Systematic Review Article

Treatment effects of fixed functional appliances alone or in combination with multibracket appliances:
A systematic review and meta-analysis

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ABSTRACT

Objective: To assess skeletal and dentoalveolar effects of fixed functional appliances, alone or in combination with multibracket appliances (comprehensive treatment), on Class II malocclusion in pubertal and postpubertal patients.

Materials and Methods: Literature survey was conducted using the Medline, SCOPUS, LILACS, and SciELO databases and The Cochrane Library, and through a manual search. The studies retrieved had to have a matched untreated control group. No restrictions were set regarding the type of fixed appliance, treatment length, or to the cephalometric analysis used. Data extraction was mostly predefined at the protocol stage by two authors. Supplementary mandibular elongation was used for the meta-analysis.

Results: Twelve articles qualified for the final analysis of which eight articles were on pubertal patients and four were on postpubertal patients. Overall supplementary total mandibular elongations as mean (95% confidence interval) were 1.95 mm (1.47 to 2.44) and 2.22 mm (1.63 to 2.82) among pubertal patients and −1.73 mm (−2.60 to −0.86) and 0.44 mm (−0.78 to 1.66) among postpubertal patients, for the functional and comprehensive treatments, respectively. For pubertal subjects, maxillary growth restraint was also reported. Nevertheless, skeletal effects alone would not account for the whole Class II correction even in pubertal subjects with dentoalveolar effects always present.

Conclusions: Fixed functional treatment is effective in treating Class II malocclusion with skeletal effects when performed during the pubertal growth phase, very few data are available on postpubertal patients. (*Angle Orthod.* 2015;85:480–492.)

KEY WORDS: Class II; Functional treatment; Timing; Growth phase; Systematic review

INTRODUCTION

Skeletal Class II malocclusion occurs in 25%–30% of the general population, is one of the most prevalent malocclusions,[1] and is mainly a consequence of mandibular retrusion.[2] Therefore, removable or fixed functional appliances were designed to increase mandibular growth by forward positioning of the mandible.[2] Previous systematic reviews of the literature[3–5] on the outcomes of functional treatment for Class II malocclusion, mainly through removable appliances, have shown substantial variability of reported results. These differences have to be ascribed mainly to the type of appliance used or duration of active treatment needed to achieve Class II correction. However, none of these reviews have focused attention on the timing of intervention, ie, the growth phase during which treatment was performed.[6] Indeed, timing has been reported as one of the key factors for successful treatment outcome with the

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Table 1. Inclusion and Exclusion Criteria Used in the Present Review

Inclusion Criteria
1. Longitudinal studies, either prospective or retrospective, on healthy growing subjects treated for skeletal Class II malocclusion
2. Use of fixed functional orthodontic appliances
3. Use of a reliable skeletal maturity indicator
4. Treatments preformed during either the pubertal or postpubertal phase
Exclusion Criteria
1. Case reports, case series with no statistical analysis, comments, letters to the Editor, reviews, article analysis
2. Studies using the headgear alone or in combination with other functional appliances, or eruption guidance appliances
3. Studies in which the compared treated groups were subjected to different treatment modalities
4. Studies in which orthodontic treatments were combined with surgery
5. Studies without cephalometric analyses
6. Studies in which a favorable response (according to the authors' definition) to treatment was an inclusion criterion
7. Studies in which control group was based on published reference standard without a specific matching of the groups by age, sex, and other features

pubertal growth phase as the optimal period for the achievement of skeletal effects.[6,7] Moreover, patient compliance is another important issue when dealing with functional treatment, which can be overcome by the use of fixed functional appliances.

Therefore, the aim of the present review and meta-analysis was to assess main skeletal and dentoalveolar effects of fixed functional appliances, alone or in combination with multibracket appliances (MBA), in the treatment of Class II malocclusion. This was done according to the pubertal or postpubertal growth phase in growing patients as compared with matched untreated controls.

MATERIALS AND METHODS

Search Strategy

The present meta-analysis follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[8] and it has been registered at the PROSPERO database (http://www.crd.york.ac.uk/PROSPERO, CRD42014009769). Articles were identified through a literature survey carried out through the following databases: (1) PubMed, (2) SCOPUS, (3) Latin American and Caribbean Health Sciences (LILACS), (4) Scientific Electronic Library Online (SciELO), and (5) The Cochrane Library. The survey covered the period from inception to the last access on July 2, 2014, without language restrictions. The search algorithms used in each database are given in Appendix 1. Finally, a manual search was also performed by scoring the references within the studies examined and the titles of the papers published over the last 20 years in the main orthodontic journals. The eligibility assessment and data collection processes were performed independently by two blinded authors. Conflicts were resolved by discussion of each article, until consensus was reached.

Eligibility Criteria

The studies retrieved had to be either randomized controlled trials (RCTs) or either prospective or retrospective controlled clinical trials (CCTs). They had to include healthy patients treated during either the pubertal or postpubertal growth phases. These studies had to investigate the skeletal and dentoalveolar effects with no restriction as to the type of parameters collected. Also, no restrictions were set regarding the type of fixed appliance used alone or in combination with MBA (comprehensive treatment), treatment length, or to the cephalometric analysis used. Studies were also excluded if a reliable indicator of the growth phase (hand-and-wrist maturation [HWM] method or cervical vertebral maturation [CVM] method) was not used. Further details are listed in Table 1.

Data Items

The following data were extracted independently by two authors: study design, enrollment of the treated group, sample size, sex distribution, age, treatment, Class II diagnosis, indicators of skeletal maturity, and distribution of subjects according to growth phase, prognostic or other features, full observational term, functional and/or comprehensive treatment length, mandibular advancement, and when treatment was stopped. Regarding the treatment effects, the following items were also collected: success rate (as defined in the different studies); skeletal, dentoalveolar, and soft tissue effects; and clinical implications with regard to the growth phase at which treatment was performed. Forms used for the data extraction were mostly predefined at the protocol stage by two authors.

Assessment of Risk of Bias in Individual Studies and Across Studies

As no single approach in assessing methodologic soundness may be appropriate for all systematic

Table 2. Assessment of Risk of Bias

Pre-established Characteristics	Score
1. Adequacy of sample selection description based on age and sex across the groups	Full: 2 points; partial: 1 point
2. Study design for the inclusion of the treated group	Prospective: 1 point; retrospective or not declared: 0 points
3. Description of the Class II (full, skeletal, and/or dental parameters; partial, only dental parameters	Full: 2 points; partial: 1 point
4. Distribution of the different maturational stages among the investigated subjects	Full: 2 points; partial: 1 point
5. Adequacy of treatment description based on three criteria: (a) orthodontic appliance; (b) mandibular advancement or information when the functional treatment was stopped; (c) length of the functional treatments (irrespective of the comprehensive multibracket appliance therapy when performed)	Full: 2 points; partial: 1 point
6. Incomplete outcome data (cephalometric magnification, success rate)	No: 1 point; yes: 0 points
7. Withdrawals declared or derivable	Yes: 1 point; no: 0 points
8. Description of the method error analysis (overall [random and systematic] errors; only systematic error; no)	Overall: 2 points, systematic: 1 point; no: 0 points
9. Blinding for measurements	Yes: 1 point; no: 0 points
10. Adequacy of statistics based on the comparisons of the intragroup changes over time among/between groups (yes, when parametric or nonparametric tests used where appropriate; no, when parametric tests used when nonparametric tests would be more appropriate, multiple comparisons with uncorrected *P* values, statistical analysis only partially described)	Yes: 2 points, no: 1 points
11. Prior estimation of sample size or a posteriori power analysis	Yes: 1 point, no: 0 points

reviews,[9] a dedicated evaluation risk of bias in individual studies (performed independently by two expert authors) was used that followed pre-established characteristics, along with the systematic scores that were assigned to the individual retrieved articles detailed in Table 2. The quality of the studies, with a maximum possible score of 17, was considered as follows:

- low: total score $\leq$7 points;
- medium: total score $>$7 and $\leq$10 points;
- medium/high: total score $>$10 and $\leq$14 points; and
- high: total score $>$14 points.

Heterogeneity was assessed using the χ^2-based Q-statistic method and I^2 Index; however, because of the moderate insensitivity of the Q statistic,[10] only an I^2 Index $\geq$50% was considered associated with a substantial heterogeneity among the studies.[11] The tau^2 was also calculated for the heterogeneity assessment. Egger test was employed to assess publication bias[12] for those parameters that showed acceptable heterogeneity (I^2 Index generally below 50%). Calculations were performed by using the Comprehensive Meta-Analysis software (Biostat Inc, Englewood, NJ).

Primary and Secondary Outcomes

Supplementary mandibular growth with respect to the untreated control group was considered as the primary outcome. This outcome was defined either as total or composite mandibular length change. The total mandibular length was derived from the following cephalometric measurements: condylion-gnathion, condylion-pogonion, and articulare-pogonion; unit of measure was expressed in millimeters. Composite mandibular length, also expressed in millimeters, was obtained by the Pancherz analysis.[13] Analyses were performed separately for the two parameters. Secondary outcomes were: SNA, SNB, and ANB angles, total facial divergence (angle between mandibular plane and S-N line or Frankfort horizontal plane), maxillary incisors inclination (relative to the S-N line or Frankfort

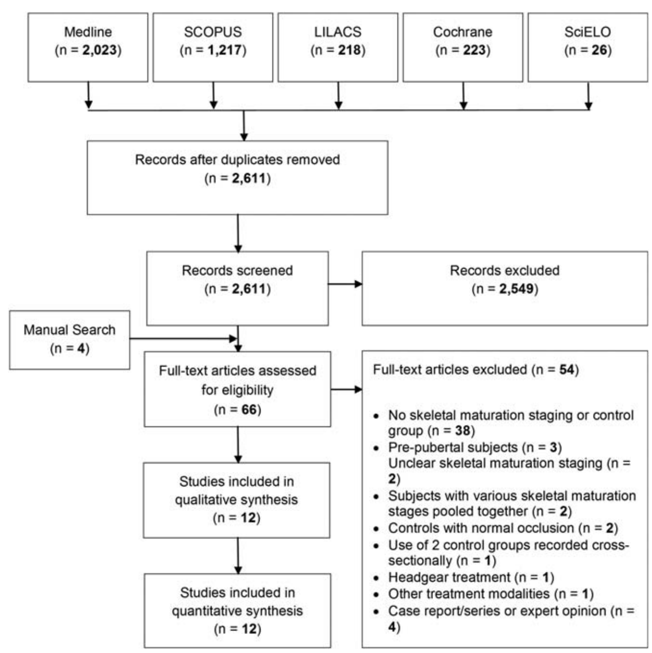


Figure 1. Flow diagram of the search strategy.

Table 3. Summarized Protocols of the 11 Studies (12 Articles) Included in the Present Systematic Review*

Study	Enrollment of the Treated Group	Sample Size and Mean Age, y (Range or SD)	Treatment	Diagnosis: Class II
Pancherz[15]	Prospective[b]	3 F; 19 M 12.1 ± 0.9	Banded Herbst appliance	1. Bilateral Class II molar relationship 2. Deep anterior overbite
		3 F; 17 M 11.2 ± 0.7	Untreated	
Franchi et al.[16]	Retrospective[b]	27 F; 28 M 12.8 ± 1.2	Acrylic splint Herbst appliance followed by MBA	1. Half cusp Class II molar relationship (at least) 2. Overjet >4 mm[b]
		15 F; 15 M 13.1 ± 1.2	Untreated	
Nalbantgil et al.[17]	Not reported	8 F, 7 M 15.1 ± 1.0	Jasper Jumpers appliance after 6 mo of arch alignment and levelling	1. Skeletal and dental Class II malocclusion due to mandibular retrusion
		9 F, 6 M 15.1 ± 0.8	Untreated	
Küçükkeleş et al.[18]	Retrospective[b]	13 F, 12 M 11.8	Jasper Jumper appliance in combination with MBA	1. Skeletal and dental Class II malocclusion due to mandibular retrusion
		10 F, 10 M 11.3	Untreated	
Baccetti et al.[19]	Prospective	14 F; 14 M 13.0 ± 0.8	Acrylic splint Herbst appliance[c]	1. ANB >4° 2. Full cusp Class II molar relationship 3. Overjet >5 mm
		14 F; 14 M 12.9 ± 1.3	Untreated	
Franchi et al.[20]	Retrospective[b]	13 F, 19 M[d] 12.7 ± 1.2	Forsus FRD appliance in combination with MBA	1. ANB ≥3° 2. Half cusp Class II molar relationship (at least) 3. Overjet >5 mm
		14 F, 13 M[d] 12.8 ± 1.3	Untreated	
Al-Jewair et al.[21]	Retrospective	18 F, 22 M 11.6 ± 1.9	MARA followed by MBA	1. SNB ≤77° 2. ANB ≥4° 3. Overjet <10 mm
		17 F, 13 M 12.3 ± 1.3	AdvanSync followed by MBA	
		11 F, 13 M 11.9 ± 1.9	Untreated	
Ghislanzoni et al.[22]	Prospective	11 F, 4 M[b] 11.4 ± 1.6 12 F, 3 M[b] 14.9 ± 1.8	MARA in combination with MBA	1. ANB >2.0° 2. Half Class II molar relationship (at least) 3. Overjet >4 mm
		11 F, 6 M[b] 12.1 ± 1.3[b] 10 F, 7 M[b] 13.2 ± 1.4[b]	Untreated	

Table 3. Extended

Diagnosis					
Skeletal Maturation Method/Stage	Prognostic or Other Features	Cephalometric Magnification	Full Observational Term (Mean and SD), mo[a]	Treatment Length: Functional/ Comprehensive, mo	Mandibular Advancement/ Treatment Stopped
HWM/not passed the pubertal growth spurt	Not reported	7%	6.2 ± 0.5	Full observational term	Incisors at edge-to-edge position/not reported
			6.2 ± 0.3		
CVM/CS3, CS4	Not reported	8%	28 ± 9	12.0 ± 6.0/Full observational term	Not reported
			25 ± 4		
HWM/postpubertal	Normal or low-angle growth pattern	Not reported	Not reported	Not reported	Stepwise activation every 8 wk/Class I canine and molar relationship
			6		
HWM/pubertal	Normal or low-angle growth pattern and well-aligned lower arch	Not reported	6	6.0/not reported	2-mm activation after 1 wk renewed once in 6 wk/ Class I molar relationship
			6		
CVM/CS3, CS4	Not reported	8%	32.4 ± 8.4	11.0/6 mo shorter than the mean full observational term	3–4 mm initial activation followed by 2–3 mm stepwise activation/Class I molar relationship
			32.4 ± 10.8		
CVM/CS2 (n = 2); CS3–CS4 (n = 14); CS5–CS6 (n = 16)	About 80% with Co-Go-Me angle <125°	8%	28.8 ± 4.8 (including an initial levelling phase)	5.2 ± 1.3/Full observational term	Not applicable/edge-to-edge incisor relationship
CVM/CS3–CS4 (n = 12); CS5–CS6 (n = 15)			31.2 ± 10.8		
CVM during the pubertal growth peak	FMA angle of 25° ± 5°	8%	39.6 ± 22.8	18.0 ± 10.8/Full observational term	Stepwise activation of 2–4 mm every 3 mo over 12-mo period when slight dental overcorrection was achieved.
			27.6 ± 8.4	14.4 ± 6.0/Full observational term	Stepwise activation of 2–4 mm every 3 mo over a 6- to 12-moperiod when moderate dental overcorrection to an anterior crossbite was achieved
			36.0 ± 12.0		
CVM/CS3–CS4	Not reported	8%	27.6 ± 10.8	16.8 ± 8.4/Full observational term	2–3 mm Stepwise activation/ slight dental Class II overcorrection
CVM/CS5–CS6			24.0 ± 9.6	16.8 ± 12.0/Full observational term	
CVM/CS3–CS4			26.4 ± 6.0[b]		
CVM/CS5–CS6			25.2 ± 3.6[b]		

Table 3. Continued

Study	Enrollment of the Treated Group	Sample Size and Mean Age, y (Range or SD)	Treatment	Diagnosis Class II
Oztoprak et al.[23]	Prospective	11 F, 9 M 15.2 ±1.2	SUS² in combination with MBA	Skeletal and dental Class II malocclusion due to mandibular retrusion
		12 F, 8 M 15.1 ± 1.0	Forsus FRD in combination with MBA	
		14 F, 5 M 14.7 ± 1.2	Untreated	
Phelan et al.[24]	Prospective	20 F; 14 M[e] 13.5 ± 1.2	Sydney Magnoglide followed by MBA	1. ANB >3.5° 2. Half Class II molar relationship (at least) 3. Overjet >6 mm
		15 F, 15 M 13.0 ±1.6	Untreated	
Baysal and Uysal[25,26]	Prospective	11 F, 9 M 12.7 ± 1.4	Banded Herbst appliance	1. SNB <78° 2. ANB >4° 3. Overjet ≥5 mm 4. Bilateral molar Class II relationship (at least 3.5 mm)
		9 F, 11 M 12.2 ± 1.5	Untreated	

* F indicates female; M, male; CS, CVM stage; CVM, cervical vertebral maturation; FMA, Frankfort/mandibular plane angle; FRD, fatigue resistant device; HWM, hand-and-wrist maturation; MARA, mandibular advancement repositioning appliance; MBA, multibracket appliance; MP3cap, medial phalanx capping stage of the third finger; SUS², Sabbagh Universal Spring; and NA, not available.

[a] Since the beginning of the functional treatment phase.

[b] Information provided by the authors.

[c] Removable splint Herbst worn full time.

[d] Full sample.

[e] Before three dropouts.

horizontal plane), and mandibular incisors inclination (relative to the mandibular plane).

Meta-analysis

For meta-analysis, data were combined using the Review Manager software 5.2 (http://www.cochrane.org). The mean difference was used for statistical pooling of data, and results were expressed as mean and 95% confidence intervals (CIs). Although the measures of total mandibular length differed slightly among the studies, these measurements were combined in the overall effects according to the concept that the differences in the intragroup changes would be poorly sensitive to the absolute measures from which they are derived. Subgroup analyses were performed whenever possible according to the growth phase (pubertal or postpubertal) during which the treatment was performed. Moreover, to account for the heterogeneity of the treatments (ie, differences among appliance used), treatment length, and cephalometric analysis, a random effect model was used for the overall effects calculations.[14] Finally, these analyses were reported according to the type of treatment (functional or comprehensive) and shown through forest plots. In studies including two or more treated groups compared to a single control group, data from treated groups were pooled according to the Cochrane Handbook indications (http://handbook.cochrane.org).

RESULTS

Study Search

The results of the electronic and manual searches are summarized in Figure 1. According to the electronic search, 2611 articles were retrieved. Among these, 12 studies[15–26] were judged to be relevant to the present study according to the inclusion/exclusion criteria. However, two articles were clearly derived from the same study sample reporting either the results about soft tissues and SNA, SNB, and ANB angles[25] or other dentoskeletal effects,[26] and may be considered as a single study. A further article[27] could not be retrieved upon Internet search, through the local library facility, and after having contacted the authors. For one study pooling pubertal and postpubertal subjects,[20] data regarding the pubertal subjects could be extracted only from the whole sample. The full details of the 12 included studies are summarized in Tables 3 and 4.

Study Designs and Treatment Interventions

Of the 12 studies included, the enrollment of the treated group was prospective in six of them[15,19,22–26] and retrospective in four[16,18,20,21]; in one study the enrollment protocol was not reported or retrieved after contacting the authors. The sample sizes ranged from a minimum of 15 subjects[17,22] to a maximum of 55

Table 3. Extended Continued

Diagnosis					
Skeletal Maturation Method/Stage	Prognostic or Other Features	Cephalometric Magnification	Full Observational Term (Mean and SD), mo[a]	Treatment Length: Functional/Comprehensive, mo	Mandibular Advancement/Treatment Stopped
CVM/CS5–CS6	SN/MP angle from 25° to 35°	Not reported	Not reported	5.2 ± 2.1/Not reported	Activation every 8 wk with steps ≤5 mm/Class I canine and molar relationship
				5.2 ± 1.2/Not reported	
CVM/CS3 (25.8%), CS4 (51.6%)	Not reported	8%	24.0	12 ± 5.0/Full observational term	Class I molar relationship/not reported
CVM/CS3 (43.3%), CS4 (46.7%)			28.8		
HWM/fourth (S and H2) or fifth (MP3cap) epiphyseal stages	SN/GoGn angle of 32° ± 6°	14%[b]	15.8 ± 6.0	6 (at least)	Incisors at edge-to-edge position/normal or corrected overjet in retruded mandibular position
			15.6 ± 3.1		

subjects,[16] and all the studies included both male and female subjects.

The fixed functional appliances used were either a banded Herbst appliance,[15,25,26] an acrylic splint Herbst[19] followed by MBA,[16] a Jasper Jumper mounted after dental arch alignment[17] or in combination with MBA,[18] Forsus fatigue resistant device (FRD) in combination with MBA,[20,23] mandibular repositioning appliance (MARA) followed by MBA,[21,22] AdvanSync followed by MBA,[21] Sabbagh Universal Spring (SUS^2) in combination with MBA,[23] and the magnetic Sydney Magnoglide followed by MBA.[24]

To assess the growth phase, seven studies[16,19–24] used the CVM method, while the other investigations[15,17,18,25,26] used the HWM method. Accordingly, treatments were performed during the pubertal growth phase in all the studies, except for three investigations that included also[22] or only[17,23] postpubertal subjects.

The mean treatment duration with a fixed functional appliance (with or without MBA) performed during the pubertal growth phase ranged from 5.2 (Forsus FRD)[20] to 18.0 (MARA)[21] months. In the postpubertal patients, the mean treatment duration ranged from 5.2 (SUS^2)[23] to 16.8 (MARA)[22] months. Comprehensive treatments lasted from 24.0 (MARA and MBA, postpubertal)[22] to 39.6 months (MARA and MBA, pubertal).[21]

A stepwise mandibular advancement of 2 to 4 mm was performed in most of the studies.[17–19,21–24] In two investigations, a mandibular advancement to an incisor edge-to-edge relationship was used,[15,26] while in one study[24] mandibular advancement to a Class I molar relationship was performed. Two studies did not report the amount of mandibular advancement during treatment.[16,20] In most of the studies, treatment was performed until a Class I molar relationship[17–19,23] or a slight overcorrection[20–22] was achieved. In one study, treatment was stopped when a normal or corrected overjet was achieved in a mandibular retruded position,[26] while three studies did not report when treatment was stopped.[15,16,24]

Main Results

Three studies reported 100% success rate.[15,24–26] Two studies reported success rates of 87.5%[20] and 92.8%,[19] while in the rest of the studies the success rate was not reported.

Regardless of the treatment timing, dentoalveolar effects were generally seen. At the mandibular level, these effects were reported as mesial movement of the mandibular dentition,[15,16] mesial movement[18,21,22] or tipping[17] of lower first molars, and proclination of lower incisors.[17,18,20–23,25,26] Dentoalveolar treatment effects at the maxillary level were reported in seven studies as distal movement of the maxillary dentition,[15,24] distal tipping of upper first molars,[17] and/or retroclination of upper incisors.[17,18,21–23,25,26] One study[19] did not report any dentoalveolar treatment effects.

Significant skeletal effects were reported mainly in the studies including pubertal patients. In two investigations including pubertal[25,26] and postpubertal[17] patients, very little skeletal effects limited to maxillary growth restraint were observed. On the contrary, eight studies on pubertal patients reported a significant increase of mandibular length,[15,16,19–22,24] with forward movement of the pogonion,[18] or restraint of the maxillary growth from minimal[18] to significant.[20,21] Finally, two studies[22,23] including postpubertal patients reported no skeletal effects. Modifications of the soft tissue profile were described in only six studies[17–20,23,25]

Table 4. Summarized Treatment Effects in the 11 Studies (12 Articles) Included in the Present Systematic Review[a]

Study	Success Rate	Main Treatment Effects			Clinical Implications
		Skeletal	Dentoalveolar	Soft Tissues	
Pancherz[15]	100%	Significant increase in mandibular length; little effect on the maxillary growth restraint	Significant distal movement of the maxillary dentition and mesial movement of the mandibular dentition	Not reported	The improvement in occlusal relationship by banded Herbst appliance treatment during the pubertal growth spurt is about equally a result of skeletal and dental changes.
Franchi et al.[16]	Not reported	More than half of the total overjet and molar Class correction due to increase in total mandibular length and ramus height	Mesial movement of the mandibular dentition represented the only significant dental change	Not reported	The acrylic splint Herbst appliance is effective for treatment of Class II malocclusion during the pubertal growth spurt with skeletal and dentoalveolar effects at the mandibular level that are stable at posttreatment evaluation.
Nalbantgil et al.[17]	Not reported	Very little skeletal effects, limited to maxillary growth restraint	Maxillary incisors reclination and maxillary molars' distal tipping and intrusion; mandibular incisors' proclination and mandibular molars' mesial tipping	Soft tissue profile improved significantly	The Jasper Jumper treatment in conjunction with MBA during the postpubertal growth spurt corrects Class II discrepancies mostly through dentoalveolar changes.
Küçükkeleş et al.[18]	Not reported	Minimal skeletal modifications as slight restraint of maxillary growth and forward movement of skeletal pogonion	Dentoalveolar compensation mainly present at the mandibular level with an important mesial movement of the first molars; maxillary incisors uprighting and extrusion and mandibular incisors' proclination and intrusion	Forward movement of the soft tissue pogonion, which improved the profile	The Jasper Jumper treatment in conjunction with MBA effectively corrects Class II malocclusion during the pubertal growth spurt, but the changes are in 80% dentoalveolar.
Baccetti et al.[19]	92.8%	Significant increase in mandibular protrusion and length	Not reported	Significant forward movement of soft tissue B-point and pogonion	The acrylic splint Herbst appliance produces favorable skeletal changes during the pubertal growth spurt.
Franchi et al.[20]	87.5%	Reduction of overjet and increase in molar relationship, proclination and intrusion of lower incisors	Restraint of the maxillary growth and increase in mandibular length	Restraint of the maxillary growth detectable at the soft tissue level	The Forsus FRD protocol is effective in correcting Class II malocclusion with a combination of skeletal (mainly maxillary) and dentoalveolar (mainly mandibular) effects.
Al-Jewair et al.[21]	Not reported	Significant increase of maxillary protrusion and significant increase in mandibular length for MARA treatment	Significant proclination of mandibular incisors and mesialization of mandibular molars	Not reported	Treatment during the pubertal growth peak using either MARA or AdvanSync resulted in normalization of Class II malocclusion. The AdvanSync showed more headgear effect and less mandibular length increase than MARA. Both appliances showed similar dentoalveolar changes.
		Significant restriction of maxillary growth and significant increase in mandibular length for AdvanSync treatment	Significant reclination of maxillary incisors, proclination of mandibular incisors, and mesialization of mandibular molars		

Table 4. Continued

Study	Success Rate	Main Treatment Effects: Skeletal	Dentoalveolar	Soft Tissues	Clinical Implications
Ghislanzoni et al.[22]	Not reported	Significant mandibular elongation only in the pubertal group	Significant dentoalveolar compensations present at the mandibular level (proclination of incisors, extrusion, and mesialization of molars) in the postpubertal group	Not reported	Optimal timing for Class II treatment with the MARA appliance is at the pubertal growth spurt, with enhanced mandibular skeletal changes and minimal dentoalveolar compensations.
Oztoprak et al.[23]	Not reported	No significant vertical and sagittal skeletal effects on maxilla and mandible in both SUS^2 and Forsus FRD treatments	Retrusion and extrusion of the maxillary incisors as well as protrusion and intrusion of mandibular incisors in both SUS^2 and Forsus FRD treatments; Forsus FRD treatment produced significantly greater mandibular incisors proclination	Soft tissue profile improvement was limited in both SUS^2 and Forsus FRD treatments	Both SUS^2 and Forsus FRD treatments in conjunction with MBA during the postpubertal growth spurt corrected Class II discrepancies through dentoalveolar changes.
Phelan et al.[24]	100%	The skeletal contribution to overjet correction exclusively due to mandibular changes	The dentoalveolar component of the overjet correction was mainly due to maxillary changes	Not reported	The Sydney Magnoglide treatment during the pubertal growth spurt was effective in Class II correction by similar skeletal and dentoalveolar effects.
Baysal and Uysal[25,26]	100%	Significant decrease of SNA and ANB angles, no significant increase in mandibular length	Significant maxillary incisors reclination and mandibular incisors protrusion and proclination	Increase of facial convexity angle and decrease of mentolabial angle	Treatment with the Herbst appliance at the pubertal growth spurt produced dental and soft tissue changes but no significant increase in mandibular length.

[a] SUS^2 indicates Sabbagh Universal Spring; FRD, fatigue resistant device; MARA, mandibular advancement repositioning appliance; and MBA, multibracket appliance.

as improvement of the profile, mainly due to soft tissue pogonion/B-point advancement.

Risk of Bias in Individual Studies

The overall quality level of the studies included was medium for six studies,[15–18,21,23] medium/high for four studies[20,22,24–26] and high for only one study[19] (Table 5). Sample description was partial in only one study.[22] Prospective enrollment was clearly reported in four studies.[19,22,24–26] For diagnosis, Class II description and maturational stage distribution were full in six[19–22,24–26] and seven[17,19–24] studies, respectively. For treatment, description was partial in only two studies.[16,17] Withdrawals were declared in three studies[15,24–26] and not mentioned in four studies[17,18,21,23]; in four studies[16,19,20,22] withdrawals were not declared but were excluded according to data reported in the tables. Incomplete data outcome was seen in six studies.[16,17,21–23,25,26] Method error analysis was included in all of the studies, even though one study[25,26] was limited to systematic error. Blinding of measurements was followed in three studies.[19,20,22] Inferential statistical analysis related to the comparisons in dental/skeletal changes between groups was judged to be adequate in three studies.[18,19,22] Finally, in two studies[19,22] a previous estimate of sample size was followed, while two more studies[19,23] reported a posteriori power analysis.[20,24]

Risk of Bias Across Studies

Among the cephalometric parameters included in the analyses, only the total and composite mandibular length changes yielded an acceptable level of heterogeneity (I^2 Indexes generally below 50%). On the contrary, all of the other parameters yielded noteworthy heterogeneity (I^2 Indexes generally above 60%). Therefore, meta-analysis was limited to the total and composite mandibular length changes. Results on the publication bias analyses when applicable to these parameters were nonsignificant ($P > .2$, at least).

Meta-analysis

The cephalometric measurements used in each study and pooled herein for the meta-analysis are reported in Table 6, with detailed results for the meta-analysis shown in Figures 2 through 5. For the functional treatment alone, the overall total mandibular

Table 5. Risk of Bias of the 11 Studies (12 Articles) Included in the Present Review

Study	Sample Description	Prospective Enrollment	Class II Description	Maturation Stages Distribution Description	Treatment Description	Incomplete Outcome Data
Pancherz[15]	Full	Not declared	Partial	Partial	Full	No
Franchi et al.[16]	Full	Not declared	Partial	Partial	Partial	Yes
Nalbantgil et al.[17]	Full	Not declared	Partial	Full	Partial	Yes
Küçükkeleş et al.[18]	Full	Not declared	Partial	Partial	Full	No
Baccetti et al.[19]	Full	Yes	Full	Full	Full	No
Franchi et al.[20]	Full	Not declared	Full	Full	Full	No
Al-Jewair et al.[21]	Full	No	Full	Full	Full	Yes
Ghislanzoni et al.[22]	Partial	Yes	Full	Full	Full	Yes
Oztoprak et al.[23]	Full	Not declared	Partial	Full	Full	Yes
Phelan et al.[24]	Full	Yes	Full	Full	Full	No
Baysal and Uysal[25,26]	Full	Yes	Full	Partial	Full	Yes

[a] Derived from tables.
[b] A posteriori power analysis.
[c] Systematic error only.

length change in pubertal patients as mean (95% CI) was 1.95 mm (1.47 to 2.44). Only one study[17] on postpubertal patients treated by functional treatment alone reported a negative total mandibular length increase for the treated group of −1.73 mm (−2.60 to −0.86) (Figure 2). Regarding the composite mandibular length changes, the overall change was 2.03 mm (1.27 to 2.80) for the pubertal patients (Figure 3). For the comprehensive treatment, the overall total mandibular length changes were 2.22 mm (1.63 to 2.82) and 0.44 mm (−0.78 to 1.66) for the pubertal and postpubertal patients, respectively (Figure 4). Finally, the composite mandibular length change for the postpubertal patients was 1.86 mm (0.83 to 2.89) (Figure 5). The subgroup analysis for the total mandibular length revealed a statistically significant greater effect for the pubertal patients as compared to the postpubertal patients for the functional treatment alone ($P < .001$; Figure 2) but not for the comprehensive treatment ($P = .10$; Figure 4).

DISCUSSION

The present review is the first using the growth phase as a main selection criterion, thus allowing a comparison of the pubertal and postpubertal patients undergoing functional treatment for skeletal Class II malocclusion with fixed appliances. Moreover, only studies with matched untreated control groups were considered. However, this often implies the use of historical Class II controls mainly due to ethical issues involved in leaving patients with relevant malocclusions without orthodontic treatment during the pubertal and postpubertal growth phases. For this reason, the inclusion of CCTs has been advocated in systematic reviews.[4] Thus, the retrieved studies were only CCTs without any RCTs (Table 3). Selective reporting of data was seen, as for instance success rate (Table 4), or cephalometric magnifications used reported in only seven studies.[15,16,19–22,24] Therefore, studies with an improved level of quality are necessary, in terms of prospective enrollment, full description of Class II

Table 6. The Cephalometric Measurements for Total and Composite Mandibular Length Used in Each Study and Pooled Herein for the Meta-analyses

Study	Parameter: Total Mandibular Length, mm	Parameter: Composite Mandibular Length, mm
Pancherz[15]		Pancherz analysis
Franchi et al.[16]	Condylion-pogonion	Pancherz analysis
Nalbantgil et al.[17]	Articulare-pogonion	
Küçükkeleş et al.[18]	Articulare-pogonion	
Baccetti et al.[19]	Condylion-gnathion	
Franchi et al.[20]	Condylion-gnathion	
Al-Jewair et al.[21]	Condylion-gnathion	
Ghislanzoni et al.[22]	Condylion-gnathion	
Oztoprak et al.[23]	Articulare-pogonion	
Phelan et al.[24]	Condylion-gnathion	Pancherz analysis
Baysal and Uysal[25,26]	Condylion-gnathion	Pancherz analysis

Table 5. Extended

Withdrawals	Method Error	Blinding for Measurements	Adequacy of Statistics	Prior Estimate of Sample Size	Quality Score	Judged Quality Standard
Yes	Yes	No	No	No	10	Medium
No[a]	Yes	No	No	No	8	Medium
Not mentioned	Yes	No	No	No	8	Medium
Not mentioned	Yes	No	Yes	No	10	Medium
No[a]	Yes	Yes	Yes	Yes	16	High
No[a]	Yes	Yes	No	Yes[b]	14	Medium/high
Not mentioned	Yes	No	No	No	10	Medium
No[a]	Yes	Yes	Yes	Yes	14	Medium/high
Not mentioned	Yes	No	No	No	9	Medium
Yes	Yes	No	No	Yes[b]	14	Medium/high
Yes	Yes[c]	No	No	No	11	Medium/high

features, adequate statistical analysis, and other information on treatment and data recording (Table 5).

Heterogeneity of the selected studies was mainly seen in the treatment interventions within pubertal and postpubertal patients (treatment duration, type of appliance; Table 3). Such differences could hardly be avoided, even though the effects of fixed functional appliances alone or in combination with MBAs were analyzed separately, and random models were used herein for meta-analysis. However, studies with more homogeneity in the interventions and data reporting are necessary.

Generally, irrespective of treatment modalities, the studies that included patients treated during the pubertal growth phase indicated that this timing would be suited for functional treatment (Table 4), whereas studies with postpubertal patients clearly reported that dentoalveolar effects were responsible for the Class II correction. However, when considering the meta-analysis on the mandibular length, the subgroup comparisons between the pubertal and postpubertal patients were significant only for the functional treatment alone ($P < .001$; Figure 2), and close to significance for the comprehensive treatment ($P = .10$; Figure 4). Therefore, while skeletal effects may be expected by functional treatment in pubertal patients, more studies are necessary to fully elucidate whether these effects are significantly greater than those achievable in patients treated post puberty.

Limitation of the Review

Several studies included herein followed a retrospective enrollment for the treated groups and/or used historical control groups. The differences in functional treatment lengths, from 6 months[15,18] to 18 months,[21] or in the cephalometric magnifications, and the pooling of slightly different parameters expressing the total mandibular length need also to be taken into account for a critical interpretation of the meta-analysis. Therefore, while a clinically relevant mandibular elongation has been shown in pubertal patients, a precise quantification of the efficiency of such treatment with

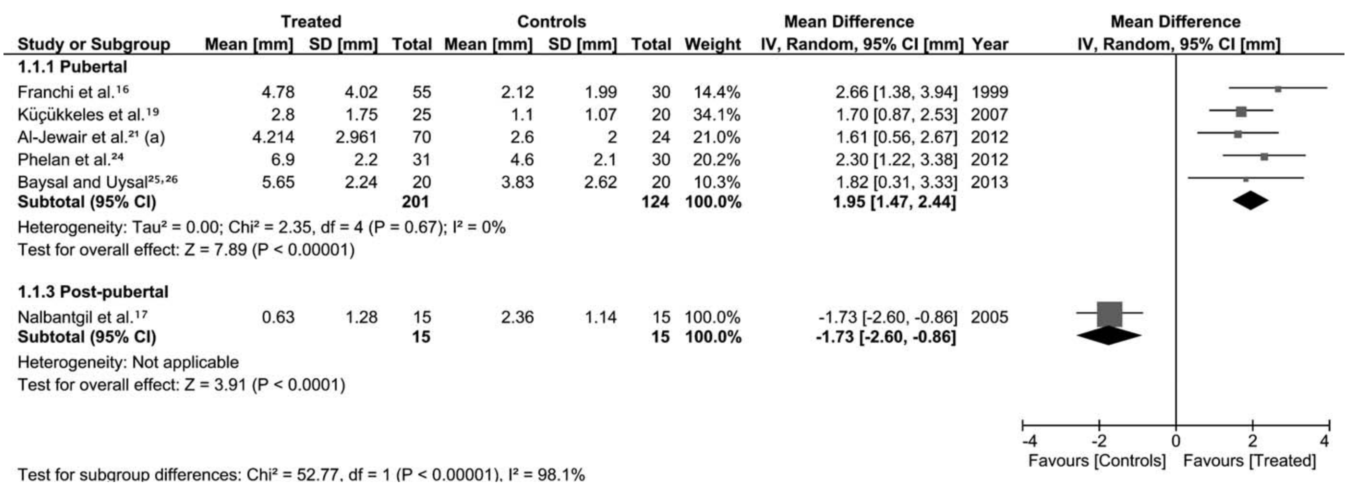


Figure 2. Forest plot (mean difference and 95% CI) for the total mandibular length changes (in mm) for pubertal and postpubertal subjects. (a) Pooled means and SDs from two groups compared to a single control group.

Study or Subgroup	Treated Mean [mm]	Treated SD [mm]	Treated Total	Controls Mean [mm]	Controls SD [mm]	Controls Total	Weight	Mean Difference IV, Random, 95% CI [mm]	Year
1.2.1 Pubertal									
Pancherz[15]	3	1.5	22	0.8	0.7	20	35.0%	2.20 [1.50, 2.90]	1982
Franchi et al.[16]	3.68	2.84	55	0.81	2.01	30	25.9%	2.87 [1.83, 3.91]	1999
Phelan et al.[24]	2.6	2.6	31	0.7	2.2	30	22.2%	1.90 [0.69, 3.11]	2012
Baysal and Uysal[25,26]	3.45	2.43	20	2.88	2.45	20	16.9%	0.57 [-0.94, 2.08]	2013
Subtotal (95% CI)			**128**			**100**	**100.0%**	**2.03 [1.27, 2.80]**	

Heterogeneity: Tau² = 0.31; Chi² = 6.21, df = 3 (P = 0.10); I² = 52%
Test for overall effect: Z = 5.20 (P < 0.00001)

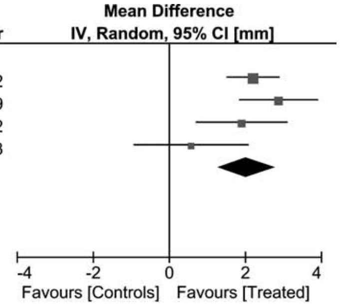
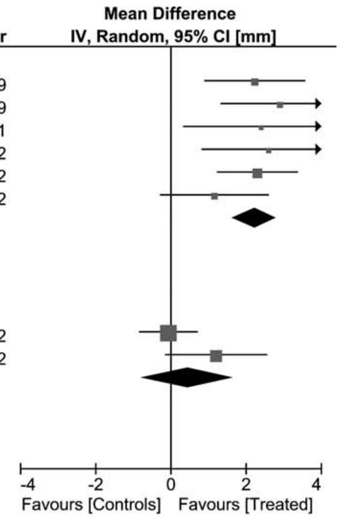


Figure 3. Forest plot (mean difference and 95% CI) for the composite mandibular length changes (in mm) for pubertal and postpubertal subjects.

Study or Subgroup	Treated Mean [mm]	Treated SD [mm]	Treated Total	Controls Mean [mm]	Controls SD [mm]	Controls Total	Weight	Mean Difference IV, Random, 95% CI [mm]	Year
2.1.1 Pubertal									
Franchi et al.[16]	6.39	3.51	55	4.16	2.72	30	19.5%	2.23 [0.89, 3.57]	1999
Baccetti et al.[19]	8.1	3.3	28	5.2	2.7	28	14.2%	2.90 [1.32, 4.48]	2009
Franchi et al.[20] (b)	9.1	3.1	14	6.7	2.3	12	8.2%	2.40 [0.32, 4.48]	2011
Ghislarzoni et al.[22]	8.6	3.1	15	6	1.7	15	11.0%	2.60 [0.81, 4.39]	2012
Phelan et al.[24]	6.9	2.2	31	4.6	2.1	30	30.3%	2.30 [1.22, 3.38]	2012
Al-Jewair et al.[21] (a)	6.557	5.47	70	5.4	1.7	24	16.8%	1.16 [-0.29, 2.61]	2012
Subtotal (95% CI)			**213**			**139**	**100.0%**	**2.22 [1.63, 2.82]**	
Heterogeneity: Tau² = 0.00; Chi² = 3.00, df = 5 (P = 0.70); I² = 0%									
Test for overall effect: Z = 7.32 (P < 0.00001)									
2.1.2 Post-pubertal									
Oztoprak et al.[23] (a)	0.73	1.986	40	0.8	1.07	19	60.0%	-0.07 [-0.85, 0.71]	2012
Ghislanzoni et al.[22]	3.6	2	15	2.4	1.8	15	40.0%	1.20 [-0.16, 2.56]	2012
Subtotal (95% CI)			**55**			**34**	**100.0%**	**0.44 [-0.78, 1.66]**	
Heterogeneity: Tau² = 0.49; Chi² = 2.51, df = 1 (P = 0.11); I² = 60%									
Test for overall effect: Z = 0.70 (P = 0.48)									



Test for subgroup differences: Chi² = 6.64, df = 1 (P = 0.010), I² = 84.9%

Figure 4. Forest plot (mean difference and 95% CI) for the total mandibular length changes (in mm) for pubertal and postpubertal subjects. (a) Pooled means and SDs from two groups compared to a single control group. (b) Only pubertal subjects of the sample.

fixed functional appliances remains undetermined. The risk of bias followed herein has not been validated. Moreover, only three studies[17,22,23] on postpubertal patients were retrieved; therefore, conclusions about inducible mandibular elongation at this stage should be interpreted with caution. Finally, long-term treatment stability, irrespective of the modalities followed, has yet to be evaluated.

Clinical Implications

Skeletal effects provided by fixed functional appliances in the correction of Class II malocclusion appear to be related to treatment timing. Skeletal corrections, including mandibular elongation, may be achieved if treatment is performed during the pubertal growth phase. Therefore, the use of a reliable skeletal maturity indicator would be advisable in everyday clinical practice in order to perform treatment during the pubertal growth phase, thus pursuing more skeletal effects. However, pure skeletal effects could not be expected even during puberty, as dentoalveolar effects, such as maxillary incisors retroclination and mandibular incisors proclination, are often present. Even though no significant effect in terms of mandibular elongation was seen herein for the postpubertal

Study or Subgroup	Treated Mean [mm]	Treated SD [mm]	Treated Total	Controls Mean [mm]	Controls SD [mm]	Controls Total	Weight	Mean Difference IV, Random, 95% CI [mm]	Year
2.2.1 Pubertal									
Franchi et al.[16]	4.94	3.86	55	2.48	2.7	30	43.2%	2.46 [1.05, 3.87]	1999
Phelan et al.[24]	2.2	2.8	31	0.8	1.8	30	56.8%	1.40 [0.22, 2.58]	2012
Subtotal (95% CI)			**86**			**60**	**100.0%**	**1.86 [0.83, 2.89]**	

Heterogeneity: Tau² = 0.12; Chi² = 1.28, df = 1 (P = 0.26); I² = 22%
Test for overall effect: Z = 3.54 (P = 0.0004)

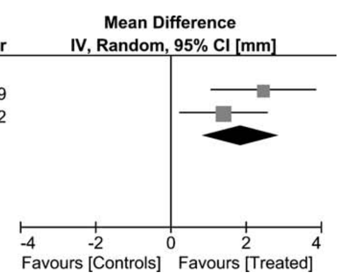


Figure 5. Forest plot (mean difference and 95% CI) for the composite mandibular length changes (in mm) for pubertal and postpubertal subjects.

patients, this does not deny the existence of such effects due to the still limited data available in the literature.

CONCLUSIONS

- Fixed functional treatment is effective in treating Class II malocclusion with skeletal effects when performed during the pubertal growth phase.
- Both mandibular elongation and maxillary growth restraint are seen.
- Skeletal effects alone would not account for the whole Class II correction, with dentoalveolar effects always present, even in patients treated during puberty.

REFERENCES

1. Proffit WR, Fields HW Jr, Moray LJ. Prevalence of malocclusion and orthodontic treatment need in the United States: estimates from the NHANES III survey. *Int J Adult Orthodon Orthognath Surg*. 1998;13:97–106.
2. McNamara JA Jr, Brudon WL. Orthodontics and dentofacial orthopedics. Ann Arbor, Mich: Needham Press; 2001.
3. Chen JY, Will LA, Niederman R. Analysis of efficacy of functional appliances on mandibular growth. *Am J Orthod Dentofacial Orthop*. 2002;122:470–476.
4. Cozza P, Baccetti T, Franchi L, De Toffol L, McNamara JA Jr. Mandibular changes produced by functional appliances in Class II malocclusion: a systematic review. *Am J Orthod Dentofacial Orthop*. 2006;129:599 e1–12.
5. Marsico E, Gatto E, Burrascano M, Matarese G, Cordasco G. Effectiveness of orthodontic treatment with functional appliances on mandibular growth in the short term. *Am J Orthod Dentofacial Orthop*. 2011;139:24–36.
6. Baccetti T, Franchi L, McNamara JA Jr. The cervical vertebral maturation (CVM) method for the assessment of optimal treatment timing in dentofacial orthopedics. *Semin Orthod*. 2005;11:119–129.
7. Petrovic A, Stutzmann J, Lavergne J. Mechanism of craniofacial growth and modus operandi of functional appliances: a cell-level and cybernetic approach to orthodontic decision making. In: Carlson DS, ed. *Craniofacial Growth Theory and Orthodontic Treatment. Monograph 23. Craniofacial Growth Series*. Ann Arbor, Mich: Center for Human Growth and Development, University of Michigan; 1990:13–74.
8. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol*. 2009;62: e1–34.
9. Centre for Reviews and Dissemination. *Systematic Reviews: CRD's Guidance for Undertaking Reviews in Healthcare*. York, UK: University of York NHS Centre for Reviews & Dissemination; 2009.
10. Lau J, Ioannidis JP, Schmid CH. Quantitative synthesis in systematic reviews. *Ann Intern Med*. 1997;127:820–826.
11. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002;21:1539–1558.
12. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629–634.
13. Pancherz H. A cephalometric analysis of skeletal and dental changes contributing to Class II correction in activator treatment. *Am J Orthod*. 1984;85:125–134.
14. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. *Introduction to Meta-Analysis*. Chichester, UK: John Wiley & Sons; 2009.
15. Pancherz H. The mechanism of Class II correction in Herbst appliance treatment. A cephalometric investigation. *Am J Orthod*. 1982;82:104–113.
16. Franchi L, Baccetti T, McNamara JA Jr. Treatment and posttreatment effects of acrylic splint Herbst appliance therapy. *Am J Orthod Dentofacial Orthop*. 1999;115: 429–438.
17. Nalbantgil D, Arun T, Sayinsu K, Fulya I. Skeletal, dental and soft-tissue changes induced by the Jasper Jumper appliance in late adolescence. *Angle Orthod*. 2005;75:426–436.
18. Küçükkeleş N, Ilhan I, Orgun IA. Treatment efficiency in skeletal Class II patients treated with the jasper jumper. *Angle Orthod*. 2007;77:449–456.
19. Baccetti T, Franchi L, Stahl F. Comparison of 2 comprehensive Class II treatment protocols including the bonded Herbst and headgear appliances: a double-blind study of consecutively treated patients at puberty. *Am J Orthod Dentofacial Orthop*. 2009;135:698.e1–10; discussion 98–99.
20. Franchi L, Alvetro L, Giuntini V, Masucci C, Defraia E, Baccetti T. Effectiveness of comprehensive fixed appliance treatment used with the Forsus Fatigue Resistant Device in Class II patients. *Angle Orthod*. 2011;81:678–683.
21. Al-Jewair TS, Preston CB, Moll EM, Dischinger T. A comparison of the MARA and the AdvanSync functional appliances in the treatment of Class II malocclusion. *Angle Orthod*. 2012;82:907–914.
22. Ghislanzoni LT, Baccetti T, Toll D, Defraia E, McNamara JA Jr, Franchi L. Treatment timing of MARA and fixed appliance therapy of Class II malocclusion. *Eur J Orthod*. 2012;35: 394–400.
23. Oztoprak MO, Nalbantgil D, Uyanlar A, Arun T. A cephalometric comparative study of class II correction with Sabbagh Universal Spring (SUS(2)) and Forsus FRD appliances. *Eur J Dent*. 2012;6:302–310.
24. Phelan A, Tarraf NE, Taylor P, et al. Skeletal and dental outcomes of a new magnetic functional appliance, the Sydney Magnoglide, in Class II correction. *Am J Orthod Dentofacial Orthop*. 2012;141:759–772.
25. Baysal A, Uysal T. Soft tissue effects of Twin Block and Herbst appliances in patients with Class II division 1 mandibular retrognathy. *Eur J Orthod*. 2013;35:71–81.
26. Baysal A, Uysal T. Dentoskeletal effects of Twin Block and Herbst appliances in patients with Class II division 1 mandibular retrognathy. *Eur J Orthod*. 2014;36: 164–172.
27. Küçükkeleş N, Sandalli T. Cephalometric evaluation of the therapeutic effects of the Herbst appliance in the treatment of Class II. Div I. malocclusion. *J Marmara Univ Dent Fac*. 1992;1:230–236.