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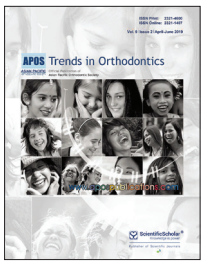

Review Article

A comparison of alternate-rapid maxillary expansion and constriction protocol with conventional rapid maxillary expansion in class III malocclusion patients – A systematic review and meta-analysis

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ABSTRACT

Class III malocclusion is a challenging orthodontic condition that can cause functional, esthetic, and psychosocial problems if untreated. Two common protocols – Alternate-Rapid maxillary expansion and constriction (Alt-RAMEC) and conventional rapid maxillary expansion (RME) – are used to manage it. However, their comparative effectiveness remains debated. The objective of the study is to compare the effectiveness of Alt-RAMEC versus conventional RME in treating Class III malocclusion with a focus on skeletal, dentoalveolar, and soft tissue outcomes. Included studies were randomized controlled trials and cohort studies comparing Alt-RAMEC and conventional RME in English. Excluded studies were without direct comparisons, those in other languages, or with insufficient outcome data. Systematic searches were conducted in PubMed/MEDLINE, Cochrane Library, and DOAJ up to January 2025. Data on study design, sample size, outcome measures, and risk of bias were extracted. Meta-analysis was performed using standard statistical techniques. Eleven studies were included. Alt-RAMEC significantly improved overjet (mean difference = 0.57 [0.18, 0.96]) versus conventional RME. No statistically significant differences were observed for other cephalometric and skeletal outcomes (e.g., Sella-Nasion-A, Sella-Nasion-B, ANB, Condyle to A, Wits appraisal). Alt-RAMEC may offer better dentoalveolar outcomes (notably overjet correction) than conventional RME, though skeletal and soft tissue changes were comparable. Long-term, high-quality studies are needed to confirm these findings. Registration PROSPERO (CRD42023456789).

Keywords: Alt-RAMEC, Class III Malocclusion, Dentoalveolar changes, Expansion technique, Maxillary Expansion, Palatal expansion technique

INTRODUCTION

Class III malocclusion affects 5–15% of the global population, with a higher prevalence in East Asian populations.[1] Class III malocclusion, characterized by the anteroposterior relationship of the lower jaw relative to the upper jaw (negative overjet), poses significant orthodontic challenges. This condition can affect facial esthetics, occlusion, and overall oral health, leading to complex treatment requirements. Untreated Class III malocclusion can lead to masticatory dysfunction, speech issues, esthetic concerns, and negative psychosocial outcomes.[2] Traditional methods for managing Class III malocclusion include conventional rapid maxillary expansion (RME), which aims to correct transverse maxillary deficiency. However, recent advancements have introduced

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the alternate RME and constriction (Alt-RAMEC) protocol, which proposes a novel approach to achieving similar or superior outcomes with potentially reduced treatment time and enhanced patient comfort.[3]

While conventional RME has shown effectiveness in enhancing skeletal and dental outcomes in Class III malocclusion, it is often associated with extended treatment duration and patient discomfort. The Alt-RAMEC protocol was introduced to overcome these drawbacks by alternating expansion and constriction phases, aiming to improve treatment efficiency and outcomes. RME combined with facemask therapy promotes skeletal changes but often results in significant dental tipping, limited maxillary advancement, and prolonged treatment duration.[4] Liou and Tsai first described Alt-RAMEC in 2005 as a method to alternate expansion and constriction to mobilize the maxillary sutures more effectively before protraction.[5] Studies report that Alt-RAMEC results in greater forward displacement of cephalometric point A, better control of vertical dimension, and less dental compensation compared to RME.[6-8] Despite this innovation, there remains a lack of comprehensive evidence comparing Alt-RAMEC directly with conventional RME regarding its efficacy and overall benefits.

However, inconsistent protocols and outcome measures across studies prevent a unified conclusion, emphasizing the need for systematic evidence synthesis.

Given these considerations, there is a critical need to systematically evaluate and compare the effectiveness of these two protocols for class III cases. Such a review could provide valuable insights into their relative benefits and guide clinicians in making informed decisions for managing Class III malocclusion.

Aims

The aims of the study are to systematically compare the skeletal, dentoalveolar, and soft tissue effects of the Alt-RAMEC protocol versus conventional RME in the management of Class III malocclusion.

Objectives

1. To assess skeletal changes (e.g., Sella-Nasion-A [SNA], Sella-Nasion-B [SNB], A-Nasion-B [ANB], point A displacement) induced by Alt-RAMEC versus conventional RME in growing Class III patients.
2. To evaluate dentoalveolar outcomes such as overjet, overbite, inter-molar and inter-canine widths, and dental tipping resulting from both protocols.
3. To compare soft tissue profile changes (e.g., nasolabial angle and facial convexity) following the protocol.
4. To analyze treatment duration, patient comfort, and compliance associated with each protocol as reported.

By addressing these objectives, the review seeks to provide a comprehensive analysis of the two protocols, offering evidence-based guidance to orthodontists and contributing to the advancement of treatment strategies for Class III malocclusion.

MATERIAL AND METHODS

Protocol and registration

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0), and the 4th Edition of the JBI Reviewer's Manual.[9] The protocol was prospectively registered with PROSPERO (Registration ID: CRD42023456789).

Focused review question

Does Alt-RAMEC protocol produce better results as compared to RME in patients with Class III malocclusion in terms of dentoalveolar, orthopedic, and soft tissue changes?

Eligibility criteria

Inclusion criteria

Population

Studies including patients aged between 7 years old and 16 years old having treatment to correct Class III malocclusion. Studies with participants with a previous history of orthodontic treatment and systemic conditions such as cleft lip and palate were excluded.

Intervention

i. Studies including the treatment of malocclusion done using Alt-RAMEC combined with or without maxillary protraction.

Comparison

i. Studies including the treatment of malocclusion done using conventional RME.

Outcome

i. Studies giving information about maxilla-mandibular skeletal and dental landmarks as seen on radiographs.
ii. Studies providing information about dentoalveolar changes produced by treatment groups.

Study design

i. Studies published in the English language.
ii. Studies published up to 31st January 2025.

iii. Clinical trials, including randomized controlled trials (RCTs), controlled clinical trials, non-randomized trials, quasi-experimental designs, cohort studies, cross-sectional studies, and other *in vivo* studies.
iv. Only studies with available full-text articles were considered for inclusion.
v. Grey literature, such as thesis, dissertations, conference abstracts, and clinical trial registries, was also screened to minimize publication bias and ensure comprehensive coverage.

Exclusion criteria

i. Studies are not fully available in the database.
ii. Single-group studies without the control group were excluded
iii. Review reports, case series, and animal studies were excluded.
iv. Studies providing only an abstract and not the full text.
v. Studies not mentioning required outcomes were excluded.

Search strategy

Studies were selected based on the Population, Intervention, Comparison, Outcome, Study design (PICOS) inclusion criteria in the review protocol. Two reviewers assessed titles and abstracts to identify potentially eligible studies. Any queries were discussed with a third reviewer.

- The PRISMA for conducting a meta-analysis was followed.
- The electronic data resources consulted for an elaborate search were Cochrane Central Register of Controlled Trials, MEDLINE, Directory of Open Access Journals (DOAJ), and PubMed Central with controlled vocabulary and free text terms [Table 1a-b].
- Articles published until 31/01/2025 were searched in English
- Following keywords and MeSH terms were used in combination with Boolean operators in the advanced search option.

The above mentioned was the final search history for the databases accessed till the month of 31st January 2025.

The search was also extended to include journals such as American Journal of Orthodontics, European Journal of Orthodontics, Progress in Orthodontics, International Orthodontics, etc. We searched gray literature by developing a detailed search plan that included searching gray literature databases, using customized Google Search engines, reviewing targeted websites such as OpenGrey, and consulting with subject experts to ensure comprehensive coverage and minimize the risk of missing relevant sources. Ongoing trials were searched through the clinical trial registry. Two authors independently performed citation search through screening the references of included articles to obtain additional articles.

Selection of studies

The title and the abstract of each study were reviewed and critically assessed by two independent reviewers (Megha Sarkar [MS] and Harsh Mishra [HM]). The methods used to apply the selection criteria were the following:

i. Integration of the searched outcomes to delete duplicate entries
ii. Examination of titles and abstracts to delete clearly irrelevant articles
iii. Recovery of the full text of potentially relevant articles
iv. Binding and gathering of multiple articles of the very same study Examination of the articles' full text to verify the degree of compliance that the studies had with the eligibility criteria
v. Establishing a connection with researchers, if necessary, to clarify the study's eligibility
vi. Deciding about the study's inclusion and proceeding with data gathering.

Data extraction

Two reviewers (MS and HM) independently extracted data from the included studies. Disagreements were again resolved through discussion with a third unbiased reviewer Laresh Mistry (LM). The gathered data was carried out using a verification list of items that were considered for data extraction. The main items of this list were as follows:

1. Authors, Year, and Title of study
2. Country
3. Study design
4. Sample size

Table 1a: Concept table.

Population	Intervention	Comparison	Outcome
Child, children, young adults, skeletal Class III malocclusion,	Alt-RAMEC protocol	Rapid maxillary expansion, rapid palatal expansion	Dentoalveolar changes, Nasolabial angle Facial convexity angle Upper lip protrusion complications, patient compliance

Alt-RAMEC: Alternate rapid maxillary expansion and constriction

Table 1b: Search strategy in different databases

Database	Search	Number of articles obtained
PubMed	("malocclusion, angle class III"[MeSH Terms] OR ("malocclusion"[All Fields] AND "angle"[All Fields] AND "class"[All Fields] AND " III "[All Fields]) OR "angle class III malocclusion"[All Fields] OR ("class"[All Fields] AND " III "[All Fields] AND "malocclusion"[All Fields]) OR "class III malocclusion"[All Fields]) AND ("alt-RAMEC"[All Fields] AND ("palatal expansion technique"[MeSH Terms] OR ("palatal"[All Fields] AND "expansion"[All Fields] AND "technique"[All Fields]) OR "palatal expansion technique"[All Fields] OR ("maxillary"[All Fields] AND "expansion"[All Fields]) OR "maxillary expansion"[All Fields]))	42
PMC/ MEDLINE	(("malocclusion, angle class iii"[MeSH Terms] OR ("malocclusion"[All Fields] AND "angle"[All Fields] AND "class"[All Fields] AND "iii"[All Fields]) OR "angle class iii malocclusion"[All Fields] OR ("class"[All Fields] AND "iii"[All Fields] AND "malocclusion"[All Fields]) OR "class iii malocclusion"[All Fields]) AND (alt-RAMEC[All Fields] AND protocol[All Fields])) AND (rapid[All Fields] AND ("palatal expansion technique"[MeSH Terms] OR ("palatal"[All Fields] AND "expansion"[All Fields] AND "technique"[All Fields]) OR "palatal expansion technique"[All Fields] OR ("maxillary"[All Fields] AND "expansion"[All Fields]) OR "maxillary expansion"[All Fields]))	60
Cochrane Central Library	Children AND class III malocclusion AND alt-RAMEC protocol AND rapid maxillary expansion	31
Google Scholar search engine	class III malocclusion AND alt-RAMEC protocol AND rapid maxillary expansion	404
Scopus	("Alt-RAMEC" OR "Alternate Rapid Maxillary Expansion and Constriction") AND ("Class III malocclusion" OR "Class III") AND ("maxillary protraction" OR "facemask")	31
Web of Science	("Alt-RAMEC" OR "Alternate Rapid Maxillary Expansion and Constriction") AND ("Class III malocclusion" OR "Class III") AND ("maxillary protraction" OR "facemask")	36

Alt-RAMEC: Alternate rapid maxillary expansion and constriction

5. Age group of participants
6. Gender
7. Intervention
8. Comparison
9. Outcomes
10. Methods of outcome assessment
11. Results
12. Conclusion and other items.

Details regarding the publication and the study, the participants, settings, the interventions, the comparators, the outcome measures, study design, statistical analysis, results, and all other relevant data (funding; conflict of interest, etc.) were carefully and accurately extracted from all included studies. Data extraction was done and accurately recorded in the Excel sheets for all the primary outcomes separately.

Risk of bias assessment

For RCTs, the Cochrane RoB-2 tool[10] was used for quality assessment.

According to this tool, the risk of bias is assessed at the study level under seven domains:

1. Random sequence generation
2. Allocation concealment
3. Blinding of participants and personnel
4. Blinding of outcome assessment
5. Incomplete outcome data
6. Selective reporting
7. Other bias.

For non-randomized studies, Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) checklist[11] was used to perform quality assessment. The ROBINS-I tool covers seven domains through which bias might be introduced into a non-RCT: Bias due to confounding, selection bias, missclassification bias, bias due to deviation from intended interventions, bias due to missing data, bias in measurement of outcomes, and reporting bias [Tables 2 and 3].

Reporting bias and certainty of evidence

Reporting bias was assessed by examining the completeness of outcome data and by reviewing trial registrations and protocols where available. Funnel plots were not generated due to the limited number of studies per outcome, which limits interpretability.

The certainty of the evidence for each outcome was considered using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. However,

Table 2: Risk of bias of included non-RCTs.

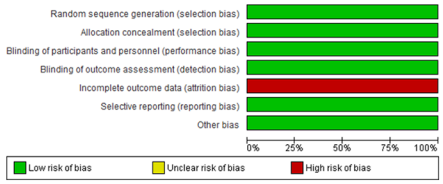
Study ID	Confounding bias	Selection bias	Misclassification bias	Bias due to deviation from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias due to selective reporting of results	Risk of bias
Masucci *et al.*, 2014[12]	Unclear	Low risk	Low risk	Unclear	Low risk	Unclear	Low risk	Moderate
Fischer *et al.*, 2018[14]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
Parayaruthottam *et al.*, 2018[15]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
Ozbilen *et al.*, 2019[16]	Unclear	Low risk	Low risk	Unclear	Low risk	Unclear	Low risk	Moderate
Buyukcavus *et al.*, 2020[17]	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Low
Kale *et al.*, 2020[18]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
Masucci *et al.*, 2022[19]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
Papadopoulou *et al.*, 2022[20]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
Ozbilen *et al.*, 2022[21]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low
Kayafoäÿlu *et al.*, 2023[6]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low

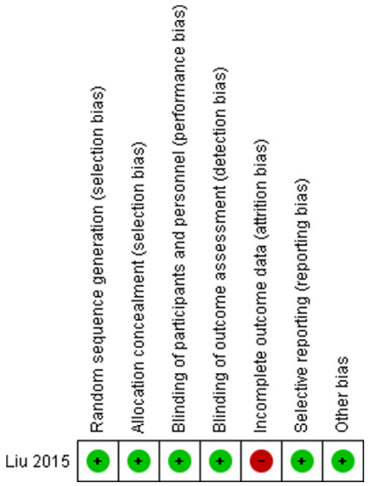
RCT: Randomized controlled trial

Table 3: Risk of bias assessment of RCT.

Study by Liu *et al.*[12], 2015 was RCT which showed high risk of bias.

The high risk of bias was due to loss to follow-up of patients in intervention group which may have introduced attrition bias in the study.





RCT: Randomized controlled trial

formal application of the GRADE framework was not performed due to substantial heterogeneity in study designs, interventions, and outcome measures across the included studies. As such, conclusions should be interpreted with caution, acknowledging the potential variability in the strength of evidence.

Meta-analysis

Meta-analysis was conducted on the studies that provided information on similar outcomes.

Assessment of heterogeneity

Clinical heterogeneity refers to differences between studies with regard to the participants, interventions, comparators, settings, and outcomes. Methodological heterogeneity refers to the study design and the methodological quality of the studies (risk of bias).

The I square statistic (I^2) represents the percentage of the variability in effect estimates that is due to statistical heterogeneity. I^2 is the proportion of observed dispersion of results from different studies included in a meta-analysis that is real, rather than spurious, measured as percentages.

Heterogeneity was considered statistically significant if $P < 0.05$. A rough guide to the interpretation of I^2 given in the Cochrane handbook is as follows:

- From 0% to 30%, the heterogeneity might not be important;
- From 30% to 60%, it may represent moderate heterogeneity;

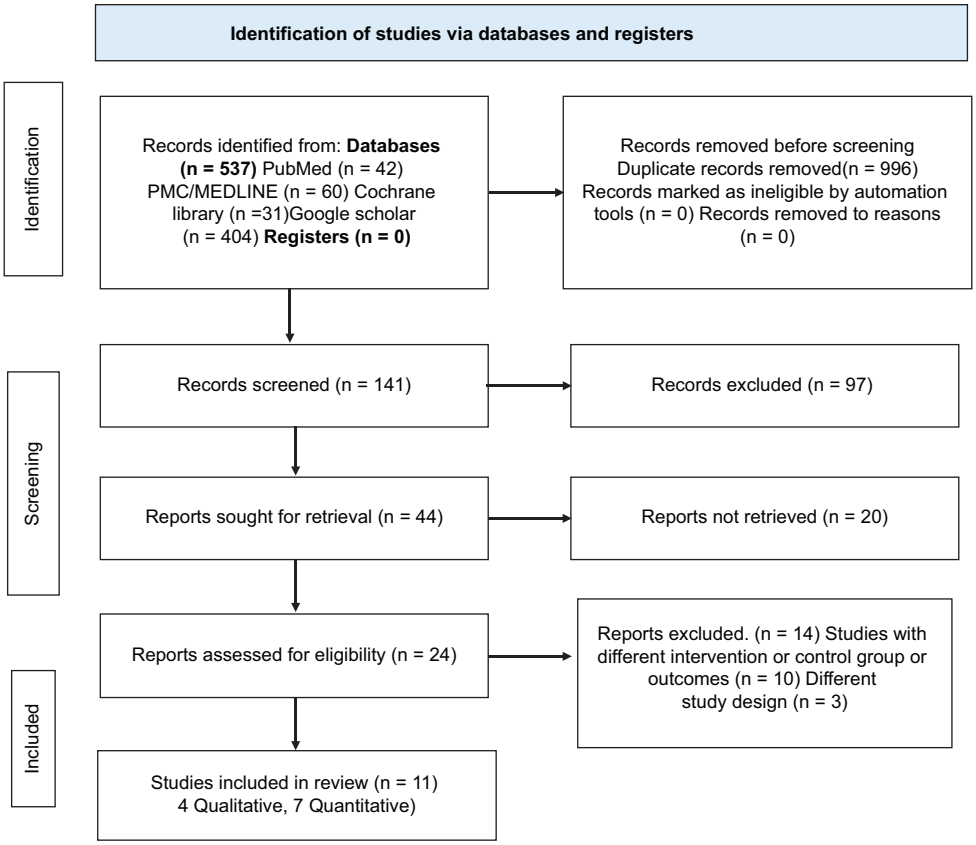


Figure 1: PRISMA 2020 flow diagram.

- From 50% to 90%, it may represent substantial heterogeneity;
- From 75% to 100%, there is considerable heterogeneity.

RESULTS

The initial electronic database search on PubMed/MEDLINE, Cochrane Library, and DOAJ resulted in 537 titles. 396 articles were cited as duplicates. After screening the abstracts, 141 relevant titles were selected by two independent reviewers were sought for retrieval and 97 were excluded for not being related to the topic. Following examination and discussion by the reviewers, 44 articles were selected for full-text evaluation. Hand searching of the reference lists of the selected studies did not deliver additional papers. Most studies had a low risk of bias, with only a few exhibiting moderate risk. The RCT by Liu *et al.*[12] had a high risk due to attrition issues. After pre-screening, application of the inclusion and exclusion criteria, and handling of the PICO questions, 11 studies remained. These 11 studies were included in the qualitative synthesis which were subjected to data extraction and statistical analysis. [Figure 1] shows the identification of studies through the database and registers.

Study characteristics

Eleven studies were included in this systematic review, the details of which are mentioned in [Table 4]. Ten of the included studies were non-randomized clinical studies, of which four studies[4,6,7,12] were designed prospectively, and the remaining data of the six studies[8-11,13,14] were obtained retrospectively. One of the included studies showed a randomized controlled study design.[5] Ethical clearance was provided for all studies. The included studies were conducted in different parts of the world, Italy[4,11] China,[5] USA,[6] India,[7] Turkey,[8-10,13,14] and Switzerland.[13] The majority of studies were conducted in Turkey.

The intervention group was treated with class III malocclusion done using the Alt-RAMEC protocol, while the comparison group was conventional RME. A total of 462 participants with Class III malocclusion were evaluated in this systematic review, of which 235 were treated by the Alt-RAMEC protocol and 227 were treated using conventional RME. Among the included participants, 212 were males and 218 were females. One study[13] did not provide information regarding the gender distribution of the participants.[15-22]

Outcomes assessed by the studies were cephalometric landmarks,[4,5,7,11,14] soft tissue landmarks,[12] airway,[8] anatomic landmarks.[6]

Table 4: Study characteristics.

Study ID	Place of study	Study design	Sample size (Intervention/ Comparison)	Age	Gender (M/F)	Malocclusion
Masucci *et al.*, 2014[13]	Italy	Prospective clinical study	31/31	6.4±0.8	33/29	Class III malocclusion, and anterior crossbite
Liu *et al.*, 2015[12]	China	RCT	22/21	7–13	20/23	Class III malocclusion and anterior crossbite
Fischer *et al.*, 2018[14]	USA	Prospective clinical study	34 17/17	7.5±1.0	16/18	Class III malocclusion with anterior crossbite or edge-to-edge incisor relationship
Parayaruthottam *et al.*, 2018[15]	India	Prospective clinical study	18	7.9–12.7	8/10	Class III malocclusion (ANB <0°) due to a retrognathic maxilla with or without associated mandibular prognathism
Ozbilen *et al.*, 2019[16]	Turkey	Retrospective	40 20/20	9.64±1.3	18/22	Skeletal Class III malocclusion due to maxillary retrognathism
Buyukcavus *et al.*, 2020[17]	Turkey	Retrospective	19//18	8–12	17/20	Negative overjet, a maxillary deficiency and a concave profile, and a decreased SNA angle and negative ANB angle
Kale *et al.*, 2020[18]	Turkey	Retrospective	22/21	11.66±1.23	23/20	Presence of transverse maxillary deficiency
Masucci *et al.*, 2022[19]	Italy	Retrospective	22/21	6.9±1.2	20/23	Class III dentoskeletal malocclusion
Papadopoulou *et al.*, 2022[20]	Switzerland	Prospective clinical study	15/16	12.5±0.9	12/19	Presence of anterior crossbite, permanent dentition with dental Class III of molars and canines, no previous orthodontic or orthopedic treatment, absence of congenital abnormalities
Ozbilen *et al.*, 2022[21]	Turkey	Retrospective	32 16/16	9.74±1.35		Anterior crossbite, skeletal class III malocclusion with maxillary deficiency
Kayafoglu *et al.*, 2023[22]	Turkey	Retrospective	79 42/37	7–14	45/34	Patients with maxillary retrusion or a combination of maxillary retrusion and mandibular protrusion

(*Contd...*)

Table 4: (*Continued*).

Study ID	Intervention (Alt-RAMEC)		Comparison (RME)		Author conclusions
	Activation	Force exerted	Activation	Force exerted	
Masucci *et al.*, 2014[13]	Twice a day (0.20 mm per turn, one turn in the morning and one turn at night) for 1 week, then it was deactivated twice a day (one turn in the morning and one turn at night) for 1 week.	400-500 g	1 or 2×per day, corresponding to 0.2 or 0.4 mm of expansion, respectively)	Not mentioned	Both the Alt-RAMEC/FM and the RME/FM protocols showed significantly favorable effects leading to correction of the Class III malocclusion
Liu *et al.*, 2015[12]	4 times/day (1 mm/day) till 7 weeks	Not mentioned	4 times/day (1 mm/day) for 7 days	Not mentioned	Facemask maxillary protraction with RPE/C might positively affect the forward movement of the maxilla compared with facemask protraction with RPE alone in the early treatment of maxillary retrusive patients.
Fischer *et al.*, 2018[14]	2×per day, corresponding to 0.4 mm of expansion) for maxillary expansion for 1 week	Not mentioned	1 or 2×per day, corresponding to 0.2 or 0.4 mm of expansion, respectively)	Not mentioned	Both Alt-RAMEC/FM and RME/FM produced favorable orthopedic changes in Class III growing patients. Neither protocol was superior to the other in terms of maxillary protraction effectiveness.
Parayaruthottam *et al.*, 2018[15]	Done twice daily for 1 week (one turn gave 0.20 mm expansion) for 5 weeks	Not mentioned	Done twice daily for 1 week (one turn gave 0.20 mm expansion)	Not mentioned	Alt-RAMEC protocol and reverse pull headgear might be more effective than conventional RME and the reverse pull headgear to correct a retruded maxilla in a developing skeletal Class III patient.
Ozbilen *et al.*, 2019[16]	1 mm/day (two turns in the morning and two turns in the evening	Not mentioned	Twice a day (0.5 mm/day) for 7 days	Not mentioned	The different expansion devices and protocols used with FM therapy do not seem to affect the forward movement of the maxilla and PA volumes. In contrast, the increase in maxillary sinus volume was greater in the Alt-RAMEC/FM protocol.
Buyukcavus *et al.*, 2020[17]	Twice per day for 1 week and to close it twice per day for the following week (0.20 mm per turn) for 5 weeks	500 g bilaterally	Twice per day for 1 week	400-500 g on each side	The most effective method in terms of skeletal effect is the application of the facemask with skeletal anchorage; the modified Alt-RAMEC protocol can be applied before the facemask to obtain faster protraction.
Kale *et al.*, 2020[18]	Twice per day for 1 week and to close it twice per day for the following week (0.20 mm per turn) for 5 weeks	Not mentioned	Twice a day for 1 week.	Not mentioned	Alt-RAMEC and RME treatment protocols are effective in orthodontic treatment with the correction of a transverse deficiency in growing subjects

(*Contd...*)

Table 4: (*Continued*).

Study ID	Intervention (Alt-RAMEC)		Comparison (RME)		Author conclusions
	Activation	Force exerted	Activation	Force exerted	
Masucci *et al.*, 2022[13]	Twice a day (0.20 mm per turn) for 1 week, and then they were instructed to deactivate it twice a day for 1 week.	Not mentioned	1–2 times/day until the desired maxillary transverse width was achieved	Not mentioned	The Alt-RAMEC/FM protocol cannot be recommended as the approach of choice for the therapy of Class III dentoskeletal disharmony in very young subjects compared to the conventional RME/FM protocol
Papadopoulou *et al.*, 2022[20]	Expansion and constriction of 1 mm/day in a weekly interchangeable manner for a total of 8 weeks and an additional 1 week of expansion.	400 g	Daily once or twice	Not mentioned	Patients treated with either early RME-FM or late Alt-RAMEC-HH-LLA had comparable overall post-pubertal skeletal and overjet corrections. However, the late Alt-RAMEC-HH-LLA showed less correction of dentoalveolar compensations and in particular of the mandibular incisors
Ozbilen *et al.*, 2022[21]	Rate of 1 mm/day in the 1st week for 9 weeks	Not mentioned	Twice daily (0.5 mm/day) until sufficient maxillary expansion (7–14 days of expansion)	Not mentioned	Both treatment protocols improved the soft tissue profile due to a forward movement of the midface and the upper lip, and a backward movement of the lower lip and chin, compared to the control group.
Kayafoglu *et al.*, 2023[22]	The screw was initially turned twice daily for 7 days to open the midpalatal suture and then once daily for 9 weeks	Not mentioned	-	-	RME/FM and Alt-RAMEC/FM therapies were found to be efficient for maxillary protraction and resulted in similar skeletal changes

SNA: Sella-Nasion-A, ANB: A-Nasion-B, RME: Rapid maxillary expansion, Alt-RAMEC: Alternate rapid maxillary expansion and constriction, RCT: Randomized controlled trial, M: Male, F: Female, Alt-RAMEC-HH-LLA: Alternate rapid maxillary expansion and contraction, Hybrid-Hyrax, Lower-lingual-Arch.

Risk of bias assessment

Among the included non-RCTs, eight studies showed low risk of bias and two showed moderate risk of bias as assessed by reviewers (MS and HM)

GRADE analysis results

Maxillary and mandibular skeletal landmarks provided moderate evidence according to the GRADE assessment tool. All the remaining outcomes provided very low evidence. In these outcomes, serious inconsistency and imprecision were noted because of the wide confidence interval of the pooled effect and high heterogeneity; because of which the evidence was downgraded. The details of assessment are mentioned in [Table 5].

Meta-analysis

Data synthesis was carried out using a descriptive synthesis, with a summary of the characteristics of each included study. For quantitative synthesis, a summary of the combined estimate related to the intervention effect was calculated as the mean of the differences of the effects of post-intervention in individual studies. Mean difference was used as a summary statistic for the quantitative assessment of cephalometric landmarks.

Maxilla

SNA

Five studies[5,8,9,12,14] were included in the pooled assessment of post-treatment SNA values. A total of 116 participants were assessed in the Alt-RAMEC group, and 112 participants

Table 5: GRADE analysis.

Outcome	Study design	No. of participants (studies)	Certainty of evidence (GRADE)
Maxilla - SNA	RCT	43 (1)	⊕⊕⊕◯ Moderate[a]
	Non-RCT	185 (4)	
Maxilla - CoA	Non-RCT	66 (2)	⊕⊕⊕◯ Moderate[a]
Mandible - SNB	RCT	43 (1)	⊕◯◯◯ Very low[a,b]
	Non-RCT	185 (4)	
Overjet	Non-RCT	116 (2)	⊕⊕◯◯ Low
Overbite	Non-RCT	145 (3)	⊕◯◯◯ Very low[a,b]
U1-PP	Non-RCT	145 (3)	⊕◯◯◯ Very low[a,b]
ANB	RCT	43 (1)	⊕⊕◯◯ Low
	Non-RCT	185 (4)	
Wits appraisal	RCT	43 (1)	⊕◯◯◯ Very low[a,b]
	Non-RCT	66 (2)	

[a]Wide 95% confidence interval, [b]High heterogeneity (I^2>50%).
RCT: Randomized controlled trial, SNA: Sella-Nasion-A,
SNB: Sella-Nasion-B, CoA: Condylion-A, U1-PP: Upper-palatal plane,
⊕ inside means present, ◯ is empty circle

with the RME. The pooled mean difference value obtained was 0.67 (−0.08, 1.41), indicating that the SNA value post treatment was greater with the Alt-RAMEC group as compared to the RME. Overall results were not statistically significant (P > 0.05). A fixed effects model was used for assessment as heterogeneity was <50%.

Condyle to A (Co-A)

Two studies[9,12] were included in the pooled assessment of post-treatment Co-A values. A total of 32 participants were assessed in the Alt-RAMEC group, and 34 participants with the RME. The pooled mean difference value obtained was −0.80 (−2.98, 1.39), indicating that the Co-A value post-treatment was less with the Alt-RAMEC group as compared to RME. Overall results were not statistically significant (P > 0.05). A fixed effects model was used for assessment, as heterogeneity was 0%. [Figure 2] shows a forest plot for maxillary relations.

Mandible

SNB

Five studies[5,8,9,12,14] were included in the pooled assessment of post-treatment SNB values. A total of 116 participants were assessed in the Alt-RAMEC group, and 112 participants with the RME. The pooled mean difference value obtained was −0.38 (−1.53, 0.77), indicating that the SNB value post-treatment was less with the Alt-RAMEC group as compared to RME. Overall results were not statistically significant (P > 0.05). A random effects model was used for assessment, as heterogeneity was 50%. [Figure 3] shows a forest plot for the SNB angle. On sensitivity analysis, it was seen that the exclusion of the study by Buyukcavus *et al.*[17] resulted in a significant reduction in heterogeneity from 50% to 0%.

Skeletal landmarks

ANB

Five studies[5,8,9,12,14] were included in the pooled assessment of post-treatment ANB values. A total of 116 participants were assessed in the Alt-RAMEC group, and 112 participants with the RME. The pooled mean difference value obtained was 0.43 (−0.06, 0.92), indicating that the ANB value post-treatment was greater with the Alt-RAMEC group as compared to RME. Overall results were not statistically significant (P > 0.05) with 0% heterogeneity.

Wits appraisal

Three studies[5,9,12] were included in the pooled assessment of post-treatment Wits appraisal values. A total of 54 participants were assessed in the Alt-RAMEC group, and 52 participants with the RME. The pooled mean difference value obtained was −0.47 (−2.56, 1.61), indicating that the Wits appraisal value post-treatment was less with the Alt-RAMEC group as compared to RME. Overall results were not statistically significant (P > 0.05) with 69% heterogeneity. [Figure 4] shows a forest plot for Skeletal Landmarks. On conducting sensitivity analysis, it was seen that the exclusion of Papadopoulou *et al.*[20] study significantly reduced the heterogeneity to 0%.

Dentoalveolar landmarks

Overjet

Two studies[9,14] were included in the pooled assessment of post-treatment overjet values. A total of 61 participants were assessed in the Alt-RAMEC group, and 55 participants with the RME. The pooled mean difference value obtained was 0.57 (0.18, 0.96), indicating that the overjet value post-treatment was greater with the Alt-RAMEC group as compared to RME. Overall results were statistically significant (P < 0.05), with 0% heterogeneity.

Overbite

Three studies[9,12,14] were included in the pooled assessment of post-treatment overbite values. A total of 74 participants were assessed in the Alt-RAMEC group, and 71 participants with the RME. The pooled mean difference value obtained was −0.55 (−1.37, 0.27), indicating that the overbite value post-

treatment was less with the Alt-RAMEC group as compared to RME. Overall results were not statistically significant ($P > 0.05$), but heterogeneity was high ($I^2 = 65\%$). On further conducting sensitivity analysis, it was found that on exclusion of the study by Buyukcavus *et al.*[17] there was a significant reduction in heterogeneity to 0% ($I^2 = 0\%$).

U1-PP

Three studies[9,12,14] were included in the pooled assessment of post-treatment U1-PP angle values. A total of 74 participants were assessed in the Alt-RAMEC group, and 71 participants with the RME group. The pooled mean difference value obtained was 3.28 (−0.45, 7.00), indicating that the U1-PP angle value post-treatment was greater with the Alt-RAMEC group as compared to RME. Overall results were not statistically significant ($P > 0.05$), but heterogeneity was high ($I^2 = 68\%$). [Figure 5] shows a forest plot for dentoalveolar landmarks. There was no difference in the amount of study heterogeneity on conducting sensitivity analysis.

Soft tissue landmarks

Nasolabial angle

Two studies[9,14] were included in the pooled assessment of post-treatment nasolabial angle values. A total of 61 participants were assessed in the Alt-RAMEC group, and 55 participants with the RME group. The pooled mean difference value obtained was 0.59 (−1.17, 2.36), indicating that the nasolabial angle value post-treatment was greater with the Alt-RAMEC group as compared to RME. Overall results were not statistically significant ($P > 0.05$), with low heterogeneity ($I^2 = 25$). [Figure 6] shows a forest plot for soft tissue landmarks.

DISCUSSION

The systematic review and meta-analysis comparing the Alt-RAMEC protocol with conventional RME in Class III malocclusion patients has yielded several important insights into their efficacy and impact on various cephalometric, dentoalveolar, and soft tissue landmarks.

Cephalometric Landmarks: The mean differences observed in cephalometric landmarks, including SNA, Co-A, SNB, ANB, and Wits Appraisal, are relatively modest and suggest that both Alt-RAMEC and conventional RME have comparable effects on these parameters.[23] Notably, the SNA and ANB angles showed slight improvements with the Alt-RAMEC protocol, though these changes are not statistically significant. This implies that while Alt-RAMEC might offer some benefits in terms of anterior-posterior skeletal

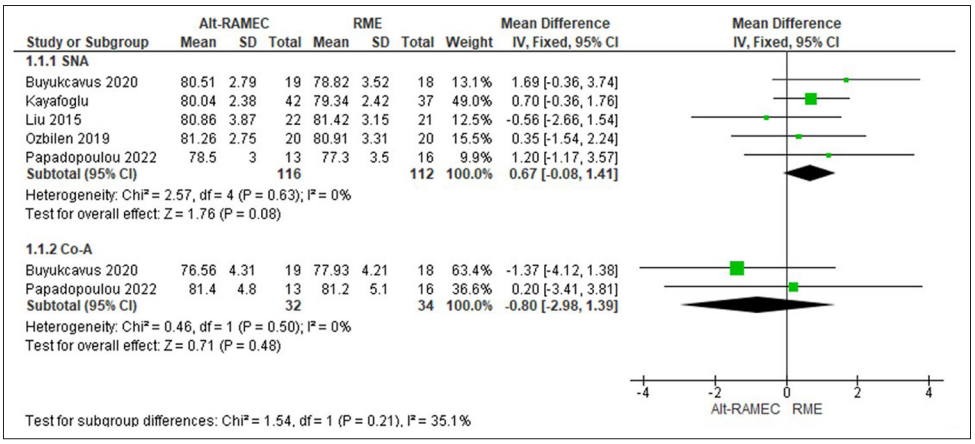


Figure 2: Forest plot for maxillary relations. SNA: Sella-Nasion-A, CI: Confidance interval.

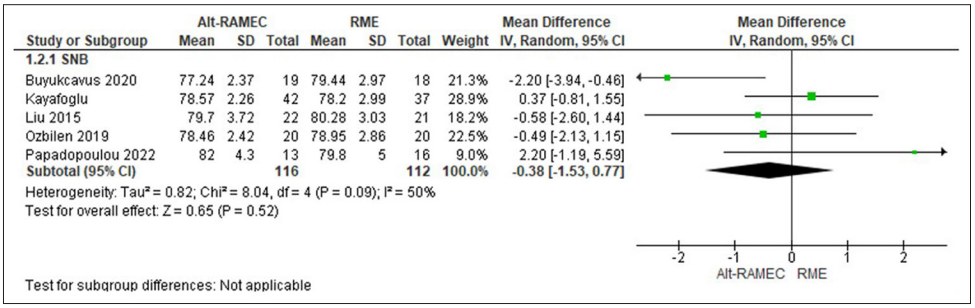


Figure 3: Forest plot for Sella-Nasion B (SNB) angle. RME: Rapid maxillary expansion, Alt-RAMEC: Alternate rapid maxillary expansion and constriction, CI: Confidence interval.

relationships, these benefits are not dramatic when compared to conventional RME [Table 6].[24]

Dentoalveolar landmarks

The Alt-RAMEC protocol demonstrated a significant improvement in overjet (mean difference = 0.57 [0.18, 0.96]), which indicates that this method is more effective in correcting overjet compared to conventional RME. This improvement could be due to the modified mechanics or protocol-specific features of Alt-RAMEC that promote enhanced dentoalveolar changes.[25] However, the changes in overbite and U1-PP angle were not significantly different between the two protocols, suggesting that their effects on these parameters are similar.

Soft tissue landmarks

The nasolabial angle, which showed a mean difference of 0.59 (−1.17, 2.36), reflects minimal impact from the treatment protocols on soft tissue esthetics. This indicates that while skeletal and dentoalveolar changes may be notable, the effect on soft tissue contours is relatively minor, consistent with previous findings that orthodontic interventions have a limited impact on soft tissue profiles.[26]

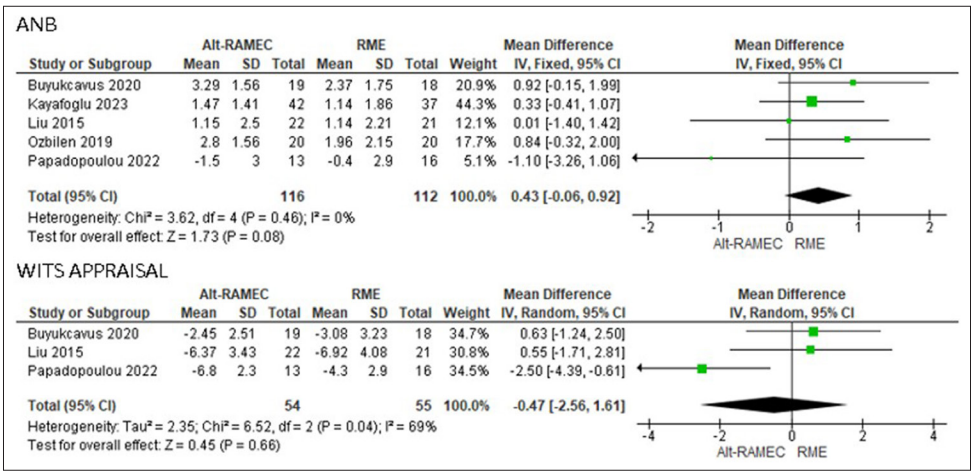


Figure 4: Forest plot for skeletal landmarks. RME: Rapid maxillary expansion, Alt-RAMEC: Alternate rapid maxillary expansion and constriction, CI: Confidence interval.

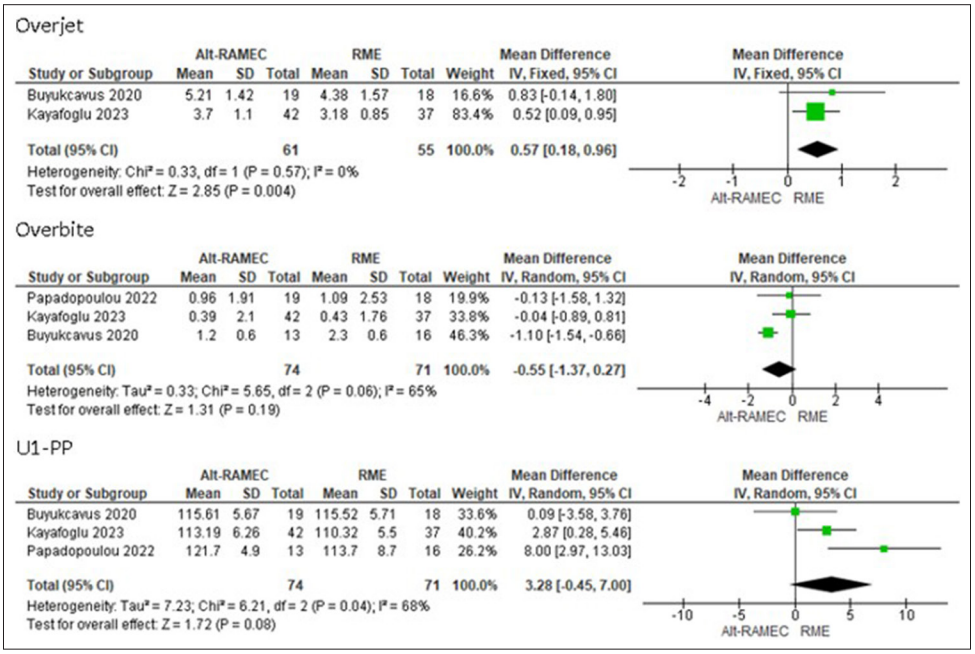


Figure 5: Forest plot for dentoalveolar landmarks. RME: Rapid maxillary expansion, Alt-RAMEC: Alternate rapid maxillary expansion and constriction, CI: Confidence interval.

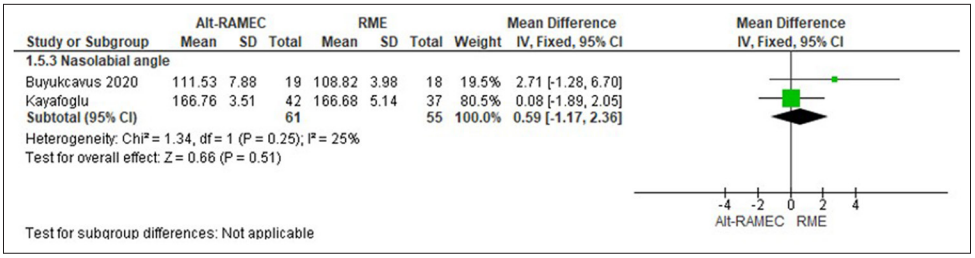


Figure 6: Forest plot for soft tissue landmarks. RME: Rapid maxillary expansion, Alt-RAMEC: Alternate rapid maxillary expansion and constriction, CI: Confidence interval.

Table 6: Summary of outcome of Alt-RAMEC versus conventional RME.

Outcome	Measure	Alt-RAMEC versus conventional RME	Mean difference (95% CI)
Cephalometric landmarks			
SNA	Angle of the Sella-Nasion-A Point	No significant difference	0.67 (−0.08, 1.41)
Co-A	Distance from Condyle to A Point	No significant difference	−0.80 (−2.98, 1.39)
SNB	Angle of the Sella-Nasion-B Point	No significant difference	−0.38 (−1.53, 0.77)
ANB	Difference between SNA and SNB	No significant difference	0.43 (−0.06, 0.92)
Wits appraisal	Occlusal relationship of the maxillary and mandibular planes	No significant difference	−0.47 (−2.56, 1.61)
Dentoalveolar landmarks			
Overjet	Horizontal distance between the upper and lower incisors	Significant improvement with Alt-RAMEC	0.57 (0.18, 0.96)
Overbite	Vertical overlap of the upper and lower incisors	No significant difference	−0.55 (−1.37, 0.27)
U1-PP angle	Angle between the upper incisors and the palatal plane	No significant difference	3.28 (−0.45, 7.00)
Soft tissue landmarks			
Nasolabial angle	Angle between the nasal base and the upper lip	No significant difference	0.59 (−1.17, 2.36)

RME: Rapid maxillary expansion, Alt-RAMEC: Alternate rapid maxillary expansion and constriction, CI: Confidence interval, SNA: Sella-Nasion-A, SNB: Sella-Nasion-B, CoA: Condyle to A

The generalizability and applicability of the evidence presented are influenced by several limitations. First, there was significant heterogeneity in study designs, with variations in methodologies, sample sizes, and treatment protocols across the included studies. This inconsistency can impact the reliability of results and hinder the formulation of definitive conclusions. In addition, many studies featured relatively short follow-up periods, which may not adequately capture the long-term stability of treatment outcomes – an important consideration given the evolving nature of orthodontic effects over time. Another concern is the variability in measurement techniques used to assess cephalometric and dentoalveolar outcomes, which introduces the risk of measurement bias and limits comparability between studies. Finally, the samples included in these studies were not consistently representative of the broader population of Class III malocclusion patients. Differences in patient demographics and the severity of malocclusion may further restrict the applicability of the findings to diverse clinical settings.

With respect to MCID justification for key outcomes, "Although a statistically significant reduction in overjet was observed between the ALT-RAMEC and conventional expansion groups (mean difference = 0.67 mm), the clinical significance of this change remains uncertain. The minimal clinically important difference (MCID) for overjet, which represents the smallest change perceived as beneficial by patients or clinicians, has been estimated in the literature to range between approximately 0.6 and 1.0 mm (Garib *et al.*, 2016; Houston, 1983; Li *et al.*, 2018).[27,28,29] Given that the observed difference lies at the lower boundary of this range, the practical impact on treatment outcomes, patient satisfaction, and clinical decision-making may be limited. Furthermore, changes of less than 1 mm are often considered within the margin of measurement error in orthodontic assessments (Houston, 1983),[28] suggesting caution when interpreting the clinical relevance of such small differences. Future studies incorporating patient-reported outcomes or longer follow-up periods are needed to confirm the meaningfulness of these findings.

The review process itself faced some limitations:

1. Publication bias: The potential for publication bias exists, as studies with significant or positive results are more likely to be published. This could skew the overall findings and limit the comprehensiveness of the review.
2. Language and accessibility constraints: Only studies published in English or accessible through the selected databases were included. This could exclude relevant research published in other languages or in less accessible journals.
3. Reviewer bias: Despite efforts to minimize bias, the subjective nature of assessing study quality and data extraction could introduce reviewer bias, affecting the robustness of the review findings.

Implications for practice, policy, and future research

Practice

The findings suggest that both Alt-RAMEC and conventional RME are effective for managing Class III malocclusion, with Alt-RAMEC offering particular benefits in improving overjet. Clinicians should consider these findings when selecting the appropriate treatment protocol based on specific patient needs and expected outcomes.

Policy

The evidence supports the continued use of both protocols in clinical practice but highlights the need for standardized treatment protocols and outcome measures to enhance comparability across studies. Policies that encourage the reporting of long-term outcomes and comprehensive data collection will contribute to more reliable and applicable evidence.

Future research

Future randomized control trials should focus on larger, more homogeneous patient populations with extended follow-up periods to assess the long-term efficacy and stability of treatment effects. Research should also explore the underlying mechanisms driving the observed differences in outcomes and investigate patient-reported outcomes to better understand the holistic impact of these treatments.

CONCLUSION

While both Alt-RAMEC and conventional RME are viable options for treating Class III malocclusion, the evidence suggests that Alt-RAMEC may offer specific advantages in overjet correction. However, the overall differences between the two protocols are not statistically significant but remain clinically comparable. Ongoing research with improved study designs and longer follow-up periods will be essential for optimizing treatment protocols and advancing the field of orthodontics.

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Declaration of patient consent: Patient's consent is not required as there are no patients in this study.

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