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EARLY TREATMENT OF SAGITTAL DISCREPANCIES: an overview of systematic reviews

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia da Pontifícia Universidade Católica de Minas Gerais, como requisito parcial para obtenção do título de Mestre em Ortodontia.

Orientador: Prof. Dr. Ildeu Andrade Júnior

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Área de concentração: Ortodontia

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ABSTRACT

One of the most topics in the orthodontic literature is the early treatment of sagittal discrepancies (Class II and Class III malocclusions). An overview of systematic reviews was developed through the electronic search of relevant articles published until October 2019 in the PUBMED, Cochrane Library, LILACS and Embase databases. Screening of eligible studies, assessment of the methodological quality of the SRs and data extraction were conducted in duplicate and independently by two reviewers. Methodological quality was assessed using AMSTAR (assessment of multiple systematic reviews) and the quality of evidence was evaluated using GRADE (Grading of Recommendations Assessment, Development and Evaluation). The search strategy identified 479 titles. Twenty-eight systematic reviews, of which seventeen meta-analyzes, were selected after applying the included criteria. Early maxillary protraction with facemask is an effective treatment for early Class III treatment. Low evidence SRs suggested that headgear, fixed and removable functional appliance and non-compliance molar distalization devices are effective for treating the Class II malocclusion, with different skeletal and dental effects. Low to moderate evidence SRs suggested that the ideal time for the treatment of Class II malocclusion appears to be in the pubertal growth stage. More evidence is still needed to draw definite conclusion related to the ideal time for early Class III treatment. There is still no evidence on the long term stability of the final results in either sagittal discrepancy. Further randomized controlled trials (RCT) with proper design and adequate sample size are needed in the future in order to reach more reliable results concerning the treatment of sagittal discrepancies in children and early adolescence in the short and the long term.

Keywords: Malocclusion, Angle Class II. Malocclusion, Angle Class III. Systematic review.

RESUMO

Um dos tópicos mais controversos da literatura ortodôntica é o tratamento precoce de discrepâncias sagitais (más oclusões de Classe II e Classe III). Uma *overview* das revisões sistemáticas (RSs) foi desenvolvida por meio da pesquisa eletrônica de artigos relevantes publicados até outubro de 2019 nas bases de dados PUBMED, Cochrane Library, LILACS e Embase. Seleção de estudos elegíveis, avaliação da qualidade metodológica das RSs e extração de dados foram realizados em duplicata e de forma independente por dois revisores. A qualidade metodológica foi avaliada usando o AMSTAR (assessment of multiple systematic reviews) e a qualidade das evidências foi avaliada usando o GRADE (Grading of Recommendations Assessment, Development and Evaluation). A estratégia de busca identificou 479 títulos. Vinte e oito RSs, das quais dezessete com meta-análises, foram selecionadas após a aplicação dos critérios incluídos. A protração maxilar precoce com máscara facial é um tratamento eficaz para o tratamento precoce da Classe III. As RSs de baixa evidência sugeriram que o AEB, o aparelho funcional fixo e removível e os dispositivos de distalização de molar não conformes são eficazes no tratamento da má oclusão de Classe II, com diferentes efeitos esqueléticos e dentários. Evidências baixas a moderadas sugeriram que o momento ideal para o tratamento da má oclusão de Classe II parece estar no estágio de crescimento puberal. Ainda são necessárias mais evidências para tirar conclusões definitivas relacionadas ao tempo ideal para o tratamento precoce da Classe III. Ainda não há evidências sobre a estabilidade a longo prazo dos resultados finais em qualquer discrepância sagital. Mais ensaios clínicos randomizados (RCT), com desenho adequado e tamanho amostral adequado, são necessários no futuro, a fim de alcançar resultados mais confiáveis no tratamento de discrepâncias sagitais em crianças e início da adolescência, a curto e longo prazo.

Palavras chave: Má Oclusão de Angle Classe II. Má Oclusão de Angle Classe III. Revisão Sistemática.

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SUMMARY

1 INTRODUCTION

Evidence-based medicine, dentistry or orthodontics is a methodological process designed to formalize the resources required to “seek, identify and interpret” the clinical studies, which offer the highest level of scientific proof (Sackett et al 2000). It involves establishing a hierarchy among scientific publications in order to enable clinicians to hight the best studies among the many publications available. The main goal is to increase the quality of the care provided by reducing the gap between scientific research and clinical practice. A Systematic Review (SR) has been considered the main key of making an evidence-based clinical decision, and offers to health professionals the present state of evidence on a specific research matter (MULROW, 1994; COOK et al. 1997; MULROW, 1997).

One of the most subjects in the orthodontic literature is the early treatment of the different kinds of malocclusion. (FLORES-MIR et al. 2006). The American Association of Orthodontists provides some educational material in their website, available for download for the general public about problems to watch for in growing children. In this material, you can find 9 conditions in the 3 planes of space (Class III malocclusion, Class II malocclusion, open bite, deep bite, posterior crossbite, crowding, space problems, eruption deviation and oral habits) that can benefit from early diagnosis and referral to an orthodontist for a full evaluation (AMERICAN ASSOCIATION OF ORTHODONTISTS, 2018).

In the early treatment literature, at the heart of the debate is the sagittal discrepancies and the need for one or two-phase treatment, despite the considerable volume of literature on this topic over the last few years. Clinical decisions, such as the ideal time to start treatment, are inevitably difficult due to patient variability and uncertainty about growth and response to treatment.

Some orthodontists believe that early treatment of sagittal discrepancies might reduce the severity of the discrepancy and also the difficulty and length of treatment with fixed appliances (PANGRAZIO-KULBERSH et al 2007; PANGRAZIO-KULBERSH et al 2018). Others stated that the overall result achieved by one phase is almost comparable, two-phase does not reduce the incidence of complex treatments

involving extractions or orthognathic surgery, and there is lack of evidence on long-term benefits (HSIEH et al 2005; O'BRIEN et al 2003).

To date, some SRs reported on early treatment of sagittal discrepancies pointed out lack of evidence to prove that early treatment brings additional benefits beyond that achieved with later treatment (SUNNAK et al 2015; THIRUVENKATACHARI et al 2013). However, this does not necessarily imply that early treatment is ineffective. It means that further high quality trials are required to assess the effectiveness of interceptive orthodontics, which are still recommended in many ways for a number of malocclusions in both skeletal and dental etiology. Therefore, it is important and timely to assemble all relevant published information to assess current evidence and to identify the availability and quality of evidence-based interventions on early treatment of sagittal discrepancies. Overviews have evolved to meet a growing need to filter information overload, improve access to targeted information, and inform healthcare decision-making. Therefore, an overview of SRs in this topic is important to analyze and summarize the reported data, and to identify any weakness, inconsistency or research gaps in this particular field.

To our knowledge, no overview of SRs has been undertaken in relation to early orthopaedic/orthodontic treatment for sagittal discrepancies. The present study aims to provide a thorough overview of the SRs and meta-analyses regarding this topic and to critically appraise the quality of the reported studies.

2 OBJECTIVES

2.1 Main objective

The aim of this overview of SRs was to investigate the methodological quality and outcomes of current SRs reporting on early treatment of sagittal discrepancies (Class II and Class III malocclusions).

2.2 Specific objectives

- To critically evaluate the quality and grade evidence from SRs on the effectiveness of early orthodontic therapies for sagittal problems (Class II and Class III malocclusions);
- To summarize and investigate the effectiveness of orthodontic therapies for Class II and Class III malocclusions in growing children;
- To evaluate the stability of early treatment of Class II and III malocclusions;
- To assess the ideal moment to treat sagittal problems.

3 MATERIAL AND METHODS

This overview of SRs was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) as a reference.

3.1 Search strategies

Published SRs were searched in the Medline (PubMed), Cochrane Library, EMBASE e *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (LILACS). For each database, search strategies were developed using indexed terms and synonyms (Table 1). The manual search was conducted by reading the bibliographic references of each included study. The last search was performed on October 2019.

Table 1. Search strategy in electronic databases

Electronic databases	Search strategy	Studies
Cochrane Library	ID Search #1 MeSH descriptor: [Malocclusion, Angle Class II] explode all trees #2 (Malocclusion, Angle Class II, Division 2) (Word variations have been searched #3 (Malocclusion, Angle Class II, Division 1) (Word variations have been searched #4 MeSH descriptor: [Malocclusion, Angle Class III] explode all trees #5 #1 or #2 or #3 or #4 Filter: Cochrane Review	**7**
Pubmed	(((((((((Malocclusion, Angle Class III[MeSH Terms]) OR Malocclusion, Angle Class III[Text Word]) OR Habsburg Jaw[Text Word]) OR Prognathism, Mandibular[Text Word]) OR Hapsburg Jaw[Text Word]) OR Angle Class III[Text Word]) OR Underbite[Text Word])) OR ((((((((((Malocclusion, Angle Class II[MeSH Terms]) OR Malocclusion, Angle Class II[Text Word]) OR Angle Class II[Text Word]) OR Class II, Angle[Text Word]) OR Malocclusion, Angle Class II, Division 1[Text Word]) OR Angle Class II, Division 1[Text Word]) OR Class II Malocclusion, Division 1[Text Word]) OR Malocclusion, Angle Class II, Division 2[Text Word]) OR Class II Malocclusion, Division 2[Text Word]) OR Angle Class II, Division 2[Text Word])) AND (((((((systematic review[ti] OR meta-analysis[pt] OR meta-analysis[ti] OR systematic literature review[ti] OR (systematic review[tiab] AND review[pt]) OR consensus development conference[pt] OR practice guideline[pt] OR cochrane database syst rev[ta] OR acp journal club[ta] OR health technol assess[ta] OR evid rep technol assess summ[ta])) OR (evidence based[ti] OR evidence-based medicine[mh] OR best practice*[ti] OR evidence synthesis[tiab])) AND (review[pt] OR diseases category[mh] OR behavior and behavior mechanisms[mh] OR therapeutics[mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline[pt])) OR (systematic[tw] OR systematically[tw] OR critical[tiab] OR (study selection[tw]) OR (predetermined[tw]	**177**

	OR inclusion[tw] AND criteri*[tw]) OR exclusion criteri*[tw] OR main outcome measures[tw] OR standard of care[tw] OR standards of care[tw])) AND (survey[tiab] OR surveys[tiab] OR overview*[tw] OR review[tiab] OR reviews[tiab] OR search*[tw] OR handsearch[tw] OR analysis[tiab] OR critique[tiab] OR appraisal[tw] OR (reduction[tw] AND (risk[mh] OR risk[tw]) AND (death OR recurrence)))) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR publication[tiab] OR bibliography[tiab] OR bibliographies[tiab] OR published[tiab] OR unpublished[tw] OR citation[tw] OR citations[tw] OR database[tiab] OR internet[tiab] OR textbooks[tiab] OR references[tw] OR scales[tw] OR papers[tw] OR datasets[tw] OR trials[tiab] OR meta-analy*[tw] OR (clinical[tiab] AND studies[tiab]) OR treatment outcome[mh] OR treatment outcome[tw])) NOT (letter[pt] OR newspaper article[pt] OR comment[pt]))	
Embase	#1 ('malocclusion, angle class ii' OR 'malocclusion, angle class iii')	**232**
	#2 ('systematic review'/exp OR 'review, systematic' OR 'systematic review' OR 'meta analysis'/exp OR 'analysis, meta' OR 'meta analysis' OR 'meta-analysis' OR 'metaanalysis' OR 'systematic review (topic)'/exp OR 'systematic review (topic)' OR 'systematic reviews' OR 'systematic reviews as topic' OR 'meta analysis (topic)'/exp OR 'meta analysis (topic)' OR 'meta-analysis as topic' OR 'metaanalyses')	
	#1 and #2	
LILACS	(tw:(Malocclusion, Angle Class II)) OR (tw:(Malocclusion, Angle Class III)) Filter: Systematic Review	**63**
	Total	**479**

3.2 Selection of studies and eligibility criteria

The SRs included were those, with and without meta-analysis, which evaluated treatments for Class II and III. There was no restriction on language and year of publication. Duplicates were identified through the End Note® program. Article selection, data extraction, and quality were independently performed by two evaluators (ASG and ACR), who applied the eligibility criteria: outcome type, patient type, and type of study. In the first stage, the studies were read by title / abstract and then by reading the full articles. Disagreements were discussed with a third evaluator (VEA). The inclusion and exclusion criteria are described in Table 2.

Table 2. Inclusion and exclusion criteria

Inclusion criteria	• SRs with and without meta-analysis • Sufficient data • SR included studies with growing patients with malocclusion Class II or Class III • SR with or without control group
Exclusion Criteria	• Other types of studies • Studies that included patients over 16 years • Studies that presented many incomplete data

3.3 Data extraction

Data from included SRs was extracted independently by two authors (ASG, ACR) and inserted in pre-tabulated data sheets (Excel, Microsoft, New Mexico). Any disagreement related to data extraction was resolved by consensus in discussion with the other authors (VA, MN, IAJ) to ensure consistency and reliability of extracted data. The data extraction included authors, publication year, sample population (number, age and gender of patients), type of intervention, methods of analyses, comparison, outcome measures and main findings, follow up period and meta-analyses' result when available Table 4 and 5.

3.4 Quality assessment

The methodological quality of the included SRs was assessed indenpendently by ASG and ACR using the Assessment of Multiple Systematic Reviews (AMSTAR) 2 tool (SHEA et al 2007), consisting of 16 items, comprising minimum requirements of an SR. The methodological quality of the included SRs is shown in Table 3.

The quality of evidence of the main outcome of the included SRs was also evaluated using the the Grading of Recommendations Assessment, Development and Evaluation (GRADE). The GRADE rating and recommendation strength of evidence are listed in Table 4 and 5.

Table 3 . General features of SRs included **(to be continued)**

Author and year	Malocclusion	Age (years)	Intervention x Comparison	Studies included	Meta analysis	AMSTAR 2
Mohammed et al 2019	Class II division 1	08 - 11	Prefabricated myofunctional appliances x No treatment	3 RCTs and 3 CCTs	No	Moderate
Woon and Thiruvenkatachari 2017	Class III	5.5 - 11.75	Orthodontic/orthopedic appliance x No treatment, delayed treatment, or intervention with the same appliance with different forces, different mechanics, or a different appliance	9 RCTs and 6 CCTs	Yes	Moderate
Rongo et al 2017	Class III	5.6 - 12.5	Orthopedic appliance x No treatment	7 RCTs, 8 CCTs and 6 retrospective	Yes	Critially Low
Janson et al 2017	Class II division 1	9.9 - 14.3	Treatment with x Without premolar extractions, all using multibracket appliance	1 CCT and 24 retrospectives	Yes	Critially Low
Al-Thomali et al 2017	Class II	10.5 - 15.4	Pendulum and modified pendulum (Effective)	9 retrospective and 16 prospective	No	Critially Low
Nucera et al 2017	Class II	08 - 09	Headgear x No treatment	4 RCTs and 2 CCTs	Yes	Critially Low

Table 3. (continuation)

Author and year	Malocclusion	Age (years)	Intervention x Comparison	Studies included	Meta analysis	AMSTAR 2
Santamaría-Villegas et al 2017	Class II	9.4 - 13	Removable functional appliances x No treatment	5 RCTs	Yes	Moderate
Papageorgiou et al 2017	Class II	7.6 - 12.9	Headgear x No treatment	5 RCTs and 13 prospectives	Yes	Critially Low
Nucera et al 2016	Class II	8.18 - 12.5	Removable functional appliances x No treatment	5 RCTs and 9 CCTs	Yes	Low
Elkordy et al 2016	Class II	12.1- 16.2	Skeletal anchors + fixed functional appliances x Fixed functional appliances	7 CCTs	Yes	Critially Low
Pacha et al 2016	Class II	12.7 - 13.6	Fixed x Removable functional appliances	2 RCTs and 2 CCTs	No	Moderate
Zymperdikas et al 2016	Class II	9.8 - 15.3	Fixed functional appliances x No treatment	8 CCTs and 1 RCT	Yes	Moderate
Al-Jewaira 2015	Class II division 1	8.7 - 13.1	MARA (with or without fixed appliance) x No treatment	7 retrospectives	Yes	Critially Low
Ehsani et al 2015	Class II division 1	9 - 11.4	Twin block x No treatment	6 Prospectives and 4 retrospectives	Yes	Moderate
Perinetti et al 2015	Class II	8.9 - 10.3	Removable functional appliances x No treatment	3 RCTs and 8 CCTs	Yes	Moderate

Table 3. (continuation)

Author and year	Malocclusion	Age (years)	Intervention x Comparison	Studies included	Meta analysis	AMSTAR 2
Chatzoudi et al 2014	Class III	8.5 - 11	Chin cup x No treatment	4 prospectives and 1 retrospectivo	Yes	Low
Koretsi et al 2014	Class II	8 - 15	Removable functional appliances x No treatment	7 RCTs and 10 CCTs	Yes	Low
Cordasco et al 2014	Class III	4.7 - 10.6	Facemask x No treatment	3 RCTs	Yes	Moderate
Watkinson et al 2013	Class III	7.3 - 11	Orthopedic appliances x May be no treatment, delayed treatment, or another active intervention	7 RCTs	No	Moderate
Perillo et al 2010	Class II	8 - 12.3	Frankel 2 x No treatment	1 RCT, 7 retrospectives and 1 prospectives	Yes	Critially Low
Antonarakis and Kiliaridis 2008	Class II	11.2 - 14.9	Noncompliance Intramaxillary Appliances (effects)	5 retrospective, 7 prospective and 1 prospective randomized	No	Low
Toffol et al 2008	Class III	4.2 - 12.3	Orthopedic appliances x No treatment	1 RCT and 18 CCTs	No	Critially Low
Flores-Mir et al 2007	Class II division 1	Growing patients	Herbst x No treatment	3 CCT	No	Critially Low
Flores-Mir and Major 2006 (Cephal)	Class II	10 - 12	Twin Block x No treatment	2 RCTs	No	Critially Low

Table 3. (continuation)

Author and year	Malocclusion	Age (years)	Intervention x Comparison	Studies included	Meta analysis	AMSTAR 2
Chen et al 2002	Class II	7 - 13	Functional appliances x No treatment	6 RCTs	No	Critially Low

Table 4 . SRs results on treatment of Class II malocclusion **(to be continued)**

Author and year	Intervention x Comparison	Primary outcome	Conclusion	GRADE	Strength of the recommendation
Mohammed et al 2019	Prefabricated myofunctional appliances x Other forms of active orthodontic treatment or untreated controls	Overjet correction, soft tissue changes, and anteroposterior sagittal improvement	There is low quality of evidence indicating that the activators were more effective than the PMAs in correcting overjet, on a short-term. However, these differences are unlikely to be of clinical significance and were not found to be profound in the longer term due to higher relapse in the activator group	Very low	Weak
Nucera et al 2017	Headgear x No treatment	Skeletal and Dental Effectiveness	Headgear treatment is effective in restricting sagittal maxillary growth and reducing the overjet in the short term.	Low	Weak
Papageorgiou et al 2017	Headgear x No treatment	The therapeutic and adverse effects	headgear is a viable treatment option to modify sagittal growth of the maxilla in the short term in Class II patients with maxillary prognathism.	Low	Weak
Janson et al 2017	Treatment with X Without premolar extractions, all using multibracket appliance	ANB mean changes	According to the existing low quality evidence, the apical base sagittal relationship in nonextraction, two-maxillary and four-premolar extractions Class II treatments decreases −1.56°, 1.88° and 2.55°, respectively	Low	Weak
Santamaría-Villegas et al 2017	Removable functional appliances x No treatment	Effects on mandibular length	All removable functional appliances, aiming to increase mandibular length, are useful. Sander Bite Jumping was observed to be the most effective device to improve the mandibular length.	High	Strong
Al-Thomali et al 2016	Pendulum and modified pendulum	Effective	Pendulum and modified pendulum appliances are effective in molar distalization.	Very low	Weak
Nucera et al 2016	Removable functional appliances x No treatment	Efficacy and the effect of these appliances on the maxilla	Removable functional appliances in Class II growing patients have a slight inhibitory effect on the sagittal growth of the maxilla in the short term, but they do not seem to affect rotation of the maxillary plane.	Low	Weak

Table 4.
(continuation)

Author and year	Intervention x Comparison	Primary outcome	Conclusion	GRADE	Strength of the recommendation
Pacha et al 2016	Fixed x Removable functional appliances	Efficacy	Fixed and removable functional appliances are effective in reducing overjet in children; however, there remains insufficient evidence to differentiate between fixed and removable variants in respect of dental and skeletal effects or indeed in terms of patient experiences.	Very low	Weak
Zymperdikas et al 2016	Fixed functional appliances x No treatment	Studies providing angular skeletal, dentoalveolar and soft tissue	According to existing evidence, FFAs seem to be effective in improving Class II malocclusion in the short term, although their effects seem to be mainly dentoalveolar rather than skeletal.	Moderate	Strong
Al-Jewaira 2015	MARA (with or without fixed appliance) x No treatment	Stability, Short- and long-term mandibular growth effects	The MARA appliance produced statistically significant mandibular growth enhancement in the short- and long-term. These findings, however, may not be clinically significant.	Low	Weak
Ehsani et al 2015	Twin block x No treatment	Skeletal and dental cephalometric findings	Changes associated with a Class II correction were identified. Most of the changes individually were of limited clinical significance, but when combined reached clinical importance.	Low	Weak
Perinetti et al 2015	Removable functional appliances x No treatment	Skeletal and dentoalveolar effects	functional treatment by removable appliances may be effective in treating Class II malocclusion with clinically relevant skeletal effects if performed during the pubertal growth phase.	Low	Weak
Yang et al 2015	Herbst x No treatment	Molar relationship, overjet, overbite and cephalometric data	The Herbst appliance is effective for patients with Class II malocclusion in active treatment period. Especially, there are obvious changes on dental discrepancy and skeletal changes on Co-Gn.	Very low	Weak

Table 4.
(continuation)

Author and year	Intervention x Comparison	Primary outcome	Conclusion	GRADE	Strength of the recommendation
Perillo et al 2010	Frankel 2 x No treatment	Skeletal mandibular changes	The FR-2 appliance had a statistically significant effect on mandibular growth. Specifically, it appeared to have an effect on total mandibular length with a low-to-moderate clinical impact.	Low	Weak
Antonarakis and Kiliaridis 2008	Palatal appliances x Buccal appliances	Dental effects (molar, premolar and incisor)	Noncompliance intramaxillary molar distalization appliances all act by distalizing molars with a concomitant and unavoidable loss of anchorage. Buccal acting and palatal acting appliances demonstrate almost similar results, with palatal acting appliances showing less tipping. Friction-free palatal acting appliances appear to produce better molar distalizing effects, but with a concomitant notable loss of anchorage.	Very low	Weak
Flores-Mir et al 2007	Herbst x No treatment	Skeletal and/or dental changes evaluated through lateral cephalograms	Dental changes are as important as skeletal changes to attaining the final occlusal results.	Low	Weak
Flores-Mir and Major 2006	Twin Block x No treatment	The soft tissue profile changes	Evidence supporting the claim for an improvement of the facial convexity with twin block treatment of Class II division I malocclusion was not found• Changes produced by the twin block appliance in the upper lip seem to be controversial, although the study with sounder methodological quality did not report significant changes;• No change in the anteroposterior position of the lowerlip and soft tissue menton was found.	Very low	Weak
Cozza et al 2006	Functional Appliances x No treatment	Effects of functional therapy on mandibular dimensions	Two-thirds of the samples in the 22 studies reported a clinically significant supplementary elongation in total mandibular length as a result of overall active treatment with functional appliances.	Very low	Weak
Chen et al 2002	Functional Appliances x No treatment	Efficacy	Results suggest the need to reevaluate functional appliance use for mandibular growth enhancement.	Moderate	Strong

Table 5 .SRs results on treatment of Class III malocclusion

Author and year	Intervention x Comparison	Primary outcome	Conclusion	GRADE	Strengh of the recommendation
Woon and Thiruvenkatachari 2017	Orthodontic/orthopedic appliance x No treatment, delayed treatment, or intervention with the same appliance with different forces, different mechanics, or a different appliance	Correction of reverse overjet	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.	Moderate	Strong
Rongo et al 2017	Orthopedic appliance x No treatment	Treatment effects (skeletal, dental, soft tissue)	There is very low to low evidence that orthopaedic treatment is effective in the correction of Class III skeletal discrepancies and moderate evidence for the correction of the overjet.	Moderate	Strong
Chatzoudi et al 2014	Chin cup x No treatment	Clinical effectiveness	Although the occipital chin cup affects significantly a number of skeletal and dentoalveolar cephalometric variables, indicating an overall positive effect for the treatment of Class III malocclusion.	Very low	Weak
Cordasco et al 2014	Facemask x No treatment	Cephalometric parameters	Facemask is effective correcting Class III malocclusion in the short term.	High	Strong
Watkinson et al 2013	Orthopedic appliances x May be no treatment, delayed treatment, or another active intervention	Effects	There is some evidence that the use of a facemask to correct prominent lower front teeth in children is effective when compared to no treatment on a short-term basis.	Moderate	Strong
Toffol et al 2008	Orthopedic appliances x No treatment	Total mandibular length, total maxillary length, and intermaxillary vertical and sagittal relationship	Data derived from medium/high quality research described over 75% of success of orthopedic treatment of Class III malocclusion (RME and facial mask therapy).	Low	Weak

4 - ARTICLE

Periodic: The Angle Orthodontist

Link to access periodic standards: https://www.angle.org/page/submit

ABSTRACT

Objectives: The aim of this overview of systematic reviews (SRs) was to investigate the level of evidence and methodological quality of current SRs that have evaluated treatments for sagittal discrepancies (Class II and Class III malocclusion) in children and preadolescents.

Material and methods: Pubmed, Medline, Embase, Cochrane Library Database and Lilacs were searched without limiting language or timeline. Screening of eligible studies, assessment of the methodological quality of the SRs and data extraction were conducted in duplicate and independently by two reviewers. Methodological quality was assessed using AMSTAR (assessment of multiple systematic reviews) and the quality of evidence was evaluated using GRADE (Grading of Recommendations Assessment, Development and Evaluation).

Results: The search strategy identified 479 titles. Twenty-eight studies were included in this Overview (5 Class III and 23 Class II) after applying the included criteria. Although nine were evaluated with moderate methodological quality, the quality of evidence was high in only two SRs.

Conclusion: Low evidence SRs suggested that headgear, fixed and removable functional appliance and non-compliance molar distalization devices are effective for treating the Class II malocclusion, with different skeletal and dental effects. Low to moderate evidence SRs suggested that the ideal time for the treatment of Class II malocclusion appears to be in the pubertal growth stage. Early maxillary protraction with facemask is an effective treatment for early Class III treatment. More evidence is still needed to draw definite conclusion related to the ideal time for early Class III treatment. There is still no evidence on the long term stability of the final results in either sagittal discrepancy.

INTRODUCTION

One of the most subjects in the orthodontic literature is the early treatment of the different kinds of malocclusion[1]. In the early treatment literature, at the heart of the debate is the sagittal discrepancies and the need for one or two-phase treatment, despite the considerable volume of literature on this topic over the last few years. Clinical decisions, such as the ideal time to start treatment, are inevitably difficult due to patient variability and uncertainty about growth and response to treatment.

Some orthodontists believe that early treatment of sagittal discrepancies might reduce the severity of the discrepancy and also the difficulty and length of treatment with fixed appliances[2,3]. Others stated that the overall result achieved by one phase is almost comparable, two-phase does not reduce the incidence of complex treatments involving extractions or orthognathic surgery, and there is lack of evidence on long-term benefits[4,5].

To date, some systematic reviews (SRs) reported on early treatment of sagittal discrepancies pointed out lack of evidence to prove that early treatment brings additional benefits beyond that achieved with later treatment[6,7]. However, this does not necessarily imply that early treatment is ineffective. It means that further high quality trials are required to assess the effectiveness of interceptive orthodontics, which are still recommended in many ways for a number of malocclusions in both skeletal and dental etiology. Therefore, it is important and timely to assemble all relevant published information to assess current evidence and to identify the availability and quality of evidence-based interventions on early treatment of sagittal discrepancies. A single SR does not approach all potential efficacy factors of orthodontic treatment and health decision makers may have difficulty finding, evaluating, comparing, and summarizing information from all relevant RSs. Thus, an overview provides an integrated summary of various studies to obtain evidence on potential clinical interventions for health status in a single document in order to reduce doubts for decision[8].

Overviews have evolved to meet a growing need to filter information overload, improve access to targeted information, and inform healthcare decision-making. Therefore, an overview of SRs in this topicis important to analyze and summarize the reported data, and to identify any weakness, inconsistency or research gaps in this particular field.

The aim of this overview of SRs is to address treatments for sagittal discrepancies (Class II and Class III malocclusion) in children and pre-adolescents, with the aim of collecting evidence from published SRs that have evaluated the effectiveness of early treatment of these poor conditions, and critically assess their quality.

MATERIAL AND METHODS

This overview of SRs was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) as a reference.

Search strategies

Published SRs were searched in the Medline (PubMed), Cochrane Library, EMBASE e *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (LILACS). For each database, search strategies were developed using indexed terms and synonyms (Table 1). The manual search was conducted by reading the bibliographic references of each included study. The last search was performed on October 2019.

Table 1. Search strategy in electronic databases

Electronic databases	Search strategy	Studies
Cochrane Library	ID Search #1 MeSH descriptor: [Malocclusion, Angle Class II] explode all trees #2 (Malocclusion, Angle Class II, Division 2) (Word variations have been searched #3 (Malocclusion, Angle Class II, Division 1) (Word variations have been searched #4 MeSH descriptor: [Malocclusion, Angle Class III] explode all trees #5 #1 or #2 or #3 or #4 Filter: Cochrane Review	**7**
Pubmed	(((((((((Malocclusion, Angle Class III[MeSH Terms]) OR Malocclusion, Angle Class III[Text Word]) OR Habsburg Jaw[Text Word]) OR Prognathism, Mandibular[Text Word]) OR Hapsburg Jaw[Text Word]) OR Angle Class III[Text Word]) OR Underbite[Text Word])) OR ((((((((((Malocclusion, Angle Class II[MeSH Terms]) OR Malocclusion, Angle Class II[Text Word]) OR Angle Class II[Text Word]) OR Class II, Angle[Text Word]) OR Malocclusion, Angle Class II, Division 1[Text Word]) OR Angle Class II, Division 1[Text Word]) OR Class II Malocclusion, Division 1[Text Word]) OR Malocclusion, Angle Class II, Division 2[Text Word]) OR Class II Malocclusion, Division 2[Text Word]) OR Angle Class II, Division 2[Text Word])) AND (((((((systematic review[ti] OR meta-analysis[pt] OR meta-analysis[ti] OR systematic literature review[ti] OR (systematic review[tiab] AND	**177**

	review[pt]) OR consensus development conference[pt] OR practice guideline[pt] OR cochrane database syst rev[ta] OR acp journal club[ta] OR health technol assess[ta] OR evid rep technol assess summ[ta])) OR (evidence based[ti] OR evidence-based medicine[mh] OR best practice*[ti] OR evidence synthesis[tiab])) AND (review[pt] OR diseases category[mh] OR behavior and behavior mechanisms[mh] OR therapeutics[mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline[pt])) OR (systematic[tw] OR systematically[tw] OR critical[tiab] OR (study selection[tw]) OR (predetermined[tw] OR inclusion[tw] AND criteri*[tw]) OR exclusion criteri*[tw] OR main outcome measures[tw] OR standard of care[tw] OR standards of care[tw])) AND (survey[tiab] OR surveys[tiab] OR overview*[tw] OR review[tiab] OR reviews[tiab] OR search*[tw] OR handsearch[tw] OR analysis[tiab] OR critique[tiab] OR appraisal[tw] OR (reduction[tw] AND (risk[mh] OR risk[tw]) AND (death OR recurrence)))) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR publication[tiab] OR bibliography[tiab] OR bibliographies[tiab] OR published[tiab] OR unpublished[tw] OR citation[tw] OR citations[tw] OR database[tiab] OR internet[tiab] OR textbooks[tiab] OR references[tw] OR scales[tw] OR papers[tw] OR datasets[tw] OR trials[tiab] OR meta-analy*[tw] OR (clinical[tiab] AND studies[tiab]) OR treatment outcome[mh] OR treatment outcome[tw])) NOT (letter[pt] OR newspaper article[pt] OR comment[pt]))	
Embase	#1 ('malocclusion, angle class ii' OR 'malocclusion, angle class iii') #2 ('systematic review'/exp OR 'review, systematic' OR 'systematic review' OR 'meta analysis'/exp OR 'analysis, meta' OR 'meta analysis' OR 'meta-analysis' OR 'metaanalysis' OR 'systematic review (topic)'/exp OR 'systematic review (topic)' OR 'systematic reviews' OR 'systematic reviews as topic' OR 'meta analysis (topic)'/exp OR 'meta analysis (topic)' OR 'meta-analysis as topic' OR 'metaanalyses') #1 and #2	**232**
LILACS	(tw:(Malocclusion, Angle Class II)) OR (tw:(Malocclusion, Angle Class III)) Filter: Systematic Review	**63**
	Total	**479**

Selection of studies and eligibility criteria

The SRs included were those, with and without meta-analysis, which evaluated treatments for Class II and III. There was no restriction on language and year of publication. Duplicates were identified through the End Note® program. Article selection, data extraction, and quality were independently performed by two evaluators (ASG and ACR), who applied the eligibility criteria: outcome type, patient type, and type of study. In the first stage, the studies were read by title / abstract and then by

reading the full articles. Disagreements were discussed with a third evaluator (VEA). The inclusion and exclusion criteria are described in Table 2.

Table 2. Inclusion and exclusion criteria

Inclusion criteria	• SRs with and without meta-analysis • Sufficient data • SR included studies with growing patients with malocclusion Class II or Class III • SR com estudos com grupo controle/comparador
Exclusion Criteria	• Other types of studies • Studies that included patients over 16 years • Studies that presented many incomplete data

Data extraction

Data from included SRs was extracted independently by two authors (ASG, ACR) and inserted in pre-tabulated data sheets (Excel, Microsoft, New Mexico). Any disagreement related to data extraction was resolved by consensus in discussion with the other authors (VA, MN, IAJ) to ensure consistency and reliability of extracted data. The data extraction included authors, publication year, sample population (number, age and gender of patients), type of intervention, methods of analyses, comparison, outcome measures and main findings, follow up period and meta-analyses result when available in Table 3.

Author and year	Malocclusion	Age (years)	Intervention x Comparison	Studies included	Meta analysis	AMSTAR 2
Mohammed 2019	Class II	06 - 14	Prefabricated myofunctional appliances x no treatment	3 RCTs and 3 CCTs	No	Moderate
Woon and Thiruvenkatachari 2017	Class III	7 - 12	Orthodontic/orthopedic appliance x no treatment, delayed treatment, or intervention with the same appliance with different forces, different mechanics, or a different appliance	9 RCTs and 6 CCTs	Yes	Moderate
Nucera 2017	Class II	08 - 09	Headgear x No treatment	4 RCTs and 2 CCTs	Yes	Critially Low
Papageorgiou et al 2017	Class II	7.6 - 12.9	Headgear x No treatment	5 RCTs and 13 prospectives	Yes	Critially Low
Janson et al 2017	Class II	9.9 - 14.3	Treatment with x Without premolar extractions, all using multibracket appliance	1 CCT and 24 retrospectives	Yes	Critially Low
Santamaría-Villegas et al 2017	Class II	9.4 - 13	Removable functional appliances x No treatment	5 RCTs	Yes	Moderate
Rongo et al 2017	Class III	5.6 - 12.5	Orthopedic appliance x No treatment	7 RCTs, 8 CCTs and 6 retrospective	Yes	Critially Low
Al-Thomali et al 2016	Class II	10.5 - 15.4	Pendulum and modified pendulum (Effective)	9 retrospective and 16 prospective	No	Critially Low
Nucera et al 2016	Class II	8 - 13	Removable functional appliances x No treatment	5 RCTs and 9 CCTs	Yes	Low

Elkordy et al 2016	Class II	11 - 15	Skeletal anchors + fixed functional appliances x Fixed functional appliances	7 CCTs	Yes	Critially Low
Pacha et al 2016	Class II	12.7 - 13.6	Fixed x Removable functional appliances	2 RCTs and 2 CCTs	No	Moderate
Zymperdikas et al 2016	Class II	9.8 - 15.3	Fixed functional appliances x No treatment	8 CCTs and 1 RCT	Yes	Moderate
Al-Jewaira 2015	Class II	10 - 16	MARA (with or without fixed appliance) x no treatment	7 retrospectives	Yes	Critially Low
Ehsani et al 2015	Class II	9 - 11.4	Twin block x No treatment	6 Prospectives and 4 retrospectives	Yes	Moderate
Perinetti et al 2015	Class II	8.9 - 10.3	Removable functional appliances x No treatment	3 RCTs and 8 CCTs	Yes	Moderate
Yang et al 2015	Class II	8.2 - 13.9	Herbst x No treatment	12 CCTs	Yes	Low
Chatzoudi et al 2014	Class III	8.5 - 11	Chin cup x No treatment	4 prospectives and 1 retrospectivo	Yes	Low
Cordasco et al 2014	Class III	6.6 - 9.2	Facemask x No treatment	3 RCTs	Yes	Moderate
Watkinson et al 2013	Class III	5 - 11	Orthopedic appliances x May be no treatment, delayed treatment, or another active intervention	7 RCTs	No	Moderate
Perillo et al 2010	Class II	8 - 11	Frankel 2 x No treatment	1 RCT, 7 retrospectives and 1 prospectives	Yes	Critially Low
Toffol et al 2008	Class III	4.2 - 12.3	Orthopedic appliances x No treatment	1 RCT and 18 CCTs	No	Critially Low
Flores-Mir et al 2007	Class II	Growing patients	Herbst x No treatment	3 CCT	No	Critially Low

Flores-Mir and Major 2006 (Cephal)	Class II	10 - 12	Twin Block x No treatment	2 RCTs	No	Critially Low
Cozza et al 2006	Class II	8.4 - 12.9	Functional appliances x No treatment	4 RCTs and 18 CCTs	No	Critially Low
Chen et al 2002	Class II	7 - 13	Functional appliances x No treatment	6 RCTs	No	Critially Low
Koretsi et al 2014	Class II	mean age: 10.6	Removable functional appliances x No treatment	7 RCTs and 10 CCTs	Yes	Low
Antonarakis and Kiliaridis 2008	Class II	11.2 - 14.9	Noncompliance Intramaxillary Appliances (effects)	5 retrospective, 7 prospective and 1 prospective randomized	No	Low

Table 3 . General features of SRs included

Quality assessment

The methodological quality of the included SRs was assessed using the AMSTAR 2 tool[9], consisting of 16 items, comprising minimum requirements of an SR. The methodological quality of the included SRs is shown in the Table 3.

The quality of evidence of the main outcome of the included SRs was also evaluated using the the Grading of Recommendations Assessment, Development and Evaluation (GRADE). The GRADE rating and recommendation strength of evidence are listed in Tables 4 and 5.

Author and year	Intervention x Comparison	Primary outcome	Conclusion	GRADE	Strength of the recommendation
Mohammed et al 2019	Prefabricated myofunctional appliances x other forms of active orthodontic treatment or untreated controls	Overjet correction, soft tissue changes, and anteroposterior sagittal improvement	There is low quality of evidence indicating that the activators were more effective than the PMAs in correcting overjet, on a short-term. However, these differences are unlikely to be of clinical significance and were not found to be profound in the longer term due to higher relapse in the activator group	Very low	Weak
Nucera et al 2017	Headgear x no treatment	Skeletal and Dental Effectiveness	Headgear treatment is effective in restricting sagittal maxillary growth and reducing the overjet in the short term.	Low	Weak
Papageorgiou et al 2017	Headgear x No treatment	The therapeutic and adverse effects	headgear is a viable treatment option to modify sagittal growth of the maxilla in the short term in Class II patients with maxillary prognathism.	Low	Weak
Janson et al 2017	Treatment with X without premolar extractions, all using multibracket appliance	ANB mean changes	According to the existing low quality evidence, the apical base sagittal relationship in nonextraction, two-maxillary and four-premolar extractions Class II treatments decreases −1.56°, 1.88° and 2.55°, respectively	Low	Weak
Santamaría-Villegas et al 2017	Removable functional appliances x no treatment	Effects on mandibular length	All removable functional appliances, aiming to increase mandibular length, are useful. Sander Bite Jumping was observed to be the most effective device to improve the mandibular length.	High	Strong
Al-Thomali et al 2016	Pendulum and modified pendulum	Effective	Pendulum and modified pendulum appliances are effective in molar distalization.	Very low	Weak
Nucera et al 2016	Removable functional appliances x no treatment	Efficacy and the effect of these appliances on the maxilla	Removable functional appliances in Class II growing patients have a slight inhibitory effect on the sagittal growth of the maxilla in the short term, but they do not seem to affect rotation of the maxillary plane.	Low	Weak

Elkordy et al. 2016	Skeletal anchors + fixed functional appliances X fixed functional appliances	Skeletal Class II correction	The studies reviewed provide insufficient evidence to form a conclusion regarding the effects of the use of skeletal anchorage with FFA. The available weak evidence suggests that the use of skeletal anchorage with FFA has no superior skeletal effects but is able to reduce proclination of the lower incisors.	Low	Weak
Pacha et al 2016	Fixed x removable functional appliances	Efficacy	Fixed and removable functional appliances are effective in reducing overjet in children; however, there remains insufficient evidence to differentiate between fixed and removable variants in respect of dental and skeletal effects or indeed in terms of patient experiences.	Very low	Weak
Zymperdikas et al 2016	Fixed functional appliances x no treatment	Studies providing angular skeletal, dentoalveolar and soft tissue	According to existing evidence, FFAs seem to be effective in improving Class II malocclusion in the short term, although their effects seem to be mainly dentoalveolar rather than skeletal.	Moderate	Strong
Al-Jewaira 2015	MARA (with or without fixed appliance) x no treatment	Stability, Short- and long-term mandibular growth effects	The MARA appliance produced statistically significant mandibular growth enhancement in the short- and long-term. These findings, however, may not be clinically significant.	Low	Weak
Ehsani et al 2015	Twin block x no treatment	Skeletal and dental cephalometric findings	Changes associated with a Class II correction were identified. Most of the changes individually were of limited clinical significance, but when combined reached clinical importance.	Low	Weak
Perinetti et al 2015	Removable functional appliances x no treatment	Skeletal and dentoalveolar effects	functional treatment by removable appliances may be effective in treating Class II malocclusion with clinically relevant skeletal effects if performed during the pubertal growth phase.	Low	Weak
Yang et al 2015	Herbst x no treatment	Molar relationship, overjet, overbite and cephalometric data	The Herbst appliance is effective for patients with Class II malocclusion in active treatment period. Especially, there are obvious changes on dental discrepancy and skeletal changes on Co-Gn.	Very low	Weak

Koretsi et al 2014	Removable functional appliances x no treatment	Skeletal, dentoalveolar, and soft tissue variables on lateral cephalometric radiographs	The short-term evidence indicates that RFAs are effective in improving Class II malocclusion, although their effects are mainly dentoalveolar, rather than skeletal.	Low	Weak
Perillo et al 2010	Frankel 2 x no treatment	Skeletal mandibular changes	The FR-2 appliance had a statistically significant effect on mandibular growth. Specifically, it appeared to have an effect on total mandibular length with a low-to-moderate clinical impact.	Low	Weak
Antonarakis and Kiliaridis 2008	Palatal appliances x Buccal appliances	Dental effects (molar, premolar and incisor)	Noncompliance intramaxillary molar distalization appliances all act by distalizing molars with a concomitant and unavoidable loss of anchorage. Buccal acting and palatal acting appliances demonstrate almost similar results, with palatal acting appliances showing less tipping. Friction-free palatal acting appliances appear to produce better molar distalizing effects, but with a concomitant notable loss of anchorage.	Very low	Weak
Flores-Mir et al 2007	Herbst x no treatment	Skeletal and/or dental changes evaluated through lateral cephalograms	Dental changes are as important as skeletal changes to attaining the final occlusal results.	Low	Weak
Flores-Mir and Major 2006	Twin Block x no treatment	The soft tissue profile changes	Evidence supporting the claim for an improvement of the facial convexity with twin block treatment of Class II division I malocclusion was not found• Changes produced by the twin block appliance in the upper lip seem to be controversial, although the study with sounder methodological quality did not report significant changes;• No change in the anteroposterior position of the lowerlip and soft tissue menton was found.	Very low	Weak
Cozza et al 2006	Functional Appliances x no treatment	Effects of functional therapy on mandibular dimensions	Two-thirds of the samples in the 22 studies reported a clinically significant supplementary elongation in total mandibular length as a result of overall active treatment with functional appliances.	Very low	Weak

Chen et al 2002	Functional Appliances x no treatment	Efficacy	Results suggest the need to reevaluate functional appliance use for mandibular growth enhancement.	Moderate	Strong

Table 4 . SRs results on treatment of Class II malocclusion

Author and year	Intervention x Comparison	Primary outcome	Conclusion	GRADE	Strengh of the recommendation
Woon and Thiruvenkatachari 2017	Orthodontic/orthopedic appliance x no treatment, delayed treatment, or intervention with the same appliance with different forces, different mechanics, or a different appliance	Correction of reverse overjet	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.	Moderate	Strong
Rongo et al 2017	Orthopedic appliance x No treatment	Treatment effects (skeletal, dental, soft tissue)	There is very low to low evidence that orthopaedic treatment is effective in the correction of Class III skeletal discrepancies and moderate evidence for the correction of the overjet.	Moderate	Strong
Chatzoudi et al 2014	Chin cup x No treatment	Clinical effectiveness	Although the occipital chin cup affects significantly a number of skeletal and dentoalveolar cephalometric variables, indicating an overall positive effect for the treatment of Class III malocclusion.	Very low	Weak
Cordasco et al 2014	Facemask x No treatment	Cephalometric parameters	Facemask is effective correcting Class III malocclusion in the short term.	High	Strong
Watkinson et al 2013	Orthopedic appliances x May be no treatment, delayed treatment, or another active intervention	Effects	There is some evidence that the use of a facemask to correct prominent lower front teeth in children is effective when compared to no treatment on a short-term basis.	Moderate	Strong
Toffol et al 2008	Orthopedic appliances x No treatment	Total mandibular length, total maxillary length, and intermaxillary vertical and sagittal relationship	Data derived from medium/high quality research described over 75% of success of orthopedic treatment of Class III malocclusion (RME and facial mask therapy).	Low	Weak

Table 5 . SRs results on treatment of Class II malocclusion

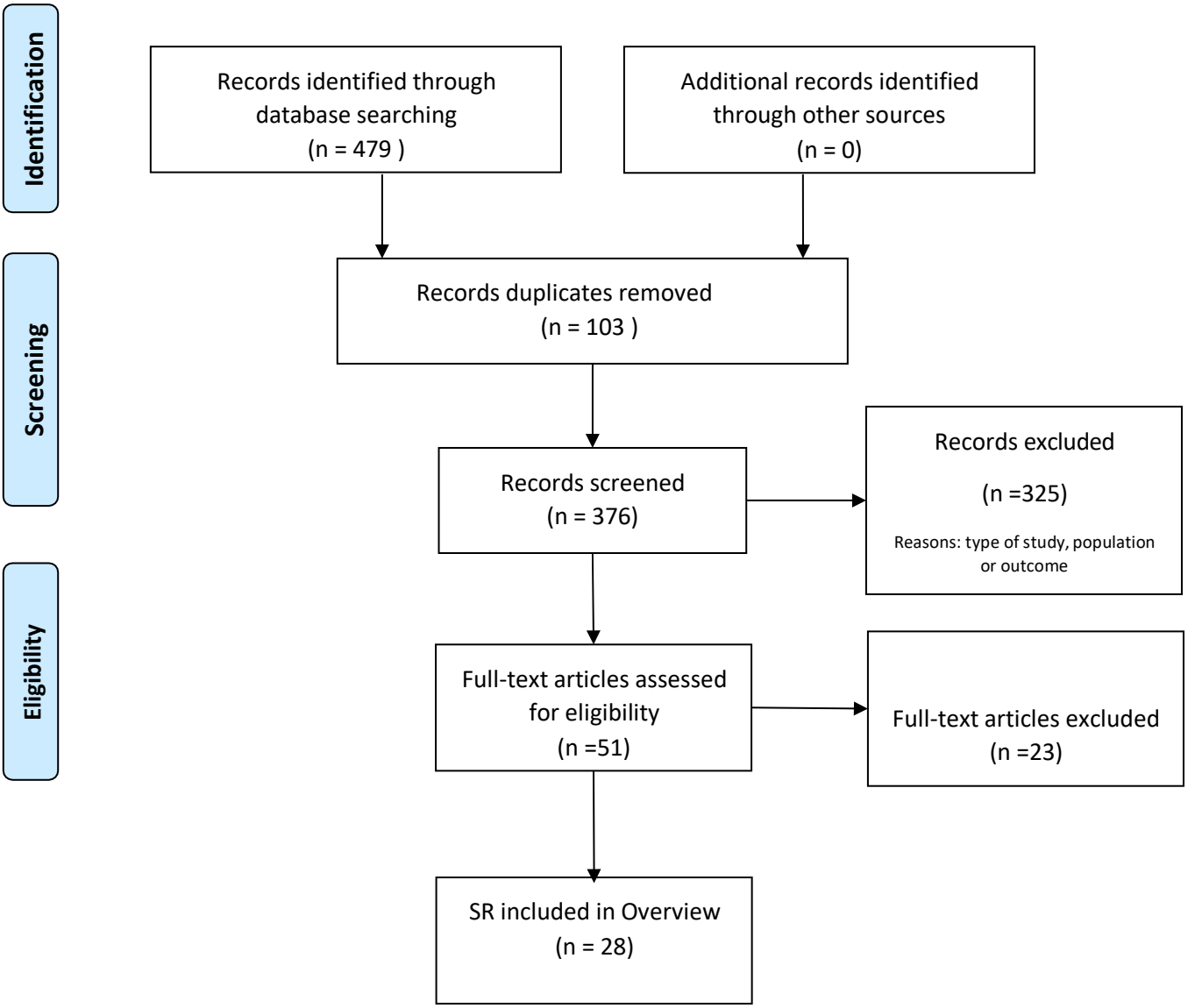
RESULTS

An electronic search of the databases has generated an overall of 479 articles. Titles and abstracts of 479 articles were screened after removing the duplicates. The full texts of 51 relevant articles were retrieved and assessed for their eligibility of inclusion. No other relevant article was found while manually searching the reference lists of those 51 articles. Ultimately, 28 SRs[10-37] have been found to match both inclusion and exclusion criteria after eliminating 23 articles[38-60]. The study selection process is summarized in the flow diagram and the excluded articles and justification for the exclusion are in table 6. Of those included, 11 did not report quantitative analysis of the results, while 17 performed meta-analysis.

Author and year	Reasons for exclusion
Mohamed et al 2018	Studies includied adults
Batista et al 2018	Outcome (moment treatment)
Janson et al 2006	Studies includied adults
Feres et al 2015	Study design included
Henriques et al 2015	Data incomplete (Study design included)
Grec et al 2013	Studies includied adults
Millet et al 2012	Studies includied adults
Antonarakis et al 2007	Only metanalysis
Flores-Mir et al 2006	Data incomplete (Study design included)
Flores-Mir et al 2006	Studies includied adults
Sunnak et al 2015	Outcome (moment treatment)
Borrie et al 2011	Study design included
Foersch et al 2015	Data incomplete (Study design included)
Fudalej et al 2011	Outcome (prediction)
Guzma´n-Barrera et al 2017	Study design included
Jäger et al 2014	Only metanalysis
Lin et al 2018	Study design included
Meyns et al 2018	Study design included
Morales-Ferna´nde et al 2013	Data incomplete (Study design included)
Pithon et al 2016	Data incomplete (Study design included)
Yang et al 2014	Study design included
Yepes et al 2013	Study design included
Zhang et al 2015	Study design included

Table 6 – Studies excluded after full reading and justification for exclusion

PRISMA 2009 Flow Diagram



Six[14,17,18,20,34,35] of the included studies referred to early Class III treatments, while 22[10-13,15,16,19,21-33,36,37] were related to Class II treatments. The age of the patients in the selected studies ranged between 6 and 15.4 years. Only one SR[36], with the objective of including only RCTs on Class II division 2 treatment, did not include any study, being an empty SR.

Out of the 28 SRs, 22 used as comparison an untreated control group. Three evaluated the effects of the appliances and 2 compared two different treatments. The devices evaluated for the treatment of the two malocclusions and the main outcome evaluated are shown in the Table 3.

Methodological quality and quality of evidence of SRs

Methodological quality was assessed using AMSTAR 2. This tool rated 9[17,18,22,23,25,26,30,35,37] RSs as moderate quality, 13[10-14,16,24,27-29,31-34-,] as critically low and 5[15,19-21,28] as low quality. The applicability of this tool in the included studies is shown in the supplementary table.

GRADE was used to assess the quality of evidence included in the SRs. For GRADE we evaluated the main outcome of each RS as shown in the supplementary table. The quality of the evidence is rated very low to high. Of the 28 included studies, only 2[30,18] had high quality of evidence, 5[10,17,25,34,35]were rated as moderate quality, 12[13,14,16,19,22-24,27-29,31,33] as low and 8[11,12,15,21,26,32,37] as very low.

From the GRADE we have the strength of recommendation of the evidence. Those high or moderate evidence qualities have their strong recommendation strength while the low or very low qualities have weak recommendation strength. Thus, 21 studies had poor recommendation while 6 had strong recommendation strength. One SR was considered and empty review[36], and the GRADE or AMSTAR evaluation could not be performed.

Description of results

Class II malocclusion

Two[29,31] SRs compared Class II treatment with headgear and control group. Both concluded that headgear restricts sagittal growth of the maxilla. One[31] also says that headgear decreases short-term overjet and the other[29] is short-term effective treatment in Class II cases with maxillary prognathism.

Two other SRs[13,21] evaluated treatments with the Herbst appliance and compared it to the untreated control group. The conclusion of SRs was that it is an effective treatment and the results achieved come from skeletal and dental changes.

Two included SRs[12,23] evaluated Twin Block treatment. One[12] of them evaluated the differences that this device can bring in the soft tissues of the face, concluding that it is not possible to affirm that the Twin Block brings changes in lips and soft tissues. The other SR[23], evaluates skeletal and dental changes with this device concluding that together the changes are significant for improvement of Class II malocclusion.

A SR[33] evaluated the Class II treatment with fixed appliances, with or without extractions of two or four premolars, and the impact on ANB angle. The results demonstrated that 4 premolar extractions is the most effective treatment for decreasing ANB.

Four studies[19,22,28,30] included in this overview analyzed treatment with removable functional appliances. One[30] concluded that it is possible to achieve mandibular growth, another[28] that the effect is on the maxilla by inhibiting its sagittal growth, another[22] that is an effective treatment if performed in the pubertal growth spurt. In contrast, the fourth[19] SR reported that these devices have minimal effect on mandibular and maxillary growth (skeletal effects) and greater dentoalveolar changes.

Four of the SRs on Class II treatment evaluated fixed functional appliances[24-27]. One compared fixed and removable functional appliances[26], another with untreated controls[25] and the third used skeletal anchorage[27], with control fixed functional appliance. The first concluded that both devices corrected the overjet and that the dental and skeletal effects are the same. The second[25] compared to untreated controls showed that there are more dentoalveolar than skeletal effects. The later had the concomitant use of skeletal anchorage[27], and pointed out that skeletal anchorage decreases the dental side effects caused by the use of these devices, especially the projection of the lower incisors. The MARA appliance was[24] compared to an untreated group. This device stimulates mandibular growth, but not in a clinically significant way. Two SRs[10,11] evaluated overall functional appliances. Both concluded that this type of treatment increases mandibular growth.

One study[37] evaluated prefabricated myofunctional appliances, and compared them with other treatments or with an untreated group. Activator devices were

considered more effective than prefabricated myofunctional appliances for overjet correction.

SR salso evaluated noncompliance intramaxillary molar distalization appliances. Al-Thomali et al[32] assessed the effectiveness of pendulum and modified pendulum appliances. The conclusion was that both are effective for distalizing molars, with no skeletal effect. Antonarakis and Kiliaridis[15] compared noncompliance intramaxillary molar palatal and buccal distalization appliances and showed that the two types of appliances are effective for molar distalization.

Class III

Six SRs[14,17,18,20,34,35] evaluated the early treatment for Class III malocclusion. Three[17,18,35] pointed out that facemask produces positive dental and skeletal effects. Rongo et al[34] showed that orthopedic appliance treatment corrects overjet. Toffol et al 2008[14] stated a 75% success is achieved with RME and facemask.

Chatzoudi et al[20] evaluated the chin cup compared to an untreated control group and reported that this appliance is effective, as it produces satisfactory skeletal and dental effects for correction of Class III malocclusion.

Stability

Out of the 28 included articles, 14 addressed stability[11,14,15,17-21,24,25,27,29,34,35]. Nine[11,14,15,19,21,24,25,27,29] were Class II and 5 Class III[17,18,20,34,35].

Fourteen did not reach conclusions because there was insufficient evidence about treatment stability. The only 2 SRs that showed any evidence of stability were headgear[29] treatment and treatment with Class III orthopedic appliances[14]. According to Papageorgiou et al[29], there is a long-term relapse in the use of dental headgear and higher in those who did not use retainers. The other[14], a Class III treatment SR with orthopedic appliances, concluded that achieving stability requires significant overjet correction.

Ideal moment to treat

Only 7[10,11,14,16,19,21,22] SRs evaluated the best time to treat sagittal problems. Five[10,11,16,19,22] of these reviews are for early Class II treatment and two[14,21] for early Class III treatment. From the early Class III SRs, one[21] stated that the best time is

before the pubertal growth stage and the other[14] showed evidence that the best moment is during the deciduous dentition. Two[16,22] of the early Class II SRs concluded that the growth phase is the ideal time. One[19] reported that the peak of growth is the ideal moment and the the other stated that it should be shortly after the peak.

DISCUSSION

In this study we performed an overview of published SRs with or without meta-analyses to investigate and summarize treatment of sagittal discrepancies in children and early adolescents. The evidence here presented is largely inconclusive, due to a variety of factors. The methodological quality of many (18 out of 28 SRs) of the included trials was low or critically low, thereby reducing the validity of reported results. Moreover, the quality of the evidence was low or vey low in 26 SRs, and therefore posed a significant threat to selection bias. Moreover, one of the included SRs is an SR[36], since no studies have met their inclusion criteria, and it is more likely to be subject to publication bias. As the quality of SRs is directly affected by the quality of included primary studies, full investigation and reporting of each included study is required.

The difficulties found in this overview were due to the heterogeneity of the samples and the wide variety of orthodontic devices used. The most frequently reported failures in the studies included poor quality articles, small or inadequate samples, lack of control group, high risk of bias, no prior power calculation and no long-term follow-up in the studies. Nevertheless, this overview summarized the outcomes of the the included SRs as follow:

Class II

Early treatment of Class II malocclusion may be applied with various orthopedic / orthodontic appliances. The devices investigated in the included SRs were: headgear, Herbst, Twin block, Conventional and modified pendulum, prefabricated myofunctional appliances, removable or fixed functional appliances, MARA, Frankel 2 and noncompliance intramaxillary molar distalization appliances (palatal and buccal). The age range included in SR studies ranged from 7 to 15.4 years.

Headgear

The 2 headgear studies[28,29] showed that this appliance restricts maxillary growth. However, both are of low quality according to GRADE and critically low methodological quality according to AMSTAR 2. Regarding stability, there is dental relapse.

Herbst

Two SRs[13,21] evaluated Herbst treatment pointed out that the Class II correction is achieved buy skeletal and mostly by dental modifications. Both were rated as of low or very low quality, so the strength of recommendation for using Herbst is weak. Regarding the methodological quality, both presented low or critically low quality. Regarding stability, there were no conclusions because there was insufficient evidence to do so. None of them investigated the ideal time of treatment.

Twin block

One[23] out of the two SRs on Twin block treatment showed that this appliance is effective to provide skeletal and dental changes. However, it was rated as of low quality of evidence and with moderate methodological quality. The other SR[12] found no changes in soft tissues after using the Twin block, but it presented very low quality of evidence and critically low methodological quality. Neither one evaluated the ideal time for treatment or its stability.

Pendulum

The conventional and modified Pendulum were effective for molar distalization[32], but they did not evaluate the ideal treatment time or the stability of the final results. They were rated as of very low quality of evidence and critically low methodological quality.

Prefabricated myofunctional appliances

On a short-term basis, low quality of evidence with moderate methodological quality suggest that prefabricated myofunctional appliances were generally less effective than the activators for Class II treatment. This SR[37] did not evaluate stability or ideal treatment time.

Removable and fixed functional appliances

Best time of treatment for two of the studies[16,22] was in the period of pubertal growth, another SR[11] that is best done at peak and another[19] that should be at or shortly after peak.

MARA

An RS[24] evaluated treatment stability and effect on mandibular growth with MARA appliance. Studies were insufficient to reach a conclusion on stability, but MARA produced mandibular growth. It is a review of low quality and critically low methodological quality.

Frankel 2

Perillo et al[16] evaluated the use of Frankel 2 on Class II treatment. Low quality of evidence with low methodological quality suggested that this appliance significantly alters the mandibular growth, but there was no long term stability evaluation.

Noncompliance intramaxillary molar distalization appliances (palatal and buccal)

A very low quality and low methodological quality SR[15] suggested that both devices provide effective molar distalization but with loss of anchorage. Stability could not be assessed due to lack of evidence.

Class III

Early treatment of Class III malocclusion may be applied with various orthopedic / orthodontic appliances. The devices investigated in the included SRs were: chin cup, facemask and orthopedic appliances. The age of the subjects in the included SRs ranged between 4.2 to 12.5 years.

Chin cup

Low quality of evidence with low methodological quality SR suggested that chin cup is effective on early Class III treatment by Chatzoudi et al[20.] It also stated that the ideal time of treatment is before the pubertal stage. It seems that occipital chin cup has more positive effects for Class III correction but that stability could not be evidentiated.

Facemask

There is a high amount of evidence[18] that the use of a facemask for early Class III treatment results in positive improvement for both skeletal and dental effects in the short term. However, there was lack of evidence on long-term benefits. The ideal treatment time has not yet been evaluated with high level trials.

The following drawbacks of this overview should be highlighted. Most of the included SRs were of moderate quality and only a few of high quality, which could have affected the quality of them. Therefore, the results of this overview should be read carefully.

Most treatment outcomes discussed in the SRs were for short-term effects of orthodontic appliances. Although many SRs had included the short and long-term effects` investigation, only 2[14,29] investigated the long-term stability and in headgear or maxillary protraction only, probably due to the limited data provided from their included articles.

Further randomized controlled trials (RCT) with proper design and adequate sample size are needed in the future in order to reach more reliable results concerning the treatment of sagittal discrepancies in children and early adolescence in the short and the long term.

The results reported in this overview that suggests a lack of evidence does not necessarily imply that the specific early treatment is ineffective. It means that further high quality trials are still required to assess the effectiveness of Interceptive orthodontics on sagittal discrepancies. Early treatment might be recommended for the treatment of sagittal discrepancies of both skeletal and dental aetiology.

CONCLUSIONS

- Early maxillary protraction with facemask is an effective treatment for early Class III treatment;
- Low evidence SRs suggested that headgear, fixed and removable functional appliance and non-compliance molar distalization devices are effective for treating the Class II malocclusion, with different skeletal and dental effects;

- Low to moderate evidence SRs suggested that the ideal time for the treatment of Class II malocclusion appears to be in the pubertal growth stage;
- More evidence is still needed to draw definite conclusion related to the ideal time for early Class III treatment;
- There is still no evidence on the long term stability of the final results in either sagittal discrepancy;
- More SRs with proper design and control of risk of bias are needed in the future in order to reach more reliable results concerning about randomized control trials (RCTs) about treatment of sagittal discrepancies in children and early adolescence in the short and the long term.

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5 - Final considerations

Far from imposing restrictions on orthodontists, evidence-based orthodontics provides an excellent tool to empower them to take control of their learning process and hone their skills. It allows them to question their clinical procedures and to evaluate them in the light of the current clinical research. In other words, evidence-based orthodontics aims to provide patients with the most effective treatment. Thus, the evidence-based approach does not simply involve using scientific literature but adopts a new approach to treatment procedures.

As a contribution to health services, this overview gathers information on early treatment of Class II and III occlusions. The applied outcomes were the ideal time for treatment, application of effects and stability.

The ideal time for the treatment of Class II malocclusion appears to be at the pubertal stage of growth, peak growth or shortly after the peak, while Class III is before the pubertal growth spurt, ie in the deciduous dentition.

Early maxillary protraction is an effective treatment, with or without rapid maxillary expansion.

Treatment for Class II malocclusion is effective using activator appliances, prefabricated myofunctional devices, upper tooth distalizers, fixed or removable functional appliances. It is important to individualize the treatment plan and make correct and indispensable diagnosis so that the treatment benefits the patient in the short and long term.

There is still no evidence on the stability of treatments for sagittal problems.

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