Systematic Review Article

Association between arch perimeter management and the occurrence of mandibular second molar eruption disturbances: *Systematic review and meta-analysis*

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ABSTRACT

Objectives: To investigate the association between the management of mandibular arch perimeter during development of the dentition and its effects on second permanent molar (M2) eruption.

Materials and Methods: Seven electronic databases were searched without restrictions up to June 2020. Assessment was performed using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool for non-randomized clinical trials (non-RCT). Odds ratio (OR) with 95% confidence intervals was calculated from random-effects meta-analyses. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) tool was used to assess the certainty of the evidence.

Results: Five non-RCTs, with serious to moderate risk of bias, were included. A low certainty of evidence indicated that individuals undergoing mandibular arch perimeter management by controlling the position of the first molar had a high prevalence of M2 eruption difficulties. The odds of eruption disorders was 7.5 times higher (OR: 7.57, [3.72, 15.41], $P < .001$) in treated individuals. Subgroup analysis revealed that appliances that increased the arch perimeter lead to a greater chance of eruption disorders compared to appliances that only maintained the perimeter. The predictive factors for the M2 eruption difficulty were its previous mesioangulation in relation to the first molar ($>24°$) and the treatment time (>2 years).

Conclusions: Mandibular arch perimeter management during development of the dentition leads to an increase in the occurrence of M2 eruption difficulties. The identification of possible risk factors as well as the choice of the appropriate appliance type and the monitoring of these individuals seems to be essential to avoid undesirable effects with this therapy. (*Angle Orthod.* 2021;91:544–554.)

KEY WORDS: Systematic review; Arch perimeter; Tooth eruption

INTRODUCTION

Arch perimeter management in the mixed dentition is a strategy often used to resolve space deficiencies in the mandibular arch.[1–3] The literature generally reported that this therapy was effective in relieving crowding in the anterior region of the mandibular arch, mainly through the preservation of the leeway space.[2–4] However, although the early preservation of space in the anterior area is usually considered a priority, less attention is given to what happens in the posterior region of the arch.

In this sense, the eruption of the mandibular permanent second molar (M2) is a complex event and the prevalence of eruption disturbances was reported to be higher in the orthodontic population compared to untreated individuals.[5,6] The etiology of M2 eruption disorders is related to systemic or local factors,[7] and the relationship between the first and second molars, with an eruption pathway oriented close along the distal root of the first molar, as well as the amount of space available in the posterior region, seems to play an important role in successful M2

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eruption.[6,8,9] Hence, the question that arises is whether the use of appliances that control the position of the permanent first molar during the development of the dentition is related to difficulties of eruption in the adjacent M2.

Previous studies[1,10,11] that evaluated the capacity of arch perimeter management therapy to favor the occurrence of M2 eruption disorders have methodological heterogeneity and the inconclusive results could bias the evidence and negatively affect clinical practice. Therefore, a systematic review addressing this topic and possible factors related to the use of arch perimeter maintainers and M2 eruption disorders would be beneficial for orthodontic clinical practice.

For these reasons, the aim of this systematic review was to provide a synthesis of the available literature to answer the following focused main question: Does management of mandibular arch perimeter (I) in children and adolescents (P) lead to an increase in M2 eruption disturbances (O) compared to untreated individuals (C)?

MATERIALS AND METHODS

Protocol and Registration

The study protocol was registered on PROSPERO (CRD42020189139). For reporting, this systematic review followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[12]

Eligibility Criteria

A PICOS acronym was established as an inclusion criterion:

- Population (P): children and adolescents in the mixed or early permanent dentition.
- Interventions (I): orthodontic treatment with appliances that maintained or increased the perimeters of the mandibular dental arch prior to M2 eruption: lingual arch, lip bumper, Schwarz appliances, Arnold appliances, or others appliances described by authors.
- Comparison (C): individuals who were not subjected to orthodontic treatment or available data from individuals treated prior to arch perimeter management.
- Outcomes (O): primary: prevalence and odds of M2 eruption disturbances; secondary: identified possible predictive risk factors.
- Study-design (S): randomized clinical trial (RCT) or non-RCT.

The exclusion criteria were: case reports, editorials, animal and in vitro studies, descriptions of clinical techniques, studies with orthodontic/orthopedic approaches performed concomitantly, treatment with mandibular tooth extractions or any other surgical procedure, and studies evaluating individuals with craniofacial deformities/syndromes or cleft lip/palates.

Information Sources and Search Strategy

An electronic search was conducted in MedLine (via PubMed), Web of Science, Cochrane Library, Scopus, Embase, and Lilacs up to June 22, 2020. Google Scholar (first 200 references) was investigated to partially access the gray literature. Detailed search strategies were developed appropriately for each database (Appendix). To check the possibility of unpublished and ongoing studies, the Clinical Trials-US National Institutes of Health (http://www.clinicaltrials.gov) was consulted. Additionally, manual searches in the reference lists of the articles included were also carried out. No restrictions on language, year, or status of publication for inclusion were applied.

Study Selection

Two authors (LGS and KA) independently and in duplicate screened the titles/abstracts of the reference lists. The full text of those references that met the eligibility criteria or with insufficient information in the title/abstract for a decision on inclusion or exclusion was retrieved. The same authors assessed independently the full text, and those studies that met the eligibility criteria were included. In both phases, any disagreements were resolved by consensus.

Data Extraction and Items Extracted

The data were collected with a standardized table. The following data were extracted: authors, year of publication, study design, characteristics of participants, description of groups, description of intervention (appliance use, treatment duration/time of records uptake), and outcomes. Data were compared for accuracy, and any discrepancy was resolved through reexamination of the original study.

Assessment of Bias Risk Within Studies

The revised Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool was used to assess the risk of bias in non-RCTs.[13] The bias due to confounding factors, selecting participants for the study, classifying the interventions, deviations from the intended intervention, missing data, measuring outcomes, and selective reported results were graded after answering the signaling questions following the recommendations of the Cochrane Handbook 6.0 (https://training.cochrane.org/handbook).[14] The risk of

overall bias for the non-RCT was judged as low, moderate, serious, critical, or no information.

If RCTs were included, the use of the revised Cochrane Collaborations-2 tool to assess the risk of bias was planned.

Summary Measurements and Synthesis of Results

Measurements were based on continuous (units) or dichotomous data from clinical indices, radiographs, or cone beam computed tomography. A meta-analysis was carried out with studies that reported comparable outcomes. When reported by the studies in percentage, the occurrence of events was converted into units to be grouped in the meta-analysis.

Data were analyzed with RevMan 5.4 software (Cochrane, London, UK). The effect measure odds ratio (OR) and the corresponding 95% confidence intervals (CI) were calculated for the occurrence of M2 eruption disturbances. A random effect was applied due to variations in terms of the implementation of interventions, design, and conduct of studies. Heterogeneity was assessed using the I^2 test, with guide for interpretation as follows: 0 to 30%, not important; 31%–50%, moderate; 51%–80%, substantial; 81%–100%, considerable.[14] Sensitivity analysis was performed based on results of subgroup analysis comparing passive appliances (that maintain the arch perimeter) and active appliances (that maintain or increase the arch perimeter). The outcomes that were not included in the meta-analysis were discussed qualitatively.

Evaluation of the Level Evidence

The quality of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool.[15] The certainty of evidence level was generated using online software (GRADEpro, available online at gradepro.org) based on assessment of the study design, risk of bias, inconsistency, indirectness, and other considerations (such as publication bias). Based on this assessment, the certainty of the evaluation of the outcome could be very low, low, moderate, or high quality.

If a sufficient number ($n > 10$) of trials were included, it was planned to assess the publication bias visually through the level of funnel plot asymmetry.

RESULTS

Study Selection

The search strategy yielded a total of 877 studies (Figure 1). After the removal of duplicates and screening the tittle/abstract, 22 references were obtained for the full-text evaluation. Among them, 17 were excluded and the reasons are provided in Table 1. Finally, five studies[5,10,11,16,17] met the eligibility criteria and were included in this systematic review.

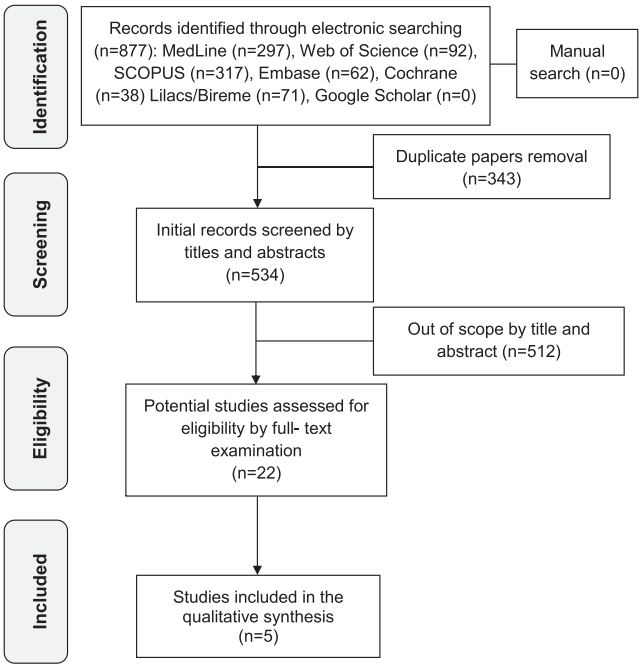

Figure 1. PRISMA flowchart of article retrieval.

Study Characteristics

Table 2 provides the descriptive characteristics of the studies included. All of them were non-RCT, three[5,11,16] were retrospective, and two studies[10,17] were prospective studies, of which three[5,10,11] were clinically controlled. Sample sizes ranged from 67[16] to 260[5] individuals per study group, and the mean age of participants at baseline ranged from 8[10,11] to 11[17] years.

Regarding the type of orthodontic appliance, two studies[5,16] used a lip bumper appliance, and another two studies[11,17] used a passive mandibular lingual arch. One study[10] compared groups of individuals treated with a Schwarz appliance, individuals treated with a mandibular lingual arch, and individuals treated with a combination of both appliances. The mean time interval between onset and the end of the therapy varied substantially from 10 months[16] to 4.6 years.[10]

Concerning the measures used to verify the M2 eruption disturbances, in two studies[10,11] the diagnosis of impaction[11] and eruption difficulties[10] was defined when the root of the M2 was formed by at least 75% but the tooth remained unerupted. In one study[5] it was necessary for the apices of the M2 to be closed for the diagnosis of impaction or ectopic eruption. In two studies,[16,17] a clinical evaluation of the M2 impaction was based on whether there was eruption into full occlusal contact and whether the mesial cusps were

Table 1. List of Excluded Studies With Reasons After Full-Text Evaluation

Reference	Reason for Exclusion
Bereket et al., 2011	Did not assess M2 eruption
Bjerregaard et al., 1980	Did not assess M2 eruption
Brothwell et al., 1997	Narrative review
Cernei et al., 2016	Did not assess M2 eruption
Ciftci et al., 2018	Did not assess M2 eruption
Gautam et al., 2006	Commentaries
Keinan et al., 2016	Case reports or case series
Keski-Nisula et al., 2008	Did not assess M2 eruption
Levit et al., 1971	Did not assess M2 eruption
Ngan et al., 1999	Editorial
Osborn et al., 1991	Did not assess M2 eruption
Owais et al., 2011	Did not assess M2 eruption
Psaltis et al., 1982	Description of clinical technique
Sable et al., 2004	Did not assess M2 eruption
Shapira et al., 2012	Did not use the therapy investigated in this review
Tsai, 2000	Did not use the therapy investigated in this review
Wendling et al., 2005	Did not assess M2 eruption

confirmed radiographically to be below the height of the distal surface of the first molar.[17]

Risk of Bias Within Studies

The methodological appraisal of the studies included and the reasons for the judgments are reported in Table 3. Overall, one study[10] was classified as having a moderate risk of bias, while four studies[5,11,16,17] were graded as having a serious risk of bias. The items affected by methodological flaws were the domains "confounding," "classifying the interventions," and "measuring outcomes."

Data Synthesis

Primary Outcome. The studies included reported a higher prevalence of M2 eruption disturbances in children and adolescents undergoing arch perimeter management therapy, with a mean frequency ranging from 7%[5] to 14.7%,[10] while untreated subjects showed a mean frequency of M2 eruption disorders of about 1.5%.

A meta-analysis was carried out regarding the odds ratio of occurrence of M2 eruption disorders (Figure 2). The I^2 test showed non-significant heterogeneity among the studies. The results showed, with statistical significance, that children and adolescents treated with appliances that maintained or increased mandibular arch perimeter in the mixed dentition were at a greater chance of the occurrence of M2 eruption disorders by 7.57 times compared to untreated individuals (OR: 7.57, 95% CI: 3.72–15.41, $I^2 = 0\%$, $P < .001$). Possibility of heterogeneity was explored with subgroup analysis based on the appliance design (Figure 3). The meta-analysis showed that the use of active appliances (that is, those that increased the arch perimeter), such as the lip bumper and Schwarz appliance, lead to greater odds of the occurrence of difficulties in M2 eruption (OR: 10.32, 95% CI: 4.09–26.01, $I^2 = 0\%$, $P < .001$) than passive arch perimeter maintainers such as the mandibular lingual arch (OR: 5.24, 95% CI: 1.94–14.16, $I^2 = 0\%$, $P = .001$).

Secondary Outcome

Regarding the investigation of predictive risk factors for eruption difficulties, an initial mesioangulation of M2 in relation to the first molar was a determining factor for the risk of impaction in two studies using passive lingual arch[17] arch and lip bumper[5] (mesial inclination greater than 24° and 30°, respectively). However, one study[10] found no statistically significant association for this variable. In one study,[5] treatment time greater than 2 years increased the risk of ectopic eruptions by 2.6 times in individuals treated with a lip bumper. Likewise, another study[10] reported that patients with M2 eruption difficulties wore the appliance, on average, 4 months longer than patients with normal eruption ($P < .001$); however, it is important to note that the authors did not analyze the effects of this outcome separately according to the type of appliance.

The initial variables of age at onset of treatment,[5,10,11,17] gender,[5,10,17] first molar/M2 spacing,[17] retromolar space,[10] crowding in mm,[5] and third molar presence[17] were not significant predictors of disturbances in the eruption of M2.

Certainty Levels and Strength of the Evidence

The certainty of evidence for the outcome prevalence of M2 eruption disorders and the odds that arch perimeter maintainers lead to eruption disorders was classified as low level. Reasons for judgment and downgrading the evidence are detailed in Table 4. The risk of bias, inconsistency, indirectness, and imprecision were the main items that affected the quality of the evidence.

DISCUSSION

Summary of Evidence

Although widely used in orthodontic practice for its immediate effectiveness in relieving crowding in the transition from the mixed to permanent dentition,[2,3] the results of this review and meta-analysis were consistent in reporting that preserving/increasing the mandibular arch perimeter by controlling the E-space increased the prevalence and lead to a greater chance of M2 eruption disorders compared to the untreated population. Lack of space is one of the main

Table 2. Summary of Study Characteristics and Results of the Included Studies[a–d]

Authors, Year	Study Design	Age, Dentition	Patients Characteristics	Descriptions of Groups (n)	Survey Method	Measurements Investigated	Results (*P* Value) EG	CG	(*P* Value)
Arevalo et al., 2020[11]	non-RCT	IG: 8.7 y CG: 9.4 y mixed	Patients between 9 to 17 y who received an lower lingual arch or a bilateral maxillary space maintainer without any others orthodontic treatment	IG: patients with leeway space preservation by means of lower lingual arch (n = 126) CG: subjects who received bilateral maxillary space maintainer without leeway space maintainers (n = 132)	Clinical examination and Panoramic radiographs	Frequency of M2 impaction n(%) OR for M2 impaction	18 (7.1) 6.5±0.8	4 (1.5) 1	.02[b] .02[b]
Jacob et al., 2014[16]	Non-RCT	IG: 10.6 y	Patients treated with lip bumper therapy in mandibular arch with, unerupted M2	IG: lip bumper was adjusted so that the acrylic shield was 2-3 mm away from the labial surface of incisors and activated to provide approximately 3-4 mm of expansion at the molar region. The mean active treatment time was 10 mo (n = 67)	Clinical examination and Panoramic radiographs	Frequency of M2 impaction n(%) Bilateral n (%) Unilateral n (%) Total n (%)	 3 (4.5) 5 (7.5) 8 (11.9)	 - - -	 - - -
Rubin et al., 2012[10]	non-RCT	IG1: 8.7 y IG2: 9.5 y IG3: 8.6 y CG: 8.8 y mixed	M1 fully erupted, M2 not yet erupted, mild to moderate crowding in the mandibular dental arch, no congenitally missing or previously extracted mandibular permanent teeth	IG1: patients treated with a removable Schwarz appliance with ball clasps incorporated in the interproximal aspect between deciduous and permanent molars. The screw was expanded by a quarter turn per week. The mean treatment time was approximately 11 mo (n = 58) IG2: passive lingual holding arch was used before the loss of the second deciduous molars and not removed until full eruption of the permanent successor. The wire lie was passively just below the cingula of the canines and the incisors. The mean treatment time was 3.8 y (n = 85) IG3: patients were treated first with the Schwarz appliance, as described in G1. Toward the end of the mixed dentition, the mandibular lingual holding arch was used as in G2. The mean treatment time was 4.6 y (n = 58) CG: Patients without treatment (n = 100)	Clinical examination and Panoramic radiographs	Frequency of M2 eruption difficulty by appliances (%): EG1 EG2 EG3 All appliance Variables investigated with M2 eruption difficulties: Inclination of M2 Space-width ratio Age at onset of treatment Total treatment time[a]	 7.8 4.7 14.7 8.5 - - - -	 1.0 1.0 1.0 1.0 - - - -	 .04[b] NS .01[b] .02[b] NS NS NS <.001

Table 2. Continued

Authors, Year	Study Design	Age, Dentition	Patients Characteristics	Descriptions of Groups (n)	Survey Method	Measurements Investigated	Results (*P* Value) EG	CG	(*P* Value)
Sonis et al., 2011[17]	non-RCT	11.2 y, mixed	patients underwent nonextraction therapy, mild to moderate crowding in the mandibular arch, nonsyndromic, with no dental or craniofacial anomalies, and position of the occlusal plane of the M2 below the cementoenamel junction at onset of therapy	EG: placement of a passive lower lingual arch prior to exfoliation of the second primary molars. Upon eruption of the second mandibular premolars, the lingual arch was removed and conventional fixed appliance therapy was initiated (n = 200)	Clinical examination and Panoramic radiographs	Frequency of M2 impaction n (%)			
						Bilateral n (%)	5 (2.5)	-	-
						Unilateral n (%)	24 (12)	-	-
						Total n (%)	29 (14.5)	-	-
						Variables investigated with M2 eruption difficulties:			
						Inclination of M2	-	-	<0.001[c]
						M1/M2 spacing	-	-	NS
						Age at onset of treatment	-	-	NS
						Third molar presence	-	-	NS
						Facial pattern	-	-	NS
						Skeletal relationship	-	-	NS
						Gender	-	-	NS
Ferro et al., 2011[5]	non-RCT	10.2 y, NR	patients with 2 mm or more of anterior crowding treated with lip bumper. Exclusion criteria were permanent M2 eruption and possible factors predisposing or impeding M2 impaction, such as agenesis, dental inclusions, destroying caries, and previous dental extractions	EG: LB was kept gingival in the vertical plane, and a distance of 1 to 2 mm from the incisor was kept in the sagittal plane. Patients could remove the LB by themselves but were asked to wear it 24 hours a day, taking it out only for meals. The mean treatment time was 28 mo (n = 260) CG: untreated (n = 135)	Clinical examination and Panoramic radiographs	Impaction of M2 :			= .027[b]
						Bilateral n (%)	9 (3.5)	1 (0.7)	
						Unilateral n (%)	9 (3.5)	1 (0.7)	
						None n (%)	242 (93)	133 (98)	
						Ectopic eruption of M2:			<.001[b]
						Bilateral n (%)	15 (6.0)	1 (0.8)	
						Unilateral n (%)	26 (10.4)	1 (0.8)	
						None n (%)	210 (83)	132 (98)	
						OR for M2 impaction	9 (2-45)	1	= .007[b]
						OR for M2 ectopic	18 (4-82)	1	<.001[b]
						OR for M2 impaction (treatment duration, >2 y)	2 (0-7)	-	NS
						OR for M2 ectopic (treatment duration, >2 y)	2.6 (1-6)	-	=.04[c]
						Inclination of M2 for impaction			
						<10° (OR)	1	-	
						21-30° (OR)	1 (0-4)	-	NS
						>30° (OR)	10 (2-43)	-	=.001[c]
						Inclination of M2 for ectopic			
						<10° (OR)	1	-	
						21-30° (OR)	1 (0-2)	-	NS
						>30° (OR)	3 (0-13)	-	NS

[a] Regarding logistic regression analysis, without control for the initial variables; [b] Concerning IG-CG difference; [c] Concerning baseline-IG; [d] CG indicates control group; IG, intervention group; M2, mandibular second molar; mo, months; non-RCT, non-randomized clinical trial; NR, not reported; NS, no significant; OR, odds ratio; y, years.

hypothesized causes to explain eruption difficulties of the M2. In this sense, late mesial migration of the first molars into the E-space during normal growth was associated with a decrease in the anterior length of the mandibular arch by approximately 4 mm[1] and, consequently, with an increase in retromolar space.[7] Therefore, appliances that act passively to prevent the migration of the first molar or that also act by distal tipping or translation of the first molar[3] could reduce the retromolar space and increase the chance of adverse effects in M2 eruption.

However, it is important to note that the evidence for the association of lack of retromolar space as a predictive factor leading to the occurrence of M2 eruption disorders after arch perimeter therapy is weak. Only one study[10] evaluated this variable and the survey method was used using two-dimensional images; however, the molars and the mandibular ramus are not situated in the same transverse plane. The other variable investigated related to space ratio, spacing of the M2 in relation to the first molar, was also not associated with impaction.[17]

Several other variables were also investigated by the studies included to provide predictive factors for M2 eruption disturbances. Pretreatment intermolar angulation (M2 mesioangulation > 24°) and treatment time (>2 years) were considered the main issues. As the initial mesioangulation suggests the M2 eruption pathway angled toward the surface of the first molar, the assessment of the prior M2/first molar angulation and the follow-up of the eruption pathway are important and should be included in the planning of any orthodontic treatment as supplementary information for making a clinical decision about the use of these

Table 3. Evaluation of Risk of Bias of the Included Studies Using ROBINS-I[a–i]

	Domain							
Study	Confounding	Selecting Participants for the Study	Classifying the Interventions	Deviations From Intended Intervention	Missing Data	Measuring Outcomes	Selecting Reported Result	Overall Risk of Bias Judgment
Arevalo et al., (2020)[11]	Moderate[a]	Low	NI[f]	Low	Low	Serious[e,g,h]	Low	Serious
Jacob et al., (2014)[16]	Serious[b]	Low	Low	Low	Low	Serious[g,h]	Low	Serious
Rubin et al., (2012)[10]	Moderate[a]	Low	Moderate[d]	Low	Low	Moderate[g]	Low	Moderate
Sonis et al., (2011)[17]	Serious[b]	Low	NI[f]	Low	Low	Moderate[g]	Low	Serious
Ferro et al., (2011)[5]	Moderate[c]	Low	Low	Low	Low	Serious[g,h]	Low	Serious

[a] Did not report match between groups on baseline for potentially predictive variables for eruption disturbances; [b] Absence of a control group; [c] Few statistical differences reported in baseline between the groups; [d] Considerable difference in treatment time between groups; [e] Did not present statistical analysis for some outcomes; [f] No information about treatment time; [g] Not blinding accessor; [h] Not measurement method error; NI indicates No information.

appliances. In addition, a concern was the possible increase in the intermolar angle due to distal tipping of the first molar caused by these appliances.[4,16] Previous studies suggested that active appliances, such as the lip bumper, could lead to the first molar tipping distally by approximately 6°–8°[3] while, with a passive lingual arch, this value was 0.5°.[18] In this sense, the subgroup analysis confirmed increased odds of M2 eruption disorders in individuals treated with active appliances. However, even with first molar distal tipping, the risk of eruption disorders appeared to be minimal when the initial M2 mesiangulation was less than 10°. In cases where the intermolar angulation is a concern, the use of passive appliances seems to be the most suitable.

There may be a perception that early perimeter management results in more effective relief of crowding. However, longer treatments should be discouraged as they have been shown to increase M2 eruption disturbances.[5,10] In cases where there was no premature loss of deciduous teeth, the ideal time for placing the appliance in the mandibular arch seems to be just before the loss of the deciduous second molars.[1–3]

Implications for Practice

Clinicians should carefully evaluate the cases in which arch perimeter management therapy will be used, considering, in addition to relieving the current space problem, the possibility of adverse effects in the medium to long term. Specifically, they should consider how treatment might affect eruption of the M2. Measurement of the intermolar angle must be performed during the diagnostic process for making appropriate clinical decisions regarding the use of this therapy. Mesioangular eruption of the M2 is often related to genetic issues of dentition development. Thus, prior identification of hereditary problems for the development of malocclusions can lead to more effective treatment strategies.[19] In addition, the optimal duration for wear of the appliance and timely removal are equally important.

Often, the absence of painful symptoms and the posterior location within the dental arch make it difficult for parents to identify the absence of a posterior tooth compared to an anterior tooth. Thus, due to the significant increase in the chance of the occurrence of M2 eruption disorders subsequent to arch perimeter management therapy in the mixed dentition, it is essential that clinicians follow these patients even in cases where other treatment will not be necessary. An early diagnosis of M2 eruption disturbances results in a better outcome, regardless of the method of treatment used.[20]

In cases where there is no monitoring of the M2 eruption process,[20] approaches involving orthodontic uprighting, surgical exposure or replacement, transplantation, or tooth extractions may be necessary.[21–23] In these cases, the early therapy with arch perimeter management that aimed to reduce the complexity of future treatment with fixed appliances may, in fact, result in the requirement for additional orthodontic intervention. This would ultimately decrease treatment efficiency and effectiveness.[20] Likewise, the initial option for a non-extraction orthodontic treatment may not always be a final non-extraction approach.

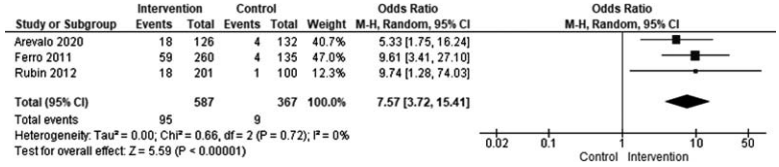

Figure 2. Forest plot representing the odds ratio for the occurrence of M2 eruption disturbances.

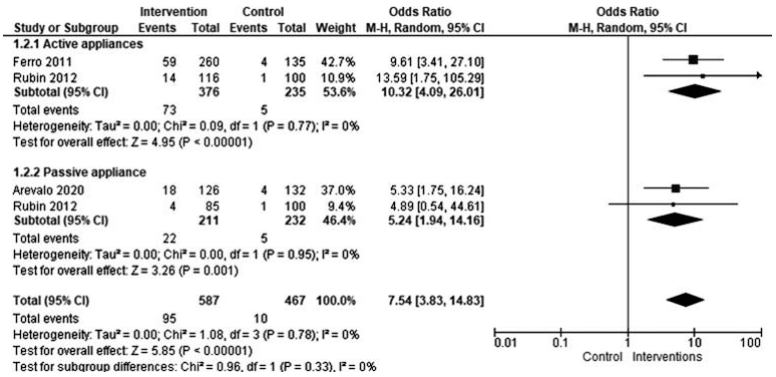

Figure 3. Forest plot representing subgroup analysis between active and passive appliances.

Strengths, Limitations, and Future Directions

Possible selection bias was avoided by extensive searches in several electronic databases and by access to partial gray literature without language restrictions or publication status. Other sources of gray literature, such as OpenGrey and Proquest, were not accessed for this review. Additionally, the risks of non-inclusion of unpublished trials were partially overcome by checking on a trial registration platform.

For rare outcomes such as M2 eruption disorders, meta-analysis may be the best way to obtain reliable evidence of the effects of healthcare interventions. Individual studies are usually underpowered to detect differences in rare outcomes. Therefore, a meta-analysis may have adequate power to investigate whether interventions do have an impact on the incidence of a rare event.[14] Although the mathematical synthesis did not demonstrate heterogeneity between studies, there are concerns about the weak estimate of I^2 when there are a small number of studies.[24] Therefore, the implementation of a random-effects model seemed more appropriate in this meta-analysis, as this model addressed the inherent diversity of the retrospective studies that used different appliance designs.[24,25]

Table 4. GRADE Evidence Profile[a–f]

Certainty Assessment								
No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Consideration	Overall Certainty of Evidence	Importance
Prevalence of eruption disturbances								
5	OS	serious[a]	not serious	serious[c]	not serious	none[e]	⊕⊕○○ LOW	The prevalence of M2 eruption disorders is higher in individuals undergoing arch perimeter management compared to the general population.
Odds Ratio for M2 eruption disturbances								
3	OS	serious[a]	not serious[b]	not serious	serious[d]	none[e]	⊕⊕○○ LOW	The odds of M2 eruption disturbances increases 7.5 times in treated individuals (OR: 7.57, 95% CI: 3.72–15.41). Appliances that increase the arch perimeter lead to a greater chance of eruption disturbances.

[a] Based on the bias of risk assessment tool; [b] Based on the heterogeneity (I^2 test); [c] Some of the studies had no control group; [d] Based on the too wide 95% CI of the estimated effect; [e] There are no other important considerations, such as potential publication bias; [f] OS indicates observational studies.

The lack of RCTs was a weakness that affected the certainty of the evidence on the outcomes assessed. Even in observational studies, future trials should be performed/reported according to guidelines such as STROBE (Strengthening the Reporting of Observational Studies in Epidemiology)[26] to increase evidence-based practice information about this topic. Finally, other outcomes, such as the identification of negative predictive factors, should be included in trials in addition to frequency and the risk of M2 eruption disorders. These factors are possibly more relevant and can be determinant for the successful management of arch perimeter in the mixed dentition.

CONCLUSIONS

- Low-quality evidence indicates that management of the mandibular arch perimeter during development of the dentition by controlling the position of the first molar increases the prevalence of M2 eruption disturbances.
- The meta-analysis found, with low certainty of evidence, that the odds of M2 eruption disturbances is 7.5 times greater in individuals undergoing management of the arch perimeter.
- The use of active appliances (that is, lip bumper and Schwarz appliance) increases the chance for eruption deviations compared to the passive lingual holding arch.
- Initial mesioangulation of the M2 in relation to the first molar ($>24°$) and the total treatment time (>2 years) seem to be the main predictive risk factors for M2 eruption disturbance.

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APPENDIX. Search Strategy for Each Database

Electronic Database	Search Strategy Used	Items Found
MedLine/ Searched via PubMed on June 22, 2020	((((((((((((((((Orthodontics, Preventive[MeSH Terms]) OR (Orthodontics, Interceptive[MeSH Terms])) OR (Space Maintenance, Orthodontic[MeSH Terms])) OR (space maint*)) OR (lingual arch*)) OR (lip bumper)) OR (lip-bumper)) OR (buccal shield)) OR (lingual holding arch)) OR (Schwarz)) OR (Arnold expanders)) OR (leeway space)) OR (E-space)) OR (maintenance of arch perimeter)) OR (arch perimeter maintenance)) AND (molar)) AND ((((((((((((((Tooth, Impacted[MeSH Terms]) OR (Failure of Tooth Eruption[MeSH Terms])) OR (Tooth Eruption, Ectopic[MeSH Terms])) OR (Tooth Eruption[MeSH Terms])) OR (Tooth, Impacted)) OR (Tooth Eruption, Ectopic)) OR (Tooth Eruption)) OR (Eruption, Tooth)) OR (Eruptions, Tooth)) OR (Tooth Eruptions)) OR (eruption disturbances)) OR (Impacted tooth)) OR (Unerupted tooth)) OR (Second molar impaction))	**297**
Web of Science Searched on June 22, 2020	#1 TOPIC: (Orthodontics, Preventive) OR TOPIC: (Orthodontics Interceptive) OR TOPIC: (Space Maintenance Orthodontic) OR TOPIC: (space maint*) OR TOPIC: (lingual arch*) OR TOPIC: (lip bumper) OR TOPIC: (buccal shield) OR TOPIC: (lingual holding arch) OR TOPIC: (Arnold expanders) OR TOPIC: (leeway space) OR TOPIC: (E space) OR TOPIC: (maintenance of arch perimeter) OR TOPIC: (arch perimeter maintenance) #2 TOPIC: (Molar) #3 TOPIC: (Tooth Impacted) OR TOPIC: (Failure of Tooth Eruption) OR TOPIC: (Tooth Eruption, Ectopic) OR TOPIC: (Tooth Eruption) OR TOPIC: (Tooth, Impacted) OR TOPIC: (Tooth Eruption, Ectopic) OR TOPIC: (Tooth Eruption) OR TOPIC: (Eruption, Tooth) OR TOPIC: (Eruptions, Tooth) OR TOPIC: (Tooth Eruptions) OR TOPIC: (Eruption disturbances) OR TOPIC: (Impacted tooth) OR TOPIC: (Unerupted tooth) OR TOPIC: (Second molar impaction) #1 AND #2 AND #3	**92**
Scopus Searched on June 22, 2020	#1 (TITLE-ABS-KEY (orthodontics, AND preventive) OR TITLE-ABS-KEY (orthodontics, AND interceptive) OR TITLE-ABS-KEY (space AND maintenance, AND orthodontic) OR TITLE-ABS-KEY (space AND maint*) OR TITLE-ABS-KEY (lingual AND arch*) OR TITLE-ABS-KEY (lip AND bumper) OR TITLE-ABS-KEY (lip-bumper) OR TITLE-ABS-KEY (buccal AND shield) OR TITLE-ABS-KEY (lingual AND holding AND arch) OR TITLE-ABS-KEY (arnold AND expanders) OR TITLE-ABS-KEY (leeway AND space) OR TITLE-ABS-KEY (e AND space) OR TITLE-ABS-KEY (maintenance AND of AND arch AND perimeter) OR TITLE-ABS-KEY (arch AND perimeter AND maintenance)) #2 TITLE-ABS-KEY (molar) #3 (TITLE-ABS-KEY (tooth, AND impacted) OR TITLE-ABS-KEY (failure AND of AND tooth AND eruption) OR TITLE-ABS-KEY (tooth AND eruption, AND ectopic) OR TITLE-ABS-KEY (tooth AND eruption) OR TITLE-ABS-KEY (tooth, AND impacted) OR TITLE-ABS-KEY (tooth AND eruption, AND ectopic) OR TITLE-ABS-KEY (tooth AND eruption) OR TITLE-ABS-KEY (eruption, AND tooth) OR TITLE-ABS-KEY (eruptions, AND tooth) OR TITLE-ABS-KEY (tooth AND eruptions) OR TITLE-ABS-KEY (eruption AND disturbances) OR TITLE-ABS-KEY (impacted AND tooth) OR TITLE-ABS-KEY (unerupted AND tooth) OR TITLE-ABS-KEY (second AND molar AND impaction)) #1 AND #2 AND #3	**317**
Embase Searched on June 22, 2020	#1 'orthodontics, preventive':ti,ab,kw OR 'orthodontics, interceptive':ti,ab,kw OR 'space maintenance, orthodontic':ti,ab,kw OR 'space maint*':ti,ab,kw OR 'lingual arch*':ti,ab,kw OR 'lip bumper':ti,ab,kw OR 'buccal shield':ti,ab,kw OR 'lingual holding arch':ti,ab,kw OR schwarz:ti,ab,kw OR 'arnold expanders':ti,ab,kw OR 'leeway space':ti,ab,kw OR 'e space':ti,ab,kw OR 'maintenance of arch perimeter':ti,ab,kw OR 'arch perimeter maintenance':ti,ab,kw #2 molar:ti,ab,kw #3 'tooth, impacted':ti,ab,kw OR 'failure of tooth eruption':ti,ab,kw OR 'tooth eruption, ectopic':ti,ab,kw OR 'tooth eruption':ti,ab,kw OR 'eruption, tooth':ti,ab,kw OR 'eruptions, tooth':ti,ab,kw OR 'tooth eruptions':ti,ab,kw OR 'eruption disturbances':ti,ab,kw OR 'impacted tooth':ti,ab,kw OR 'unerupted tooth':ti,ab,kw OR 'second molar impaction':ti,ab,kw #1 AND #2 AND #3	**62**
Cochrane Central Register of Controlled Trials Searched via The Cochrane Library on June 22, 2020	#1 ('orthodontics, preventive' OR 'orthodontics, interceptive' OR 'space maintenance, orthodontic' OR 'space maint*' OR 'lingual arch*' OR 'lip bumper' OR 'buccal shield' OR 'lingual holding arch' OR 'schwarz' OR 'arnold expanders' OR 'leeway space' OR 'e space' OR 'maintenance of arch perimeter' OR 'arch perimeter maintenance'):ti,ab,kw #2 (Molar):ti,ab,kw #3 ('tooth, impacted' OR 'failure of tooth eruption' OR 'tooth eruption, ectopic' OR 'tooth eruption' OR 'eruption, tooth' OR 'eruptions, tooth' OR 'tooth eruptions' OR 'eruption disturbances' OR 'impacted tooth' OR 'unerupted tooth' OR 'second molar impaction'):ti,ab,kw #1 AND #2 AND #3	**38**

APPENDIX. Continued

Electronic Database	Search Strategy Used	Items Found
LILACS database (via Bireme) Searched via Bireme on June 22, 2020	tw:((tw:((tw:(orthodontics, preventive)) OR (tw:(orthodontics, interceptive)) OR (tw:(space maintenance, orthodontic)) OR (tw:(space maint*)) OR (tw:(lingual arch*)) OR (tw:(lip bumper)) OR (tw:(buccal shield)) OR (tw:(lingual holding arch)) OR (tw:(schwarz)) OR (tw:(arnold expanders)) OR (tw:(leeway space)) OR (tw:(e-space)) OR (tw:(maintenance of arch perimeter)) OR (tw:(arch perimeter maintenance)))) AND (tw:(molar)) AND (tw:((tw:(tooth, impacted)) OR (tw:(failure of tooth eruption)) OR (tw:(tooth eruption, ectopic)) OR (tw:(tooth eruption)) OR (tw:(eruption, tooth)) OR (tw:(eruptions, tooth)) OR (tw:(tooth eruptions)) OR (tw:(eruption disturbances)) OR (tw:(impacted tooth)) OR (tw:(unerupted tooth)) OR (tw:(second molar impaction)))))	**71**
Google Scholar (first 200 references) Searched on June 22, 2020	"arch perimeter management AND molar eruption"	**0**
Manual Search		**0**
Sum		**877**