in intermaxillary relationship. Due to the force being directed at the bone, rather than the teeth, there is a reduction in the changes in incisal inclination.[92]

Similar work has been carried out by Sar et al.[93] Their protocol involves 2 miniplates placed lateral to the aperture piriformis regions of the maxilla. After a week the protraction starts using elastics from the hooks connected to a facemask. A splint removes occlusal interferences (Figure 10). Again, results are short-term but appear promising, achieving maxillary protraction quickly and with reduced dentoalveolar side-effects.[93]

Figure 10: Maxillary protraction with skeletal anchorage.[93]

2.5.6 Camouflage

In some cases with Class III incisal relationships, the maxillomandibular disharmony is mild and the ANB angle close to normal. These cases may be treated by camouflage, for example by proclining the upper labial segment and retroclining the lower labial segment.[94] It has been shown that a wide range of skeletal discrepancy may be successfully camouflaged with solely tooth movement, however, it is only possible with mild to moderate skeletal malocclusions and realistic treatment objectives on behalf of the clinician are imperative.[36, 95, 96] Kerr et al. found threshold values for the ANB and lower incisor angles at which point surgery was carried out over camouflage. These angles were ANB of -4° and lower incisor angle of 83°.[36]

Similar work by Stellzig-Eisenhauer et al. found that Wits appraisal, length of the anterior cranial base, ratio of the anteroposterior length of the maxilla to the anteroposterior length of the mandible and gonial angle could be used as predictors for which cases were treated by camouflage compared with surgery.[97] A considerable problem is the inability to predict future growth and Bishara suggests treatment planning should be based on 'worst case scenario' assuming facial growth will continue unfavourably.[98] Camouflage can be achieved using either fixed or removable appliances.

2.5.6.1 Fixed Appliances

Camouflage is most commonly carried out using fixed appliances.[96] They are often used on the non-growing patient when other, orthopaedic or functional, treatments are no longer possible.[95, 96] A fixed appliance that has been shown to be particularly successful in the early mixed dentition is the 2 x 4 appliance that successfully proclines the maxillary incisors using an advancing loop connected to the first permanent maxillary molars.[23]

2.5.6.2 Removable Appliances

The use of removable maxillary appliances to procline the maxillary incisors has also been shown to be successful.[99] It has been shown that, as would be expected, there are no skeletal effects and all improvement in anterior relationship is solely due to maxillary incisor proclination.[100] The proclination may be achieved with the use of a spring or screw in the appliance and aims to produce a positive, stable overjet at the end of treatment. Used in mild cases this has been shown be stable long term.[101]

2.6 Conclusion

Many appliances have been advocated for use in the correction of a Class III malocclusion in childhood. They have been used at different stages of development and for different

aetiological reasons. The methodology of some of the studies appears to be weak, especially with respect to the use of appropriate controls.

It is the purpose of this Cochrane systematic review to identify all the literature in this area, collate the evidence from controlled and randomised clinical trials, determine the relative effectiveness of these interventions and suggest future areas for research.

Chapter 3: Systematic Review

3.1 Objectives

The purpose of this systematic review was to test the null hypotheses that there were no differences in outcomes between:

- different orthodontic interventions for correcting a reverse bite,
- the age at which orthodontic treatment for a reverse bite is carried out,

against the alternative hypotheses that there were differences.

3.2 Methods

3.2.1 Criteria for Considering Studies for the Review

3.2.1.1 Types of Studies

All randomised controlled clinical trials of orthodontic treatments to correct prominent lower front teeth.

3.2.1.2 Types of Participants

Trials were eligible for inclusion in the review if they had recruited children and/or adolescents (aged 16 or less) receiving orthodontic treatment to correct prominent lower front teeth.

Trials including patients with a cleft lip and/or palate or other cranio-facial deformity/syndrome were excluded as were trials that had recruited less than 80% children or adolescents or patients who had previously received surgical treatment for their prominent lower front teeth.

3.2.1.3 Types of Interventions

Active interventions included:

- Orthodontic braces (removable, fixed, functional)

- Chin cups

- Face masks

- Reverse headgear

- Bone-anchored appliances.

Controls included:

- No treatment

- Delayed treatment

- Other active intervention.

3.2.1.4 Types of Outcome Measures

- **Primary**: Prominence of the lower front teeth (measured in mm or by any index of malocclusion).

- **Secondary**: Relationship between upper and lower jaw (measured in degrees or mm); psychosocial measures (using any measure of self-esteem, self-concept or self-perception); patient satisfaction (using any form of questionnaire); jaw joint problems (using any index of temporomandibular jaw assessment tool).

- **Adverse effects**: Health of the gums; damage to the teeth e.g. tooth decay.

Outcomes have been recorded at all ages reported. The results have been reported according to the most common endpoints. Adverse effects have been recorded and the results reported in descriptive terms.

3.2.2 Search Methods for Identification of Studies

For the identification of studies included or considered for this review, detailed search strategies were developed for each database searched. These were based on the search strategy developed for MEDLINE (OVID) but revised appropriately for each database. The search strategy used a combination of controlled vocabulary and free text terms and was linked with the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials (RCTs) in MEDLINE: sensitivity maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011).[13] Details of the

MEDLINE search are provided in Appendix 3. The search of EMBASE was linked to the Cochrane Oral Health Group filters for identifying RCTs (see Appendix 4).

3.2.2.1 Databases Searched

The following databases were searched:

- The Cochrane Oral Health Group Trials Register (to 7 January 2013) (See Appendix 1)

- The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, 2012, Issue 12) (See Appendix 2)

- MEDLINE via OVID (1946 to 7 January 2013) (See Appendix 3)

- EMBASE via OVID(1980 to 7 January 2013) (See Appendix 4)

3.2.2.2 Handsearching

Only handsearching done as part of the Cochrane Worldwide Handsearching Programme and uploaded to CENTRAL was included for the following journals:

- American Journal of Orthodontics and Dentofacial Orthopedics

- The Angle Orthodontist

- European Journal of Orthodontics

- Journal of Orthodontics

- Seminars in Orthodontics

- Clinical Orthodontics and Research

- Australian Journal of Orthodontics

- Journal of Clinical Orthodontics

The bibliographies of the clinical trials identified were checked for references to trials published outside the handsearched journals.

Personal references were checked.

3.2.2.3 Language

Databases were searched to include all languages and non-English language papers were translated.

3.2.2.4 Unpublished Studies

The first authors of all trial reports were contacted in an attempt to identify unpublished studies and to obtain any further information about the trials. In addition, trial registries were searched to identify on-going studies. These included www.clinicaltrials.gov, clinicaltrials-dev.ifpma.org, and isrctn.org.

3.2.3 Data Collection and Analysis

3.2.3.1 Study Selection

- The titles and abstracts of the search results were examined to remove obviously irrelevant reports, being generally over inclusive at this stage. This was done by two review authors (from Simon Watkinson (SW), Jayne Harrison (JH) or Sue Furness (SF)) independently and in duplicate. Disagreements would have been resolved by discussion between these review authors. If arbitration was required, it would have been provided by Annabel Teague (AT).

- Full text reports of potentially eligible studies were examined for compliance with the eligibility criteria. This was performed by two review authors (from SW, JH or SF) independently and in duplicate. We corresponded with investigators, where appropriate, to clarify study eligibility. Disagreements would have been resolved by discussion between these review authors. If arbitration was required, it would have been provided by AT. If additional information was required, the corresponding author of the trial was contacted and the study categorised as one awaiting assessment. Study eligibility was performed with the aid of a piloted study eligibility form.

- A list of excluded studies was recorded giving the primary reason for exclusion following the screening of the titles and abstracts stage.

3.2.3.2 Data Extraction

Data extraction was performed independently and in duplicate by two review authors (from SW, JH and SF). A piloted data extraction form was used independently to record the year of publication, interventions assessed, outcomes, sample size and age of the subjects. The primary outcome was the prominence of the lower front teeth and the secondary outcomes were the relationship between the upper and lower jaws, psychosocial outcomes and patient satisfaction and jaw joint problems. Other outcomes were recorded for descriptive purposes e.g. relationship of the upper jaw (Sella-Nasion-A point), relationship of the lower jaw (Sella-Nasion- B point), and incisor angle to the lower jaw. Adverse effects, e.g. health of the gums, damage to the teeth e.g. tooth decay, would have been recorded and the results reported in descriptive terms.

Outcome data would have been grouped into those measured post phase I (growth modification phase) and post phase II (fixed brace phase) and, where available, post-retention outcomes would be recorded and reported. If outcome data were recorded at other time points, consideration would have been given to recording these as well.

3.2.3.3 Assessment of risk of bias in included studies

The Cochrane risk of bias tool was used to assess the methodological quality of the studies. This was undertaken independently and in duplicate by two review authors (from SW, JH or SF) as a part of the data extraction process. Six specific domains were investigated: sequence generation; allocation concealment; blinding of participants; personnel and outcome assessors; incomplete outcome data; selective outcome reporting and 'other sources of bias'.

Each domain was given a judgement that could be high, low or unclear. 'High' indicated and high risk of bias, 'Low' a low risk of bias and 'Unclear' indicated an unclear or unknown level of bias. The risk of bias tool was undertaken as described in the Cochrane Handbook for Systematic Reviews of Interventions. Sequence generation was assessed for the study as a whole. Blinding, incomplete outcome data and selective outcome reporting were assessed on the level of the study and for each outcome as appropriate.

3.2.3.4 Measures of Treatment Effect

The Cochrane Collaboration statistical guidelines were followed and the data analysed using RevMan and reported according to Cochrane Collaboration criteria.

For dichotomous data, the estimates of effect of an intervention would have been expressed as risk ratios together with 95% confidence intervals.

For continuous outcomes, mean differences and 95% confidence intervals were used to summarise the data for each group where the mean difference and standard deviations were calculable from the data presented.

3.2.3.5 Dealing with Missing Data

If there were any missing data, an attempt was made to contact the original trial investigators. A study was not excluded from the review because of missing summary data, however the potential implications of its absence from any meta-analysis were discussed.

3.2.3.6 Assessment of Heterogeneity

Clinical heterogeneity was assessed by examining the type of participants, interventions and outcomes in each study. Meta-analysis was only used when studies of similar comparisons were reporting comparable outcome measures. A random-effects model was planned for use for all analysis with more than three studies, otherwise a fixed-effect model was used. I^2 statistics were used as measures of statistical heterogeneity.

3.2.3.7 Assessment of Reporting Biases

Only a proportion of research projects conducted are ultimately published in an indexed journal and become easily identifiable for inclusion in systematic reviews. Reporting biases arise when the reporting of research findings is influenced by the nature and direction of the findings of the research.[102] We investigated and attempted to minimise potential reporting biases including publication bias, multiple (duplicate) publication bias and language bias in this review.

If there were more than ten studies in one outcome we planned to construct a funnel plot. If there was asymmetry in the funnel plot, indicating possible publication bias, we planned to undertake statistical analysis using the methods introduced by Egger (continuous outcome) and Rücker (dichotomous outcome).[103, 104] Insufficient studies were identified to investigate reporting biases.

3.2.3.8 Data Synthesis

A random-effects meta-analysis, using the inverse variance method, was planned for use for all primary and secondary outcomes for all analyses with more than three studies. Studies of each intervention were analysed and presented separately.

A general framework for data synthesis was used to report the adverse effects. The following questions were considered when analysing these effects:

- What was the size of the effect?

- Was the effect consistent across studies?

- What was the strength of evidence for the effect?

3.2.3.9 Subgroup analysis and investigation of heterogeneity

We planned to investigate clinical heterogeneity by examining: the nature of the interventions; ages; background and number of participants and reported outcomes. No subgroup analyses were planned.

3.2.3.10 Sensitivity analysis

Providing there were sufficient studies for each intervention and outcome, we planned to undertake sensitivity analysis based on risk of bias (including low risk of bias studies only).

3.2.3.11 Presentation of main results

A summary of findings table was developed for the primary outcomes of this review using GRADEPro software. The quality of the body of evidence was assessed with reference to the overall risk of bias of the included studies; the directness of the evidence; the inconsistency of the results; the precision of the estimates; the risk of publication bias and the magnitude of the effect. The quality of the body of evidence for each of the primary outcomes was categorised as high, moderate, low or very low and summary of findings tables have been produced for the main outcomes of this review.

Chapter 4: Results

4.1 Description of Studies

4.1.1 Results of the search

The database search found 440 articles. Of these 19 were duplicates. Of the remaining 421, 391 were discarded during the screening of the titles and abstracts. Of the remaining 30 articles, for which the full text was examined, 22 were excluded leaving 8 included articles, 2

of which were reporting the outcomes of the same study, at different time points, leaving 7

randomised controlled trials to be included in this review. (Figure 11)

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┌─────────────────────────────────────┐
│  440 records identified through database  │
│                                       │
│              searching                │
└─────────────────────────────────────┘
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│  421 records after duplicates removed │
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│     421 records screened      │───────▶│     391 records excluded      │
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┌─────────────────────────────────────┐           ┌─────────────────────────────────┐
│ 30 full-text articles assessed for   │ ────────> │ 22 records excluded             │
│ eligibility                          │           │                                 │
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│ 7 trials (2 articles reporting the   │
│ same study)                          │
│ included in the qualitative synthesis│
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│ 7 trials included in quantitative    │
│ synthesis                            │
│ (meta-analysis)                      │
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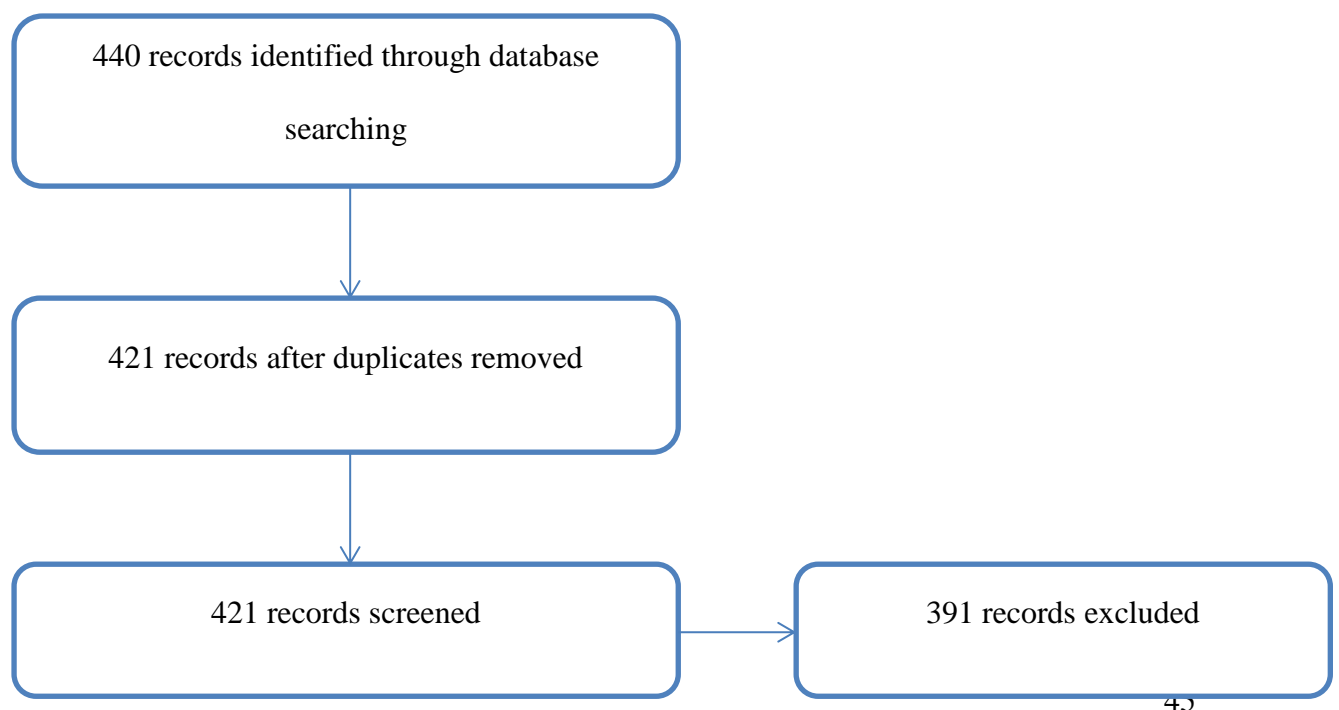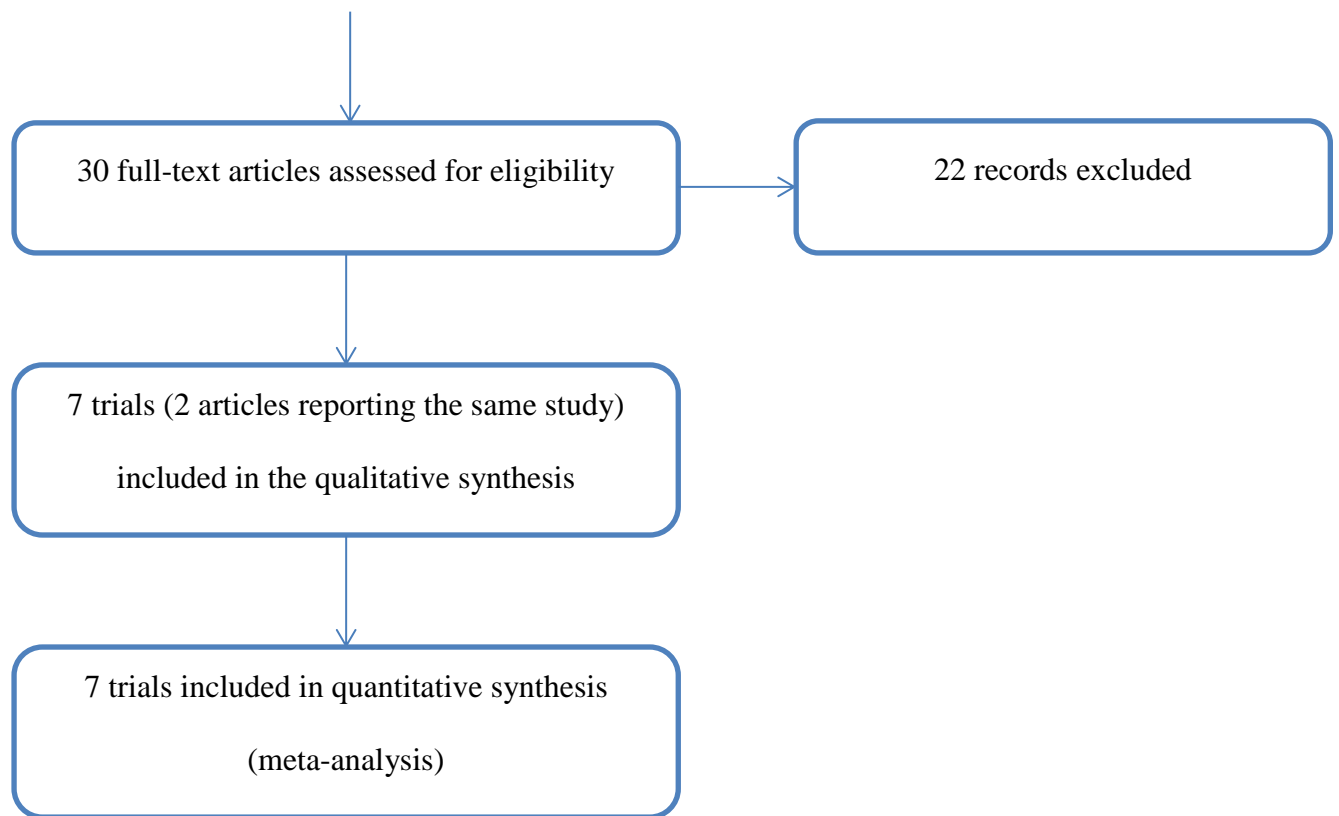
Figure 11: Study flow diagram

4.1.2 Included studies

Seven trials were included in this review (see Table 2). All trials were parallel randomised controlled trials. Three trials were conducted in Turkey,[87, 105, 106] one in Egypt,[33] one in the United Kingdom,[72, 107] one in the United States of America,[81] and one in China.[108] Six trials reported outcome data solely immediately post treatment. One trial had outcomes reported at both 15 months and 3 years after the start of treatment.[107] (see Appendix 5)

4.1.2.1 Characteristics of the trial setting and investigators

All of the included trials were conducted in college/university orthodontic departments. Six of the trials were carried out in a single institution,[33, 81, 87, 105, 106, 108] one in 8 centres in the same country.[72, 107]

Orthodontists provided the care for the children in all the trials. Only one paper stated they had 2 operators,[81] the remainder did not disclose the number of operators.

Only one trial disclosed external funding.[72, 107]

4.1.2.2 Characteristics of the participants

All trials were conducted on children aged between 5 and 11 years. They were from different ethnic backgrounds, dependant on the trial setting. There were between 20[105] and 73[72] children included in the 7 trials, with a median of 46. Approximately equal numbers of boys and girls were included in each trial.

4.1.2.3 Characteristics of the interventions

Four different types of intervention and an untreated control group were compared in the 7 included trials. The comparisons were:

- Facemask versus Untreated Control[72, 81, 107, 108]

- Facemask with expansion versus Facemask only[81]

- Nanda facemask versus Conventional facemask[105]

- 600g Chin cup versus 300g Chin cup versus Untreated Control[33]

- Tandem traction bow appliance versus Untreated Control[87]

- Mandibular headgear versus Chin cup versus Untreated Control[106]

Characteristics of the outcomes

Five outcomes were presented in the results for the 7 included trials.

- Overjet[72, 87, 107]

- ANB[33, 72, 81, 87, 105-108]

- Wits appraisal[33, 81]

- Piers Harris children's self-concept scale[72, 107]

47

- Oral Aesthetic Subjective Impact Score (OASIS)[72, 107]

Study	Country	Interventions	Number of participants	Outcomes measured
Abdelnaby and Nasser[33]	Egypt	300g chin cup 600g chin cup Untreated control	50	ANB Wits
Arun et al.[106]	Turkey	Mandibular headgear Chin cup Untreated control	60	ANB
Atalay and Tortop[87]	Turkey	TTBA Untreated control	30	Overjet ANB
Keles et al.[105]	Turkey	Nanda facemask Conventional facemask	20	ANB
Mandall et al.[72, 107]	UK	Facemask Untreated control	73	Overjet ANB Piers Harris children's self-concept scale OASIS
Vaughn et al.[81]	USA	Facemask with expansion Facemask without expansion	46	ANB Wits

Xu[108]	China	Facemask Untreated control	60	ANB

Table 2: Summary of characteristics of included trials

4.1.3 Excluded studies

A reason for exclusion of each trial of which the full text was assessed is given in Appendix 6. Of the 22 excluded studies:

- 13 were excluded as they were not RCTs

- 6 used retrospective control groups

- 1 was entirely retrospective

- 1 did not report an outcome of interest to this review

- 1 reported outcomes for patients over age 16.

4.2 Risk of bias in included studies

The risk of bias assessment for each trial can be found in Appendix 7.

4.2.1 Allocation (selection bias)

4.2.1.1 Sequence Generation

Sequence generation was adequate for four of the trials[72, 81, 87, 106, 107] and unclear for the remaining trials. Whilst the Arun et al.[106] and Atalay and Tortop[87] papers were unclear in the text, contact with the authors revealed the use of a random number generator for patient

assignment on registration to the trial. Mandall et al.[72, 107] used randomisation blocks of 10 with stratification according to gender and a computer generated randomisation sequence. Vaughn et al.[81] also used a block randomisation table to assign to one of the 3 groups. The remaining papers did not mention how a sequence was generated and no response has been received from the authors for further clarification.

4.2.1.2 Allocation concealment

Allocation concealment was adequate in only the Mandall et al. trial,[72, 107] using a sequence that was concealed centrally and each clinician telephoned the research assistant for allocation once the patient was registered. It was unclear for four of the trials,[33, 81, 105, 108] in which there was no mention of allocation concealment in the articles and there has been no response from the authors to clarify. There was a high risk of bias from the remaining two articles with whom contact was made and they disclosed that no allocation concealment was used.[87, 106]

4.2.2 Blinding (performance bias and detection bias)

The blinding of participants would not have been possible in 6 of the 7 trials due to the nature of the treatments in comparison with other treatments and the untreated controls. However, it may have been possible to blind patients in the Abdelnaby and Nassar trial that compared the strength of force of the chin cups.[33] No mention of an attempt to do this was mentioned in the paper and the author has not responded to clarify the situation.

The blinding of the personnel taking part in the trials would not have been possible due to the nature of the treatments being used.

The blinding of the outcome assessment would have been possible in all cases as cephalometric measures were used as outcomes in all trials. There was a low risk of bias in the Mandall et al. trial in which the researchers measuring the radiographs and study models, as well as the statistician, were all blinded.[72] There was also low risk of bias in the Vaughn et

al. trial as the principal investigator carrying out the analysis was blinded to the patient assignment.[81] The blinding of outcome assessment was unclear in the Abdelnaby and Nassar, Keles et al. and Xu trials in which no mention of blinding was made and no response from the authors has been received to clarify.[33, 105, 108] The authors of the Arun et al. and Atalay and Tortop trials confirmed that there were no attempts at blinding at any stage in these trials and therefore the risk of bias is high.[87, 106]

4.2.3 Incomplete outcome data (attrition bias)

There was a low risk of attrition bias for the Arun et al., Atalay and Tortop, Mandall et al. and Xu trials as the participants included in the analysis are exactly those randomised in the trial.[72, 87, 106, 107, 108] The number of dropouts in the remaining three trials is unclear and the authors have not responded to clarify, so the risk of attrition bias in these trials was assessed as unclear.[33, 81, 105]

4.2.4 Selective reporting (reporting bias)

There is a low risk of reporting bias for all trials. All trials reported on the outcomes that they set out to report and there were no obvious anomalies.

4.2.5 Other potential sources of bias

The Abdelnaby and Nassar trial states that the groups are randomly allocated yet has 20 patients in groups 1 and 2 and only 10 in group 3.[33] Clarification on the exact method of randomisation has not been possible as the author has not responded to contact, however this leads to an assumption of high risk of bias.

The authors of the Arun et al. and Atalay and Tortop trials have clarified all our questions regarding other bias, and have been assessed at low risk of other bias.[87, 106]

The Mandall et al. paper disclosed that some patients included in this trial had a centric relation to centric occlusion displacement.[72, 107] This may have influenced the perception of the skeletal discrepancy from the lateral cephalogram. The actual effects of this on the results are uncertain. Randomisation of groups, which was carried out adequately, should have minimised any bias introduced by this and therefore the study has still been graded as being of low risk of bias.

There are no other obvious potential sources of bias for the Keles et al. or Vaughn et al. trials.[81, 105]

4.2.6 Overall risk of bias

The trial by Mandall et al. shows overall low risk of bias.[72, 107] Three trials are assessed at high risk of bias due to the absence of allocation concealment and blinding of outcome assessment (Arun et al. and Atalay and Tortop) and inadequate randomisation (Abdelnaby and Nassar).[33, 87, 106] The remaining three trials (Keles et al., Vaughn et al. and Xu) are assessed as unclear risk of bias.[81, 105, 108] These conclusions can be seen in Figures 13 and 14.
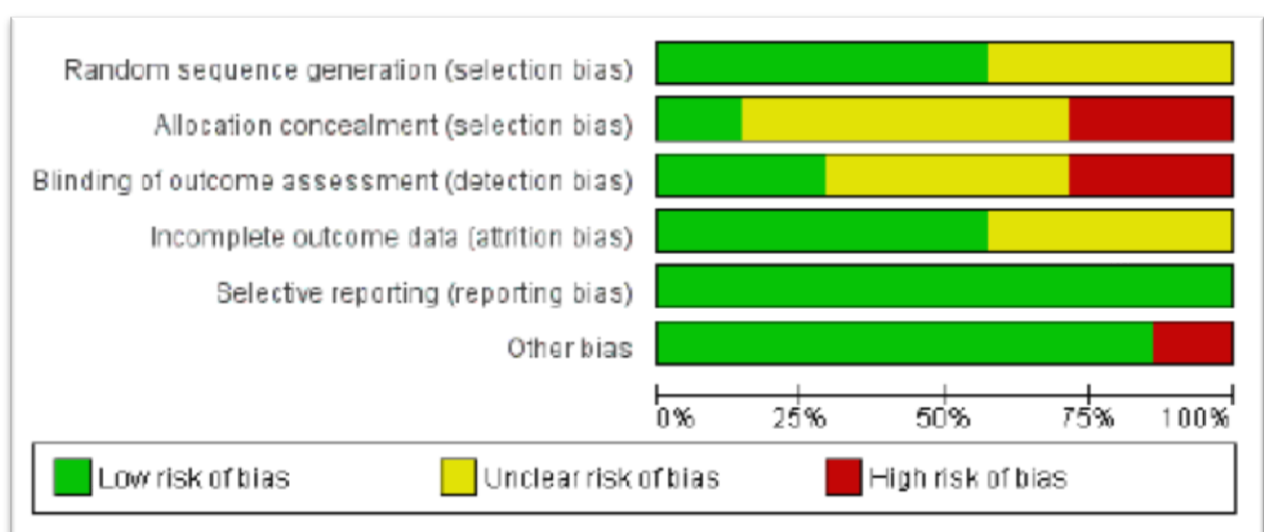
Figure 13: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included trials.

Figure 14: Risk of bias summary: review authors' judgements about each risk of bias item for each included trial.

4.3 Effects of interventions

There were 8 comparisons in the 7 included trials. The results for each comparison are summarised below. All data and analysis tables can be found in Appendix 8 (Tables 3-11, Figure 15).

4.3.1 Facemask versus Untreated control

Three trials investigated the use of a facemask versus an untreated control (Mandall et al., Vaughn et al. and Xu).[72, 81, 107, 108] I have combined the results from the trial using the facemask with and without rapid maxillary expansion as they showed no statistical difference (see later).[81] The only outcome considered by all three trials was ANB. The Mandall et al. trial also assessed overjet and self-concept measures whilst Vaughn et al. also assessed Wits appraisal (another measure of the relative positions of the maxilla and mandible).[72, 81, 107] The Mandall et al. trial reported outcomes at the end of treatment and at 3 years' follow-up.[72, 107] (See Tables 3, 4)

4.3.1.1 Overjet

The Mandall et al. trial was the only one that reported overjet and found a statistically significant difference of 4.10 mm (95%CI 3.04 to 5.16; P<0.0001) in favour of the facemask post-treatment.[72, 107] They also found a statistically significant difference of 2.50 mm (95%CI 1.21 to 3.79; P=0.0001) at 3 years' follow-up.[107]

4.3.1.2 ANB

Three trials included the outcome ANB (Mandall et al., Vaughn et al. and Xu),[72, 81, 107, 108] and it was possible to undertake a meta-analysis at the post-treatment stage. The pooled estimate was 3.93 degrees (95% CI 3.46 to 4.39; P<0.0001) in favour of the facemask. There was substantial heterogeneity (P=0.004; I^2=82%) between the trials which may be due to several factors including: different inclusion criteria, different ethnic groups, different populations and different ages of the patients at the start of treatment. However, each trial demonstrated a statistically significant benefit for the facemask and we thought it appropriate to pool the

results. The random effects model gave rise to a similar estimate of 3.70 degrees (95%CI 2.50 to 4.91; P<0.0001). (See Figure 15)

The Mandall at al. trial assessed ANB at 3 years' follow-up and found that the statistically significant benefit of 1.4 degrees (95%CI 0.43 to 2.37; P=0.004) persisted in favour of the facemask.[107]

4.3.1.3 Wits appraisal

The Vaughn et al. trial looked at Wits and showed a benefit in favour of the facemask of -3.84 mm (95%CI -5.31 to -2.37; P<0.0001).[81]

4.3.1.4 Psychosocial Outcomes

There was no difference between the facemask and untreated control groups in the Mandall et al. trial in the outcome of self-concept measured on the Piers-Harris self-concept index at either the post-treatment or 3 year follow-up time points.[72, 107]

The OASIS assessment of oral self-perception, however, did demonstrate a statistically significant benefit for the facemask at the post-treatment stage of -4.00 (95%CI -7.40 to -0.60; P=0.02). However, there was no significant difference at 3 years' follow-up: -3.40 (95%CI -7.99 to 1.19; P=0.15).[72, 107]

4.3.1.5 Adverse Effects

Only the Mandall et al. trial reported on temporomandibular joint (TMJ) signs and symptoms. It noted that due to low prevalence of TMJ signs and symptoms at all time points no statistical analysis was carried out.[72, 107]

4.3.2 Facemask with expansion versus Facemask only

The Vaughn et al. trial compared the facemask with and without expansion.[81] There was no evidence of a difference between treatment using a facemask with or without the use of rapid maxillary expansion for the outcomes of ANB (-0.13 degrees (95%CI -1.40 to 1.14; P=0.84)) and Wits (-0.16 mm ((95%CI -1.63 to 1.31; P=0.83)). (See Tables 3, 5)

4.3.3 Nanda facemask versus Conventional facemask

The Keles et al. trial compared Nanda facemask versus Conventional facemask.[105] There was weak evidence of a difference in ANB between the groups using each design of facemask in favour of the Nanda facemask: 1.29 degrees (95%CI 0.16 to 2.42; P=0.02). (See Tables 3, 6)

4.3.4 Chin cup (600g and 300g) versus Control, and 600g vs 300g

The Abdelnaby and Nassar trial compared 600g and 300g chin cup with an untreated control group in a three arm trial.[33] Both chin cup groups had improved ANB and Wits when compared to the untreated control:

- 600g ANB 2.00 degrees (95% CI 1.61 to 2.39; P<0.001)

- 300g ANB 1.90 degrees (95%CI 1.43 to 2.37; P<0.001)

- 600g Wits 4.80 mm (95%CI 4.13 to 5.47; P<0.0001)

- 300g Wits 5.10 mm (95%CI 4.43 to 5.77; P<0.0001)

With respect to 600g versus 300g chin cup there was no difference in ANB (0.10 degrees (95%CI -0.31 to 0.51; P=0.63)) or Wits (-0.30 mm (95%CI -1.12 to 0.52; P=0.47)). (See Tables 3, 7, 8, 9)

4.3.5 Tandem traction bow appliance versus Untreated control

The Atalay and Tortop trial compared Tandem traction bow appliance with an untreated control.[87] Two outcomes, overjet and ANB were reported and both demonstrated a statistically significant benefit in favour of the Tandem traction bow appliance. Overjet 3.30 mm (95%CI 2.46 to 4.14 P<0.0001); ANB 1.70 degrees (95%CI 1.09 to 2.31; P<0.0001). (See Tables 3, 10)

4.3.6 Mandibular headgear versus Chin cup versus Untreated control

The Arun et al. trial compared mandibular headgear or a chin cup with an untreated control.[106] It provided outcome data for ANB, however no standard deviations were given and P-values from the Mann Whitney test were presented, so I was unable to use the data. Both mandibular headgear and chin cup showed statistically significant benefit for ANB compared to the control P<0.001; however, there was no statistically significant difference between the two active interventions (P>0.05). (See Table 11)

Chapter 5: Discussion

5.1 Summary of main results

5.1.1 Facemask Therapy

There was some evidence that facemask therapy was more effective at improving overjet, ANB and Wits appraisal immediately post treatment when compared with an untreated control. The improvements in overjet and Wits were still statistically significant at 3 years' follow-up, although reduced in comparison to the changes immediately post-treatment. These changes can still be considered to be of clinical significance. Whilst immediately following treatment there was a statistically significant improvement in the OASIS score, there was no evidence that facemask treatment produced clinically important changes in patients' self-concept or self-perception measures.

There was insufficient evidence to determine whether there was a difference between the outcomes reported in a comparison between facemask with and without the use of rapid maxillary expansion from the single small trial which evaluated this comparison. Therefore, its use solely as an adjunct to improve the efficacy of facemask therapy, can not be recommended.

One trial compared the use of a Nanda facemask (force applied at parallel to the Frankfort plane at a level 20mm above the occlusal plane) with a conventional facemask (force applied at 30 degrees at the level of the occlusal plane).[105] This very small trial showed weak evidence of a difference in ANB between the two appliances in favour of the Nanda facemask, however due to the size of the trial and its risk of bias no recommendation can be made to support one design over the other.

The ultimate aim of facemask treatment is to correct the jaw discrepancy at an early stage so reducing the need for any orthognathic surgical intervention at a later stage. It must be noted that only one published trial has reported data beyond the end of orthodontic treatment,[107] and this only at 3 years' follow-up, so no evidence was found for a long term benefit for facemask

therapy beyond 3 years. Discussion with the authors of this trial has revealed that the trial is on-going. The final report of this trial is due for publication in the near future and we hope it will be included in future issues of this review. For ethical reasons there is a limit as to how long treatment can be withheld from a patient and, therefore, a limit as to how long term a trial of this nature can be followed up. We hope that the final results of the trial will give us an indication as to what percentage of patients avoided a surgical intervention to correct their malocclusion due to the early intervention with the facemask.

The papers by Mandall et al. were overall of low risk of bias, however, one potential area for bias was noted.[72, 107] Some of the patients had a displacement from centric relation into maximum intercuspation. The lateral cephalograms and overjet measurements were taken in maximum intercuspation. Therefore, this may have made the pre-treatment overjet and ANB appear worse than was actually the case, so influencing the results. Whilst the overall impact of this on the results is unclear it must be considered a potential source of bias in the trial design.

Only one trial reported on adverse effects and showed no changes in TMJ signs and symptoms as a result of facemask therapy.[72]

5.1.2 Chin cup Therapy

There were two trials showing evidence that the use of a chin cup led to statistically significant benefit in ANB when compared to an untreated control.[33, 106] A meta-analysis was not possible due to missing data from one trial.[106] Again, the trials were short-term and there was no evidence of any long term benefit.

There was no statistically significant difference found between the use of 300g and 600g force when used with the chin cup.

These trials were of high risk of bias and as such their results should be interpreted with caution. At this stage the authors are unable to recommend the use of the chin cup for early correction of a Class III malocclusion.

5.1.3 Tandem Traction Bow Appliance (TTBA)

One trial reported results on the use of the TTBA when compared with an untreated control.[87] It showed that there was a statistically significant benefit in favour of the TTBA. Again, the trial was short term and there was no evidence for long term benefit. In addition, the trial was of high risk of bias and therefore even the short term results should be interpreted with caution.

5.1.4 Mandibular Headgear

One trial reported results on the use of mandibular headgear compared to an untreated control and the chin cup.[106] Statistical analysis was not possible due to missing data, however, it was reported that there was significant benefit in favour of the mandibular headgear with respect to ANB when compared to the untreated control. There was no statistically significant difference between the mandibular headgear and the chin cup. In addition, this trial was of high risk of bias and therefore all results should be interpreted with caution.

5.2 Overall completeness and applicability of evidence

Overall, seven trials were found investigating multiple comparisons to treat Class III incisors in children and adolescents and reported multiple outcomes. Four of the trials investigated the facemask, two the chin cup, one TTBA and one mandibular headgear. Only one investigated beyond the treatment phase and that only at 3 years' follow-up. This has major implications

for the applicability of the evidence. An aim of early intervention for a Class III malocclusion is to prevent subsequent need for corrective orthognathic surgery. The current evidence does not allow us to assess if any of the interventions have succeeded in this aim, due to their short term nature.

The concern of many patients seeking treatment for a Class III malocclusion is that their lower front teeth meet in front of their upper front teeth and therefore they have a reverse overjet. The patients are unaware of their cephalometric measurements and the use solely of these measures does not allow adequate assessment of patient-centred outcomes. However, only two of the trials reported overjet as an outcome.[72, 87] This must be considered a significant flaw in the current evidence. Whilst cephalometric measurements can be useful indicators for clinical benefit, they mean little to a patient. Large changes in a patients ANB or Wits appraisal do not necessarily mean that the treatment outcome has been successful. Future research must aim to report outcomes of interest to patients. I therefore recommend a much greater use of patient-centred outcomes and patient satisfaction measurements, with less emphasis on the use of cephalometric measurements as primary outcomes.

The use of a sample size calculation allows the researcher to be sure that there is sufficient power in the trial design that if a true difference exists then the trial should detect it. It can prevent the waste of research resources and also prevent undue inclusion of excessive patient numbers which may be considered unethical. Only one trial carried out a sample size calculation,[72, 107] and it is possible that the Vaughn et al. trial was underpowered to find a difference between their facemask groups.[81]

The lack of accurate reporting, especially with respect to unclear methodology, and in one case, missing statistical data, means much of the evidence was of low or very low quality and overall the results must be interpreted with caution.

5.3 Quality of the evidence

The overall quality of the evidence can be seen in the Summary of Findings tables (Tables 12, 13, 14)

The evidence regarding overjet and ANB changes, when comparing the use of a facemask with an untreated control, has been graded as moderate. This implies that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate but is unlikely to overturn the direction of the effect.

All other comparisons and outcomes have been graded as a low or very low level of evidence. The reasons for this are the low number of trials and participants, the unclear or high risk of bias in these trials and in the meta-analysis, the high level of heterogeneity.

5.4 Potential biases in the review process

The manner in which a Cochrane systematic review is undertaken minimises the risk of bias being introduced into the review. Bias has been reduced in this systematic review by using a broad sensitive search of multiple databases with no restrictions on language. We have also searched for unpublished studies and data, and included studies reported in all languages (involving the translation of one Chinese paper and several Turkish papers).

5.5 Agreements and disagreements with other studies or reviews

Five other reviews were found that reported on similar comparisons and outcomes to this study.[83, 109, 110, 111, 112]

de Toffol et al., Jager et al. and Kim et al. all report with greater confidence the efficacy of the facemask than we have reported.[83, 109, 111] The difference in confidence is due to the greater number of studies that the other systematic reviews have included. This discrepancy is due to the differing inclusion criteria used in our systematic review when compared to the previous reviews. We have only included prospective randomised controlled trials, whilst the

other reviews have included retrospective studies. This is inherent in the methodology used in a Cochrane systematic review when compared with other reviews. Whilst the inclusion of a greater number of studies and, therefore, a greater number of participants allows a more powerful result to be produced it inevitably allows a much greater influence of bias. Therefore, the results of this systematic review are more reliable than those that were carried out previously. From the results that we have obtained only the paper by de Toffel et al. has included any of the studies on facemasks that we have included.[109]

The review by Kim et al. supports the use of rapid maxillary expansion prior to facemask therapy, whilst we have found insufficient evidence to support this protocol.[83] Again, the difference is due to the inclusion of retrospective studies in the previous review. Only one randomised controlled trial has been carried out in this area and this showed no significant differences.[81] The recommendations made by Kim et al. were based on two retrospective studies.

Liu et al. reports on the efficacy of the chin cup appliance and agrees with our conclusion that there are insufficient data in the current trials to make clear recommendations regarding the efficacy of chin cup therapy.[112] This review, whilst allowing controlled clinical studies and cohort studies, was closer in nature to a Cochrane systematic review and therefore explains why the results in this area were similar.

5.6 Implications for practice

At the current stage there is insufficient evidence to recommend the use of chin cups, mandibular headgear or the TTBA. There is evidence that the use of a facemask produces short term improvements in overjet and ANB. However, the aim of early interventions may

be considered two-fold. Firstly, they aim to correct the presenting malocclusion in an attempt to reduce the need for later intervention, which in this case will usually involve the use of orthognathic surgery. Whilst the evidence thus far suggests that they are effective at correcting the presenting Class III malocclusion, it does not allow us to know whether the use of the facemask reduces the need for later intervention. It is hoped that the results of the on-going trial by Mandall et al., combined with future research, may allow a greater understanding of the effectiveness of the facemask at reducing later surgery. Secondly, early intervention may reduce the psychosocial impact of the malocclusion. If the child is being teased or bullied due to their malocclusion it would be hoped that if there is an early intervention to reduce this malocclusion, the teasing and bullying will be reduced and therefore psychosocial measures will be improved. The evidence from the only trial using these measures suggests that up to 3 years after treatment this is not the case.[107] Therefore, at this time, early intervention in order to improve the psychosocial impact of the malocclusion, can not be recommended.

5.7 Implications for Research

This review has shown that there is only one trial in this field that has been carried out with an overall low risk of bias, and there was possible methodological bias even with this trial, due to the inclusion of children with a displacement from centric relation to maximum intercuspation. In order for clinicians to be carrying out sound evidence based treatments, the evidence should be of the highest standard. Therefore, there needs to be considerably more research carried out in this field, and that research should be carried out to a much higher standard than the majority of existing studies have been.

When designing future trials, the following need to be considered:

- Clear inclusion and exclusion criteria should be set.

- An a priori sample size calculation should be carried out.

- The use of outcomes relevant to the patient (not solely a list of cephalometric measures) should be used. The following are recommended:

  - Overjet

  - Overjet change.

  - Correction of an anterior crossbite.

  - ANB.

  - Psychosocial measures.

- The following methodological points are recommended:

  - Recording if there is a discrepancy between centric relation and maximum intercuspation.

  - All lateral cephalograms should be taken in the centric relation.

- Adverse effects should be reported

- Long term follow-up, to assess fully if the treatment has been successful at the end of growth, should be considered.

Reports on clinical trials would be improved by following the guidelines produced by the CONSORT Group to ensure that all relevant information is provided.[113]

If these recommendations are followed it will allow much more reliable conclusions to be drawn in future issues of this review and therefore allow clinicians to base their treatment decisions on much greater evidence base.

Chapter 6: Conclusions

6.1 Overall Conclusions

There is some evidence that the use of facemask therapy, between the ages of 6-10 years, leads to short term improvements in overjet and ANB. These improvements have been shown, in high level evidence, to be maintained until 3 years after treatment.

There is insufficient evidence to support the use of any other intervention for the early treatment of a child with Class III incisors.

There is insufficient long term evidence to fully understand the benefit of early intervention for a patient with Class III incisors.

6.2 Implications for practice

There is some evidence to support the use of the facemask for early treatment of Class III incisors. The long term benefits, however, are still unknown.

There is insufficient evidence to support the use of any other appliance for early treatment of Class III incisors.

6.3 Implications and recommendations for research

In view of the quality of the trials identified in this systematic review, it has been difficult to draw definitive conclusions. This review suggests the need for more long term, well designed and reported randomised controlled clinical trials to assess the efficacy of early orthodontic treatment for prominent lower front teeth. When designing future trials, consideration should be given to use of the recommendations made in the discussion.

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Appendix 1: Cochrane Oral Health Group Trials Register Search Strategy

A search was undertaken using the Cochrane Register of Studies and the search strategy below:

 #1   ("prominent lower front teeth" or underbite* or under-bite* or "under bite*" or reverse-bite* or "reverse bite*" or prognath* or "Malocclusion Angle Class III" or "Angle* class III") AND (INREGISTER)

#2   (("Class III" AND (malocclusion or bite))) AND (INREGISTER)

#3   (#1 or #2) AND (INREGISTER)

#4   (("orthodontic appliance*" OR "orthodontic device*" OR "removable appliance*" OR "removable device*" OR "functional appliance*" OR "functional device*" OR "fixed appliance*" OR "growth modif*" or brace* OR ((extraoral OR "extra oral" or extra-oral) AND traction) OR "chin cap*" or chin-cap* or chincap* OR "chin cup*" or chin-cup* or chincup* or "face mask*" OR facemask* or face-mask* OR "reverse head gear" OR "reverse head-gear")) AND (INREGISTER)

#5   (((orthopedic* OR orthopaedic*) AND (dental OR orthodontic* OR facial))) AND (INREGISTER)

#6   (#4 or #5) AND (INREGISTER)

#7   (#3 AND #6) AND (INREGISTER)

 A previous search of the Register was undertaken in July 2011 using the Procite software and the search strategy below:

(("prominent lower front teeth" or underbite* or under-bite* or "under bite*" or reverse-bite* or "reverse bite*" or prognath* or "Malocclusion Angle Class III" OR "Angle* class III" OR ("Class III" AND (malocclusion* OR bite))) AND ("orthodontic appliance*" OR "orthodontic device*" OR "removable appliance*" OR "removable device*" OR "functional appliance*" OR "functional device*" OR "fixed appliance*" OR "growth modif*" or brace* OR ((extraoral OR "extra oral" or extra-oral) AND traction) OR "chin cap*" or chin-cap* or chincap* OR "chin cup*" or chin-cup* or chincup* or "face mask*" OR facemask* or face-mask* OR "reverse head gear" OR "reverse head-gear" OR ((orthopedic* OR orthopaedic*) AND (dental OR orthodontic* OR facial))))

Appendix 2: Cochrane Central Register of Controlled Trials (CENTRAL) Search Strategy

#1   MeSH descriptor Malocclusion, Angle Class III

#2   ("Class III" in All Text and (Angle in All Text or Angle's in All Text or malocclusion* in All Text or bite* in All Text))

#3   (underbite* in All Text or under-bite* in All Text or "under bite*" in All Text or "reverse bite*" in All Text or reverse-bite* in All Text or prognath* in All Text)

 #4   "prominent lower front teeth"

#5   (#1 or #2 or #3 or #4)

#6   MeSH descriptor Orthodontic Appliances, Functional explode all trees

 #7   MeSH descriptor Orthodontic Appliances, Removable explode all trees

#8   ("growth modif*" in All Text and (jaw in All Text or maxilla* in All Text or mandible in All Text))

#9   (("fixed appliance*" in All Text or brace* in All Text) and orthodontic* in All Text)

#10   ((extraoral in All Text or extra-oral in All Text or "extra oral" in All Text) and traction in All Text)

#11   ("chin cap*" in All Text or chin-cap* in All Text or chincap* in All Text)

#12   (("face mask*" in All Text or face-mask* in All Text or facemask* in All Text or "reverse head-gear" in All Text or "reverse headgear" in All Text) and orthodontic* in All Text)

#13   ((orthopedic* in All Text or orthopaedic* in All Text) and (dental in All Text or orthodontic* in All Text or facial in All Text))

#14   (#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13)

#15   (#5 and #14)

Appendix 3: MEDLINE (OVID) Search Strategy

1. Malocclusion, Angle Class III/

2. ("Class III" and (Angle or Angle's or malocclusion$ or bite$)).mp.

3. (underbite$ or under-bite$ or "under bite$" or "reverse bite$" or reverse-bite$ or prognath$).mp.

4. "prominent lower front teeth".mp.

5. or/1-4

6. exp Orthodontic Appliances, Functional/

7. exp Orthodontic Appliances, Removable/

8. ("growth modif$" and (jaw or maxilla$ or mandible)).mp.

9. (("fixed appliance$" or brace$) and orthodontic$).mp.

10. ((extraoral or extra-oral) and traction).mp.

11. "chin cap$".mp.

12.   (("face mask$" or facemask$ or face-mask$ or "reverse head-gear" or "reverse headgear") and orthodontic$).mp.

13.   ((orthopedic$ or orthopaedic$) and (dental or orthodontic$ or facial)).mp.

14.   or/6-13

15.   5 and 14

The above subject search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomized trials in MEDLINE: sensitivity maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of The Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0 [updated March 2011].

1. randomized controlled trial.pt.

2. controlled clinical trial.pt.

3. randomized.ab.

4. placebo.ab.

5. drug therapy.fs.

6. randomly.ab.

7. trial.ab.

8. groups.ab.

9. or/1-8

10. exp animals/ not humans.sh.

11. 9 not 10

Appendix 4: EMBASE (OVID) Search Strategy

1.   Malocclusion/

2.   ("Class III" and (Angle or Angle's or malocclusion$ or bite$)).mp.

3.   (underbite$ or under-bite$ or "under bite$" or "reverse bite$" or reverse-bite$ or prognath$).mp.

4.   "prominent lower front teeth".mp.

5.   or/1-4

6.   Orthodontic device/

7.   ("growth modif$" and (jaw or maxilla$ or mandible)).mp.

8.   (("fixed appliance$" or brace$) and orthodontic$).mp.

9.   ((extraoral or "extra oral" or extra-oral) and traction).mp.

10.   ("chin cap$" or chin-cap$ or chincap$).mp.

11.   ((facemask$ or face-mask$ or "face mask$" or "reverse headgear" or "reverse head-gear") and orthodontic$).mp.

12.   ((orthopedic$ or orthopaedic$) and (dental or orthodontic$ or facial)).mp.

13.   or/6-12

14.   5 and 13

Appendix 5: Characteristics of Included Studies:

Abdelnaby 2010

Methods	3 arm parallel randomised controlled trial
Participants	**Number recruited:** 50 growing patients (26 males and 24 females) **Mean age:** 9.7 years (range not given) **Inclusion criteria:** Patients had skeletal Class III (ANB < 1 degree) and mandibular prognathism (SNB > 80 degrees) and an anterior crossbite. Assessed for skeletal maturation with hand-wrist radiographs and shown to have not passed the peak of the pubertal growth spurt. **Exclusion criteria:** Not reported **Setting:** Recruited from the Faculty of Dentistry, Mansoura University, Mansoura, Egypt.
Interventions	**Comparisons:** 600g Chin cup versus 300g Chin cup versus Untreated control. Group 1: Occipital pull soft chin cup (Dentaurum, Ispringen, Germany) with an acrylic occlusal bite plane of a thickness that just freed the occlusion anteriorly. Force applied was 600g force per side. Patients were instructed to wear the appliance for 14 hours each day. (n=20) Group 2: As above using 300g per side. (n=20) Group 3: No orthodontic or orthopaedic treatment (n=10)
Outcomes	All measures taken prior to treatment and after 1 year. Outcomes relevant to the review: ANB, Wits
Notes	Sample size calculation was not described

Arun 1994

Methods	3 arm parallel randomised controlled trial
Participants	**Number recruited:** 60 patients (26 males and 34 females). **Mean age:** 8.23 years. Range 7.44 to 8.97 years **Inclusion criteria:** ANB<2.5 degrees, Jarabak ratio greater than 59%, antegonial notch depth less than 2mm. **Exclusion criteria:** Not reported **Setting:** Treated in the Marmara University Dental Faculty, Turkey.
Interventions	**Comparisons:** Mandibular headgear versus Chin cup versus Untreated control. Group 1: Mandibular headgear group: Prefabricated tubeless bands were thoroughly adapted to the lower molar teeth. They were then removed from the mouth and orthobuccal tubes were spot welded in the middle of their buccal surfaces. The bands were seated back on the molar teeth and a facebow, with downward facing U bends of its inner bow, was inserted in to the tubes. The desired force was applied to the facebow. The bands were cemented and the patients instructed to use their appliance 24 hours later. The outer bow was initially positioned parallel to the inner bow. Later, its arms were bent downwards in the parallel position. (n=20) Group 2: Chin-cap group: Force directed obliquely on a line from the symphysis to the condyle. The head straps of the chin cap passed 1cm above the earlobes in the temporal region and enwrapped the cranial vault. Topical application of the talcum powder was recommended in case the metal connections of the chin cap caused allergic reactions. In both treatment groups, the first review was one week after the insertion of the appliance and thereafter at three week intervals. Both groups were advised to use the appliances 16 hours per day during the one year treatment period. Forces were maintained at 480-500g in both groups. The effects of any anterior crossbite were eliminated and the mandibular distal movement freed from occlusal interferences through application of posterior bite planes. (n=20) Group 3: No treatment. (n=20)
Outcomes	Open and closed mouth lateral cephalograms were taken of all 60 patients at the beginning and end of the 12 month treatment and control period. The condylion point was first traced on the open-mouth lateral cephalogram then, using its mandibular projection as a guide, it was superimposed on the closed-mouth lateral cephalogram on which 18 cephalometric points were selected for analysis. Outcomes relevant to this review: ANB

Notes	Sample size calculation was not described

Atalay 2010

Methods	2 arm parallel randomised controlled trial
Participants	**Number recruited:** 30 patients (16 males and 14 females) **Mean age:** 8.04 years.

	Inclusion criteria: Skeletal Class III (ANB < 0 degree), due to maxillary retrusion, or a combination of maxillary retrusion and mandibular protrusion. Angle Class III malocclusion with an anterior crossbite. An optimum SN/GoGn angle (between 26 and 38 degrees). Fully erupted maxillary incisors. **Exclusion criteria:** Congenitally missing teeth or congenital syndromes such as a cleft lip/palate. Previous orthodontic treatment. **Setting:** Patients recruited from Gazi University, Turkey
Interventions	**Comparison:** Tandem Traction Bow Appliance (TTBA) versus Untreated control. Group 1: The modified tandem traction bow appliance: After dental casts were obtained, a wax construction bite was obtained with a 5-6 mm vertical opening at the molar region and without any sagittal activation. The modified TTBA comprised an upper splint, a lower splint, and a traction bow. The upper splint had Adams' clasps in the posterior region for retention and elastic hooks between the maxillary central and lateral incisors. The upper splint covered the palatal and occlusal surfaces, in addition to 1–2 mm of the buccal surfaces of the maxillary teeth. The lower splint covered the buccal and lingual surfaces of the mandibular teeth. Activator tubes were embedded in the posterior region of the lower splint. A conventional headgear facebow was modified and used as the traction bow. The outer bows of the face bow were cut to approximately 3 cm and shaped as a letter 'S'. Two elastics that exerted a force of 400–500g on one side were worn between the labial hooks and the traction bow. The elastic force was directed between 35 and 40 degrees to the occlusal plane by arranging the position of the outer traction bows. The patients were instructed to wear the appliance approximately 14–16 hours a day. The average treatment time for this group was 9 months. (n=15) Group 2: Control group: Observed without treatment for 8 months. (n=15)
Outcomes	Lateral cephalometric radiographs were taken before treatment and after a Class I molar relationship and a minimum overjet of 2 mm was obtained. Pre- and post-treatment lateral cephalograms were traced by hand and measured by one author. Twenty-one parameters were evaluated. Outcomes relevant to this review: Overjet, ANB
Notes	Sample size calculation was not described.

Keles 2002

Methods	2 arm parallel randomised controlled trial.
Participants	**Number recruited:** 20 patients (10 males and 10 females) **Mean age:** 8.54 years. Range 7.3-10.9 years. **Inclusion criteria:** Healthy patients without any hormonal or growth discrepancy. Anterior cross bite with Class III molar relationship. True class III patients. Class III patients with maxillary retrognathism. **Exclusion criteria:** Pseudo or functional Class III.

	Setting: Recruited from Marmara University, Istanbul, Turkey.
Interventions	**Comparison:** Nanda facemask versus Conventional facemask.
	Group 1: Facemask with modified angle of force direction (Nanda group): Composed of three parts: a modified full-cover acrylic cap splint expansion appliance, a specially designed face bow, and a Petit type protraction headgear. The cap splint expansion appliance was modified by adding two tubes (3M Unitek, USA, item no. 325–303) on the buccal side of the acrylic in the premolar area. The tubes were soldered to the RME screw (Leone, item A620-09) and the acrylic was constructed. The purpose of these tubes was to accommodate the inner bows of the specially designed face bow. The face bow was constructed from an adjustable face bow (Ormco, item 200- 0227 Glendora, CA, USA). The inner bows of the face bow ended in the mouth with a special U-shaped bend in order to enter the buccal tubes from the distal, and thus be able to retain itself when an anterior pull was applied. In order to carry the level of force application above the occlusal plane, the outer bows of the face bow were bent in a 30 degree upward direction and ended with two hook bends in order to hold the elastics used for the face mask. These hooks were positioned around the root tips of the first and second premolars and 500g of force was applied parallel to the Frankfort plane in an anterior direction. The same Petit-type face mask was used and the direction of the force was adjusted by moving the wire piece upward on the face mask for elastic engagement. (n=11)
	Group 2: Conventional facemask: This consisted of a cap splint–type rapid palatal expander modified by adding two hooks in the canine area. The purpose of these hooks was to hold the elastics in place for protraction. The protraction headgear was a Petit type (Ormco Corporation, Glendore, Calif), and a force of 500g was applied to each hook at a 30 degree angle to the occlusal plane. (n=9)
	In both groups, treatment was started with 10 days of rapid maxillary expansion. Following the expansion, a facemask was applied to the patients of both groups and the appliance was used for six months after the onset of treatment. Patients were advised to wear the face mask for a minimum of 16 hr/d in the first three months and 12 hours in the second three months. In both groups a 500g force was used. In group 1 the force was applied parallel to the Frankfort horizontal plane, in group 2 it was angled downward 30 degrees to the occlusal plane.
Outcomes	Lateral cephalometric films were taken both at the beginning and the end of treatment (6 months). Eighteen linear and angular cephalometric measurements were made for all patients. Outcomes relevant to this review: ANB
Notes	Sample size calculation was not described.

Mandall 2010

Methods	2 arm parallel randomised controlled trial
Participants	**Number recruited:** 73 patients (34 males and 39 females). **Mean age:** 8.86 years. **Inclusion criteria:** 7-9 years old at the time of registration. Three or four incisors in crossbite in the intercuspal position. Clinical assessment of a class III skeletal problem. **Exclusion criteria:** Child of non-Caucasian origin. Cleft lip and palate and/or craniofacial syndrome. A maxillo-mandibular planes angle greater than 35 degrees or lower face height greater than 70 mm. Previous history of TMJ signs or symptoms. Lack of consent. **Setting:** Patients were recruited through UK orthodontic departments at five district general hospitals and three university teaching hospitals. Patient recruitment was optimised by writing to all general dental

	practitioners, who referred to each unit, explaining the type of patient we were looking to recruit. Additionally, the consultant orthodontist in each centre screened up to five local primary schools for suitable children in the 8–9 years old age group.
Interventions	**Comparison:** Facemask versus Untreated control Group 1: Facemask group: A bonded maxillary acrylic expansion device was placed. This consisted of a metal framework and a midline expansion screw to which 3 mm acrylic was adapted. The appliance was modified, if needed, with acrylic extending over the upper incisor edges to increase appliance retention. One vestibular hook was located, on each side, in the upper deciduous first molar position, for elastic traction. The appliance was cemented with glass ionomer cement, but if it later debonded, it was re-cemented with composite, following acid etching of the buccal and palatal cusps of the upper first permanent molars. For patients with posterior crossbites, the expansion screw was activated one quarter turn (0.25 mm) per day until the lingual cusps of the upper posterior teeth approximated the buccal cusps of the lower posterior teeth. If no transverse change was required, the maxillary splint was still activated once a day for 7–10 days in order to disrupt the circum-maxillary sutures. A commercially available adjustable facemask was used (TP Orthodontics), which had bilateral vertical rods connected to both chin and forehead pads. This design was adjustable vertically to customize the fit. If patients experienced chin reddening, ventilation holes were drilled through the plastic chin pad or soft padding was added. Elastics were connected bilaterally to the adjustable midline crossbow in a downwards and forwards direction. Patients were asked to wear the facemask for 14 hours per day, continuously, during the evening and night. A co-operation calendar was used in an attempt to increase treatment compliance, although this was not formally statistically evaluated. Extra oral elastics of increasing strength were used (3/80 8 oz. elastics for 1–2 weeks; then 1/20 14 oz. elastics; then 5/160 14 oz. elastics) until a force of 400g per side was delivered. The direction of elastic traction was downwards and forwards 30 degrees from the vestibular hooks on the bonded maxillary expander to the adjustable crossbar of the facemask. Additionally, the elastics could be crossed over to prevent catching or interference. (n=35) Group 2: Control: Following collection of initial records the patients allocated to the control group received no clinical intervention. They were recalled 15 months after registration for collection of final records. (n=38) Both groups were then recalled for follow up at 3 years.
Outcomes	Data were collected at the following time points: DC1: baseline data at trial registration. DC2: 15 months after baseline data collection. DC3: 3 years after baseline data collection. Cephalometric and occlusal measurements: The lateral cephalograms were traced by an experienced clinician who was blinded as to group allocation.

To determine the rotations of the maxillary and occlusal planes superimposition of the DC1, DC2 and DC3 lateral cephalometric radiographs was undertaken by another author using Bjork's structural method which employs the anterior zygomatic process as the reference landmark. PAR scores were measured by a calibrated examiner. Overjet measurements were recorded from study models, with a steel millimetre ruler, by an experienced examiner.

Psychosocial measures. The short form of the Piers–Harris children's self-concept scale (60 questions) was used to evaluate self-concept. This may have been influenced by receiving early class III treatment. Psychosocial/oral health related quality of life effects of treatment were assessed using the OASIS, which sums the impact of concern about appearance of teeth, including nice comments, unpleasant comments, teasing, avoidance of smiling, covering the mouth because of the teeth and self-perceived aesthetic component of the Index of Orthodontic Treatment Need.

TMJ examination. All the orthodontists involved in the trial received training from a TMJ specialist before the start of the trial to ensure that the TMJ examination was standardized. This TMJ specialist also advised that an examination appropriate for this age group of children should assess pain (lateral and intra-auricular), clicking, crepitus, locking, muscle tenderness (temporalis, masseter, and lateral pterygoid), and restriction of jaw movement (maximum opening and lateral movement). In addition, the presence of forward mandibular displacement on closure was recorded. TMJ signs or symptoms were recorded at DC1 to ensure no patients might be treated with protraction facemask that may exacerbate any TMJ problems through potential downwards and backwards rotation at the chin point. No patients were excluded at baseline because of pre-existing TMJ signs or symptoms.

Outcomes relevant to this review: Overjet, ANB, Piers-Harris score, OASIS score, TMJ outcomes.

Notes	Sample size calculation estimated that 23 children per group would give 90% power to detect a PAR reduction of 25% with a 0.05 two sided significance level.

Vaughn 2005

Methods	3 arm parallel randomised controlled trial
Participants	**Number recruited:** 46 patients (24 male and 22 female) **Mean age:** 7.33 years (range not given). **Inclusion criteria:** Zero or negative overjet on 2 or more incisors, Class III molar relationship with the mesiobuccal cusp of the maxillary permanent first molar distal to the buccal groove of the mandibular first permanent molar, or a mesial step terminal plane relationship of 3.0 mm or more if the deciduous molars were present (measured clinically). When the clinical or dental criteria were borderline, cephalometric criteria of ANB angle of 0 degrees or less, Wits analysis of 3 mm or more, and nasion perpendicular to A-point of 2 mm or less. **Exclusion criteria:** Any craniofacial anomaly, psychosocial impairment or skeletal open bite. **Setting:** University hospital in USA.
Interventions	**Comparison:** Facemask with expansion versus Facemask only versus Untreated control

	Group 1: Facemask with expansion group: Treated with palatal expansion with facemask therapy. A banded, soldered, jackscrew palatal expansion appliance was used for each subject. Two teeth per side were banded: the first and second deciduous molars, the first permanent molar and the second deciduous molar, or the first permanent molar and premolar. The appliance was activated twice daily (0.5 mm/day) for a minimum of 7 days. Soldered hooks (.045 in) were extended to the mesial of the canine for attachment of the force-delivering elastics. Each facemask was fabricated on a model made from an impression of the patient's face. The facemask was fitted 7 to 10 days after the placement of the palatal appliance. Elastics, directed 15 to 30 degrees downward from the occlusal plane, delivered a force of 300 to 500g per side, as determined by a force gauge. The participants were instructed to wear the appliance full time at the beginning of treatment. Compliance was closely monitored with timecards. Once positive overjet and overbite and Class I molar occlusion were obtained, facemask wear was reduced to 14 hours a day. In anticipation of some relapse, over correction, approaching an end-to-end molar relationship and overjet of 4 to 5 mm, were the treatment objectives. The treatment results were maintained for 3 to 6 months with night-time wear. (n=15)
	Group 2: Facemask only group: The protocol in group 2 was identical to that for group 1 except that the palatal expander was not activated. If patients required transverse expansion, this was performed after final records (T2) were obtained. (n=14)
	Group 3: Control group: Initial records (T0) were taken at enrolment and 1 year later. (n=17)
Outcomes	Lateral cephalometric radiographs were taken at T0, T1, and T2 for the control group, and at T1 and T2 for the 2 treatment groups. Fifty-five standard cephalometric landmarks were digitised in a predetermined order with a digitiser accurate to 0.001 mm. Traditional cephalometric measurements were used to describe changes between pre-treatment, posttreatment, and control lateral cephalograms. Measurements included a combination of the Steiner, McNamara, Ricketts, Riedel, and Wits analyses. Changes in 55 landmarks were also evaluated relative to an x-y coordinate system. The Johnston analysis also was used to differentiate between skeletal and dental changes and to provide a method to evaluate the combined treatment effects (skeletal and dental) along the mean functional occlusal plane. Outcomes of relevance to the review: ANB, Wits
Notes	No sample size calculations reported, and study likely to be under powered to detect a difference between groups 1 and 2.

Xu 2001

Methods	2 arm parallel randomised controlled trial.
Participants	**Number recruited:** 60 patients (27 male and 33 female) **Mean age:** 9.3 years. Range 8 to 11 years. **Inclusion Criteria:** Children with skeletal anterior cross-bite and abnormal facial morphology. **Exclusion Criteria:** Tooth or functional Class III patients. This lead to the exclusion of 20 of the 60 patients leaving 40 to be randomised. **Setting:** University hospital in China
Interventions	**Comparison:** Facemask versus Untreated control Group 1: A jackscrew rapid palatal expander welding with the bands of maxillary first molar and first premolar was attached to the patient posterior teeth. The protraction hook was located in the position of maxillary canines. After the first-week of expander placement, the expander was activated with 90 degree winding each time twice per day. After two weeks, active expansion treatment was stopped and the maxillary protraction started. The protraction treatment used a force of 400-500g lasted 12 hours per day. (n=20) Group 2: Observation only (n=20) Duration of Treatment: 11-13 months (mean 11.3 months)

Outcomes	Lateral cephalometric films taken at baseline and 11-13 months (right after the treatment), on which 9 linear and 6 angular measurements were made. Outcomes relevant to this review: ANB
Notes	Sample size calculation not described.

Appendix 6: Characteristics of Excluded Studies:

Reference	Reason for exclusion
Altug[114]	Retrospective control group therefore not a prospective RCT.
Arman[1]	Retrospective control group therefore not a prospective RCT.
Arman[79]	Retrospective control group therefore not a prospective RCT.
Baik[115]	Retrospective control group therefore not a prospective RCT. (author contacted)
Barrett[58]	Retrospective control group therefore not a prospective RCT.
Biren[116]	Not a randomised controlled trial.
Cozza[53]	Not a randomised controlled trial.
El[117]	Analysed condylar position during treatment, not an outcome of interest to this review.
Gokalp[118]	Not a randomised controlled trial.

Goyenc[69]	Not a randomised controlled trial.
Isci[119]	Not a randomised controlled trial.
Jamilian[120]	Not a randomised controlled trial.
Kurt[121]	Not a randomised controlled trial.
Mucedero[122]	Not a randomised controlled trial.
Pavoni[123]	Not a randomised controlled trial.
Sar[93]	Not a randomised controlled trial.
Tortop[80]	Retrospective control group therefore not a prospective RCT.
Ucem[124]	Not a randomised controlled trial.
Ulgen[47]	No randomisation process. Author contacted for clarification.
Wilmes[125]	Patients over the age of 16.
Yagci[126]	Not a randomised controlled trial.
Yagci[127]	Retrospective study so therefore not a prospective randomised controlled trial.

Appendix 7: Risk of Bias Assessments

Abdelnaby 2010

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear	The method of randomisation was not described. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Allocation concealment (selection bias)	Unclear	The method of allocation concealment was not described. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Blinding of outcome assessment (detection bias)	Unclear	There was no mention of blinding of the assessor. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Incomplete outcome data (attrition bias)	Unclear	There was no mention of any loss of patients during the study. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Selective reporting (reporting bias)	Low risk	The authors solely aimed to report on cephalometric measures and all were reported.
Other bias	High risk	Stated that patients 'randomly divided into three groups' however groups 1 and 2 have double the number of patients compared to group 3.

Arun 1994

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Contact from author confirms that a random number generator was used for patient assignment on registration to the study.
Allocation concealment (selection bias)	High risk	Contact from author confirms there was no allocation concealment used.
Blinding of outcome assessment (detection bias)	High risk	Contact from author confirms there was no blinding of any assessors during the study.
Incomplete outcome data (attrition bias)	Low risk	All patients completed the study and were included in the analysis.
Selective reporting (reporting bias)	Low risk	All cephalometric measurements were recorded and analysed.
Other bias	Low risk	Authors clarified all other queries.

Atalay 2010

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Contact from author confirms the use of random sequence generator using the patient application numbers.
Allocation concealment (selection bias)	High risk	Contact from author confirms no allocation concealment was used.
Blinding of outcome assessment (detection bias)	High risk	Contact from author confirms that no blinding of assessors was used.
Incomplete outcome data (attrition bias)	Low risk	All patients completed the study and were accounted for in the analysis
Selective reporting (reporting bias)	Low risk	All cephalometric measurements were recorded and analysed
Other bias	Low risk	Authors clarified all other queries

Keles 2002

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The method of randomisation was not described. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment was not described. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Blinding of outcome assessment (detection bias)	Unclear risk	There was no mention of blinding of the assessor. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Incomplete outcome data (attrition bias)	Unclear risk	There was no mention of any loss of patients during the study. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Selective reporting (reporting bias)	Low risk	The authors solely aimed to report on cephalometric measures and all were reported.
Other bias	Low risk	None detectable

Mandall 2010

Bias	Authors' judgement	Support for judgement

	judgement	
Random sequence generation (selection bias)	Low risk	The randomisation list was generated in randomisation blocks of 10 with stratification according to gender. Stratification meant that a separate randomisation list was generated for girls and boys, since gender was considered to be a potential confounding factor. This was because girls and boys will grow at different times during the study and, thus, potentially confound class III skeletal measurements.
Allocation concealment (selection bias)	Low risk	The computer generated randomisation sequence was concealed centrally and each clinician telephoned a research assistant to receive the treatment allocation after each patient was registered.
Blinding of outcome assessment (detection bias)	Low risk	The lateral cephalograms were traced by an experienced clinician who was blinded as to group allocation It was not possible to blind the clinician or the patient in this study. However, the trial was single-blind, as the researchers measuring the radiographs and study models and the statistician were blind to the treatment/control allocation until the data were analysed and the code broken. Ideally the clinician collecting the records at the 15 month DC2 time point would have also been blinded as to group allocation. However, this was not attempted, because with only one operator was involved at each centre they would have had the patient's notes in front of them at the time of data collection. Also, it was likely that the clinicians would have remembered who had received protraction facemask treatment.
Incomplete outcome data (attrition bias)	Low risk	Two patients were lost to follow up in each group, and excluded from the analysis. This is unlikely to have introduced bias.
Selective reporting (reporting bias)	Low risk	Cephalometric and occlusal measurements, psychosocial measures and TMJ examination results were planned and reported.
Other bias	Unclear risk	Some patients included in this study had a centric relation to centric occlusion displacement. This may have influenced the perception of the skeletal discrepancy from the lateral cephalogram.

Vaughn 2005

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	We used a block randomisation table to assign the subjects to 1 of 3 groups after obtaining proper informed consent.
Allocation concealment (selection bias)	Unclear risk	There was no method of allocation concealment. Attempts were made to contact the authors for clarification but we

Bias		Support for judgement
		are yet to receive a response.
Blinding of outcome assessment (detection bias)	Low risk	The principal investigator (G.A.V.) was blinded to the assignment.
Incomplete outcome data (attrition bias)	Unclear risk	Number of dropouts was not clear in the text. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Selective reporting (reporting bias)	Low risk	All cephalometric measures recorded and reported as intended.
Other bias	Low risk	None detectable.

Xu 2001

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The article states: 'the children were randomly divided into two groups' but no further details were given. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Allocation concealment (selection bias)	Unclear risk	The method of allocation concealment was not described. Attempts were made to contact the authors for clarification but we are yet to receive a response.
Blinding of outcome assessment (detection bias)	Unclear risk	There was no mention of blinding of the assessor. Attempts were made to contact the authors for clarification but we are yet

		to receive a response.	
Incomplete outcome data (attrition bias)	Low risk	All the participants with skeletal Class III were assessed.	
Selective reporting (reporting bias)	Low risk	All measures targeted were reported	
Other bias	Low risk	No other sources of bias identified.	

Appendix 8: Data Tables and Figures

Comparison	Outcome	Study	Effect measure	P-value
Facemask versus control	Overjet (post-treatment)	Mandall	4.10 mm (95%CI 3.04 to 5.16)	<0.0001
	Overjet (3 years' follow-up)	Mandall	2.50 mm (95%CI 1.21 to 3.79)	0.0001
	Piers-Harris (post-treatment)	Mandall	1.50 (95%CI -0.96 to 3.96)	0.23
	Piers-Harris (3 years' follow-up)	Mandall	0.60 (95%CI -2.57 to 3.77)	0.71
	OASIS (post-treatment)	Mandall	-4.00 (95%CI -7.40 to -0.60)	0.02
	OASIS (3 years' follow-up)	Mandall	-3.40 (95%CI -7.99 to 1.19)	0.15
Facemask with expansion vs Facemask only	ANB	Vaughn	-0.13 degrees (95%CI -1.40 to 1.14)	0.84
	Wits	Vaughn	-0.16 mm (95%CI -1.63 to 1.31)	0.83

Nanda facemask vs Conventional facemask	ANB	Keles	1.29 degrees (95%CI 0.16 to 2.42)	0.02
600g Chin cup vs Control	ANB	Abdelnaby	2.00 degrees (95%CI 1.61 to 2.39)	<0.0001
	Wits	Abdelnaby	4.80 mm (95%CI 4.13 to 5.47)	<0.0001
300g Chin cup vs Control	ANB	Abdelnaby	1.90 degrees (95%CI 1.43 to 2.37)	<0.0001
	Wits	Abdelnaby	5.10 mm (95%CI 4.43 to 5.77)	<0.0001
600g Chin cup vs 300g Chin cup	ANB	Abdelnaby	0.10 degrees (95%CI -0.31 to 0.51)	0.63
	Wits	Abdelnaby	-0.30 mm (95%CI -1.12 to 0.52)	0.47
Tandem traction bow appliance vs Control	Overjet	Atalay	3.30 mm (95%CI 2.46 to 4.14)	<0.0001
	ANB	Atalay	1.70 degrees (95%CI 1.09 to 2.31)	<0.0001

Table 3: Data for comparisons with single study

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
Overjet [mm]	1		Mean Difference (IV, Fixed, 95% CI [mm])	Subtotals only
1 year follow-up	1	69	Mean Difference (IV, Fixed, 95% CI [mm])	4.10 [3.04, 5.16]
3 year follow-up	1	63	Mean Difference (IV, Fixed, 95% CI [mm])	2.50 [1.21, 3.79]
ANB [Degrees]	3		Mean Difference (IV, Fixed, 95% CI [Degrees])	Subtotals only
1 year follow-up	3	155	Mean Difference (IV, Fixed, 95% CI [Degrees])	3.93 [3.46, 4.39]
3 year follow-up	1	63	Mean Difference (IV, Fixed, 95% CI [Degrees])	1.40 [0.43, 2.37]
Piers-Harris self-concept	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1 year follow-up	1	69	Mean Difference (IV,	1.50 [-0.96,

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
			Fixed, 95% CI)	3.96]
3 year follow-up	1	63	Mean Difference (IV, Fixed, 95% CI)	0.60 [-2.57, 3.77]
OASIS	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1 year follow-up	1	69	Mean Difference (IV, Fixed, 95% CI)	-4.00 [-7.40, -0.60]
3 year follow-up	1	63	Mean Difference (IV, Fixed, 95% CI)	-3.40 [-7.99, 1.19]
Wits [mm]	1	46	Mean Difference (IV, Fixed, 95% CI [mm])	-3.84 [-5.31, -2.37]

Table 4: Facemask versus untreated control

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 ANB [Degrees]	1	29	Mean Difference (IV, Fixed, 95% CI [Degrees])	-0.13 [-1.40, 1.14]
2.2 Wits	1	29	Mean Difference (IV, Fixed, 95% CI)	-0.16 [-1.63, 1.31]

Table 5: Facemask with expansion versus facemask only.

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 ANB [Degrees]	1	20	Mean Difference (IV, Fixed, 95% CI [Degrees])	1.29 [0.16, 2.42]

Table 6: Nanda facemask versus conventional facemask

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
4.1 ANB [Degrees]	1	30	Mean Difference (IV, Fixed, 95% CI [Degrees])	2.00 [1.61, 2.39]
4.2 Wits [mm]	1	30	Mean Difference (IV, Fixed, 95% CI [mm])	4.80 [4.13, 5.47]

Table 7: 600g chin cup versus untreated control

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
5.1 ANB [Degrees]	1	30	Mean Difference (IV, Fixed, 95% CI [Degrees])	1.90 [1.43, 2.37]
5.2 Wits [mm]	1	30	Mean Difference (IV, Fixed, 95% CI [mm])	5.10 [4.43, 5.77]

Table 8: 300g chin cup versus untreated control

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
6.1 ANB [Degrees]	1	40	Mean Difference (IV, Fixed, 95% CI [Degrees])	0.10 [-0.31, 0.51]
6.2 Wits [mm]	1	40	Mean Difference (IV, Fixed, 95% CI [mm])	-0.30 [-1.12, 0.52]

Table 9: 600g chin cup versus 300g chin cup

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
7.1 Overjet [mm]	1	30	Mean Difference (IV, Fixed, 95% CI [mm])	3.30 [2.46, 4.14]
7.2 ANB [Degrees]	1	30	Mean Difference (IV, Fixed, 95% CI [Degrees])	1.70 [1.09, 2.31]

Table 10: Tandem traction bow appliance versus untreated control

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
8.1 ANB	1		Other data	No numeric data

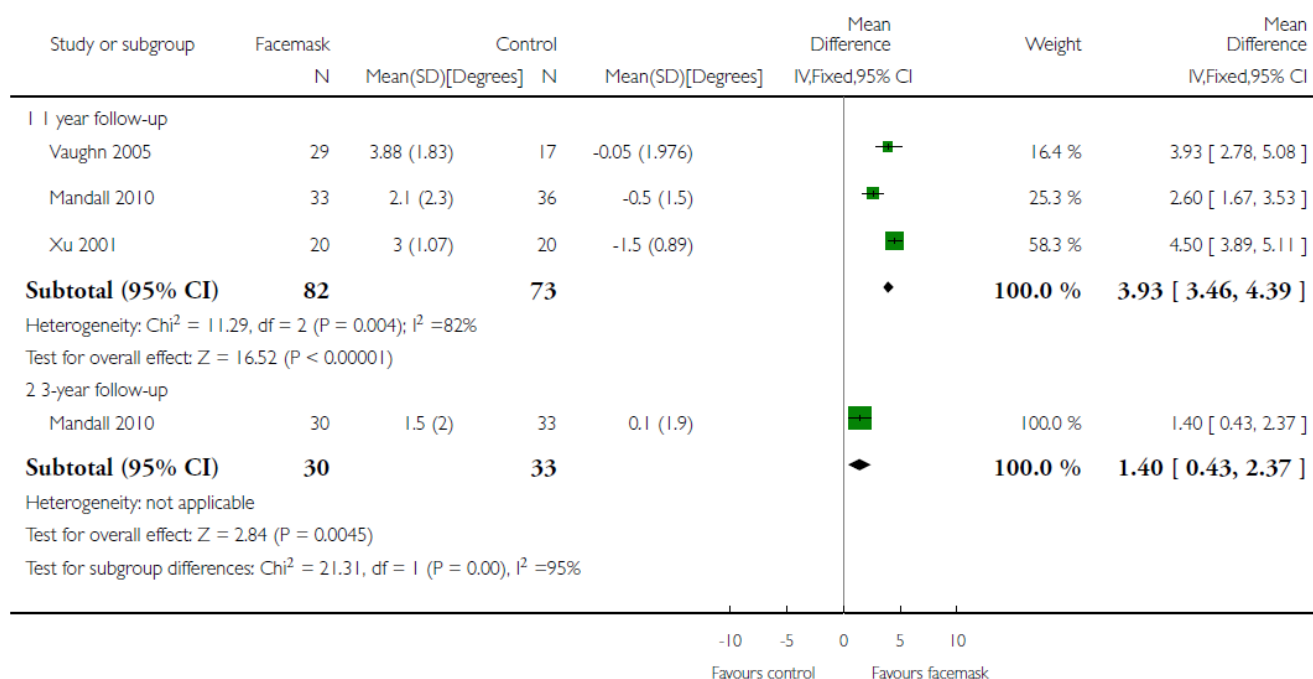Table 11: Mandibular headgear versus chin cup

Figure 15: Forest plot for pooled data for facemask versus untreated control for ANB

Appendix 9: Summary of Findings Tables

Facemask compared to no treatment for prominent lower front teeth in children					
Patient or population: Patients with prominent lower front teeth in children **Settings:** Dental hospital **Intervention:** Facemask **Comparison:** No treatment					
Outcomes	**Illustrative comparative risks* (95% CI)**		**No of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk	**Corresponding risk**			
	No treatment	**Facemask**			
Overjet - 1 year treatment Follow-up: at end of treatment		The mean overjet - 1 year follow-up in the intervention groups was **4.1 higher** (3.04 to 5.16 higher)	69 (1 study)	⊕⊕⊕⊖ **moderate**[1]	
Overjet - 1 year treatment Follow-up: mean 2		The mean overjet - 3 year follow-up in the intervention groups was **2.5 higher** (1.21 to 3.79 higher)	63 (1 study)	⊕⊕⊕⊖ **moderate**[1]	

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years post treatment					
ANB - 1 year follow-up Follow-up: mean 1 year		The mean ANB - 1 year follow-up in the intervention groups was **3.93 higher** (3.46 to 4.39 higher)	155 (3 studies)	⊕⊕⊖⊖ **low**[2,3]	
ANB - 3 year follow-up		The mean ANB - 3 year follow-up in the intervention groups was **1.4 higher** (0.43 to 2.37 higher)	63 (1)	⊕⊕⊕⊖ **moderate**[1]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes

[1] Downgraded because only one study with this comparison reported overjet.
[2] Downgraded because one study at low risk of bias, and 2 at unclear risk of bias
[3] Downgraded due to Heterogeneity: Chi² = 11.29, df = 2 (P = 0.004); I² = 82%

Table 12: Facemask compared to no treatment for prominent lower front teeth in children

Chin cup compared to no treatment for prominent lower front teeth in children					
Patient or population: Patients with prominent lower front teeth in children **Settings:** Dental hospital **Intervention:** Chin cup (300g or 600g) **Comparison:** No treatment					
Outcomes	**Illustrative comparative risks* (95% CI)**		**No of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk **Control**	**Corresponding risk** **600g Chin cup**			
600g Chin cup **ANB** Follow-up: mean 1 years	No treatment	The mean ANB in the intervention groups was **2 higher** (1.61 to 2.39 higher)	30 [1] (1 study)	⊕⊖⊖⊖ **very low**	Insufficient evidence from a single study at high risk of bias to determine whether or not chin cup is an effective treatment.
300g Chin cup **ANB** Follow-up: mean 1 years	No treatment	The mean ANB in the intervention groups was **1.9 higher** (1.43 to 2.37 higher)	30 [1] (1 study)	⊕⊖⊖⊖ **very low**	Insufficient evidence from a single study at high risk of bias to determine whether or not chin cup is an effective treatment.
*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval;					
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in					

the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Downgraded because only one small study at high risk of bias reported this outcome.

Table 13: Chin cup compared to no treatment for prominent lower front teeth in children

Tandem traction bow appliance compared to no treatment for prominent lower front teeth in children					
Patient or population: Patients with prominent lower front teeth in children **Settings:** Dental hospital **Intervention:** Tandem traction bow appliance **Comparison:** Control					
Outcomes	**Illustrative comparative risks* (95% CI)**		**No of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk	**Corresponding risk**			
	No Treatment	**Tandem traction bow appliance**			
Overjet at end of 1 year of treatment		The mean overjet in the intervention groups was **3.3 higher** (2.46 to 4.14 higher)	30 [1] (1 study)	⊕⊖⊖⊖ **very low**	Insufficient evidence from a single study at high risk of bias to determine whether or not tandem traction bow is an effective treatment.
ANB at end of 1 year of treatment		The mean ANB in the intervention groups was **1.7 higher** (1.09 to 2.31 higher)	30 [1] (1 study)	⊕⊖⊖⊖ **very low**	Insufficient evidence from a single study at high risk of bias to determine whether or not tandem traction bow is an effective treatment.
*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval;					
GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in					

the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes

[1] Downgraded because only one small study at high risk of bias reported this outcome.

Table 14: Tandem traction bow appliance compared to no treatment for prominent lower front teeth in children