Early orthodontic treatment for Class III malocclusion: A systematic review and meta-analysis

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Introduction: Class III malocclusion affects between 5% and 15% of our population. The 2 most common dilemmas surrounding Class III treatment are the timing of treatment and the type of appliance. A number of appliances have been used to correct a Class III skeletal discrepancy, but there is little evidence available on their effectiveness in the long term. Similarly, early treatment of Class III malocclusion has been practiced with increasing interest. However, there has been no solid evidence on the benefits in the long term. The aim of this systematic review was to evaluate the effectiveness of orthodontic/orthopedic methods used in the early treatment of Class III malocclusion in the short and long terms. **Methods:** Several sources were used to identify all relevant studies independently of language. The Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Embase (Ovid), and MEDLINE (Ovid) were searched to June 2016. The selection criteria included randomized controlled trials (RCTs) and prospective controlled clinical trials (CCTs) of children between the ages of 7 and 12 years on early treatment with any type of orthodontic/orthopedic appliance compared with another appliance to correct Class III malocclusion or with an untreated control group. The primary outcome measure was correction of reverse overjet, and the secondary outcomes included skeletal changes, soft tissue changes, quality of life, patient compliance, adverse effect, Peer Assessment Rating score, and treatment time. The search results were screened for inclusion, and the data extracted by 2 independent authors. The data were analyzed using software (version 5.1, Review Manager; The Nordic Cochrane Centre, The Cochrane Collaboration; Copenhagen, Denmark). The mean differences with 95% confidence intervals were expressed for the continuous data. Random effects were carried out with high levels of clinical or statistical heterogeneity and fixed affects when the heterogeneity was low. **Results:** Fifteen studies, 9 RCTs and 6 CCTs, were included in this review. In the RCT group, only 3 of 9 studies were assessed at low risk of bias, and the others were at high or unclear risk of bias. All 6 CCT studies were classified as high risk of bias. Three RCTs involving 141 participants looked at the comparison between protraction facemask and untreated control. The results for reverse overjet (mean difference, 2.5 mm; 95% CI, 1.21-3.79; $P = 0.0001$) and ANB angle (mean difference, 3.90°; 95% CI, 3.54-4.25; $P < 0.0001$) were statistically significant favoring the facemask group. All CCTs demonstrated a statistically significant benefit in favor of the use of each appliance. However, the studies had high risk of bias. **Conclusions:** There is a moderate amount of evidence to show that early treatment with a facemask results in positive improvement for both skeletal and dental effects in the short term. However, there was lack of evidence on long-term benefits. There is some evidence with regard to the chincup, tandem traction bow appliance, and removable mandibular retractor, but the studies had a high risk of bias. Further high-quality, long-term studies are required to evaluate the early treatment effects for Class III malocclusion patients.
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Early treatment of Class III malocclusion has been attempted with varying success. The main advantage of early Class III malocclusion treatment is to avoid surgical intervention and thus reduce the morbidity of the surgery. The timing of early treatment is crucial for a successful outcome. Some studies have reported that treatment should be carried out in patients less than 10 years of age to enhance the orthopedic effect.[1-4] In contrast, other studies have

found that patient age had little influence on treatment response and outcome.[5,6] Hence, there is no strong evidence to support that early treatment would be beneficial.

The main goals of early intervention are to provide a more favorable environment for growth and to improve the occlusal relationship: eg, correcting the crossbite and facial esthetics.[4] Many orthopedic appliances have been explored including protraction facemask, chincup, FR-3 appliance of Frankel, bionator, reverse Twin-block, removable mandibular retractor, double-piece corrector, Class III elastics, and mandibular headgear to achieve this goal. Among these, the protraction facemask is favored by many to correct a retronagthic maxilla. On the other hand, the chincup is believed to retard or redirect the growth of a prognathic mandible. The previous Cochrane systematic review concluded that although there was some evidence for the effectiveness of the facemask appliance in the short term, there is no evidence that the results are maintained in the long term.[7] Furthermore, the review included only 3 randomized controlled trials (RCTs). When there are not many high-quality RCTs in the literature, it is appropriate to look at prospective controlled clinical trials (CCTs). Additionally, further randomized studies have been published since the review. Hence, this systematic review is to update the Cochrane review and also to include prospective CCTs to evaluate the evidence base for Class III early treatment.

The aim of this systematic review was to evaluate the effectiveness of orthodontic methods used in the early treatment of Class III malocclusion in the short and long terms.

MATERIAL AND METHODS

Protocol and registration

This systematic review protocol was registered under the PROSPERO register with the number CRD42015024252 (www.crd.york.ac.uk/prospero).

Eligibility criteria

The criteria for considering studies for this review (PICO) were the following: (1) types of studies: RCTs and prospective CCTs; (2) participants: studies of subjects with Class III malocclusion between 7 and 12 years of age; (3) intervention: orthodontic treatment with a removable or fixed orthodontic/orthopedic appliance for early correction of Class III malocclusion; (4) comparison: no treatment, delayed treatment, or intervention with the same appliance with different forces, different mechanics, or a different appliance; and (5) primary outcome: correction of reverse overjet (measured in millimeters or by other index of malocclusion) with the measurements based on study models, or cephalometric or clinical assessment.

Secondary outcomes were skeletal changes, soft tissue changes, quality of life, patient compliance, adverse effects, Peer Assessment Rating score, and treatment time.

Table I. MEDLINE search strategy

#1 Malocclusion-Angle-Class-III (ME)
#2 (Class III AND (Angle OR bite))
#3 Orthodontic-Appliances-Functional (ME)
#4 Facemask OR chin cup
#5 ((Extraoral OR extra oral OR extra-oral) AND appliance*)
#6 reversehead gear OR reverse headgear
#7 growth modif* AND maxilla*
#8 (early AND (treatment OR therapy)) AND orthodontic*
#9 ((orthopedic* OR orthopaedic*) AND (orthodontic* OR facial))
#10 #1 OR #2 AND #3 OR #4 OR #5 OR #6 AND #7 OR #8 OR #9
#11 Randomised controlled trial.pt.
#12 Controlled clinical trial.pt.
#13 Randomised.ab.
#14 Clinical trials as topic.sh.
#15 Randomly.ab
#16 #11 OR #12 OR #13 OR #14 OR #15
#17 #10 AND #16

Information sources, search strategy, and study selection

Several sources were used to identify all relevant studies independently of language. The Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Embase, and MEDLINE (Ovid) were searched to April 2016. To identify relevant records, 3 basic sets of terms were used. These included those that identified records related to early Class III malocclusion treatment, records related to intervention involved, and records related to outcome. Details of the MEDLINE search are provided in Table I. Hand searching was carried out for the journals that were identified on the Cochrane Oral Health Group Web site (http://ohg.cochrane.org). Articles not in English from the search were translated. References in the full-text articles selected were scanned for relevant studies. Unpublished studies were searched on ClinicalTrials.gov.

Articles and abstracts from the search were examined to exclude irrelevant studies. The article selection process was carried out independently by both authors. All doubts and disagreements were resolved after discussion.

Full texts of the potentially eligible studies were retrieved and examined carefully for compliance with the inclusion and exclusion criteria independently by

both authors. All disagreements were resolved after discussion.

Data items and collection

A customized data collection form was created and used to gather information from the selected studies. This information included authors, year of publication, details of the trial, details of the interventions, characteristics of participants, duration of treatment, and outcome measures. The data extraction was performed by both authors independently and in duplication. An attempt to contact the authors was made for any missing information.

Risk of bias and quality assessment in the studies

The risk of bias for the RCTs was evaluated using the Cochrane Collaboration's tool for assessing the risk of bias, as described in the *Cochrane Handbook for the Systemic Reviews of Interventions*.[8] For the CCTs, the quality assessment was adopted from the checklist described by Downs and Black.[9] We pilot tested a subset of our studies with the Downs and Black and the Newcastle-Ottawa scales.[10] Although both have been widely used for quality assessment, we found the former to be a more comprehensive asessment with a 27-point scale.

Summary measures, approach to synthesis and analysis

The data were grouped and classified according to the study methodology into 2 categories: RCT and CCT.

The collected data were analyzed using Review Manager software (version 5.1; The Nordic Cochrane Centre, The Cochrane Collaboration; Copenhagen, Denmark). Risk ratios with 95% confidence intervals (95% CI) were shown for dichotomous data and mean differences with 95% CI for continuous data.

Data collection was completed without missing data from the eligible studies during the review. If there were any missing data, an attempt was made to contact the original author.

Clinical heterogeneity was assessed by examining the participant types, interventions, and outcomes. Statistical heterogeneity among the trials was assessed by chi-square test where a P value of <0.1 was considered as significant heterogeneity. The I^2 test was also carried out. The studies with more than 50% I^2 were assessed as having significant heterogeneity. Random effects were carried out with high levels of clinical or statistical heterogeneity, and fixed affects when the heterogeneity was low.

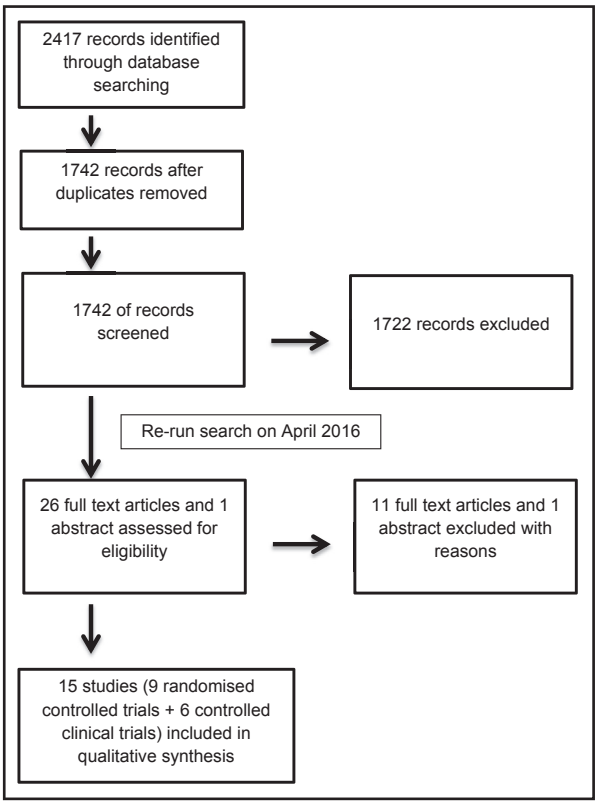

Fig 1. Study flow diagram.

Table II. Excluded studies of early treatment of Class III malocclusion

Author/year	*Reason of exclusion*
Sheera et al[11] (2012)	Retrospective comparative study
Kidner et al[12] (2003)	Case series
Liu et al[13] (2011)	Studies included in systematic review were prospective cohort
Kurt et al[14] (2011)	Did not fulfill inclusion criteria
Minami-Sugaya et al[15] (2012)	Studies included adult sample
Solano-Mendoza et al[16] (2012)	Literature review that included retrospective studies
Arun and Erverdi[17] (1994)	Did not fulfill inclusion criteria
Saleh et al[18] (2013)	Did not fulfill inclusion criteria
Lione et al[19] (2015)	Did not fulfill inclusion criteria
Ngan et al[20] (2015)	Retrospective comparative study

RESULTS

Study selection and characteristics

A total of 2417 records were identified from the initial search. A further search was carried out in April 2016. From the records that were identified, 26 full-text articles were retrieved for further evaluation (Fig 1). Eleven

Table III. Characteristics of included RCTs

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Abdelnaby and Nassar [25] (2010)							
Parallel group RCT	50 randomized (26 boys, 24 girls) Groups 1 and 2 were intervention groups; group 3 was control group Group 1: n=20 Group 2: n=20 Group 3: n=10	Group 1: 9.6 years Group 2: 10.1 years Group 3: 9.2 years	1. Patients with skeletal Class III (ANB<1°) 2. Mandibular prognathism (SNB >80°) 3. Anterior crossbite	Not reported	Patients recruited from the Faculty of Dentistry, Mansoura University, Mansoura, Egypt	Comparison between chincup and control Patients divided into 3 groups Intervention groups: Group 1: treated with chincup and occlusal bite plane using 600 g of force per side Group 2: treated with a chincup and occlusal bite plane using 300 g of force per side Control group: Group 3: no treatment provided	Skeletal changes: ANB All measurements taken before treatment and after 1 year
Atalay and Tortop [6] (2010)							
Parallel group RCT	45 randomized (26 boys, 19 girls) Patients divided into treatment and control groups Groups 1 and 2 were intervention groups, group 3 was control group Group 1: 15 patients Group 2: 15 patients Group 3: 15 patients	Group 1: 8.18 years Group 2: 11.75 years Group 3: 7.90 years	1. Skeletal Class III (ANB < 0°), due to maxillary retrusion or a combination of maxillary retrusion and mandibular protrusion 2. Angle Class III malocclusion with anterior crossbite. 3. Optimum SN/GoGn angle (between 26° and 38°) 4. Fully erupted maxillary incisors 5. No congenitally missing teeth or congenital syndromes such as a cleft lip/palate	1. Congenitally missing teeth or congenital syndromes 2. Previous orthodontic treatment	Patients recruited from Gazi University, Turkey	Comparison between modified tandem traction bow appliance and untreated group Intervention: Group 1: early treatment group treated with modified tandem traction bow appliance Group 2: late treatment group treated with modified tandem traction bow appliance Control: Group 3: observation without treatment for 8 months	1. Dental changes: overjet 2. Skeletal changes: ANB All measurements taken before and after treatment

Table III. Continued

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Keles et al [26] (2002)							
Parallel group RCT	20 randomized (10 boys, 10 girls) Group 1: 9 patients Group 2: 11 patients	Group 1: 8.58 years Group 2: 8.51 years	1. Healthy patients without any hormonal or growth discrepancy 2. Anterior crossbite with Class III molar relationship 3. True Class III patients (pseudo or functional Class III patients excluded) 4. Class III patients with maxillary retrognathism were selected for treatment.	1. Pseudo or functional Class III	Patients recruited from Marmara University, Istanbul	Comparison between Nanda facemask and conventional facemask Group 1: Conventional facemask. Force was applied intraorally from canine region in a forward and downward direction at 30° angle to occlusal plane Group 2: Modified protraction headgear. Force was applied extraorally 20 mm above the maxillary occlusal plane In both groups a unilateral 500 g force was applied; patients were instructed to wear the facemask for 16 h/d for the first 3 months and 12 h/d for the next 3 months	Skeletal changes: ANB All measurements were taken before and after treatment on lateral cephalograms
Mandall et al [28,29] (2010, 2013)							
Parallel group RCT	73 randomized (34 boys, 39 girls) Group 1: 35 patients Group 2: 38 patients	Group 1: 8.7 years Group 2: 9.0 years	1. Age 7 -9 years old at registration 2. Three or 4 incisors in crossbite in intercuspal position 3. Clinical assessment of Class III skeletal problem	1. Nonwhite origin 2. Cleft lip/ palate or craniofacial syndrome 3. Maxillo-mandibular plane angle >35° or lower face height >70 mm 4. Previous history of TMJ signs or symptoms 5. Lack of consent	Patients recruited through UK orthodontic departments at 5 district general hospitals and 3 university hospitals	Comparison between facemask and untreated group Intervention Group 1: facemask Control: Group 2: untreated patients followed for 15 months. Initial and post-15-month records were taken	1. Skeletal changes: ANB 2. Reverse overjet 3. Self-esteem (Piers Harris) and OASIS scores 4. TMJ problem 5. PAR score

Table III. Continued

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Vaughn et al [27] (2005)							
Parallel group RCT	46 randomized (24 boys, 22 girls) Patients divided into 2 groups: intervention and control. Intervention group subdivided into 2 subgroups: expansion and nonexpansion Group 1: 15 patients Group 2: 14 patients Group 3: 17 patients	Group 1: 7.83 years Group 2: 8.10 years Group 3: 6.62 years	Zero or negative overjet on 2 or more incisors and Class III molar relationship with mesiobuccal cusp of maxillary permanent first molar distal to buccal groove of mandibular permanent first molar, or mesial step terminal plane relationship of 3.0 mm or more if deciduous molars were present (measured clinically) When clinical or dental criteria were borderline, cephalometric criteria of ANB angle of 0° or less, Wits analysis of 3 mm or more, and nasion perpendicular to A-point of 2 mm or less were used	Any craniofacial anomaly, psychosocial impairment, or skeletal open bite	University hospitals in United States	Comparison between facemask and observation group Intervention: Group 1: Expansion group. Palatal expansion with facemask therapy Group 2: Nonexpansion group. Passive palatal appliances with facemask therapy Control: Group 3: Untreated patients followed up 1 year. Initial and after-1-year records were taken	Skeletal changes: ANB
Xu and Lin [24] (2001)							
Parallel group RCT	60 randomized (27 boys, 33 girls); 20 patients later excluded Group 1: 20 patients Group 2: 20 patients	Mean age: 9.3 years	Skeletal anterior crossbite and skeletal Class III	Dental or functional Class III	Patients were recruited from hospital in Beijing, China	Comparison between facemask and untreated group Intervention: Group 1: facemask Control: Group 2: observation only	Skeletal changes: ANB

Table III. Continued

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Showkatbakhsh et al [23] (2013)							
Parallel group RCT	50 randomized (24 boys, 26 females) Group 1: 24 patients Group 2: 23 patients	Group 1: 9 years Group 2: 9.1 years	1. SNA 80°, SNB 80°, ANB 0° 2. No syndromic or medically compromised patients 3. No previous surgical intervention 4. No other appliances before or during functional treatment 5. No skeletal asymmetry 6. Class III molar relationship 7. Prepubertal (CS1, CS2, and CS3) according to recently improved CVM		Department of Orthodontics, SB University of Medical Sciences Dental School, Tehran, Iran	Comparison between facemask and tongue plate group Intervention: Group 1: facemask Group 2: tongue plate Active treatment times 18 mo (SD 3) for facemask and 16 mo (SD 2) for tongue plate	1. Skeletal changes: ANB
Saleh et al [22] (2013)							
Parallel group RCT	67 randomized (32 boys, 35 girls) Group 1: 33 patients Group 2: 34 patients	Group 1: 7.5 years Group 2: 7.3 years	1. Age 5-9 years at assessment with permanent first molars erupted 2. Class III molar relationship 3. Anterior crossbite on 2 or more incisors with or without mandibular displacement or closure 4. Clinical assessment of skeletal Class III relationship 5. No cleft lip/palate or other craniofacial syndromes 6. No or minimal facial asymmetry 7. No previous orthodontic treatment 8. Syrian ancestry		Department of Orthodontics, University of Al-Baath Dental School, Hamah, Syria	Comparison between removable mandibular retractor and untreated control Intervention: Group 1: removable mandibular retractor Control: Group 2: untreated control Treatment times for both removable mandibular retractor groups, 14.5 mo (SD 0.1)	1. Skeletal changes: A and B points (linear measurement)

Table III. Continued

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Liu et al [21] (2015)							
Parallel group RCT*	43 randomized (20 boys, 23 girls) Groups 1 and 2 were intervention groups Group 1: 21 patients Group 2: 22 patients	Group 1: 9.8 years Group 2: 10.1 years	1. Age 7-13 years before treatment with midface soft tissue deficiency 2. Fully erupted maxillary first molars, Class III malocclusion, and anterior crossbite 3. ANB less than 0°, Wits appraisal less than -2 mm (corrected cephalometric tracing technique applied for patients with functional shift), and distance from Point A to nasion perpendicular less than 0 mm	1. Previous orthodontic treatment 2. Other craniofacial anomalies, such as cleft lip and palate 3. Maxillary dentition unsuitable to bond hyrax expander	Patients were recruited from the Department of Orthodontics, Peking University, Beijing, China	Comparison between facemask protraction combined with alternating rapid palatal expansion and constriction (RPE/C) vs rapid palatal expansion (RPE) alone Patients divided into 2 groups Group 1: treated with RME for 1 week followed by facemask maxillary protraction, delivering force of 400-500 g per side Group 2: treated with RME/C for 7 weeks (7 days expansion, 7 days constriction) followed by facemask maxillary protraction, delivering force of 400-500 g per side	Skeletal changes All measurement taken before treatment and when positive overjet with Class I or Class II molars were achieved
Note: Sample size calculation was estimated using the previous study on 2-hinged expander RPE/C and intraoral maxillary protraction (95% power; 5% significance level; 2-tailed); minimum sample size of 16 in each group required to detect significant difference in ANS between groups; sample size was increased by 40% to account for dropouts, resulting in 22 patents in each group							

Table IV. Characteristics of the included CCTs

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Barrett et al [30] (2010)							
CCT Note: Sample size calculation not described Groups not balanced for sex and age Inclusion and exclusion criteria were unclear Patients were not treated equally: 12 of 26 were treated with quad helix	46 patients (17 boys, 29 girls) included Treatment group: 26 patients Control group: 20 patients	Treatment group: 8.5 years Control group: 7.3 years	Occlusal signs of Class III malocclusion with Wits appraisal of −2 mm or more		Patients recruited from hospitals in Ann Arbor, Mich, and Florence, Italy	Comparison between light force chincup and control group Intervention: light force chincup Control: observation only Posttreatment cephalograms were taken on average 2.6 years later	Dental changes: reverse overjet Skeletal changes: ANB
Cozza et al [32] (2010)							
CCT Note: Sample size calculation was adequate: 85% Groups were not well balanced for sex and age Exclusion criteria were not described P values not provided	34 patients (16 boys, 18 girls) included Treatment group: 22 patients Control group: 12 patients	Treatment group: 8.9 years Control group: 7.6 years	1. Class III malocclusion in the mixed dentition characterized by Wits appraisal of −2 mm or less, anterior crossbite or incisor end-to-end relationship, and Class III molar relationship 2. No permanent teeth were congenitally missing or extracted before or during treatment 3. No transverse discrepancy between the dental arches		Patients recruited from Department of Orthodontics at the University of Rome, Rome, Italy	Comparison between facial mask and bite-block appliance and control group Intervention: Facial mask and bite-block appliance Lateral cephalograms were taken at beginning and end of treatment Control: observation only Treated sample was collected prospectively; control sample was collected retrospectively	Dental changes: reverse overjet Skeletal changes: ANB

Table IV. Continued

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Cozza et al [33] (2004)							
CCT Note: Sample size calculation not described Statistical analysis incomplete	54 patients (31 boys, 23 girls) included Treatment group: 30 patients Control group: 24 patients	Treatment group: 5.85 years Control group: 5.9 years	1. Skeletal Class III relationship caused by maxillary retronagthism without other craniofacial anomalies or history of orthodontic treatment	1. Craniofacial anomalies 2. History of orthodontic treatment	Patients recruited from university hospital and private practice in Rome, Italy	Comparison between Delaire facemask and Bionator III appliance and control group Intervention: Delaire facemask and Bionator III Lateral cephalogram obtained before treatment, after facemask removal, and at end of retention Control: observation only Three series of cephalometric registrations with 1-year interval	Skeletal changes: ANB
Kajiyama et al [33] (2000)							
CCT Note: Sample size calculation not described	54 patients (21 boys, 33 girls) included Treatment group: 29 patients Control group: 25 patients	Treatment group: 8 y 7 mo Control group: 8 y 1 mo	1. Anterior crossbite (negative overjet) 2. Stage III-B of Hellman's developmental stages (4 maxillary and mandibular incisors have erupted) 3. Angle Class III molar relationship 4. No previous orthodontic treatment	History of orthodontic treatment	Patients treated at orthodontic clinic, Kyushu University Dental Hospital, Fukuoka, Japan	Comparison between maxillary protraction bow appliance and control group Intervention: Maxillary protraction bow Two cephalographs for each subject, 1 before and 1 after treatment Control: observation only Two cephalographs of each control subject were taken Mean treatment period to achieve normal overjet was 10.2 mo (range, 5-18 mo)	Dental changes: correction of the reverse overjet in angular measurement Skeletal changes: ANB

Table IV. Continued

Method	*Participants*	*Age*	*Inclusion criteria*	*Exclusion criteria*	*Setting*	*Interventions*	*Outcomes*
Kajiyama et al [34] (2004)							
CCT Note: Sample size calculation not described	120 patients (42 boys, 78 girls) included Treatment and control groups were subdivided into deciduous and mixed groups Treatment group: Deciduous dentition: 34 patients Mixed dentition: 29 patients Control group Deciduous dentition: 32 patients Mixed dentition: 25 patients	Treatment group: Deciduous dentition: 5 y 6 mo Mixed dentition: 8 y 7 mo Control group Deciduous dentition: not reported Mixed dentition: not reported	1. Anterior crossbite (negative overjet) 2. Class III deciduous canine relationship 3. Bilateral mesial step type of terminal plane or Class III permanent molar relationship 4. No craniofacial anomalies (cleft lip or palate) 5. No previous orthodontic treatment		Patients treated at orthodontic clinic, Kyushu University Dental Hospital, Fukuoka, Japan	Comparison between modified maxillary protractor (deciduous and early mixed dentitions) and control Intervention: modified maxillary protraction Lateral cephalograms taken at beginning of treatment without appliance and at removal of maxillary protraction bow appliance after achieving positive overjet Control: observation only. 2 cephalograms taken at start and end of observation periods, corresponding with timing in treatment group Mean periods of treatment were 5.2 months in patients with deciduous dentition and 10.2 months in those with mixed dentition	Skeletal changes: ANB

Table IV. Continued

Method	Participants	Age	Inclusion criteria	Exclusion criteria	Setting	Interventions	Outcomes
Lin et al [35] (2010)							
CCT Note: Sample size calculation not described	40 patients (20 boys, 20 girls) included Treatment group: 20 patients Control group: 20 patients	Treatment group: 9 y 11 mo Control group: 9 y 6 mo	1. SNA = 78° - 81°, sella-nasion-B (SNB) = 81°- 84° and ANB = −6°- 0° for Class III patients with both midface deficiency and mandibular prognathism 2. Negative incisal overjet and Class III molar relationship 3. ANB angle not smaller than −7°.		Patients recruited from Kaohsiung Medical University, Taiwan	Comparison between occipitomental anchorage appliance plus chincup and control Intervention: occipitomental anchorage appliance plus chin cup Lateral cephalometric radiographs taken at 2 times: pretreatment or initial stage and posttreatment or final stage Control: observation only Mean observation period, 1 y 5 mo	Dental changes: correction of the reverse overjet Skeletal changes: ANB

Fig 2. Risk of bias summary: review authors' judgments about each risk of bias item presented across all included RCTs.

articles were subsequently excluded with reasons for exclusion shown in Table II.[11-20] A total of 15 articles—9 RCTs[6,21-30] and 6 CCTs[30-35]—were included in the final analysis.

The characteristics of the included studies are shown in Tables III and IV.

Risk of bias in studies

The quality assessments of the RCTs are given in Figures 2 and 3.

Selection bias

Nine of the 15 included studies were RCTs.[6,21-29] Randomization and allocation concealment were

adequate for Mandall et al,[28,29] Liu et al,[21] and Showkatbakhsh et al.[23] The remaining studies were judged as either high risk or unclear on allocation concealment.[6,22,24-27]

Performance and detection bias

Because of the nature of orthodontic studies, blinding of the patients and clinicians could not be performed and therefore was not assessed. However, blinding of the outcome assessors was carried out and judged as having a low risk of bias in Mandall et al,[28,29] Vaughn et al,[27] Liu et al,[21] and Showkatbakhsh et al,[23] and unclear for the others.[6,22,24-26]

Attrition bias

The withdrawal rates were clearly reported in Mandall et al,[28,29] Liu et al,[21] Atalay and Tortop,[6] Showkatbakhsh et al,[23] and Saleh et al,[22] judged as having low risk of bias. Interestingly, Atalay and Tortop reported no loss at follow-up in their study. The remaining studies were judged as having an unclear risk.[24-27]

Overall, Mandall et al,[28,29] Liu et al,[21] and Showkatbakhsh et al[23] were assessed as having low risk of bias. One study was classified as having a high risk of bias,[6] and the remaining 5 studies were assessed as having an unclear risk of bias.[23,24-27]

Quality assessment of CCTs

The quality assessment criteria for the CCTs were adopted from the checklist by Downs and Black[9] (Table V). All included studies showed high risk of bias, with the total quality score less than 20 (Table V).[30-35] Although these studies had a clear objective and an intervention of interest, there were several biases including lack of sample size calculation and blinding.

Summary of the studies and meta-analysis

A summary of the findings is reported in Table VI.

RCTs: appliance vs untreated control

Three studies looked at comparisons between facemask and untreated control.[24,27-29] Only Mandall et al[28,29] followed up the outcomes achieved by facemask treatment for 15 months and 3 years. The other studies evaluated the short-term outcomes.[24,27] Changes in ANB were the only outcome evaluated by the studies. Mandall et al[28,29] also assessed the correction of reverse overjet, Piers-Harris concept scores, and OASIS.

Facemask studies showed positive results in both skeletal and dental variables. For the changes in ANB, a meta-analysis was performed for the 3 studies. The pooled estimate was 3.90° (95% CI, 3.54-4.25; P <0.0001) (Fig 4). It was statistically significant and favored the facemask group. However, the I^2 for heterogeneity was high (82%).

For overjet, only Mandall et al[29] reported the outcome at 3 years. Analysis showed a statistically significant difference for the outcome (2.5 mm [mean difference], 2.5 mm; 95% CI, 1.21-3.79; P = 0.0001) (Fig 4).

Mandall et al[28,29] also assessed self-esteem using the Piers-Harris concept scores and OASIS. No statistically significant differences were found at 15 months (MD, 1.5; 95% CI, −0.96-3.96; P = 0.23) (Fig 5) and at 3 years (MD, 0.6; 95% CI, −2.57-3.77; P = 0.71) (Fig 5) for the Piers-Harris score. Conversely, for the OASIS, there was a significant difference at 15 months with −4.00 (95% CI, −7.40 to −0.60; P = 0.02) (Fig 5) in favor of the control group. However, there was no difference in the results for the 3-year follow-up (MD, 3.40; 95% CI, −7.99-1.19; P = 0.15) (Fig 5).

Atalay and Tortop[6] compared the tandem traction bow appliance with an untreated control. There was strong evidence in favor of the tandem traction bow appliance in both measured outcomes: ANB changes (MD, 1.7°; 95% CI, 1.54-1.86; P <0.00001) (Fig 6) and overjet correction (MD, 3.30 mm; 95% CI, 3.08-3.52; P <0.00001) (Fig 6).

Saleh et al[22] compared the removable mandibular retractor with an untreated control. The evidence favored the use of the appliance for changes of A point (MD, 1.47°; 95% CI, 1.20-1.74; P <0.00001) (Fig 6) and B point (MD, 1.87°; 95% CI, −2.03 to −1.71; P <0.00001) (Fig 6).

Appliance 1 vs appliance 2

Keles et al[26] compared conventional facemask with modified protraction headgear, and Showkatbaksh et al[23] compared facemask with tongue plate appliance. The meta-analysis showed a statistically significant difference for ANB measurement favoring the conventional facemask groups (MD, 0.97°; 95% CI, 1.79-0.15; P = 0.02) (Fig 7).

The resuts of Vaughn et al[27] showed no statistically significant difference for ANB between the 2 groups: facemasks with and without rapid maxillary expansion (MD, −0.13; 95% CI, −0.60 to 0.34; P = 0.59) (Fig 7).

Abdelnaby and Nassar[25] compared the use of 400-g and 200-g chincups. There was no statistically significant difference in the ANB changes (MD, 0.1°; 95% CI, −0.21-0.41; P = 0.53) (Fig 6) and the Wits analysis (MD, 0.3 mm; 95% CI, −1.12-0.52; P = 0.47) (Fig 7).

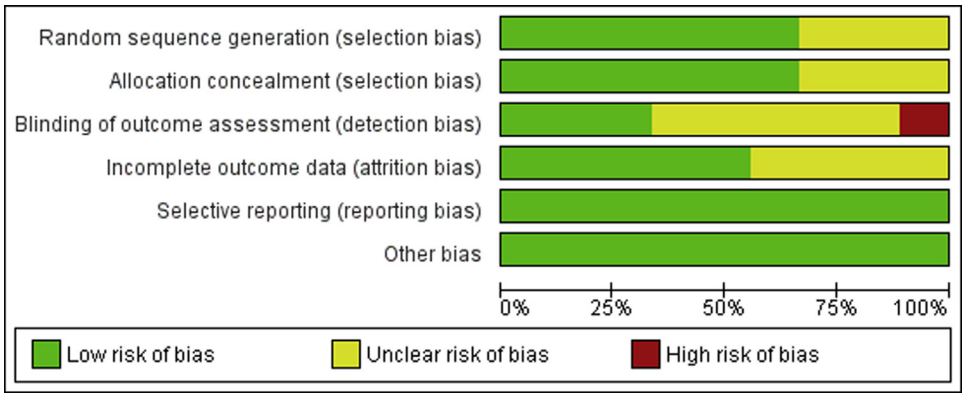

Fig 3. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included RCTs.

Liu et al[21] compared facemask appliances with expansion only vs expansion and constriction. The results showed no statistically significant difference for ANB between groups (MD, 0.14; 95% CI, 0.74 to −1.02; $P = 0.76$) (Fig 7).

CCTs

A total of 6 studies tested 6 different appliances.[30-35] A summary of the analyses for dental and skeltal changes is given in Figure 7. The results showed a statistically significant difference for the treatment groups compared with the control groups in all studies. Three studies looked at reverse overjet, and the results were statistically significant for the treatment groups in all studies (Fig 8).

DISCUSSION

Eight studies assessed the effectiveness of the facemask in early treatment.[23,26-29,31,32] Three studies[25,30,35] used chincups, and 2 studies[33,34] used maxillary protraction devices.

Quality of the RCTs

Only Mandall et al,[28,29] Liu et al,[21] and Showkatbakhsh et al[23] were judged as having low risk of bias. Five studies[9,21-24] were judged as having unclear risk of bias, and 1 study[6] was judged as having high risk of bias.

Quality of the CCTs

All included studies had high risk of bias.[31-35] The smaller numbers of participants with no sample size estimations and lack of blinding were some of the main shortcomings.

Heterogeneity

Overall, the facemask studies showed positive corrections in the skeletal and dental variables. However, because of the high heterogeneity in the pooled studies, the evidence was classified as moderate. Interestingly, we found no standardized design of the facemask for Class III treatment or a standardized outcome method for evaluating the effect of the appliance. The variations in the design of the facemask appliance used are discussed below.

Intraoral appliance

Mandall et al,[28,29] Liu et al,[21] Keles et al,[26] and Vaughn et al[27] used fixed rapid maxillary expansion devices, Cozza et al[31,32] used fixed buccal and palatal arches, and Xu and Lin[24] and Showkatbakhsh et al[23] used removable appliances.

Direction of force

The direction of force was reasonably consistent in the studies of Vaughn et al,[27] Liu et al,[21] Mandall et al,[28,29] Keles et al,[26] and Cozza et al[31,32] using about 30° of downward and forward force. Xu and Lin[24] and Showkatbakhsh et al[23] did not specify the direction of force application.

Force level

The force applied varied between 300 and 600 g. Cozza et al[31,32] used 600 g in their 2010 study and 400 g in their 2004 study, respectively. Mandall et al,[28,29] Vaughn et al,[27] and Xu and Lin[24] used about 400 g; Keles et al[26] and Showkatbakhsh et al[23] used 500 g, and Liu et al[21] used between 400 and 500 g of force.

Table V. Quality assessment of the CCT based on checklist of Downs and Black[9]

Study	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*	*19*	*20*	*21*	*22*	*23*	*24*	*25*	*26*	*27*	*Total*
Kajiyama et al[33] (2000)	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	1	0	1	1	1	0	0	0	0	1	0	14
Cozza et al[32] (2004)	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	1	0	14
Kajiyama et al[34] (2004)	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0	1	0	15
Lin et al[36] (2007)	1	1	1	1	0	1	1	1	1	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	1	0	13
Barrett et al[30] (2010)	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	1	0	15
Cozza et al[31] (2010)	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	1	0	13

Reporting: *1*, yes: *0*, no.

QUESTIONS:

1. Is the hypothesis/aim/objective of the study clearly described?
2. Are the main outcomes to be measured clearly described in the introduction or methods section?
3. Are the characteristics of the patients/samples in the study clearly described?
4. Are the interventions of interest clearly described?
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described? (*2*, yes; *1*, partially; *0*, no)
6. Are the main findings of the study clearly described?
7. Does the study provide estimates of the random variability in the data for the main outcomes?
8. Have all important adverse events that may be a consequence of the intervention been reported?
9. Have the characteristics of patients lost to follow-up been described?
10. Have actual probability values been reported (eg, 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001? (external validity: *1*, yes; 0, no and unable to determine)
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?
12. Were the subjects who were prepared to participate representative of the entire population from which they were recruited?
13. Were the staff, places, and facilities where the patients were treated representative of the treatment the majority of patients received? (Internal validity/bias: *1*, yes; *0*, no and unable to determine)
14. Was an attempt made to blind the subjects to the intervention they received?
15. Was an attempt made to blind those measuring the main outcomes of the intervention?
16. If any of the results of the study were based on "data dredging," was this made clear?
17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time between the intervention and outcome the same for subjects and controls?
18. Were the statistical tests used to assess the main outcomes appropriate?
19. Was compliance with the intervention reliable?
20. Were the main outcome measures used accurate (valid and reliable)? (Internal validity/confounding (selection bias): *1*, Yes; *0*, no and unable to determine)
21. Were the patients in different intervention groups (trials and cohort studies) or were the subjects and controls (case-control studies) recruited from the same population?
22. Were study subjects in different intervention groups (trials and cohort studies) or were the subjects and controls (case-control studies) recruited over the same period of time?
23. Were study subjects randomized to intervention groups?
24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?
26. Were losses of patients to follow-up taken into account?-

POWER:

27. Did the study have sufficient power to detect a clinically important effect where the probability for a difference due to chance was less than 5%? Sample sizes have been calculated to detect a difference of x% and y%.

Table VI. Summary of findings for RCTs

Study	*Location*	*Design*	*Groups*	*n*	*Age in years (SD)*	*Duration of follow up*	*ANB change (°)*	P *value*	*Overjet change (mm)*	P *value*
Vaughn et al[27]	Seattle, Phoenix, and Los Angles	RCT	A = FM with expansion	15	7.3	1.16 y	3.82	A vs B = NS (MD = 0.13)	NR	NR
			B = FM nonexpansion	14	8.1	1.15 y	3.95	A v C = SS (MD = 3.87)	NR	NR
			C = untreated control	17	6.6	1 y	−0.05	B vs C = SS (MD = 3.99)	NR	
Liu et al[21]	Beijing, China	RCT	A = FM with expansion	21	9.81 (1.72)	11.19 (2.75) mo	4.29 (1.54)	NS (P = 0.772)	NR	NR
			B = FM with expansion/ constriction	22	10.11 (1.44)	10.95 (2.73) mo	4.15 (1.41)			
Mandall et al[28,29]	United Kingdom	RCT	A = FM	30	8.7 (0.9)	3 years	1.5 (2.0)	SS (P = 0.001)	3.6 (2.6)	SS (P = 0.001)
			B = Untreated control	33	9.0 (0.8)	3 years	0.1 (1.9)		1.1 (2.6)	
Xu and Lin[24]	Beijing, China	RCT	A = FM with expansion	20	9.3	11.3	3.0 (1.7)	SS (P = 0.000)	NR	NR
			B = untreated control	20	9.3	11.3	−1.5 (0.89)			
Keles et al[26]	Istanbul, Turkey	RCT	A = conventional facemask	9	8.58	6 mo	3.89 (1.17)	NS (P = 0.052)	NR	NR
			B = Modified protraction headgear	11	8.51	6 mo	5.18 (1.4)			
Abdelnaby et al[25]	Mansour, Egypt	RCT	A = chincup with occlusal biteplate 600-g force	20	9.6	1 y	2.5 (0.51)	SS for treatment vs control group	NR	NR
			B = chincup with occlusal biteplate 300-g force	20	10.1	1 y	2.4 (0.5)			
			C = untreated control	10	9.2	1 y	0.5 (0.52)			
Atalay and Tortop[6]	Ankara, Turkey	RCT	A = modified tandem traction bow-early treatment	15	8.18 (0.5)	9 mo	1.7 (0.24)	SS for treatment vs control group	3.6 (0.36)	SS for treatment vs control group
			B = modified tandem traction bow-late treatment	15	11.75 (1.0)	11 mo	2.1 (0.18)		4.4 (0.34)	

Table VI. Continued

Study	Location	Design	Groups	n	Age in years (SD)	Duration of follow up	ANB change (°)	P value	Overjet change (mm)	P value
			C = untreated control	15	7.9 (0.62)	8 mo	0.0 (0.20)		0.3 (0.23)	
Saleh et al[22]	Saudi Arabia	RCT	A = removable mandibular retractor	34	7.5 (1.33)	14.5 (0.1) mo	NR	NR	NR	NR
			B = untreated control group	33	7.3 (1.58)	14.5 (0.1) mo				
Showkatbakhs et al[23]	Tehran, Iran	RCT	A = FM	24	9 (1.2)	18 (3) mo	1.2 (1.6)	NS ($P = 0.1$)	NR	NR
			B = tongue plate	23	9.1 (0.9)	16 (2) mo	1.8 (1.2)			

FM, Facemask; *MD*, mean difference; *NR*, not recorded; *SS*, statistically significant; *NS*, not significant.

Point of force application

There were wide variations between the studies on the point of force application for facemask appliances. Mandall et al[28,29] included hooks near the center of rotation of the maxilla, Vaughn et al[27] added hooks mesial to the canines, and Keles et al[26] placed the hooks distal to the canines. Liu et al[21] positioned hooks around the canine area, and Showkatbakhsh et al[23] and Cozza et al[31,32] added hooks near the first molar region.

Overall, 8 studies used 8 different type of facemask appliance design. A similar situation was noticed for the outcome measures. There was a lack of reporting on the dental changes induced by the facemask.

The quality of evidence in the studies looking at the chincup, tandem traction bow appliance, maxillary protraction bow appliance, modified maxillary protractor, and tongue plate was considered to be low. Although the results were favorable in terms of skeletal and dental changes, the high risk of bias made the positive results questionable.

All included studies focused only on the short-term treatment results, with a lack of long-term follow-up. Conventionally, the orthodontic treatment for a patient with Class III skeletal problem is to defer treatment until the patient passes the growth phase, since we are aware that if treatment is provided early, further growth will undo the good done by the early treatment and, in the worst case, compromise further orthognathic treatment. In short, the short-term favorable results are not conclusive and robust to allow any recommendation and prediction of the long-term treatment effects achieved by the appliances.

Outcomes

Reverse overjet was the main reason for a patient to seek orthodontic treatment. However, this finding was not assessed in most of the included studies. It might be due to the perception that skeletal changes are more crucial in Class III malocclusion correction because they will eventually help in the correction of reverse overjet. This makes it impossible to do a meta-analysis if the studies do not report on similar outcome measures. This shows the importance of developing core outcome sets in orthodontics so that every study has a minimum set of data that needs to be reported on.[36]

Three RCTs[6,26,27] and 5 CCTs[30,31,33-35] reported a positive result regarding reverse overjet correction. Mandall et al[28] and Atalay and Tortop[6] showed short-term improvements of 4.4 and 3.6 mm, respectively. In addition, at the 3-year follow-up, Mandall et al[29] demonstrated that the corrected overjet was maintained

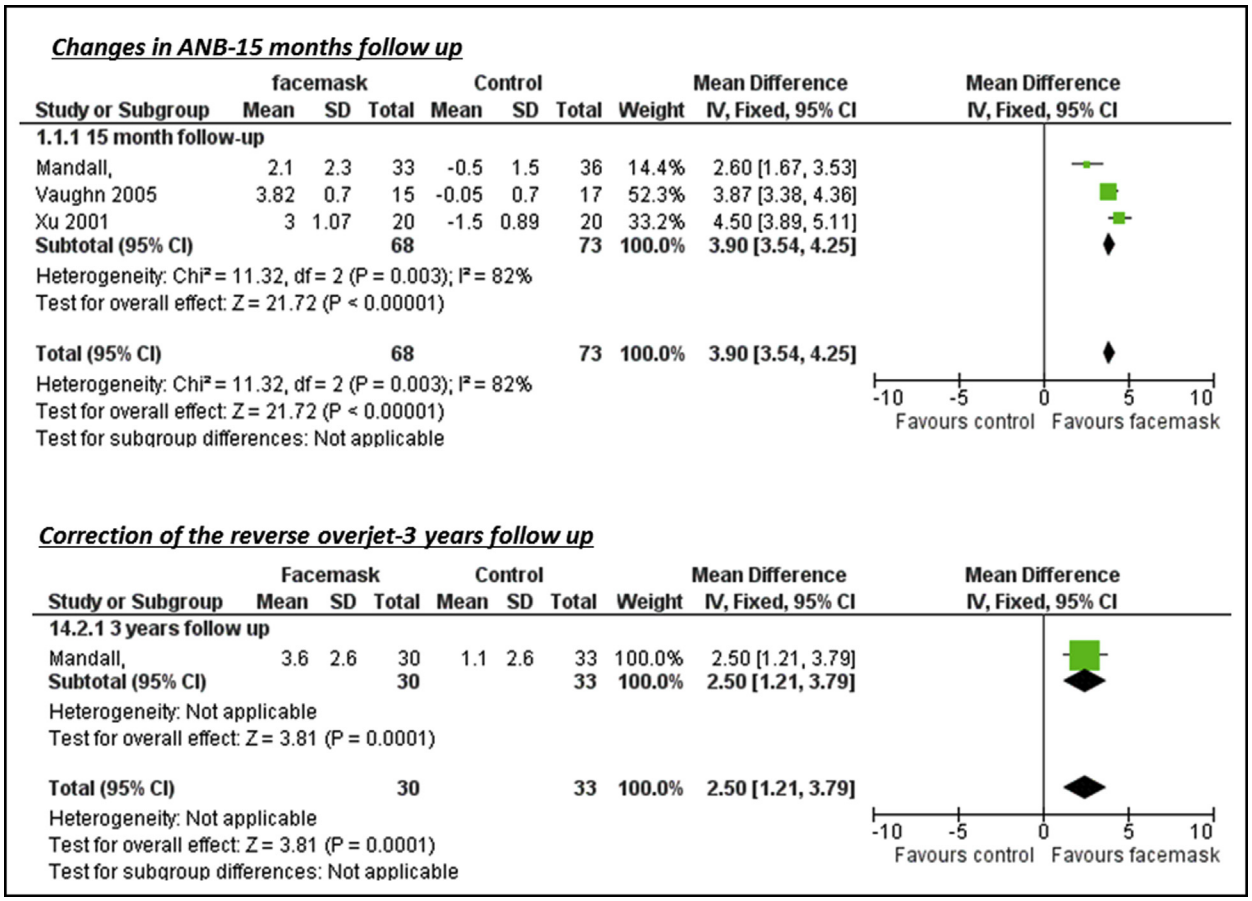

Fig 4. ANB and overjet changes in facemask studies.

at a mean value of 3.6 mm. This is an exciting finding; however, we have yet to receive any long-term follow-up data.

Skeletal changes

Skeletal changes in early Class III treatment are always the main focus of studies and were mostly reported as values for ANB angle and the Wits appraisal. For the facemask appliance, the reported ANB changes ranged from 2° to 5°. Conversely, the chincup studies displayed a smaller range of changes from 0.3° to 2.5°. However, no long-term data are available. For the other appliances, because of the small sample sizes and poor study quality, it is not possible to make any conclusion.

When the data for the SNA and SNB angles were looked at descriptively for treatment groups, the facemask produced improvement in both SNA and SNB consistently, whereas the chincup mainly worked on restriction of mandibular growth (SNB) (Table VII). However, the data for the chincup were derived from just 1 study.

Quality of life

The assessment of quality of life in early Class III treatment was evaluated by Mandall et al.[28,29] They concluded that early treatment does not seem to confer a clinically significant psychosocial benefit.[28] It is not surprising because, although the skeletal changes were statistically significant, they were only a few degrees, which might not be significant enough for patients to appreciate.

Reliability assessment in the studies

Intraexaminer reliability asessement for cephalometric radiograph assessment was reported in 6 studies.[21-23,25,27,28] Keles et al[26] Atalay and Tortop,[6] and Xu and Lin[24] did not report on reliability assessment. Four[21,22,25,27] of the 6 studies used Dahlberg's formula, whereas Showkatbakhsh et al[23] used Cronbach's alpha, and Mandall et al[28] used the intraclass correlation coefficient for reliability assessment.

Limitation of Class III studies

The main limitation for early Class III treatment studies is the delay in treatment for the control subjects.

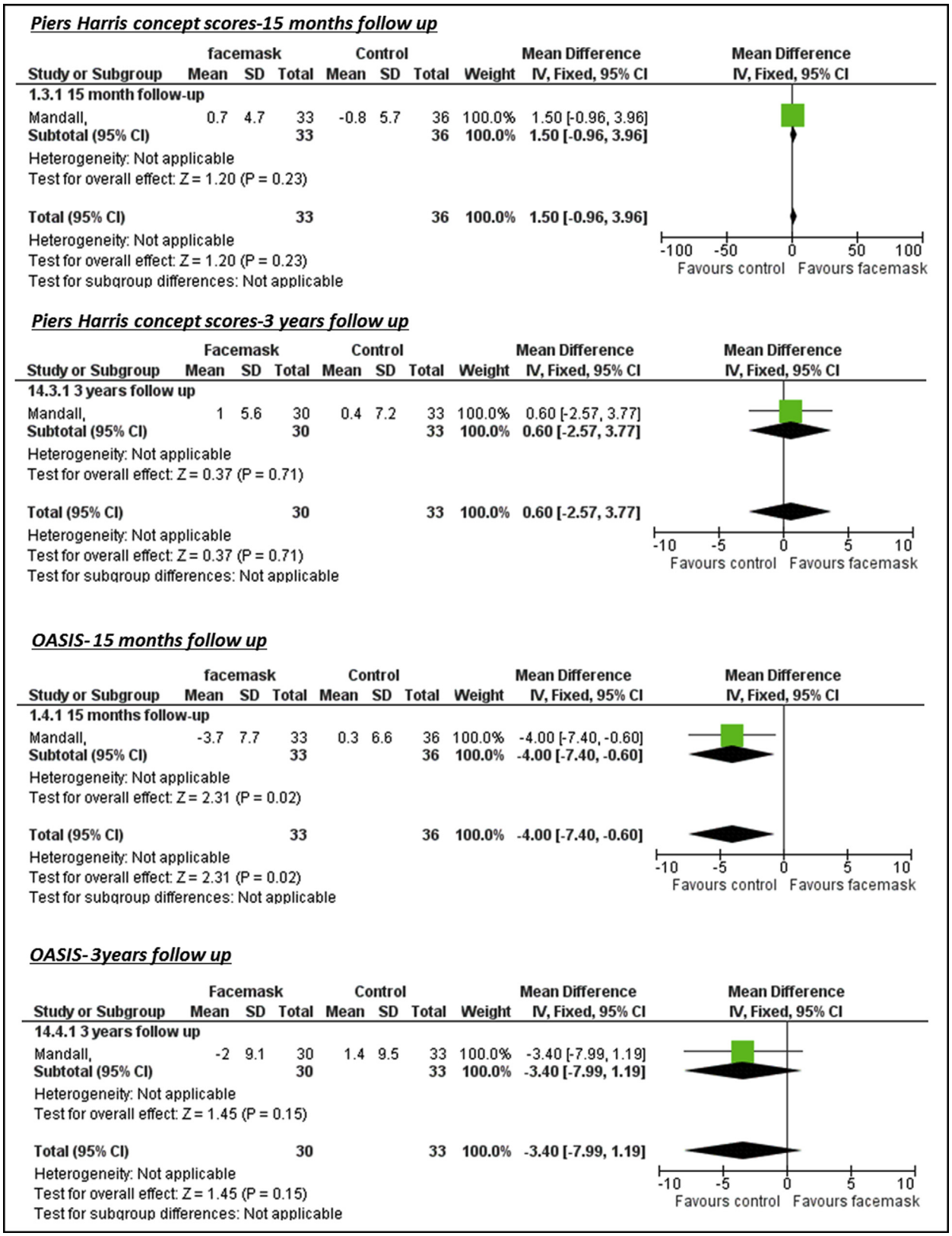

Fig 5. Piers-Harris and OASIS scores in facemask studies.

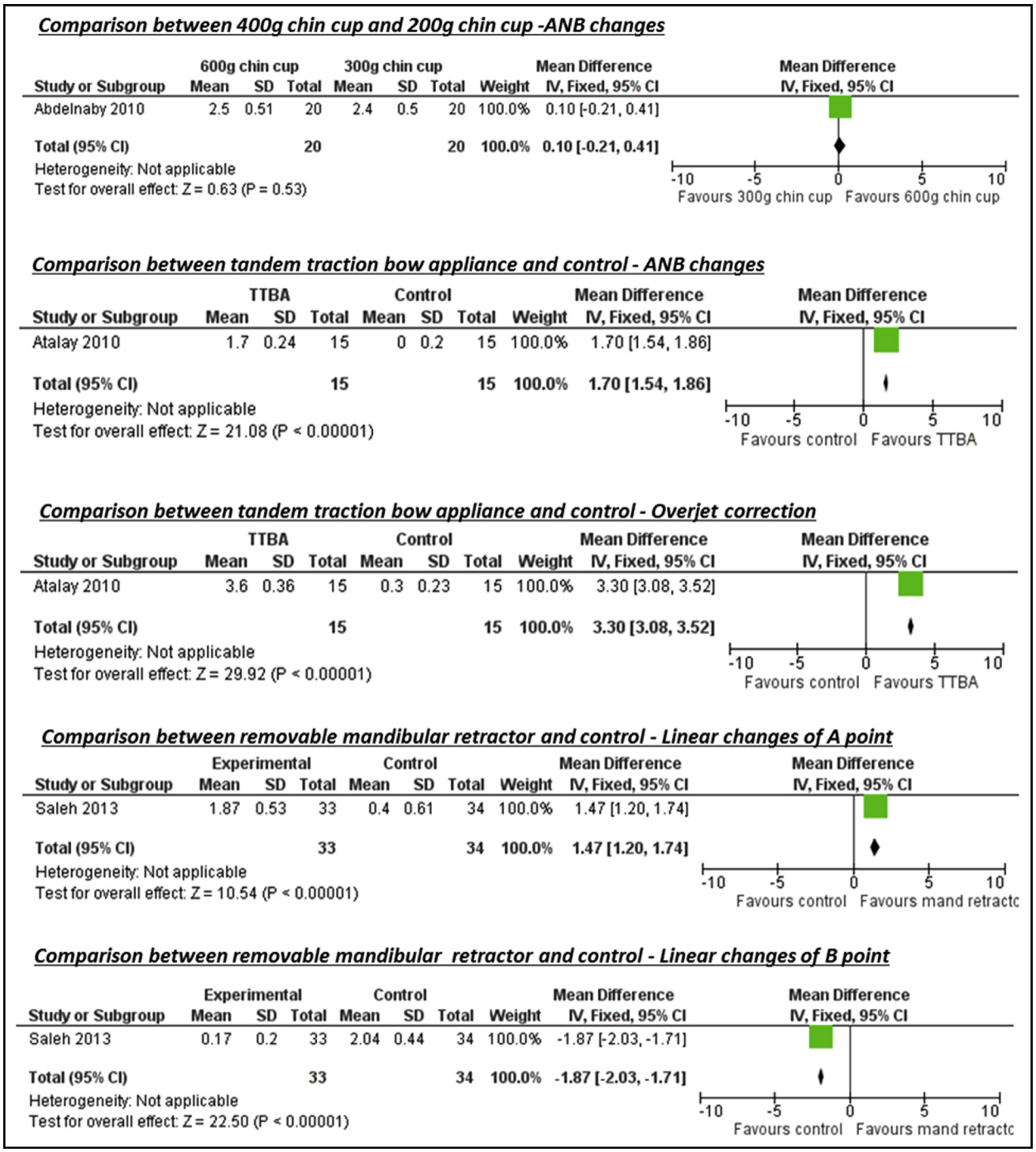

Fig 6. Meta-analysis of RCTs comparing treatment vs untreated controls: skeletal and dental changes.

Although RCTs are the gold standard to evaluate the effectiveness of 1 intervention, it is unethical to have a control group that does not receive treatment. Furthermore, after recruitment, patients need to be followed until the age of 16 or 17 when mandibular growth ceases, to evaluate the real benefit. This increases the cost and, more importantly, burns off patient compliance, leading to high a dropout rate. Another barrier for early Class III treatment is age limit. Patients need to be recruited as early as 8 years. Along with the age

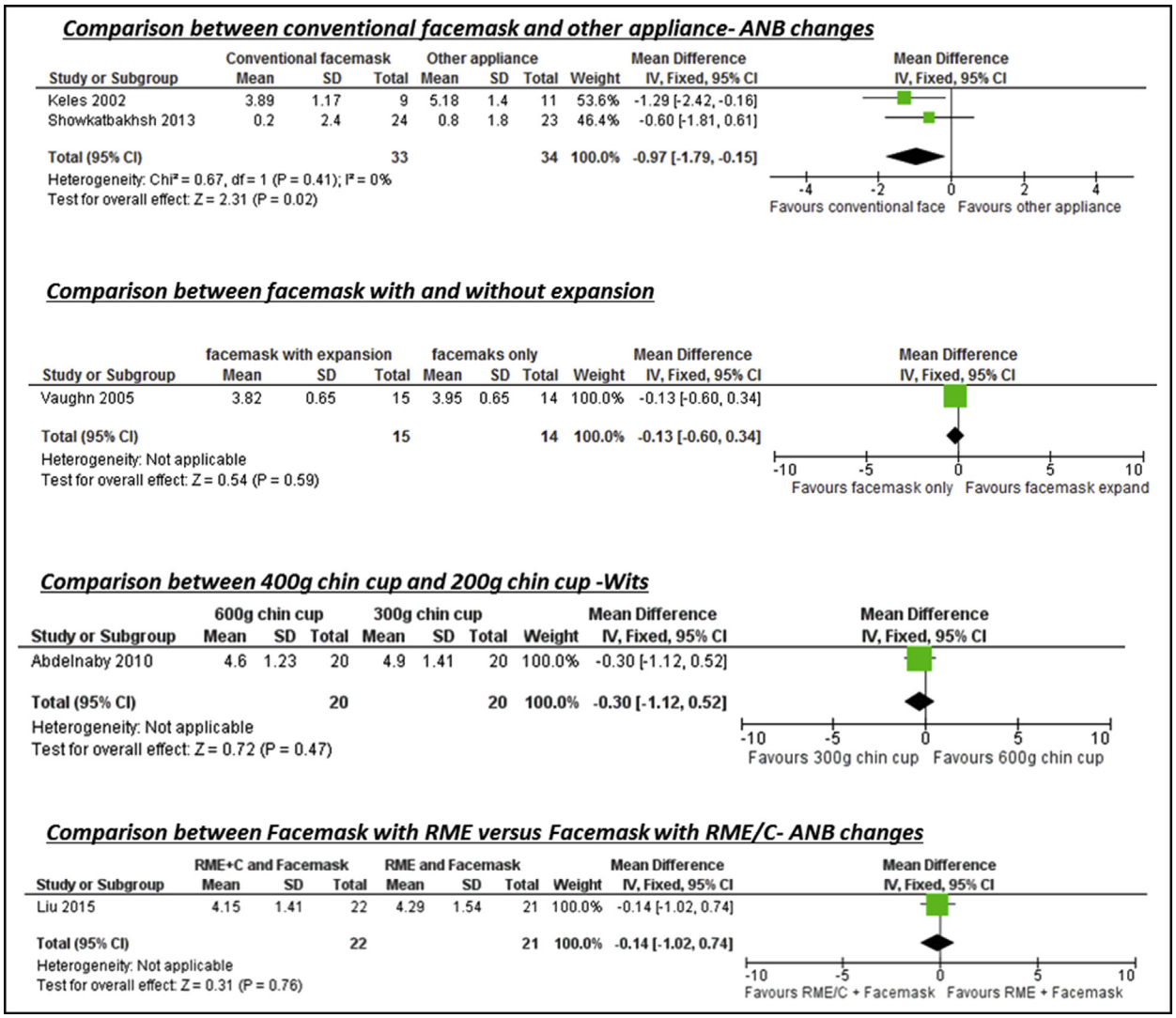

Fig 7. Meta-analysis of RCTs comparing treatment 1 vs treatment 2: skeletal and dental changes.

of referral, compliance of these young patients is another challenge for early treatment. However, data on patient perceptions toward early treatment, which could answer this, are the part least reported by most studies.

The prevalence of Class III malocclusion varies widely among different regions and ethnic groups. It has been reported to be as low as 5% in European countries.[37,38] Funding bodies are biased to studies that make the most impact, and it is unlikely that they will fund for diseases with rare occurrences. This makes it difficult to acquire big research funding in orthodontics, especially when competing with medical illnesses such as cancer and diabetes studies. Additionally, recruitment becomes a challenge and has a direct impact on the cost.

The Cochrane review by Watkinson et al[7] included only RCTs and concluded that there is some evidence about the effectiveness of the facemask in treating prominent mandibular teeth in the short term. Additionally, the review did not include the 3-year follow-up results of Mandall et al,[19] Showkatbakhsh et al,[13] and Liu et al.[11] These studies showed low risk of bias and had a positive result on the outcome.

The systematic review by Liu et al,[29] on the use of a chincup indicated insufficient data to make a clear recommendation. The review found no RCT and included only cohort studies with high risk of bias. In

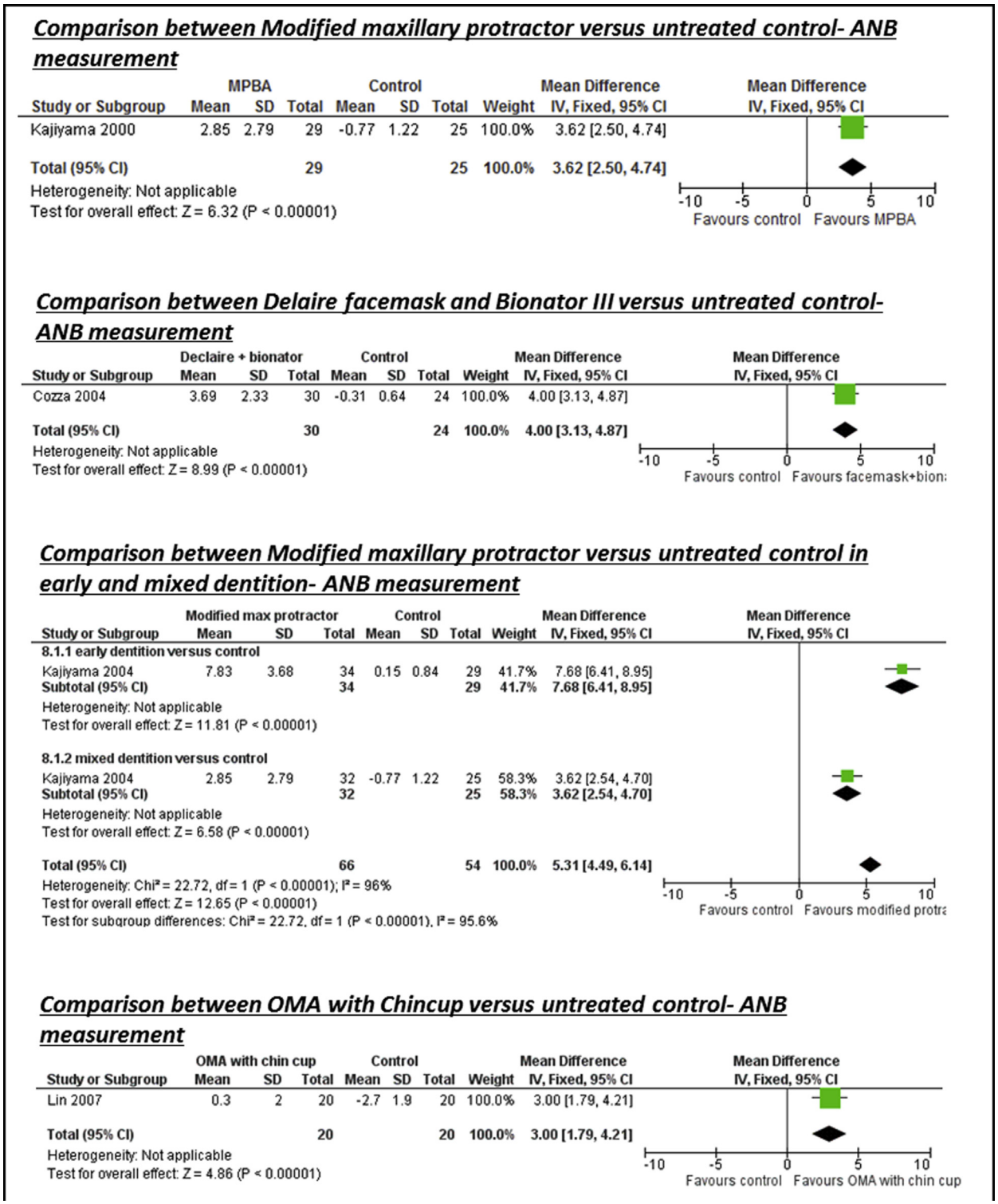

Fig 8. Meta-analysis of CCTs: skeletal and dental changes.

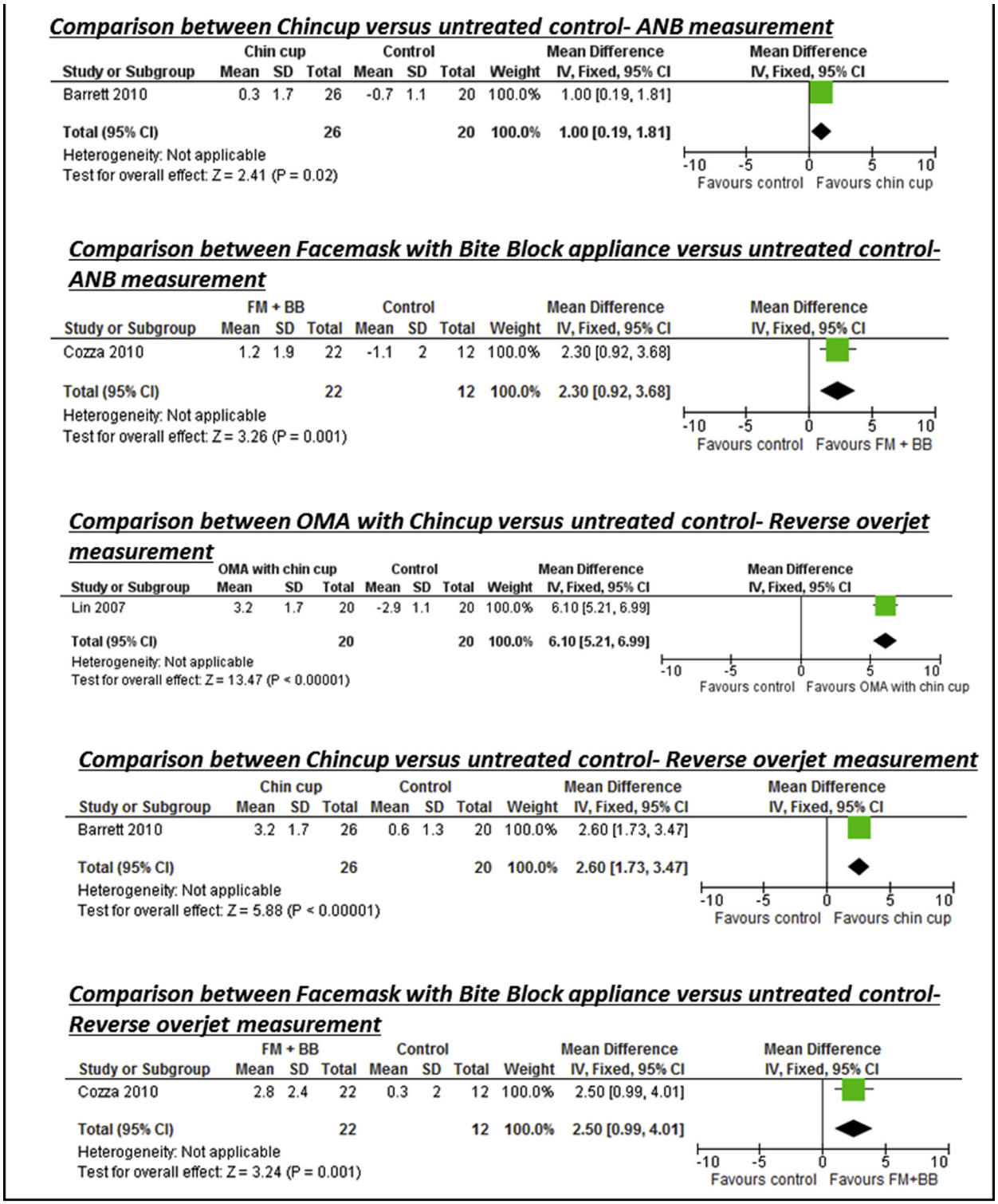

Fig 8. (continued).

Table VII. SNA and SNB changes for treatment groups in RCTs

		Treatment group changes in degrees (DC2–DC1)	
Study	*Groups*	*SNA mean (SD)*	*SNB mean (SD)*
Vaughn et al[27]	A = FM with expansion	2.77	−1.06
	B = FM nonexpansion	2.51	−1.43
Liu et al[21]	A = FM with expansion	1.93 (0.79)	−2.35 (1.21)
	B = FM with expansion/constriction	2.67 (1.31)	−1.49 (0.89)
Mandall et al[28,29]	A = FM	2.3 (2.1)	0.8 (1.5)
Xu and Lin[24]	A = FM with expansion	1.25 (1.32)	−1.69 (0.99)
Keles et al[26]	A = FM	3.11 (1.05)	−0.78 (1.48)
	B = modified protraction headgear	3.09 (1.7)	−2.1 (1.58)
Abdelnaby and Nassar[25]	A = chincup with occlusal biteplate 600-g force	0.3 (0.47)	−2.2 (0.41)
	B = Chincup with occlusal biteplate 30-g force	0.4 (0.5)	−2.0 (0.79)
Atalay and Tortop[6]	A = modified tandem traction bow-early treatment	0.7 (0.28)	−1.1 (0.32)
Showkatbakhsh et al[23]	A = FM	1.0 (1.5)	−0.2 (1.5)
	B = Tongue plate	2.2 (1.5)	0.4 (0.5)

DC, data collection; *FM*, facemask.

our review, we found 1 RCT, but it was judged as having a high risk of bias. Hence, no recommendation can be drawn because of the weak evidence.

CONCLUSIONS

1. The overall quality of evidence was low. Only 3 of the 15 studies were classified as having a low risk of bias.
2. There is moderate evidence to show that early treatment with a facemask resulted in positive improvements in both skeletal and dental changes in the short term. However, there is a lack of evidence for the long-term benefits.
3. Although the chincup appliance showed greater skeletal changes when compared with the untreated control group, due to high heterogeneity and high risk of bias, the results should be interpreted with caution.
4. Further long-term, high-quality studies are needed to determine the long-term effects of orthopedic treatment for Class III patients.
5. The results from this study could be a starting point for clinicians to have a discussion with both patients and their parents to make an informed decision regarding early treatment.

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