Systematic Review Article

Effect of mandibular third molars on crowding of mandibular teeth in patients with or without previous orthodontic treatment: a systematic review and meta-analysis

Georgia Palikaraki[a]; Anastasia Mitsea[b]; Iosif Sifakakis[c]

ABSTRACT

Objectives: To assess the scientific evidence related to the role of the mandibular third molars on the late crowding of the lower anterior teeth in patients with or without previous orthodontic treatment. The secondary outcomes included changes in mandibular arch width and arch length.

Materials and Methods: The databases PubMed, Scopus, ProQuest, and Google Scholar were searched from inception until April 2022. The included papers were studies evaluating the role of mandibular third molars on crowding of mandibular anterior teeth in patients of any age and gender, with mandibular third molars impacted or semi-impacted or erupted. Predetermined and prepiloted data collection forms were used to record the necessary information.

Results: Thirteen observational studies were included in the present systematic review. Most of them were assigned an overall risk of bias of moderate risk while the rest of them were at high risk. Four studies found an association between the presence of mandibular third molar and mandibular incisor crowding. Finally, seven studies were included in the quantitative analysis. Three different meta-analyses were conducted: for patients (a) with or (b) without previous orthodontic treatment and (c) in combination for patients with and without previous orthodontic treatment. According to the pooled results of all three meta-analyses, random effects model yielded a significant benefit for those without third molars compared to those with third molars regarding crowding, mean Little's irregularity index and mean arch length.

Conclusions: Lower third molars may contribute to mandibular crowding and lower arch constriction. Further prospective research of high quality is needed to clarify the impact of third molars on anterior mandibular crowding. (*Angle Orthod*. 2024;94:122–132.)

KEY WORDS: Anterior crowding; Tertiary crowding; Third molar; Wisdom teeth; Relapse; Systematic review

INTRODUCTION

Dental crowding is a common orthodontic problem defined as the discrepancy between tooth size and available space for proper alignment. It may be classified into primary, secondary, and tertiary crowding.[1] Tertiary crowding also can be described in the literature as "late dental crowding," since it appears mostly in the mandibular incisors during adolescence or later.[2,3] In patients who had received previous orthodontic treatment, relapse of pretreatment crowding also may occur during this life period.[4,5]

Late crowding of the mandibular incisors has been reported in treated and untreated individuals and is particularly common. Half of the general population may present moderate to severe crowding.[6,7] This is a major concern among older orthodontic patients since, with increasing age, there is a gradual decrease in the exposure of the upper anterior teeth and an increase in the

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Accepted: September 2023. Submitted: March 2023.
Published Online: October 18, 2023

Table 1. Eligibility Criteria Based on the PICOS (Participants, Intervention, Comparison, Outcomes, Study Design) Strategy

Participants (population)	Patients of any age and sex in permanent dentition with or without previous orthodontic treatment
Intervention	Patients presented with mandibular third molars impacted or semi-impacted or erupted
Comparisons	Patients with absence of mandibular third molars (agenesis; extracted)
Outcome	(a) Primary: Little's irregularity index, Ganss ratio, Lundström analysis (b) Secondary: arch length, arch width Outcome measured: on casts, panoramic radiographs, lateral cephalometric radiographs, or cone beam computed tomography
Study design	Randomized clinical trials, non- or quasi-randomized controlled trials, prospective or retrospective studies evaluating the association of third molars and late anterior crowding or relapse

exposure of the lower incisors. As a result, crowding of the lower anterior teeth becomes more visible and has a greater impact on the esthetics of the smile.[8] The mandibular dental arch becomes more square-shaped with increasing age and crowding tends to increase due to a decrease in arch length and perimeter.[9–13]

Late mandibular crowding is a multifactorial phenomenon and its etiological factors may differ among individuals.[9] It is often attributed to a disturbance of the equilibrium between the dentition and pressure of the tongue, lips, cheeks, and periodontium. In this case, the teeth tend to move until a new state of equilibrium is reached.[10] The effect of mandibular third molars on late crowding remains controversial.[3,4] It has been reported that the lower third molars may generate a mesial pressure that moves the lower posterior teeth forward, causing mandibular anterior crowding.[14–16] An increase in mandibular crowding has been reported in adolescents and young adults between the ages of 13 and 26 years, during the time of eruption of the third molars.[12,17] On the other hand, other reports claim that this pressure is not capable of causing anterior crowding.[1,15,16] Currently, some orthodontists refer their patients to an oral surgeon for third molar extraction to avoid recrowding of the anterior teeth. A recent systematic review (SR) with meta-analysis evaluated only patients after previous orthodontic treatment and suggested mandibular third molar removal for preventing or alleviating long-term incisor irregularity.[18] Whether third molars contribute to anterior mandibular crowding and their relationship with orthodontic treatment remains controversial.

The present SR was conducted to answer the research question of whether there is any association between the presence of lower third molars and late crowding of the lower anterior teeth. The objective was to map the scientific evidence related to the role of mandibular third molars on late crowding of the lower anterior teeth in patients with or without previous orthodontic treatment. Secondary outcomes included changes in mandibular arch width and arch length.

MATERIALS AND METHODS

Protocol and Registration

This SR was conducted according to a specific protocol developed and piloted with respect to the guidelines outlined in the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P).[19] The study was registered at PROSPERO (CRD42023331648).

Eligibility Criteria

Eligibility criteria were based on the PICOS (Participants, Intervention, Comparison, Outcomes, Study design) strategy (Table 1). The population was patients of any age and sex, in permanent dentition, with or

Table 2. Electronic Search Strategy

Databases	Search Strategy/Keywords
Medline/PubMed	(secondary crowding OR relapse OR anterior crowding OR incisor crowding OR mandibular crowding OR incisor relapse OR anterior post retention OR anterior post-retention OR re-crowding) AND (third molar OR third molars OR wisdom tooth OR wisdom teeth OR 3rd molar Or teeth wisdom OR tooth wisdom OR molar third)
Scopus	KEY ((secondary crowding OR relapse OR anterior crowding OR incisor crowding OR mandibular crowding OR incisor relapse OR anterior post retention OR anterior post-retention OR re-crowding) AND (third molar OR third molars OR wisdom tooth OR wisdom teeth OR 3rd molar))
Google Scholar	allintitle: (secondary crowding OR relapse OR anterior crowding OR incisor crowding OR mandibular crowding OR incisor relapse OR anterior post retention OR anterior post-retention OR re-crowding) AND (third molar OR third molars OR wisdom tooth OR wisdom teeth OR 3rd molar)
ProQuest Dissertations and Theses Global	Ti (secondary crowding OR relapse OR anterior crowding OR incisor crowding OR mandibular crowding OR incisor relapse OR anterior post retention OR anterior post-retention OR re-crowding) AND (third molar OR third molars OR wisdom tooth OR wisdom teeth OR 3rd molar)

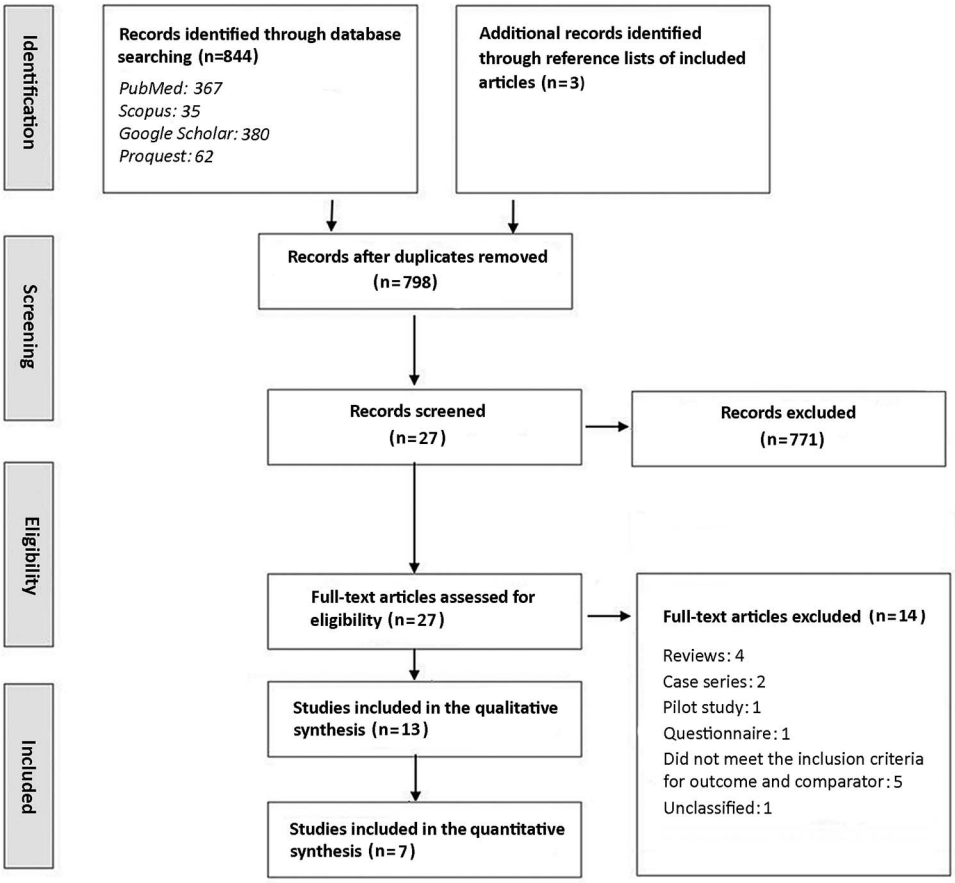

Figure 1. Flow chart diagram.

without previous orthodontic treatment, presented with impacted or semi-impacted or erupted mandibular third molars. These patients were compared with patients with absence of mandibular third molars (agenesis or extracted).

Finite element analyses, follow-ups, case reports, reviews (systematic and literature), author responses, letters to the editor, editorial summary, books and/or book chapters, abstracts, congress abstracts, personal opinions, author debates, summary articles, non-English articles, or no author response to inquiry email for data clarification were excluded.

Information Sources and Search Strategy

The search databases included PubMed, Scopus, ProQuest, and Google Scholar. The databases were searched from inception until April 30, 2022. Research was specified and performed to identify any relevant study based upon various combinations of key words (Table 2).

Developed detailed search strategies for each database were conducted by one of the authors (GP) and assessed by the other two authors (AM and IS) independently. The search strategies developed for MEDLINE were adopted and were revised appropriately for each

Table 3. Risk of Bias Summary

Studies	Zigante et al., 2021[23]	Husain et al., 2021[30]	Shah et al., 2018[24]	Esan et al., 2017[29]	Stanaityté et al., 2014[25]
Bias due to confounding	Serious	Serious	Serious	Serious	Serious
Bias in selection of participants into the study	Low	Low	Low	Low	Low
Bias in classification of interventions	Low	Low	Low	Low	Low
Bias due to departures from intended interventions	Low	Low	Low	Low	Low
Bias due to missing data	Low	Low	Low	Low	Low
Bias in measurement of outcomes	Low	Low	Low	Low	Low
Bias in selection of the reported result	Low	Low	Low	Low	Low
Overall RoB	**Moderate**	**Moderate**	**Moderate**	**Moderate**	**Moderate**

[a] RoB indicates ROBINS-I assessment tool.

database to include differences in controlled vocabulary and syntax rules (Table 2). No restrictions were applied on the date and status of publication except that only English language papers were considered for inclusion. The reference lists of all the eligible studies, as well as these of relevant reviews, were searched. The authors of retrieved studies were contacted for further clarification if needed.

Study Selection

Two authors (GP and AM) assessed the titles and the abstracts of the retrieved records for inclusion independently and in duplicate. They were not blinded to the identity of the authors, institution of origin, or the results of the research. Any article title that met the objectives of the study but did not have an available abstract was fully analyzed in the final evaluation. Full texts of the selected studies were obtained and evaluated to verify whether they fulfilled the eligibility criteria. Disagreements were resolved by discussion or consultation with a third author (IS) before the final decision. The reference lists of all retrieved full text articles were searched for relevant articles that might have been missed through the electronic search. Finally, the articles that did not answer the clinical research questions were excluded.

Risk of Bias in Individual Studies

Two authors (GP and AM) assessed the risk of bias in individual studies independently and in duplicate using the "ROBINS-I" (RoB) assessment tool. Any disagreements were resolved by discussion or consultation with the last author (IS).[20]

Data Collection and Data Items

The same two authors (GP and AM) performed data extraction independently and in duplicate. Any disagreements were resolved through discussion with the last author (IS). Predetermined and prepiloted data collection forms were used to record the necessary information: first author, age, type of study, previous orthodontic treatment, sample size, presence of third molars, analysis tools, crowding measurement, angulation of lower teeth, and outcome of the study.

Summary Measures and Synthesis of Results

The summary characteristics of the included studies were reviewed. The mean values and the corresponding SDs were extracted independently from each article that used quantitative measures for outcome assessment. The random effects model was used. Forest plots were also used to visualize the pooled estimates across studies. Statistical analysis of the data was conducted with the statistical package R (www.r-project.org, v3.6.2) and the level of statistical significance was set at 0.05.

Additional Analyses and Risk of Bias Across Studies

Egger's test was used to assess potential publication bias in the meta-analysis via funnel plot asymmetry. If there were at least two studies with the same outcome and having sufficient homogeneity regarding the compared groups and the time frame, meta-analysis was planned. Otherwise, a qualitative synthesis of the results was reported. Statistical heterogeneity was inspected with the DerSimonian and Laird's Q statistic and I^2 statistic. If split-mouth studies were included in meta-analysis, the correlation coefficient was planned to be computed to calculate the adjusted standard error (SE), as described in chapter 23 of the Cochrane handbook. The difference in means of both arms and the adjusted standard error were used in the meta-analysis.[21]

RESULTS

Study Selection

The results of literature searching identification, inclusion, and exclusion of the articles are presented

Table 3. Extended

Hasegawa et al., 2013[33]	Sidlauskas & Trakiniene, 2006[1]	Niedzielska, 2005[31]	Lindqvist & Thilander, 1982[32]	Harradine et al., 1998[26]	Van der Scoot et al., 1997[27]	Ades et al., 1990[22]	Kaplan et al., 1974[28]
Serious	Serious	Serious	Serious	Serious	Serious	Serious	Serious
Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Low	Low	Low	Low	Low	Low	Low	Low
Low	Low	Low	Low	Low	Low	Low	Low
Low	Low	Low	Low	Low	Low	Low	Low
Low	Low	Low	Low	Low	Low	Low	Low
Low	Low	Low	Low	Low	Low	Low	Low
Serious	**Moderate**	**Moderate**	**Serious**	**Serious**	**Serious**	**Serious**	**Serious**

Table 4. Summary Characteristics of Included Studies

		Type of Study	Age (y)	Sample Size (N)	Inclusion / Exclusion
Without previous orthodontic treatment	**Zigante et al., 2021**[23]	Cross-sectional	12, 15, 18, and 21	72 (F: 34, M: 38)	No significant malocclusions nor facial disharmonies at the start of follow-up (6 y), no orthodontic treatment. Presence of panoramic radiographs and plaster casts at the ages of 12, 15, 18, and 21
	Husain et al., 2021[30]	Cross-sectional	18–30	40 patients in 2 groups: (a) without third molars (20) and (b) with third molars (20)	Inclusion criteria: Class I malocclusion, CBCT images of patients in the 18–30 age group, CBCT images recorded in the database of the University, CBCT images with the presence of all the permanent dentition Exclusion criteria: presence of impacted teeth, presence of deciduous teeth, presence of skeletal asymmetries, presence of any underlying pathologies, partial or complete absence of teeth, other than third molars
	Shah et al., 2018[24]	Cross-sectional	>25	90 (F 50, M 40) in 3 groups: (a) group E with erupted M3: 58, (b) group UE with unerupted M3: 18, and (c) group AB with agenesis of M3: 14	Exclusion criteria: patients with a history of previous orthodontic, orthopedic, or facial and surgical treatment; systemic disease, developmental anomalies, or syndromes; abnormal habits and third molar extraction
	Esan et al., 2017[29]	Cross-sectional	M 19–70 (43.66 SD 12.00)	535 in 6 groups: (a) bilateral M3 present: 439, (b) unilateral agenesis: 23, (c) bilateral agenesis: 14, (d) unilateral impaction: 36, (e) bilateral impaction: 21 and (f) agenesis and impaction: 2	Inclusion criteria: Black South African males
	Stanaityté et al., 2014[25]	Prospective non randomized controlled trial	25,5 (16,2–55,1)	30 (F 19, M 11) before and after lower M3 removal	• complete lower dental arch • age at least 16 y • no orthodontic treatment before records collected • bilateral LM3 removal • good quality OPT and plaster casts
	Hasegawa et al., 2013[33]	Cross-sectional	21,0 (18,3–24,1)	34 in 2 groups: (a) Class I normal occlusion (<3.5 mm) with F 10 and M 4, and (b) Class I crowding (≥3.5 mm) with F 10 and M 10)	Inclusion criteria: Angle Class I molar relationship, all four M3 impacted, all teeth were caries-free, no previous dental treatment, no anomalies of crown morphology, no orthodontic treatment in either maxillary or mandibular arch
	Sidlauskas & Trakiniene, 2006[1]	Cross-sectional	21,01 (SD 4,13)	91	Inclusion criteria: age at least 17 y, complete lower dental arch (except M3), no orthodontic treatment before records collected, good state of care of the lower teeth with no artificial dental crowns, good quality OPTs and plaster casts available
	Niedzielska, 2005[31]	Cross-sectional	14–32	47 (F 36, M 11) in 4 groups: (a) bilaterally extracted: 17, (b) unilaterally extracted: 12, (c) control group (bilaterally retained): 16 and (d) M3 agenesis: 2	Exclusion criteria: previous orthodontic treatment or patients presented with malocclusions
	Lindqvist & Thilander, 1982[32]	Cross-sectional	15,5 (13–19), with a 3 y follow-up	52	
Previous orthodontic treatment	**Harradine et al., 1998**[26]	Cross-sectional	14,8 (SD 16,2)	77 (F 45, M 32) in 2 groups: (a) M3 extracted: 44 and (b) M3 nonextracted: 33	Inclusion criteria: Class I malocclusion, CBCT images of patients in the 18–30 y age group, CBCT images recorded in the database of the University, CBCT images with the presence of all permanent dentition. Exclusion criteria: presence of impacted or deciduous teeth, presence of skeletal asymmetries, presence of any underlying pathologies, partial or complete absence of teeth, other than third molars
	Van der Scoot et al., 1997[27]	Cross-sectional	22,3 (SD 4,2)	99 (F 60, M 39) in 4 groups: (a) both M3 erupted (lower arch n = 24, upper arch n = 23, (b) neither of M3 erupted (lower arch n = 19, upper arch n = 22, (c) both M3 extracted (lower arch n = 43; upper arch n = 37 and (d) one or both M3 congenitally absent (lower arch n = 8, upper arch n = 7)	-
	Ades et al., 1990[22]	Cross-sectional	28,6 (18,6–39,4)	97 in 4 groups: (a) erupted: 32, (b) impacted: 14, (c) extracted: 34 and (d) absent: 17	1. All participants were Caucasian 2. Participants free of all retention for at least 10 y
	Kaplan et al., 1974[28]	Cross-sectional	26.6 (at postretention)	75 in 3 groups: (a) erupted: 30, (b) impacted: 20 and (c) agenesis: 25	Orthodontically treated Caucasian patients

[a] CBCT indicates cone beam computed tomography and OPT orthopantomogram.

Table 4. Extended

Groups	Analysis Tools	Outcomes	Results
(a) agenesis (b) extracted (c) nonerupted (d) impacted	OPT casts	Little's irregularity index	No difference
(a) without third molars (b) with third molars	CBCT	Little's irregularity index	Association between the presence of mandibular third molar and mandibular incisor crowding
(a) erupted (visible in oral cavity, either partially or completely), (b) unerupted (not visible in oral cavity), (c) agenesis (neither visible in oral cavity nor in OPT)	OPT casts	Lundström analysis	No difference
(a) bilateral M3 present (b) unilateral agenesis (c) bilateral agenesis (d) unilateral impaction (e) bilateral impaction and (f) agenesis and impaction	Casts (jaws)	Little's irregularity index	Third molar impaction plays a role in anterior crowding
(a) Before M3 removal and (b) after M3 removal	OPT casts	Lower dental arch width changes	No difference
(a) without and (b) with crowding	OPT casts Cephalogram	Little's irregularity index , Ganss ratio	No difference
(a) erupted M3, (b) unerupted M3 and (c) M3 agenesis	OPT casts	Mesiodistal width related to the length from central incisor to canine, Lundström analysis	No difference
(a) bilaterally extracted (b) unilaterally extracted (c) bilaterally retained (d) M3 agenesis	OPT casts	Lundström's method, Ganss ration	Retained M3 associated with increased tooth crowding in relation to Ganss ratio
	Casts Cephalograms	Arch length, Cephalometric analysis	Extraction side had a more favorable development than the control side on 70% of the patients
(a) M3 extracted (b) M3 non-extracted	OPT casts Cephalograms	Little's irregularity index, intercanine width and arch length; cephalometric analysis	No difference
(a) right and left M3 had emerged, (b) neither of M3 had erupted, (c) right and left M3 were extracted, (d) one or both M3s were congenitally absent	OPT casts	Little's irregularity index, Arch length	No difference
(a) erupted, (b) impacted, (c) extracted, (d) agenesis	Casts Cephalograms	Little's irregularity index Arch length	No difference
(a) bilaterally erupted, in occlusion (b) bilaterally impacted (c) bilateral agenesis	Casts Cephalograms	Little's irregularity index Arch length Intermolar width	No difference

Table 5. General Characteristics of the Studies Included in the Quantitative Synthesis

			Number	
		Groups	With M3	Without M3
Without previous orthodontic treatment	**Zigante et al., 2021**[23]	(a) agenesis, (b) extracted, (c) impacted, (d) unerupted	present 48 (impacted at 21 y: 16; unerupted at 21 y: 10; erupted at 21 y: 22)	extracted: 16 hypodontia: 8
	Husain et al., 2021[30]	(a) without M3 (b) with M3	20	20
	Shah et al., 2018[24]	E: erupted (visible in oral cavity, either partially or completely) UN: unerupted (not visible in oral cavity) AB: agenesis (neither visible in oral cavity nor in OPT)	E:119 UE:38	AB: 23
	Sidlauskas & Trakiniene, 2006[1]	E: erupted M3 UE: unerupted M3 A: agenesis of M3	E: 88 UE: 85	A: 9
Previous orthodontic treatment	**Harradine et al., 1998**[26]	3EX: extracted M3 3NEX: non-extracted M3	3NEX: 33	3EX: 44
	Ades et al., 1990[22]	Impacted Erupted Extracted Agenesis	Erupted: 32 Impacted: 14	Absent: 17 Extraction: 34
	Kaplan et al., 1973[28]	Bilaterally erupted: M3E Bilaterally impacted: M3I Bilateral agenesis: M3A	Erupted: 30 Impacted: 20	Agenesis 25

in the flow diagram according to the PRISMA statement (Figure 1). Initially, 847 relevant records were identified after the electronic and manual search, while only 798 remained after manual duplicate removal. After title and abstract screening, 27 articles were selected for full-text review according to the inclusion and exclusion criteria. Finally, nine papers were excluded because four were reviews, five did not meet the criteria for outcome and comparator, two were case series, one pilot study, one questionnaire, and one unclassified. The remaining five did not meet the inclusion criteria for outcome and comparator. Finally, 13 articles were included in the qualitative synthesis.[1,22–33] However, only seven articles were included in the quantitative synthesis since the remaining studies were heterogeneous.[1,22–24,26,28,30]

Risk of Bias in Individual Studies

Risk of bias for the included studies[1,22–33] is depicted in Supplemental Table 1 and Table 3 (in summary). Eight studies were assigned an overall risk of bias of moderate risk,[1,23,25,29–31,33] while the rest (five studies) were of high risk.[22,26–28,32]

General Characteristics of Included Studies

The general characteristics of the studies included in the present SR, as well as the sample characteristics, are depicted in Tables 4 and 5. A total of 1342 participants was calculated from the included studies. All included studies were observational by design (cross-sectional and prospective nonrandomized controlled trials)[1,22–33] and used two-dimensional radiographs (orthopantomographs, lateral cephalometric radiographs) and casts as analysis tools, except two studies that used only casts[29] or cone beam computed tomography (CBCT).[30] Crowding was quantified with Little's irregularity index in eight studies,[22,23,26–30,33] three used Lundstrom analysis,[1,20,31] and two studies used Ganss ratio.[31,33] Five studies measured arch length[22,26–28,32] and four studies measured arch width.[1,25,26,28] In four studies, the participants had undergone orthodontic treatment.[22,26–28] Four out of the 13 eligible studies supported a cause-and-effect relationship among third molars and anterior crowding.[29–32]

Quantitative Synthesis of Included Studies: Synthesis of Results

Seven studies were included in the quantitative analysis and three different meta-analyses were conducted. The first was conducted in patients without previous orthodontic treatment,[1,23,24,30] and the second in patients with previous orthodontic treatment.[22,26,28] The third analysis was implemented in combination for patients with and without previous orthodontic treatment.[1,22–24,26,28,30]

The first meta-analysis of four studies was performed on patients without previous orthodontic treatment and compared mean differences in crowding between cases with or without third molars (agenesis or extracted).

Table 5. Extended

Crowding (mm)		Arch Width (mm)		Arch Length (mm)	
With M3 Mean (SD)	Without M3 Mean (SD)	With M3	Without M3	With M3	Without M3
present: 1,8 (1,6) (impacted at 21 y: 1,3 (1,4), unerupted at 21 y: 1,9 (1,5), erupted at 21 y 1,7 (1,6))	extracted: 1,7 (2,0), agenesis: 0,5 (1,8)	–	–	–	–
group b: 6,79 (5,45)	group a: 4,26 (4,88)	–	–	–	–
right side: E 2,02 (1,42), UE 1,3 (0,68), left side: E 1,6 (1,46), UE 1,4 (0,89)	right side: AB 1,5 (0,66), left side: 1,32 (0,57)	–	–	–	–
E: 1,50 (1,77) UE: 1,70 (2,20)	A: 0,78 (1,13)	–	–	–	–
3NEX: 1,10 (2,72)	3EX: 0,80 (1,23)	3NEX: −0,38 (0,38)	3EX: 0,37 (0,73)	3NEX: −2,13 (0,96)	3EX: −1,10 (1,13)
Impacted: 2,27 (1,81) Erupted: 3,19 (2,20)	Extracted: 3,25 (5,24) Agenesis: 2,55 (1,40)	Impacted: −1,52 (1,23) Erupted: −1,71 n(1,45)	Extracted: −1,86 (1,29) Agenesis: −1,47 (1,76)	Impacted: −2,01 (1,41) Erupted: −2,81 (2,12)	Extracted: −2,02 (1,71) Agenesis: −2,17 (2,10)
M3E: 3,00 (2,15) M3I: 3,35 (2,20)	M3A: 1,99 (1,76)	M3E: −1,38 (1,19) M3I: −1,49 (1,24)	M3A: −1,94 (1,27)	M3E: −2,50 (1,57) M3I: −2,39 (1,83)	M3A: −2,20 (1,55)

Crowding was statistically significant with random-effects model (**$P = .01$). According to the pooled results of meta-analysis, random effects model yielded a significant benefit for those without third molars compared to those with third molars (Figure 2). Specifically, those with third molars had greater mean Little's irregularity index scores compared to those without third molars. Egger's test *P* value was .09, which implies borderline significant publication bias.

The second meta-analysis of three studies on patients with previous orthodontic treatment compared mean differences in cases with and without third molars (agenesis or extracted) regarding crowding, arch width, and arch length. The pooled estimate of crowding and arch width was not statistically significant ($P = .23$, $P = .69$). According to the pooled results of meta-analysis, random effects model showed that those with third molars had lower mean arch length scores than those without third molars ($P = .07$) (Figure 3). Additionally, Egger's test *P* value was .73, which implies no publication bias.

The third meta-analysis of seven studies on patients with and without previous orthodontic treatment compared mean differences in crowding between patients with and without third molars (agenesis or extracted). Crowding was statistically significant with random effects model (**$P = .005$). According to the pooled results of meta-analysis, random effects model yielded a significant benefit for those without third molars compared to those with third molars. Specifically, those with third molars had greater mean Little's irregularity index scores compared to those without third molars (Figure 4). Egger's test *P* value was .10, which implies no publication bias.

DISCUSSION

Three SRs have been conducted to assess the possible association between mandibular third molars and lower anterior crowding.[18,34,35] However, only the most recent (2018) included a meta-analysis.[18] The first

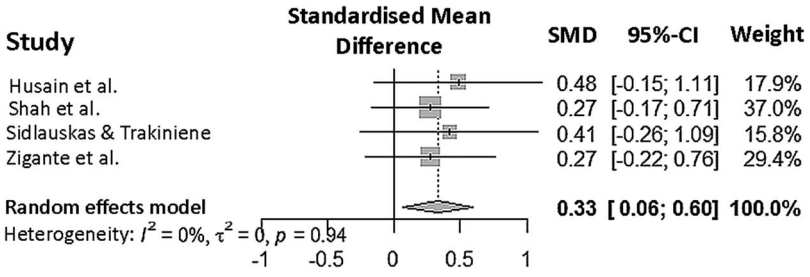

Figure 2. Forest plot for studies on patients without previous orthodontic treatment for crowding.

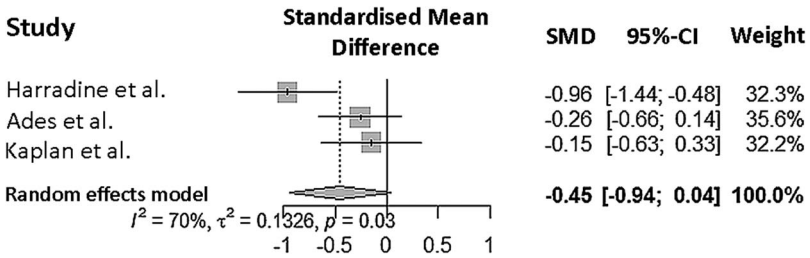

Figure 3. Forest-plot for studies on patients with previous orthodontic treatment for arch length.

available SR assessed the literature by using the Medline database between 1971 and 2011 and included 21 articles in the qualitative analysis.[35] The results were contradictory: some researchers concluded that lower third molars favored crowding; however, this finding was not confirmed by the other articles. The second was a systematic literature review that selected 12 observational studies to evaluate the role of third molars in late mandibular anterior crowding in post-orthodontic patients. Qualitative analysis of the results failed to support the cause-and-effect relationship between third molars and lower anterior tooth crowding. However, according to the authors, definitive conclusions on the role of the third molars in the development of anterior tooth crowding could not be drawn.[34] Finally, the third SR evaluated three retrospective studies conducted on patients in the retention phase after orthodontic treatment quantitatively with a meta-analysis. They found statistically significant differences between the erupted third molar extraction group and agenesis third molar group regarding the Little's irregularity index, whereas the arch length and intermolar width did not differ between these patient groups. The authors recommended mandibular third molar removal for preventing or alleviating long-term incisor irregularity.[18] The present SR was the first to investigate the role of the mandibular third molars on the space conditions of the mandibular teeth in patients with and/or without previous orthodontic treatment.

The present SR identified no randomized trials on the effect of third molars on anterior teeth. The eligible studies were intervention studies with a control group, without randomization or double blinding, and most of them did not find such an association, suggesting a coincidence between the two events. The studies examined orthodontically treated and untreated subjects with impacted, erupted, extracted, or congenitally absent (agenesis) third molars.[1,22–28,33] Four studies reported a different outcome and supported a cause-and-effect relationship between third molars and anterior crowding.[29–32]

These contradictory results may be explained by differences in study design and methodology, sample size, inclination, and degree of impaction (impacted, semi-impacted, erupted) of the third molars. The present meta-analyses suggested that third molars may contribute to mandibular crowding. However, the etiology of this phenomenon is multifactorial and the extraction of third molars per se may not prevent tertiary crowding or dental relapse after orthodontic treatment. Thus, removing third molars, whether impacted or not, only for preventing crowding is not justified or recommended by the present results. The extraction of third molars is indicated in cases of posterior crowding, if distalization is needed, or when the unfavorable orientation of third molars compromises the stability of the arch or the prognosis of the adjacent second molar.[26,36] Nevertheless, strict retention protocols should be used after orthodontic treatment in patients with lower third molars left in situ.

The extracted data were classified according to the presence or absence (agenesis/extracted) of the third

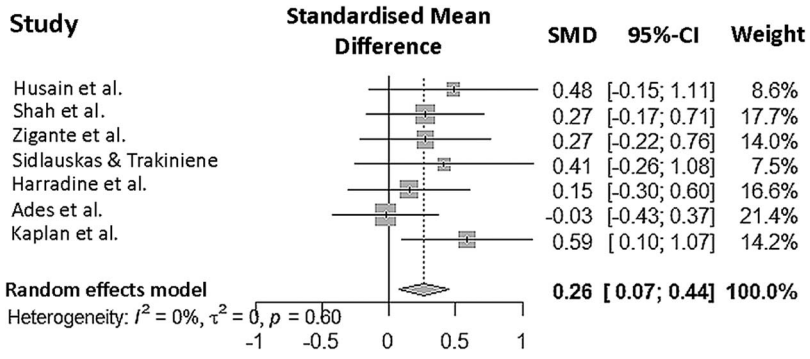

Figure 4. Forest plot for all the included studies (on patients with and without previous orthodontic treatment) for crowding.

molar and three meta-analyses were conducted: for patients with or without orthodontic treatment as well as in combination for patients with and without previous orthodontic treatment. According to the pooled results of the meta-analysis, random effects models yielded a significant benefit for those without third molars compared to those with third molars in all three meta-analyses. Specifically, patients with third molars had greater mean Little's irregularity index scores compared to those without third molars in the nonorthodontic patient group. Additionally, random effects models showed that, in postorthodontic patients, the presence of third molars was associated with lower mean arch length scores. When all patients (with and without previous orthodontic treatment) were pooled together, the meta-analysis revealed a statistically significant effect of the third molar on random effects model ($*P = .02$).

Strengths and Limitations

A protocol was developed a priori and the present review followed clear-cut guidelines. The search strategies employed were exhaustive, covering electronic, manual, and gray literature material up to April 2022. Their character was comprehensive, irrespective of date and status of publication. Every effort to decrease bias in the methodology employed was made. Screening, verification of eligibility, abstraction of information, assessment of risk of bias, and of the quality of evidence were all performed in duplicate, and any disagreement was resolved by discussion or consultation until a final consensus was achieved.

However, a potential source of bias in the present review could be the exclusion of articles not written in English. Further limitations in this study arose mainly from the nature and the characteristics of the retrieved data during the review process. Factors such as extractions, interproximal enamel reduction, or compliance with fixed/removable retention protocols were not evaluated in the included studies. However, the main limitation was related to the heterogeneity of the studies and the inadequate control of confounding in the included studies. These were nonrandomized trials, with risk of bias and differences in the methods of assessing the crowding. Differences in the study groups (impacted or erupted or present third molars vs agenesis or extracted) may have confounded the present findings and the impact of the third molars on the mandibular incisors may have occurred before their extraction. Additionally, each of the first and second meta-analyses included three studies. Egger's test may lack the statistical power to detect bias when the number of studies is small (<10). Additionally, there are several other factors that may affect anterior crowding, such as growth-related changes, muscular factors, periodontal ligament traction, bone adaptation, masticatory force, etc.[17,18] Further research is necessary to clarify the etiology of mandibular anterior crowding and to quantify the relapse tendency in each individual case.

CONCLUSIONS

- Within the limitations of the present systematic review, it can be concluded that lower third molars may contribute to mandibular crowding.
- Specifically, the degree of lower anterior dental crowding was higher in patients with presence of mandibular third molars, at least in the included studies.
- Postorthodontic patients with third molars presented with significantly lower mean arch length compared to those without third molars.

SUPPLEMENTAL DATA

Supplemental Table 1 available online.

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