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Assessment of short-term skeletal and dental effects of mandibular advancement with aligners in class II patients: a systematic review and meta-analysis

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Aim: This systematic review and meta-analysis aimed to assess the short term skeletal and dental effects of clear aligners with mandibular advancement feature (CAMA) in class II malocclusion due to mandibular retrognathism. **Methods:** An electronic data search was performed without any restriction in the year of publication in five search engines. Data were extracted and Newcastle–Ottawa Scale for observational studies was used to assess the risk of bias. As necessary, statistical heterogeneity was examined, random effects model was used in meta-analyses and parameters assessed by meta-analysis across studies were graded for quality of evidence. **Results:** Seven retrospective and five prospective studies were included. Five studies had low risk, two had moderate and five had high risk of bias. There was a significant increase in mandibular length following CAMA therapy. There was no significant difference in the skeletal changes brought about by twin block and CAMA. There was no significant change in maxillary and mandibular incisor inclination after twin block or CAMA therapy. **Conclusion:** It can be concluded that CAMA promoted mandibular growth, but it was not significantly greater than twin block. There was no difference in the maxillary and mandibular incisor inclination with twin block or CAMA therapy.

Keywords: Mandibular advancement. Orthodontic appliances, removable. Orthodontic appliances, functional. Retrognathia. Malocclusion, Angle Class II.

Introduction

The global prevalence of class II malocclusion has been found to be 19.56% in the permanent dentition and 23% during the mixed dentition period. It can be caused by mandibular retrognathism, maxillary prognathism or both[1,2]. Functional appliances are designed to achieve the correction of retrognathic mandible through forward posturing of the lower jaw during the pubertal spurt. The cervical vertebrae maturity indicator (CVMI) is a valid method of assessing skeletal growth, and stages CS3/4 are considered ideal for achieving maximum skeletal changes[3].

The efficacy of various removable and fixed functional appliances has been studied extensively over the years. Many researchers are under the consensus that a short-term supplemental increase in mandibular length coupled with changes in the dentoalveolar structures have been found to aid in class II correction following functional appliance therapy[4-7]. The Invisalign® system (Align Technology) introduced a mandibular advancement feature with precision wings in the buccal vestibular aspect, which incorporated inclined planes to advance the mandible[8]. Other companies have recently incorporated a mandibular advancement feature into their aligners or clear trays to facilitate class II correction[9-12].

Removable functional appliances are viewed as bulky, and they lead to excessive salivation and disturbance of speech[13]. There has been a growing interest among clinicians in attempting to achieve the skeletal correction of retrognathic mandible by using clear aligner mandibular advancement appliance (CAMA). The optical properties of the clear aligners make them nearly invisible, thus contributing to improved aesthetics[14,15].

It is crucial that the alternative treatment options provided to orthodontic patients are supported by credible data that proves their clinical efficacy[16]. A systematic review comparing the skeletal and dental efficiency of the CAMA with that of conventional functional appliances was conducted. This review only used local databases and was not representative of the global literature[17]. The current review included more recent studies, inclusion of research from across globe and not confined to one aligner system or one region, conducted a more thorough meta-analysis, and included broader international databases (such as SciELO, Virtual Health Library, and Cochrane). As a result, it provides updated and globally applicable summary of CAMA's short-term skeletal and dental effects. The primary aim of this systematic review and meta-analysis was thus to evaluate the efficacy of mandibular advancement with the CAMA in producing skeletal changes in class II subjects with mandibular retrognathism. The secondary aim was to evaluate the dental effects of the CAMA on maxillary and mandibular incisor inclination. These aims were formulated into the following research questions: Does mandibular advancement with clear aligner therapy produce significant changes in the effective mandibular length? Does mandibular advancement with clear aligners produce greater skeletal and dental changes than when it is carried out with conventional functional appliances?

Materials and Methods

Protocols and registration

This systematic review was registered with the International Prospective Register for Systematic Reviews (PROSPERO) (CRD42023407203) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[18].

Eligibility criteria

The inclusion and exclusion criteria were as follows:

Population: Patients with class II malocclusion due to a retrognathic mandible.

Intervention: A clear aligner appliance with a mandibular advancement feature.

Comparison: A control group treated with conventional functional appliances and/or an untreated control group. Studies without a control group were included due to the scarcity of research on this topic in existing literature.

Outcomes: Changes in the effective mandibular length (Co-Gn/Pg- distance from the condylion to the gnathion or pogonion) and unit mandibular length (Go-Gn/Pg - distance from the gonion to the gnathion or pogonion).

Secondary outcomes: Changes in the maxillary and mandibular incisor inclination.

Study design: Randomised clinical trials, non-randomised prospective clinical studies and retrospective cohort studies were included.

Case reports or series, letters to editor, expert opinion, review articles, studies in languages other than english and those that used other methods of class II correction were excluded.

Information sources, search strategy and study selection

MEDLINE, Cochrane Library, Virtual Health Library, Google Scholar and SciELO were systematically searched without restrictions in the year of publication till January 2024. The search strategy included the terms “mandibular advancement” AND “aligners” OR “clear aligners” AND “Class II” AND “malocclusion”. (supplementary appendix 1) Rayyan software was used to import results[19].

Data collection process and data Items

Authors PJ and RG worked independently to collect the data and compiled them together. Details of the data collected are given in Table 1. Measures of skeletal and dental changes and conclusions provided by the authors were gathered for the systematic review. After comparison of collected data, conflicts were resolved with the third and fourth reviewers until a consensus was achieved.

Table 1. Study characteristics

Author & Year	Type of study	Participants	Intervention and control	Age (years)	CVMI stage	Treatment duration (months)	Outcome measurement	
							Primary	Secondary
Retrospective studies								
Wu et al.[20], 2023	Retrospective study	63 37 males 26 females	VA n=14 7 boys 7 girls	10.71 ± 1.44	CS2	7.28 ± 2.30	Co-Pg Go-Pg	L1- MP U1-PP
			Herbst n=11 4 boys 7 girls	11.55 ± 0.69		10.18 ± 3.06		
			TB n=12 7 boys 5 girls	11.00 ± 1.04		10.16 ± 5.46		
			Invisalign MA n= 14 12 boys 2 girls	12.11 ± 1.16		22.84 ± 8.98		
			UC n=12 7 boys 5 girls	10.41 ± 0.90		10.25 ± 3.74		
Caruso et al.[21], 2021	Retrospective cohort study	20 10 males 10 females	Invisalign MA n-10 5 males 5 females	10 ±1.05	CS3	-	Data not available	L1- MP U1-PP
			Twin block n=10 5 males 5 females	10 ±1.05				
Lombardo et al.[22], 2023	Retrospective cohort study	56	TB n=35 17 males 18 females	12±1.3	CS3	20	Co-Gn	L1-MP U1-PP
			Invisalign MA n= 21 9 males 12 females	11.2±1.1		29		
			UC n=15 4 males 11 females	10.9±1.1		37		
Sabouni et al.[8], 2022	Retrospective clinical cohort study	32	Invisalign MA n= 32 13 females 19 males	9.9 to 14.8	CS3 or CS4	9.2 (7.5 to 13.8)	Co-Gn	IMPA
			No control group					
Sun et al.[23], 2022	Retrospective comparative cohort study	46 23 females 23 males	A6 appliance n=23 12 male 11 female	13.66 ± 4.25	-	9.40±4.23	Co-Gn Go-Gn	U1-PP IMPA
			Twin block n=23 12 male 11 female			10.23±3.27		

Continuation								
Hosseini et al.[24], 2023	Retrospective cohort study	40 18 males 22 females	Invisalign MA n=20 9 male 11 female	13.1±1.5	CS2,3,4	32.3	Co-Pg	1S-NL 1i-ML
			Herbst n=20 9 male 11 female	12.7±1.8		36.8		
Blackham[25], 2020	Prospective study	96	Invisalign MA n=32	11.82±1.74 to 13.15±1.37	CVM2 CVM3	12	Co-Gn	U1-PP L1-MP
			Twin block n=32					
			Control n=32					
Prospective studies								
Ravera et al.[26], 2021	Prospective controlled study	72	Invisalign MA n= 40 — CVM2 n= 20	9.2±1.4	CVM2 CVM3	18	Co-Gn Go-Gn	X11-SpP X41-GoGn
			Invisalign MA n= 40 — CVM3 n=20	12.10± 1.4		17		
			UC n=32 — CVM2 n= 15	10.9± 1.8		18		
			UC n=32 — CVM3 n=17	14.2± 1.0		18		
Kong and Liu[27], 2023	Prospective Non-randomised clinical study	30	Invisalign MA n=30 15 male 15 female	11.6±0.9	CVM1-CVM3		Co-Pg Go-Pg	U1-SN L1-MP
			No control					
Cremonini et al.[10], 2022	Longitudinal prospective clinical study	15	F22 Young device n=15 7 females 8 males	10.3	CVM3- CVM4	10±0.5	Co-Gn Go-Pg	U1-PP IMPA
			No control group					
Glaser et al.[28], 2022	Prospective non-randomized multicenter clinical study	60 (47 plus 23 withdrawal)	Invisalign MA n=47 55% male 45% female	12.75	-	12.6	Co-Gn	L1-MP
			No control group					
Zaky and Negm[29], 2022	Longitudinal prospective study	25	Clear mandibular advancement appliance n=25 female	8 to 12	CVM2 –CVM3	13	Co-Gn Go-Me	L1-MP
			No control					

CVMI- cervical vertebra maturity indicator, Co-Pg Condylion-Pogonion distance in millimeters, Co-Gn Condylion- Gnathion(mm), Go-Pg Gonion-Pogonion(mm), Go-Gn Gonion-gnathion (mm), U1-PP upper incisor -palatal plane(degree), L1-MP lower incisor -mandibular plane(degree), IMPA – incisor mandibular plane angle,U1-SN upper incisor to anterior cranial base (degree), 1s-NL- Maxillary incisor to Nasal Line (degree), 1i-ML- Mandibular incisor to Mandibular Line (degree), X11-SpP- angle between the 1.1 long axis and the Bispinal Plane (degree), X41-GoGn- angle between the 4.1 long axis and the Mandibular Plane (degree)

Risk of bias assessment:

Newcastle–Ottawa Scale was used for assessing the risk of bias for non-randomized retrospective and prospective studies[30].

Data synthesis and summary measures

Due to limited availability of clinical trials, an effort was made to include all existing studies in the systematic review. All the relevant data were summarized in tables, and any missing data was calculated using appropriate methodologies. Review Manager 5.4 was used for quantitative analysis of data. As the outcome may be influenced by patient or appliance related factors, Random effects model was used. Standardized mean difference (SMD) was estimated for parameters that assessed incremental changes in mandibular length (Go-Pg, Co-Gn) with aligner mandibular advancement and twin block; changes in incisor inclination were quantified using two parameters (L1-MP, U1-PP)[31].

τ^2 and I^2 statistics were used to assess the heterogeneity between the studies and I^2 greater than 75% indicated considerable heterogeneity between the studies. Sensitivity analysis was performed to address heterogeneity that may be associated with factors like extreme deviation in results and difference in the brand of appliance. Publication bias was addressed by including a study from unpublished literature. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) was used to identify level of evidence[32].

Results

Study selection

A comprehensive literature search was conducted across PubMed, Google Scholar, Cochrane, SciELO, and the Virtual Health Library using keywords such as "mandibular advancement", "clear aligners," and "Class II malocclusion." Literature search provided 693 results in five search engines and after elimination of duplicates, 663 abstracts were obtained. Screening of title and abstracts eliminated 643 and finally 20 full text articles were extracted. 12 studies qualified for systematic review; Figure 1 sums up the reason for elimination of the 8 articles.

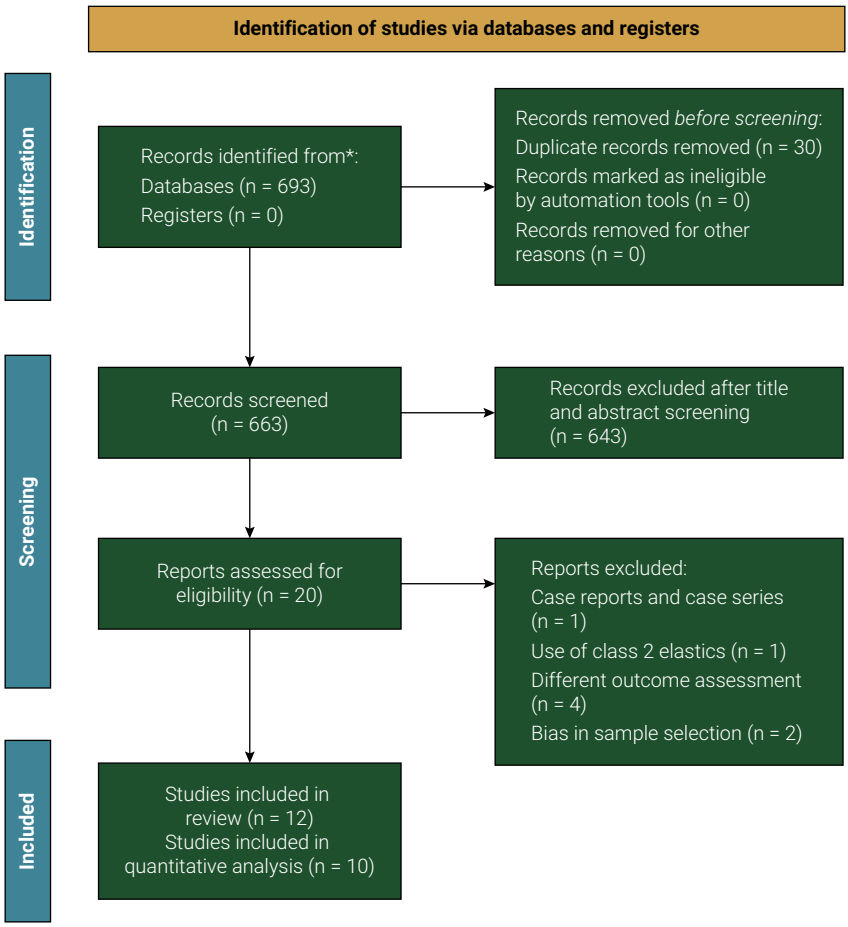

Figure 1. PRISMA Flow Chart

Study Characteristics

The summary of characteristics of the studies is given in Table 1. Five Prospective and seven retrospective studies were included with the total patient count of 555[8,10,20-29]. The patient population included those treated with clear aligner mandibular advancement appliances, twin block, Herbst, Vanbeek activator and untreated controls. The patient's age ranged from 10 to 14 years. Five of the twelve studies did not have a control group[8,10,27-29]. Five studies had twin block, two had Herbst and four had untreated control groups[8,26,20-25].

Measurements were made on lateral cephalometric radiographs using digital software except Caruso et al.[21] and Lombardo et al.[22] Zaky and Negm[29] measured on CBCT images.

The parameters included to assess the changes in mandibular length varied with every study[20,23,25-27]. Parameters used to assess maxillary and mandibular incisor inclinations across studies were similar. A detailed overview of the study results is given

in Table 2. The parameters analyzed were unit length of mandible (Go-Pg or Go-Gn), effective mandibular length (Co-Pg or Co-Gn), lower and upper incisor inclination to mandibular and palatal planes respectively.

Risk of Bias and Quality of Evidence

Risk of bias for the studies was done using Newcastle–Ottawa Scale for observational studies (Table 3). Four retrospective studies had low risk of bias because of a well-defined study population, blinding of operators and inclusion of control[20,22,24,25]. Caruso et al.[21] and Sun et al.[23] did not include an untreated control group.

Zaky and Negm[29] included only female subjects, Cremonini et al.[10] prescribed class II elastics to be worn at night and Kong and Liu[27] used an expansion arch in pre-CAMA stage of treatment, Glaser et al.[28] didn't have a control group. Sabouni et al.[8] had high risk because of the absence of a control group.

Following were the results arrived at after the descriptive analysis of the findings of all the studies in Table 2.

Results of Mandibular length

Studies that assessed the skeletal effects of clear aligner mandibular advancement appliance showed significant increase in mandibular unit length after treatment[8,10,27-29]. Similar results were obtained when the skeletal effects of CAMA were compared with untreated control[20,22,26]. Blackham[25] concluded that twin block produced significant increase in mandibular length when compared to CAMA. Wu et al.[20], Lombardo et al.[22] and Sun et al.[23] found no preferential increase in mandibular length between twin block and CAMA group.

Results of Lower incisor inclination

Four groups reported a reduction in lower incisor inclination following CAMA treatment (-1.68º,- 0.11º,-0.44º and-0.58º)[8,24-26]. In contrast, few reported mild increase in lower incisor inclination following treatment with similar appliances[27-29]. Caruso et al.[21] reported a reduction of 1.5º in lower incisor inclination following twin block treatment[23]. Hosseini et al.[24] and Wu et al.[20] reported a substantial increase in lower incisor inclination following Herbst therapy.

Results of Upper incisor inclination

Reduction in maxillary incisor inclination following CAMA therapy was reported in all the studies, Blackham reported a reduction in upper incisor inclination following twin block treatment (Table 2).

Meta-analysis

Ten studies were included for meta-analysis, excluding the research that had potential confounder[10]. Data for changes in mandibular length could not be effectively extracted from report of Hosseini et al.[24] Meta-analysis was performed for the following parameters: comparison of changes in mandibular length after CAMA therapy with pretreatment levels - effective mandibular length (Co-Gn) and unit mandibular length (Go-Pg),

Table 2. Results: Skeletal and Dental changes from pre-treatment to post-treatment

Author & Year	Group	Difference in Unit mandibular length(mm)	Sig.	Difference in Effective mandibular length (mm)	Sig.	Lower incisor inclination (°)	Sig.	Upper incisor inclination (°)	Sig.	Results
Wu et al.[20] 2023		Go-Pog	0.425	Co-Pog	0.015*	L1-Mp	0.027*	U1-PP †	0.028*	Co-Go of TB and MA groups increased significantly more than VA and control. Co-Pog of Herbst, TB and MA groups increased significantly than in the control group. TB and MA groups was comparable to VA group. MA group had significant reduction in U1-PP than the other groups but not TB. L1-MP of Herbst increased significantly than VA, MA and control while VA group decreased by 0.26°
	Vanbeek	T0: 59.59 ± 4.87 D:1.30 ± 0.98		T0:95.83±6.48 D:2.84 ± 1.23 bc		T0: 99.37 ± 2.98 D: 0.15/3.52[b]		T0: 28.35/2.30 D: 0.00/0.80b		
	Herbst	T0:57.36±4.71 D:1.82 ± 1.68		T0:95.27±5.91 D:3.84 ± 2.31 ab		T0: 99.34 ± 5.80 D: 7.80/11.40[a]		T0: 27.70/5.00 D: 0.10/0.70b		
	Twin-Block	T0:57.14±3.97 D:1.81 ± 1.58		T0:94.58±5.27 D:4.87 ± 2.26 a		T0: 97.89 ± 8.58 D: 3.20/5.80[ab]		T0: 26.30/4.20 D: 0.45/1.22 ab		
	Mandibular advancement	T0:69.20±3.33 D:2.25 ± 1.67		T0:102.14±4.06 D:4.93 ± 1.59 a		T0: 97.23 ± 6.28 D: 0.95/4.05[b]		T0: 27.65/3.30 D: 0.70/1.85 a		
	Control	T0:56.50±3.22 D:1.39 ± 1.38		T0:93.96±4.83 D:2.06 ± 1.35 c		T0: 97.95 ± 6.66 D: 0.30/1.28[b]		T0: 27.45/4.30 D: 0.20/1.38b		
Ravera et al.[26] 2021		Gn_Go	0,668	Gn_Co	0,306	X41_GoGn	0,757	X11_SpP	0.00034***	At CVM2 in MA significant reduction in upper incisor inclination was seen. At CVM3 increase in total mandibular length Co-Gn was seen.
	MA (CVM2)	T0: 64.63 ± 14.39 T1: 66.79 ± 15.54 D:2.16±21.17		T0: 111.22 ± 23.83 T1: 117.15 ± 25.00 D:5.93±34.53		T0: 93.89±7.80 T1: 94.13±7.09 D:0.24±10.54		T0: 114.27 ± 8.335 T1: 107.93 ± 4.43 D:-6.34± 9.44		
	Control (CVM2)	T0: 68.46 ± 5.49 T1: 71.12 ± 4.88 D:2.66±7.34		T0: 106.8 ± 6.40 T1: 111.0 ± 6.80 D:4.2±9.3		T0: 96.64 ± 9.06 T1: 97.30 ± 7.41 D:0.66±11.70		T0: 110.52 ± 4.94 T1: 110.23 4.68 D:-0.29±6.80		
	MA (CVM3)	T0: 66.36 ± 6.19 T1: 69.99 ± 9.85 D:3.63± 11.63	0,455	T0:107.93±8.89 T1:117.39±11.11 D:9.46±14.22	0.034*	T0:100.73±5.60 T1:99.05±6.13 D:-1.68±8.30	0,057	T0: 111.35±8.88 T1:111.55±4.41 D:0.2±9.91	0,410	
	Control (CVM3)	T0: 71.36 ± 4.94 T1: 73.02 ± 7.44 D:1.66±8.9		T0: 113.24 ± 6.18 T1: 113.07 ± 6.04 D:-0.17±8.64		T0: 97.23 ± 7.03 T1: 98.34 ± 6.69 D:1.11±9.70		T0: 109.80 ± 4.45 T1: 106.07 ± 2.89 D:-3.73±5.31		

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Caruso et al.[21] 2021	Mandibular advancement Twin block	Data not available		Data not available		L1 ^ GoMe T0: 95.7 ±7.8 T1: 98.1 ±6.8 D: 2.4 ± 10.34 T0: 93.6 ± 4.7 T1: 92.1 ±4.3 D: -1.5 ±6.4	0.580	U1 ^ ANSPNS T0: 111.2 ±10.0 T1: 109.9 ±6.8 D: -1.3 ±12 T0: 119 ± 2.3 T1: 109 ± 9.3 D:-10 ±9.6	0.010*	TB treatment resulted in statistically significant changes In U1^ANSPNS The comparison between the two treatments over time revealed a different response for U1^ANSPNS
Hosseini et al.[24] 2023	Mandibular advancement appliance (MA) Herbst	Data not available		Co-Pg D:4.96±2.80 D:5.23±3.37	NI	L1-ML T1:101.80±6.23 T2:101.36 D:-0.44±4.10 T1:94.59±7.12 T2:101.98 D:7.39±6.91	<0.0001***	U1-NL T1:114.2±9.57 T2:112.34 D:-1.86±9.25 T1:113.10±8.35 T2:106.33 D:-6.77±8.73	0.09	There was a statistically significant increase in growth at condylion in MA group (0.02). L1-ML increased(7.39°) in Herbst group but it reduced by 0.44° in MA group. U1-NL decreased by 6.77° in Herbst group and 1.86° in MA group.
Kong and Liu[27] 2023	Mandibular advancement	Go-Pg T0:76.18±5.43 T1:80.43±3.90 D:4.25±2.87	0.001***	Co-Pg T0:108.58±7.08 T1:113.60±6.58 D:5.02±1.83	0.038*	L1-MP T0:95.20±2.93 T1:96.43±2.86 D:1.23±0.40	0.000***	U1-SN T0:108.04±3.01 T1:103.98±4.78 D:-4.06±4.88	0.000***	The average increase of Go-Pg in mandibular body length was 4.25 mm and Co-Pg was 5.02mm and was statistically significant. The inclination of upper central incisor U1-NA significantly decreased by 3.44° and the angle of the lower central incisor significantly increased 1.23°

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Lombardo et al.[22] 2023	Twin block	Data not available		Co-Gn T0:100.3± 5.7 D:8.4±2	0.000***	L1-MP T0:97.2±5.9 D:1.6±1.4	0.345	U1-PP T0:112.4±7.6 D:0.1±1.7	0.079	The TB group and MA group showed statistically significant difference in Co-Gn between pre and post treatment when compared with the UC group with a total increase of 8.4mm in patients treated with the TB appliance and of 8.3mm in MA patients. No significant difference in incisor inclination was seen.
	MA			T0:101.9±6.5 D:8.3±3.1		T0:100.2± 9 D:1.4±3.2		T0:112±9.6 D:-0.4±2.6		
	Untreated control			T0:98.7±5.7 D:3.3±1.2		T0:97.1±7.3 D:0.4±1.1		T0:112.2±6.1 D:-0.7±1.5		
Sabouni et al.[8] 2022	Mandibular advancement	Data not available		Mandibular length T0:94.3±4.8 T1:95.8±4.9 D:1.5	<0.001***	IMPA T0:97.66±6.6 T1:97.56±6.2 D:-0.11	0.454	Data not available		Statistically significant increase in mandibular length was evident post treatment.
Cremonini et al.[10] 2022	F22 Young device	Go-Pg T0:59.01± 3.752 T1:62.44±4.343 D:3.43	0.00003***	Co-Gn T0:94.80± 5.586 T1:97.82± 5.811 D:3.02	0.00001***	IMPA T0:97.7±5.493 T1:99.0±4.545 D:1.3		U1- Pp T0:111.8±9.914 T1:111.0±15.216 D:-0.8	0.7	Significant increase in IMPA and mandible length, both total (Co-Gn) and at the base (Go-Pg) was evident as a result of treatment with the F22® Young appliance .
Glaser et al.[28] 2022	Invisalign mandibular advancement	Data not available		Co-Gn T0:104.06 ± 7.13 T1:107.01±7.50 D:2.95± 10.35	<0.002**	L1- MP T0:99.30 ±6.85 T1:99.57±6.52 D:0.27± 9.46	0.925	Data not available		Statistically significant increase in mandibular length (CoGn = +3.59mm) and no statistically significant change in IMPA.
Sun et al.[23] 2022	A6 appliance	Go-Gn T0: 74.95±10.06 T1: 76.67±8.56 D: 1.72±3.11	0.651	Co-Gn T0: 98.66±5.97 T1: 103.53±6.28 D: 4.87±3.89	0.822	IMPA T0:99.96±5.80 T1:102.80±6.74 D:2.91±4.05	0.438	U1-PP T0: 120.90±6.55 T1: 115.12±6.50 D: −5.78±3.71	0.068	Both appliances had significant effects on increasing the effective mandibular length (Co-Gn), inclination of upper and lower incisors.
	Twin block	T0: 80.70±4.83 T1: 84.15±4.24 D: 3.45±3.57		T0: 102.07±5.26 T1: 107.04±5.70 D: 4.97±3.87		T0:98.35±5.97 T1:100.22±5.80 D1.87±6.57		T0: 118.27±6.87 T1: 114.81±6.98 D: −3.46±6.22		

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		Go-Me		Co-Gn		LL1-MP			
Zaky and Negm[29] 2022	Clear mandibular advancement appliance	T0: 72.54 ± 5.48 T1: 75.77 ± 6.07 D: 3.22 ± 2.95	<0.001**	T0: 106.6 ±6.28 T1: 111.6 ±6.79 D: 5.02 ±2.58	<0.001**	T0: 101.06 ±4.62 T1: 103.69 ±6.16 D: 2.63 ± 3.09	0.002**	Data not available	Statistically significant increase in effective mandibular length, mandibular body length and the lower incisor inclination in relation to the mandibular plane.
				Co-Gn		L1-MP		U1-PP	
Blackham[25] 2020	Clear mandibular advancement appliance	Data not available		T1:104.32±6.14 D:3.35±3.40	<0.05	T1:99.73±6.70 D: -0.58±4.33	NS	T1: 111.94±9.92 D: -0.14±7.13	<0.01	Statistically significant increase in mandibular length in effective mandibular length in twin block treated group when compared to clear aligner mandibular advancement appliance
	Twin block			T1:102.58±6.22 D:5.57±3.19		T1:96.96±6.42 D: 1.48±4.50		T1:114.81±7.51 D: -4.45±5.77		
	Control			T1:112.24±6.09 D:3.02±3.10		T1:94.80±4.96 D: -0.69±3.22		T1:109.31±5.78 D: 0.56±3.11		

T0- Pre-treatment, T1- Post-treatment (functional), D- post-treatment changes (T1-T0)
† Non parametric test; Groups with the same letter indicated no statistically significant difference
Sig. –Significance, *P < 0.05 **: P <0.01 ***: P <0.001 -NI – No Information
CVMI- cervical vertebra maturity indicator, Co-Pg Condylion-Pogonion distance in millimeters, Co-Gn Condylion- Gnathion(mm), Go-Pg Gonion-Pogonion(mm), Go-Gn Gonion-gnathion (mm), U1-PP upper incisor -palatal plane(degree), U1-SN upper incisor to anterior cranial base (degree)L1-MP lower incisor -mandibular plane(degree), IMPA – incisor mandibular plane angle , L1- GoMe- lower incisor inclination to gonion menton mandibular plane

Table 3. Risk of Bias assessment using Newcastle–Ottawa Scale for non-randomized prospective and retrospective cohort studies.

Studies	SELECTION (maximum 4 stars)				COMPARABILITY (maximum 2 stars)	OUTCOME (maximum 3 star)			Total stars (9)	Risk of Bias
Cohort studies	Representativeness of the exposed cohorts	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration of the outcome of interest was not present at the start of the study	Comparability of cohorts on basis of design or analysis	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow up of cohorts		
	a) Truly representative of the average in the target population* (all subjects or random sampling); b) Somewhat representative of the average in the target population* (nonrandom sampling); c)Selected group of patients; d)No description of the sampling strategy.	a) drawn from the same community as the target population *; b) drawn from a different source. c)no description of the derivation of the comparison population.	a) secure record (eg surgical records)* b) structured interview * c) written self-report d) no description	a) yes* b) no	The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled. a)The study controls for age , sex*; b) The study controls for CVMI, ANB. * c) Cohorts are not comparable on the basis of design or analysis is controlled for confounders	a) Independent blind assessment*; b)Record linkage*; c)Self-report; d)No description.	a) yes * b) no	a) complete follow up - all subjects accounted for* b) subjects lost to follow up unlikely to introduce bias - small number lost (follow up, or description provided of those lost) * c) follow up rate and no description of those lost d) no statement		
Caruso et al.[21] 2021	c	b	a*	a*	b*	a*	a*	a*	6	Moderate
Sabouni et al.[8] 2022	c	c	a*	a*	c	a*	a*	a*	5	High
Sun et al.[23] 2022	c	b	a*	a*	a*,b*	a*	a*	a*	7	Moderate
Zaky and Negm[29] 2022	c	c	a*	a*	c	a*	a*	a*	5	High

Continue

Continuation

Kong and Liu[27] 2023	c	c	a*	a*	c	a*	a*	a*	5	High
Glaser et al.[28] 2022	c	c	a*	a*	c	a*	a*	b*	5	High
Cremonini et al.[10] 2022	c	c	a*	a*	c	a*	a*	a*	5	High
Hosseini et al.[24] 2023	a*	a*	a*	a*	a*,b*	a*	a*	a*	9	Low

Studies	SELECTION (maximum 4 stars)				COMPARABILITY (maximum 2 stars)	EXPOSURE (maximum 4 star)			Total stars (9)	Risk of Bias
Case control studies	Is the case definition adequate	Representativeness of the cases	Selection of controls	Definition of control	Comparability of cases and controls on basis of design or analysis	Assessment of exposure	Same method of ascertainment for cases and controls	Non-response rate		
Lombardo et al.[22] 2023	a*	a*	a*	a*	a*, b*	a*	a*	a*	9	Low
Wu et al.[20] 2023	a*	a*	a*	a*	a*,b*	a*	a*	a*	9	Low
Ravera et al.[26] 2021	a*	a*	a*	a*	a*,b*	a*	a*	a*	9	Low
Blackham[25] 2020	a*	a*	a*	a*	a*	a*	a*	a*	9	Low

comparison of changes in effective mandibular length (Co-Gn) between CAMA and Twin block, comparison of changes in lower and upper incisor inclination between CAMA and twin block (Figure 2-6).

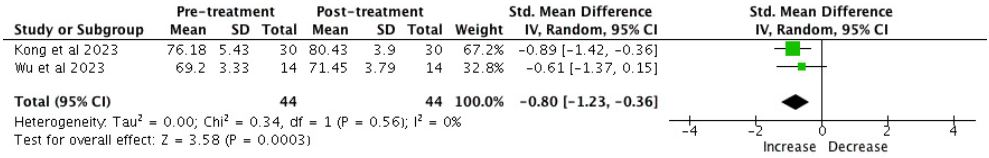

Figure 2. Forest plot comparing pre- and post-treatment changes in Go-Pg with clear aligner mandibular advancement (CAMA) therapy.

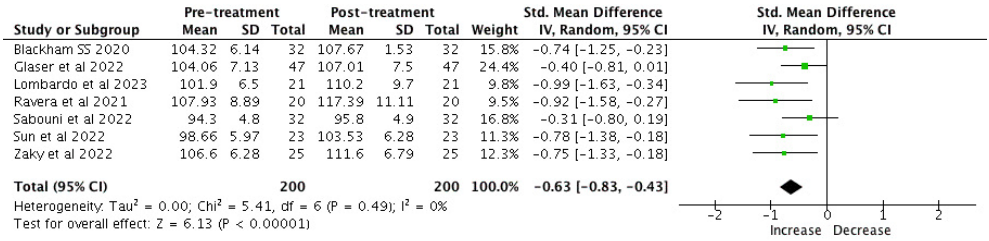

Figure 3. Forest plot comparing pre- and post-treatment changes in Co-Gn with CAMA therapy.

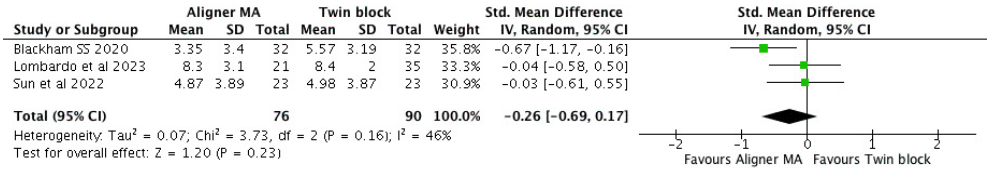

Figure 4. Forest plot comparing Co-Gn changes between CAMA and twin block (TB).

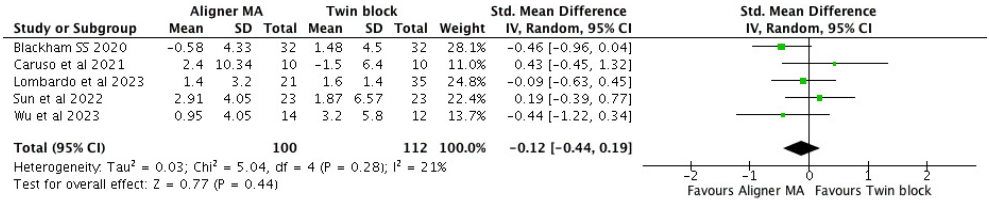

Figure 5. Forest plot comparing lower incisor inclination changes between CAMA and TB.

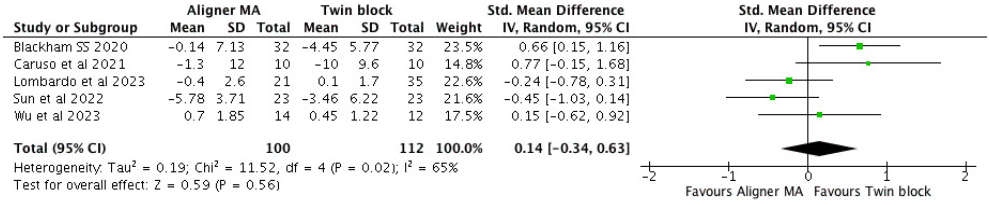

Figure 6. Forest plot comparing upper incisor inclination changes between CAMA and TB.

Skeletal changes in effective mandibular length (Co-Gn) were not different between CAMA and twin block p=0.23, SMD-0.26[-0.69,0.17] though one of the studies reported significant increase in mandibular length with twin block when compared to CAMA (Figure 4)[25]. There was significant difference in Go-Pg and Co-Gn measurements after treatment with CAMA, the p-values were 0.0003, SMD-0.80[-1.23, -0.36] and <0.00001, SMD-0.63[-0.83, -0.43] respectively (Figure 2,3).

There was no significant change in mandibular incisor inclination in patients treated with either CAMA or twin block p=0.44, SMD-0.12[-0.44,0.19] (Figure 5). No difference was found when the inclination of maxillary incisor was compared between the two appliances, p=0.56, SMD0.14[-0.34,0.63] (Figure 6).

GRADE was assessed to analyze quality of evidence across studies (Table 4). Two of the five analyses done had high level of certainty, one was moderate, one low and one had very low levels of certainty.

Table 4. GRADE assessment

Certainty assessment							№ of patients		Effect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Aligner mandibular advancement	Twin block	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
Changes in effective mandibular length												
3	non-randomised studies	not serious	not serious	not serious	not serious	none	76	90	-	SMD 0.26 SD lower (0.69 lower to 0.17 higher)	⊕⊕⊕⊕ High	
Changes in lower incisor inclination												
5	non-randomised studies	not serious	not serious	not serious	not serious	none	100	112	-	SMD 0.12 SD lower (0.44 lower to 0.19 higher)	⊕⊕⊕⊕ High	
Changes in upper incisor inclination												
5	non-randomised studies	not serious	serious[a]	not serious	not serious	none	100	112	-	SMD 0.14 SD higher (0.34 lower to 0.63 higher)	⊕⊕⊕◯ Moderate	
changes in unit mandibular length in MA group												
2	non-randomised studies	serious[b]	not serious	not serious	not serious	all plausible residual confounding would suggest spurious effect, while no effect was observed	44		-	SMD 0.8 SD lower (1.23 lower to 0.36 lower)	⊕⊕◯◯ Low	
changes in effective mandibular length in MA group												
7	non-randomised studies	not serious	serious[c]	not serious	not serious	none	200		-	SMD 0.63 SD lower (0.83 lower to 0.43 lower)	⊕◯◯◯ Very low	

CI: confidence interval; SMD: standardised mean difference
a. Inconsistency in upper incisor inclination following twin block treatment across studies
b. Kong and Liu[27] used expansion device in the Pre MA stage that would have led to the forward mandibular growth
c. In the study by Blackham there was a statistically significant increase in mandibular length with Twin block treatment when compared to Clear Aligner Mandibular Advancement

Discussion

Literature is replete with evidence proving the efficacy of appliances like twin block (TB) in treating retrognathic mandible[5,6,7,33,34]. There has been a constant increase in the number of patients opting for aligners and the use of mandibular advancers with aligners have increased[8,10,20-23,26,35]. Aim of the present systematic review was to compare the skeletal and dental effects of CAMA with conventional functional appliances.

Analysis of the studies revealed that subjects were included based on SNB angle of Steiner to assess mandibular retrognathia and CVMI staging to assess the growth status. The time taken for CAMA phase ranged from 9.2 to 10.23 months and 17 to 36 months were the total treatment duration. Mandibular advancement in nine studies was performed with Invisalign Mandibular Advancement appliance[8,20-22,24,26-28]. Sun et al.[23] and Zaky and Negm[29] studied an appliance having bite blocks. Cremonini et al.[10] studied an aligner with an anterior bite ramp.

Results of this systematic review and meta-analysis indicated that clear aligners with mandibular advancement feature were efficacious in increasing the mandibular length in subjects with class II malocclusion (Figure 2,3), but when the skeletal effects were compared with twin block, there was no statistically significant increase in the effective mandibular length (Figure 4). It is understandable that the clear aligner advancing appliances do not increase the mandibular length more than twin block. Koretsi et al.[36] compared the effects of five removable functional appliances and concluded that there were more pronounced skeletal changes with twin-block.

Data indicating changes in effective mandibular length (Co-Gn) were retrieved from seven studies and checked for heterogeneity. There was significant increase in mandibular length with CAMA (Figure 3)[8,22,23,26,28,29]. Eshani et al.[37] reported consistent increase in mandibular length after twin-block treatment.

There have been varied results on mandibular incisor inclination. Meta-analysis comparing the lower incisor inclination after CAMA and TB treatment proved that there was no significant difference in lower incisor inclination after treatment with CAMA or TB (Figure 5). Franchi et al.[5] reported that there was no significant increase in lower incisor inclination following activator or bionator treatment, while Pacha et al.[38] reported significant increase in lower incisor inclination following Herbst advancement.

Analyzing the changes in maxillary incisor inclination after treatment with CAMA and TB showed that no significant proclination or retroclination occurred with either CAMA or TB (Figure 6)[20-23]. Caruso et al.[21] reported significant reduction in upper incisor inclination after TB treatment. Labial bow incorporated in TB might reduce the upper incisor inclination if activated.

The results of the current meta-analysis and systematic review partially concur with those of Yu et al.[17] who compared clear aligners with mandibular advancement to conventional functional appliances in the treatment of Class II malocclusion in subjects with mandibular retrognathism. Following CAMA therapy, both studies found a significant increase in mandibular length, demonstrating the effectiveness of this

treatment in fostering skeletal advancement. In the present study, there was no statistically significant difference in overall mandibular length (Co-Gn) between the CAMA and twin block groups, even though Yu et al.[17] reported a significantly greater increase in mandibular ramus length (Co-Go) with traditional appliances. In terms of dental effects, Yu et al. found that aligners were better at controlling lower incisor proclination than traditional appliances, demonstrating a 1.94° reduction in proclination. However, the present meta-analysis revealed no statistically significant difference in lower incisor inclination between the two groups, indicating that the incisor control offered by both appliances was comparable across the included studies. Furthermore, both reviews concluded that differences in upper incisor inclination were negligible in the studied appliances, be it CAMA or twinblock.

The present systematic review and meta-analysis have provided some important insights into the functional correction of class II malocclusion by advancing the mandible forward. There was no significant difference in the amount of mandibular growth when skeletal changes following treatment with TB and CAMA were compared (p=0.23) (Figure 4). Twin block is a removable appliance, so are the clear aligner mandibular advancement devices. Though studies comparing the effects of these two appliances are scarce at this point in time, there is enough evidence in literature to prove the effectiveness of twin block in promoting the growth of mandible[7,37,39]. CAMA appliances have incorporated either occlusal bite blocks or vestibular wings similar to the bite blocks in TB for advancing mandible. The choice of a time-tested appliance like twin block or the expensive alternative of CAMA therapy can be left to the clinician and patients. Long-term evaluation of treatment results with aligners using mandibular advancement feature needs to be studied to prove that CAMA provides an enhanced experience of comfortable care better than conventional appliances, that are still relevant.

There are limitations in the present study: I- Prospective research comparing the effectiveness of CAMA with untreated controls or other functional appliances is scarce. Evaluating the effects of a single appliance without a comparative group leads to risk of selection of study participants directly related to outcome, and five studies did not have a control group[8,10,22,27,28]. The confounding effect of natural growth is a significant limitation when interpreting the observed skeletal changes. The lack of reliable comparator groups makes it difficult to clearly attribute changes to the intervention alone, even though some studies tried to account for this by matching participants based on skeletal maturity indicators like CVMI stages. Prospective studies with such robust design are required to further the present available knowledge.

II- Use of mandibular advancement features in aligner is a comparatively novel treatment modality for growth modification and there are no definitive long-term studies showing skeletal changes as in twin block appliance. Hence, long term evaluation of treatment results is imperative, but it was not done in any of the included studies.

Conclusion

Based on the low-to-moderate quality evidence, the following conclusions arrived from this systematic review and meta-analysis: I- Clear aligners with mandibular

advancement feature provided an increase in mandibular growth when compared to pre-treatment levels. II- Clear aligners with mandibular advancement feature and twin block produced similar skeletal effects in promoting mandibular growth. III- There was no significant change with maxillary and mandibular incisor inclination when the dental effects of CAMA and twin block were compared.

Acknowledgments

None.

Conflict of Interest

None.

Data Availability Statement

Datasets related to this article will be available upon request to the corresponding author.

Author Contributions

Poornima Jnaneshwar: Conceptualization, Methodology, Formal Analysis, Investigation, Writing - Original Draft, Writing - Review and Editing and Visualization. **Rasiga Gandhi:** Conceptualization, Methodology, Writing - Original Draft and Writing - Review and Editing. **Krishnaraj Rajaram:** Validation and Writing - Review and Editing. **Ravi Kannan:** Validation and Writing - Review and Editing. All authors contributed to the study's design, data collection, and analysis. They actively participated in discussing the manuscript's findings and critically revised and approved the final version of the manuscript.

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Supplementary appendix 1. Search strategy

Search engine	No	Key words
Pubmed	598	((“mandibular advancement”[All Fields] OR “mandibular advancement”[MeSH Terms]) AND “clear aligner”[All Fields]) OR “clear aligners”[All Fields]
Google Scholar	63	“mandibular advancement” and “mandibular retrognathism” and “clear aligners”
Cochrane	1	(“ mandibular advancement”) AND (“clear aligner”)
SciELO	0	(“mandibular advancement”) AND (“clear aligner”) AND (“class II”)
Virtual health library	31	(“mandibular advancement”) AND (“clear aligner”) AND (“class II malocclusion”)