



# Clinical effectiveness of clear aligner treatment compared to fixed appliance treatment: an overview of systematic reviews

Yassir A. Yassir<sup>1,2</sup> · Sarah A. Nabbat<sup>3</sup> · Grant T. McIntyre<sup>4</sup> · David R. Bearn<sup>4</sup>

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## Abstract

**Objective** To evaluate the available evidence regarding clinical effectiveness of clear aligner treatment (CAT).

**Materials and methods** A comprehensive literature search was conducted for systematic reviews investigating effectiveness of CAT published up to July 15, 2021. This was accomplished using different electronic databases. No language restriction was applied. Screening, quality assessment, and data extraction were performed by two authors independently. Information was categorized and narratively synthesized for the key findings from moderate and high-quality reviews.

**Results** A total of 361 potentially eligible reviews were identified. After excluding the non-relevant/low-quality reviews, 18 systematic reviews were included. CAT was found to be effective for mild to moderate malocclusions, and was associated with inferior outcomes when treating severe cases or with achieving specific tooth movements. There were conflicting results regarding treatment duration; however, CAT may be associated with shorter treatment in mild to moderate cases. Relapse was greater with CAT, while periodontal health was better. The risk of root resorption tended to be lower with CAT. Regarding pain, the results were unclear, although CAT was found to be more comfortable and associated with a reduced impact on eating and chewing.

**Conclusions** The level of evidence regarding CAT is moderate; hence, further high-quality randomized clinical trials are required. Evidence supports use of aligners as an alternate to fixed appliances in patients with mild-to-moderate malocclusion but not in severe cases. Advancement in technology could enhance the accuracy of CAT in delivering planned outcomes.

**Clinical relevance** CAT can be used effectively for selected cases with mild to moderate malocclusion.

**Registration** PROSPERO registration number: CRD42021246855.

**Keywords** Orthodontic appliances · Clear aligner · Removable appliance · Overview of systematic reviews

## Introduction

With the increase of esthetic requirements, the demand for orthodontic treatment has increased in both adult and young patients [1, 2]. Orthodontic fixed appliance treatment (FAT) is the most common and traditional method for comprehensive treatment [3]. However, conventional FAT has been associated with some compromises in terms of appliance

appearance, patient comfort, and achieving adequate oral hygiene [4–6]. On the other hand, clear aligner treatment (CAT) has developed as an esthetic alternative option for patients seeking orthodontic treatment.

The idea of CAT was initially introduced by H.D. Kesling in 1945 [7], who suggested the use of a single positioner after orthodontic treatment with fixed appliances to achieve final settling/corrections. As thermoplastic materials became more widely available in orthodontics, Sheridan et al. [8] used a removable plastic retainer (Essix®; Dentsply, York, PA, USA) in combination with interproximal reduction (IPR) to apply force to teeth to make minor tooth movements. In 1997, commercially produced series of aligners were introduced by Invisalign® (Align Technology, Santa Clara, Calif.) as removable, clear semi elastic polyurethane aligners [9] and have been followed by many other variants produced by other manufacturers. These were initially indicated for cases with mild

✉ Yassir A. Yassir  
yassirkyassir@gmail.com

<sup>1</sup> Orthodontic Department, College of Dentistry, University of Baghdad, Baghdad, Iraq

<sup>2</sup> School of Dentistry, University of Dundee, Dundee, UK

<sup>3</sup> Ministry of Health, Baghdad, Iraq

<sup>4</sup> School of Dentistry, University of Dundee, Dundee, UK

malocclusion. Subsequently, with the significant improvement in computer-aided design/computer-aided manufacturing (CAD/CAM) and materials, it has been able to forecast treatment outcomes and fabricate a series of custom-made aligners using a single silicone or digital impression [10] with the potential to treat more complex malocclusions.

Many positive advantages of CAT have been proposed, such as overall reduction in treatment and chair time [11], being safe and esthetic, more comfortable, reduced problems with eating, simplicity of ensuring adequate gingival/periodontal health, and optimal oral hygiene compared with FAT [4, 5, 12–16], and hence with a lower impact on patient's quality of life [15]. In contrast, there are some reported limitations of CAT, for instance, limited control over root movements, limited intermaxillary sagittal/overjet correction, dependence on patient compliance on their wear with little or no control by the operator, reduced effectiveness in closing extraction spaces, and in achieving adequate occlusal contact and arch expansion when compared to FAT [17–20].

With the recent increase in popularity of CAT and the claims of Invisalign® to effectively perform major tooth and root movements [21], controversy exists in terms of whether CAT could be a suitable alternative to FAT. Several systematic reviews have been conducted to investigate different aspects of the effectiveness of CAT [22–42], but no single clear and conclusive result can be obtained from each of these reviews. Therefore, this study was designed to provide an overview (on a systematic review level) to answer the following research question: is CAT as effective as FAT? The strategy used in this study was to use the overview method to synthesize the evidence available (for patients of any age with any malocclusion).

## Materials and method

### Protocol and registration

The protocol for the present overview was registered in the International Prospective Register of Systematic Review (<https://www.crd.york.ac.uk/prospero/>; Registration number: CRD42021246855). This overview was conducted and reported in line with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) checklist [43]. Ethical approval was not required as there was no individual participation, no intervention or personal data collection.

### Eligibility criteria

The eligibility criteria were determined according to the Population, Intervention, Comparison, Outcome, and Study design (PICOS) scheme:

Population: patients of any age with any type of malocclusions undergoing orthodontic treatment.

Intervention: orthodontic treatment with clear aligners (any type).

Comparison: orthodontic treatment with fixed orthodontic appliances (any type) or untreated control group or predicted digitally planned tooth movement models.

Outcome: evaluation of the clinical effectiveness of CAT (treatment outcomes, treatment duration, and stability), and its effects on periodontal health, root resorption, and oral health-related quality of life (OHRQoL).

Study design: systematic reviews with or without meta-analysis, assessed as moderate or high-quality according to AMSTAR 2 quality assessment tool (A Measurement Tool to Assess Systematic Reviews) [44]. In case of Cochrane reviews, the most recent publication was included, and all previous versions were excluded. Studies with any other design were also excluded as well as any systematic review with only in-vitro or animal studies.

### Information sources, search strategy, and study selection

A comprehensive literature search was conducted for systematic reviews published up to July 15, 2021, using the following key terms: “aligners,” “Invisalign,” “orthodontic aligner,” “thermoplastic aligner,” “clear aligner,” “teeth positioner,” “invisible appliance,” “orthodontic appliance,” “fixed appliance,” “removable appliance,” “braces,” “treatment outcome,” “systematic review,” and “meta-analysis.” This was accomplished using electronic databases: MEDLINE via OVID (1946 to July 15, 2021), EMBASE (1974 to July 15, 2021), AMED (Allied and Complementary Medicine Database) (1985 to July 15, 2021), PubMed (inception to July 15, 2021), Cochrane Library (inception to July 15, 2021), and Web of Science (1900 to 2021). Any ongoing systematic reviews were searched using Prospero and a gray literature search was undertaken using Google Scholar and OpenGrey ([www.opengrey.eu/](http://www.opengrey.eu/)). The reference lists of the eligible reviews were also checked for additional relevant reviews. No restrictions were applied in terms of language, date, and status of publication, and age of treated patients. All relevant reviews were identified, retrieved, and assessed for eligibility of inclusion by two authors independently (Y.A.Y. and G.T.M.) who screened the titles, abstracts, and, if necessary, the full texts. Any disagreement was resolved by discussion to reach consensus or alternatively by consulting a third author (D.R.B.).

### Data items and collection

After screening the eligible systematic reviews, the following data were extracted independently and in duplicate by two authors (Y.A.Y. and G.T.M.): (1) authors; (2) year of publication; (3) study design; (4) number of studies

included; (5) type of studies; (6) number of participants; (7) period of search; (8) name of journal; and (9) objectives of the study (Table 1).

### Quality assessment in individual studies

Two authors (Y.A.Y. and G.T.M.) assessed the included reviews independently using the AMSTAR 2 quality assessment tool (Table 2). Any disagreement was initially resolved by discussion or in conjunction with a third author (D.R.B.), if necessary.

The level of evidence according to the AMSTAR 2 is presented in Table 3.

### Summary measures and approach to synthesis

Data pooling was planned to qualitatively assess the effectiveness of CAT as systematic reviews per se do not have primary data. However, according to the PROSPERO protocol and the data synthesis, quantitative analysis was also planned in case of clinical homogeneity between the reviews.

### Orthodontic treatment with clear aligners

The following categories of treatment with CAT will be taken into consideration: treatment effectiveness/efficiency (treatment outcomes, treatment duration, and stability), periodontal health, root resorption, and OHRQoL.

## Results

### Study selection and characteristics

A total of 361 potentially eligible studies were identified. After excluding the duplicates, 299 studies were left. Then, initial screening for the titles and abstracts reduced the number to 29 reviews. Following full-text assessment, eight reviews were excluded (three reviews included laboratory-based in vitro studies and five reviews were not relevant to the aim) leaving 21 systematic reviews for inclusion in the quality assessment. The PRISMA flow diagram of the literature selection process is presented in Fig. 1.

A summary of systematic review characteristics is presented in Table 1. Only systematic reviews that followed the PRISMA checklist were included and these were then evaluated for their quality with the AMSTAR2 tool. The included reviews were published from 2005 to 2021. Meta-analyses were carried out in 42.9% of the included systematic reviews (9/21 systematic reviews). Nine of the reviews included studies with Invisalign® only and the rest included Invisalign® among other types of aligners.

### Quality of the evidence

According to the AMSTAR 2 checklist, the quality of the included reviews was variable: three reviews (14.3%) were considered of low/critically low quality of evidence, 17 reviews (80.9%) were considered of moderate quality of evidence, and one review (4.8%) was considered of high quality of evidence (Table 1). Most of the AMSTAR 2 items were covered to a varying degree (Table 2). There was complete consensus between the reviewers regarding the quality assessment.

In this overview review, the main findings from the moderate and high-quality systematic reviews were considered in the thematic synthesis (18 systematic reviews). Therefore, the results of Mortazavi et al. (2020) [31] (low quality), Lagravère and Flores-Mir (2005) [22], and Elhaddaoui et al. (2017) [36] (critically low quality) were not considered further in the results and discussion.

### Data synthesis

Due to the lack of primary data, standardized treatment protocols, differences in interventions, clinical and methodological heterogeneity across the studies, further meta-analysis was not feasible. The data were, therefore, synthesized qualitatively using thematic synthesis by identifying the most prominent and important themes with the findings summarized accordingly.

### Orthodontic treatment with clear aligners

The results of orthodontic treatment with clear aligners in terms of: treatment effectiveness/efficiency (treatment outcomes, treatment duration, and stability), periodontal health, root resorption, and OHRQoL are presented in Table 4.

## Discussion

### Summary of evidence

Clear aligners represent an esthetic and more comfortable alternative to fixed orthodontic appliances [5, 6]. This study was designed to overview the available evidence-based information regarding the clinical effectiveness of clear aligners, mainly in comparison with fixed orthodontic appliances. Therefore, data synthesis was based on systematic reviews only. The 18 included systematic reviews were published during the last 6 years in high-quality journals. About half of these systematic reviews have investigated Invisalign® only, and the rest investigated different types of

**Table 1** Systematic reviews that have assessed orthodontic treatment with clear aligners

Author	Year	Study design	No. of studies	No. of participants	Type of studies	Period of search	Journal	Objective	Quality of evidence
Lagravère and Flores-Mir [22]	2005	Systematic review	2	89	Clinical Trials	Up to April 15, 2005	Journal of the American Dental Association	To determine the treatment effectiveness of Invisalign	Critically Low
Zheng et al. [23]	2017	Systematic review and meta-analysis	4 (2 for meta-analysis)	270	1 RCT 3 Cohort studies	Up to October, 2014	Orthodontics and Craniofacial Research	To evaluate efficiency, effectiveness and treatment stability of clear aligners	Moderate
Papadimitriou et al. [24]	2018	Systematic review	22	1216 (one study did not report the number of participants)	3 RCTs 8 Prospective studies 11 Retrospective studies	Up to August 28, 2017	Progress in Orthodontics	Clinical effectiveness of Invisalign®	Moderate
Ke et al. [25]	2019	Systematic review and meta-analysis	8 (5 for meta-analysis)	706	2 RCTs 1 Prospective cohort study 5 Retrospective cohort studies	Up to August 20, 2018	BMC Oral Health	To compare treatment effectiveness between clear aligner and fixed appliance therapies	Moderate
Papageorgiou et al. [26]	2019	Systematic review and meta-analysis	11	887	4 RCTs 7 Retrospective non-randomized studies	Up to April 25, 2019	European Journal of Orthodontics	To assess treatment outcome with orthodontic aligners and fixed appliances	Moderate
Python et al. [27]	2019	Systematic review	4	396	1 RCT 3 NRCT	Not reported	Journal of Investigative and Clinical Dentistry	To compare treatment effectiveness between clear aligner and fixed appliance therapies	Moderate
Robertson et al. [29]	2019	Systematic review	7	254	1 RCT 6 Retrospective cohort studies	From 2014 to 2019	Orthodontics and Craniofacial Research	To compare treatment effectiveness between clear aligner and fixed appliance therapies	Moderate
Rossini et al. [29]	2015a	Systematic review	11	480	2 RCTs 5 Prospective studies 4 Retrospective studies	Up to June 15, 2014	The Angle Orthodontics	To assess the efficacy of clear aligners in controlling orthodontic tooth movement	Moderate

**Table 1** (continued)

Author	Year	Study design	No. of studies	No. of participants	Type of studies	Period of search	Journal	Objective	Quality of evidence
Galan-Lopez et al. [30]	2019	Systematic review	20	1508	1 Systematic review 7 Prospective clinical trial 2 Retrospective clinical trial 6 Retrospective cohort study 4 Retrospective case series	From August 2007 to August 2017	The Korean Journal of Orthodontics	To assess the accuracy and efficiency of dental movements with Invisalign®	Moderate
Mortazavi et al. [31]	2020	Systematic review	18	637	15 Retrospective studies 1 Observational study 1 Prospective clinical trial 1 RCT	From 2014 to December 2020	Journal of Craniomaxillofacial Research	To assess the effectiveness of clear aligner therapy	Low
Koletsis et al. [32]	2021	Systematic review and meta-analysis	7 (3 for meta-analysis)	202 patients (teeth)	4 Retrospective cohort 3 Prospective cohort	Up to August 4, 2020	Journal of Orthodontics	Predictability of rotational tooth movement with orthodontic aligners comparing software-based and achieved data	Moderate
Rossini et al. [33]	2015b	Systematic review	5	173	1 RCT 4 Prospective studies	From January 1945 to September 2014	European Journal of Orthodontics	To assess periodontal health during CAT and FAT	Moderate
Jiang et al. [34]	2018	Systematic review and meta-analysis	8 (5 for meta-analysis)	464	3 RCTs 7 Cohort studies	Up to August 14, 2017	Journal of the American Dental Association	To assess periodontal health during CAT and FAT	Moderate
Lu et al. [35]	2018	Systematic review and meta-analysis	7	368	7 Prospective cohort studies	Up to October, 2017	Medicine	To assess periodontal health during CAT and FAT	Moderate
Elhaddaoui et al. [36]	2017	Systematic review	3	217	1 RCT 1 NRCT 1 Retrospective cohort study	Up to December, 2015	International Orthodontics	To compare the incidence and severity of OIHR caused by aligners with that caused by fixed appliance	Critically Low

Table 1 (continued)

Author	Year	Study design	No. of studies	No. of participants	Type of studies	Period of search	Journal	Objective	Quality of evidence
Aldeeri et al. [37]	2018	Systematic review	2	87	1 RCT 1 Retrospective Cohort study	1980 to June, 2017	The Journal of Contemporary Dental Practice	To compare OIIRR between clear aligners and fixed appliance	Moderate
Fang et al. [38]	2019	Systematic review and meta-analysis	11 (3 for meta-analysis)	1026	4 Cohort studies 1 Case-control study 6 Before and after studies	Up to December, 2018	Orthodontics and Craniofacial Research	To compare OIIRR between clear aligners and fixed appliance	Moderate
Gandhi et al. [39]	2021	Systematic review and meta-analysis	16	523	4 Prospective studies 12 Retrospective studies	Up to December 31, 2019	European Journal of Orthodontics	To compare OIIRR between clear aligners and fixed appliance	Moderate
Cardoso et al. [40]	2020	Systematic review	7	533	1 RCT 5 NRCT 1 Cross-sectional study	Up to February, 2019	Progress in Orthodontics	To compare pain level between CAT and FAT	Moderate
Pereira et al. [41]	2020	Systematic review and meta-analysis	5	273	1 RCT 4 Prospective studies	Up to May, 2020	Applied Sciences	To compare pain level between CAT and FAT	High
Zhang et al. [42]	2020	Systematic review	2	102	1 Cohort study 1 Cross-sectional study	From January, 2000 to July, 2019	Orthodontics and Craniofacial Research	Effect of clear aligners on oral health-related quality of life	Moderate

RCT, randomized controlled trial; CCT, controlled clinical trial; NRCT, non-randomized controlled trial; OIIRR, orthodontically induced inflammatory root resorption

**Table 2** A Measurement Tool to Assess Systematic Reviews (AMSTAR 2) items

AMSTAR 2 Items	Meeting the criteria			
	Yes	Partial	Yes	No
1. Did the research questions and inclusion criteria for the review include the components of PICO?	18		3	
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	11			10
3. Did the review authors explain their selection of the study designs for inclusion in the review?	20		1	
4. Did the review authors use a comprehensive literature search strategy?	14	7		
5. Did the review authors perform study selection in duplicate?	17		4	
6. Did the review authors perform data extraction in duplicate?	14		7	
7. Did the review authors provide a list of excluded studies and justify the exclusions?	3	9		9
8. Did the review authors describe the included studies in adequate detail?	8	8		5
9. Did the review authors use a satisfactory technique for assessing the risk of bias in individual studies that were included in the review?	18	1		2
10. Did the review authors report on the sources of funding for the studies included in the review?	3			18
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	9			
12. If meta-analysis was performed, did the review authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis or other evidence synthesis?	8			1
13. Did the review authors account for risk of bias in individual studies when interpreting/ discussing the results of the review?	19			2
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	15			6
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	3			6
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	16			5

**Table 3** Level of evidence according to the AMSTAR 2 assessment tool

Level	Description
High	No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest
Moderate	More than one non-critical weakness*: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review
Low	One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest
Critically low	More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies

\*Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence

aligners (but mainly Invisalign®); therefore, the results can be inferred in general to Invisalign®, although other aligner types could confound the results.

### Treatment effectiveness/efficiency (CAT vs. FAT)

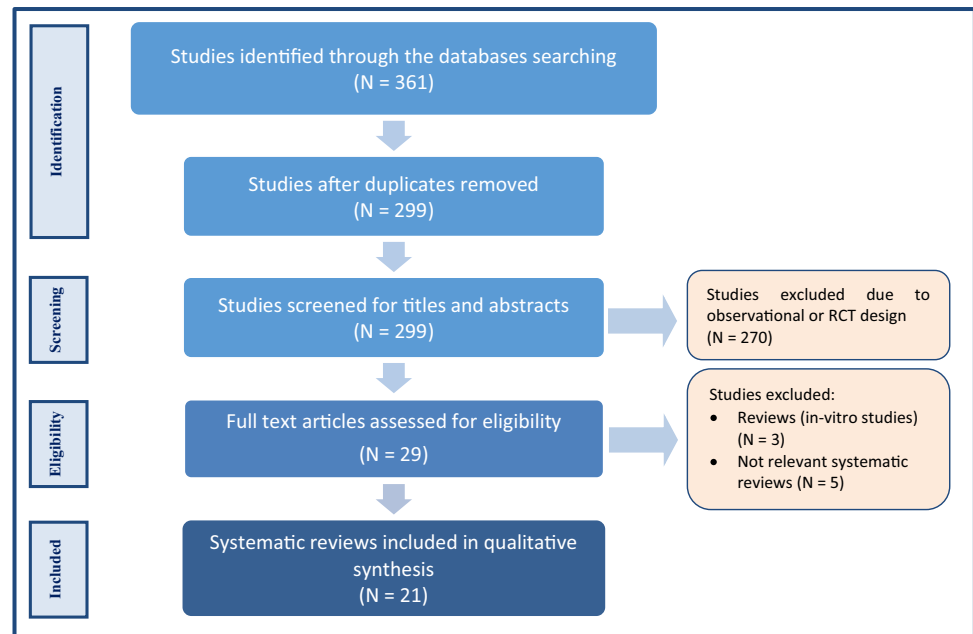
#### Treatment outcomes

It had been concluded that CAT is effective for mild to moderate cases of malocclusion in patients where simple tooth movement is required without the need of bodily/root

movement and/or extraction, while, it is not as successful as fixed appliances for more severe crowding and complex cases, especially when extractions are included [24, 27, 29]. Generally, in minor cases (without extraction), aligners can increase arch perimeter, but in severe crowding (greater than 6 mm), this can result in significant incisor proclination and protrusion which is neither desirable nor stable [24, 30].

The capability of achieving intrusion with CAT was found to be comparable to that of FAT. This can be explained by the ability of force application directed apically through the incisal edge with or without attachments. Therefore, mild

**Fig. 1** PRISMA flow diagram of the literature selection process



deep bite cases that can be treated with true intrusion can be managed with CAT. Paradoxically, extrusive movements have been found to be the least precisely achieved by CAT as it is difficult to apply the force in a suitable direction and magnitude to extrude teeth. Despite this neither the American Board of Orthodontics Cast-Radiograph Evaluation Index (ABO CR-EVAL) nor Peer Assessment Rating Index (PAR index) revealed any discrepancy with CAT in vertical tooth movement. Consequently, treatment of open bite cases that require extrusion of anterior teeth is still not recommended with CAT [29]. Galan-Lopez et al. (2019) [30] also agreed that one of least predictable movements by CAT is vertical movement, especially for posterior teeth. They recommended incorporation of attachments to improve outcomes. With fixed appliances, bracket position can be adjusted with or without the use of auxiliaries and elastics to intrude or extrude teeth as required. With aligners these movements, especially extrusion can be difficult to achieve. Besides, the presence of aligner material that covers the occlusal surfaces of the teeth as a physical barrier prevents adequate settling of the teeth during the finishing stage of treatment [25, 27]. This could explain the inability of CAT to establish adequate occlusal contacts, as found by several reviews [24–26, 30].

It was evident from the literature that there is limited control of rotational tooth movement with CAT for canines and premolars. This may be related to the difficulty in applying a force couple system on a round surface with an aligner [43, 45], but the use of IPR, attachments (vertical ellipsoid, centrally located) [45], overcorrection, and reduced staging to less than 1.5°/aligner can improve CAT ability to deliver such movement [24, 27, 29, 30].

Both controlled and uncontrolled tipping can be achieved by CAT. This is logical as tipping movements are the simplest types of tooth movement and can be achieved by applying a single force on the crown; however, the ability for bodily tooth movement is limited due to the difficulty in controlling root movement where a force couple is required [24–27, 29, 30]. Likewise, arch perimeter can be increased effectively with aligners by increasing intercanine, interpremolar, and intermolar widths [30], whereas arch expansion with bodily tooth movement represents one of the limitations of CAT [24, 29]. The main reason for the limitation in achieving bodily tooth movement is due to the difficulty in applying a moment of couple to control root movement with aligners. With fixed appliances, the predetermined tooth inclination (within the bracket) when using a rectangular wire can deliver not only tipping of teeth but also torquing of their roots [25]. The use of attachments (ellipsoid precision attachments) [46], altered aligner geometries, and reducing the amount of activation per aligner could improve root control [29]. In spite of this, it has been shown that aligners are capable of controlling bodily distalization of maxillary molars of 1.5 mm or  $\leq \frac{1}{2}$  cusp [24, 29, 30]. This may be due to the anatomy of the molar crown allowing greater engagement with the aligner to generate more complex forces.

Robertson et al. (2020) [28] found that CAT may produce clinically acceptable outcomes which are comparable to FAT regarding buccolingual inclination (torque) of maxillary incisors and proclination of mandibular incisors in mild to moderate malocclusions. Nevertheless, these findings were considered to be at a low level of evidence. Moreover, their finding of buccolingual inclination contradicts the abovementioned evidence. Hence a decision algorithm by



**Table 4** The results of the included systematic reviews in terms of CAT vs. FAT outcomes

Treatment effectiveness/efficiency (CAT vs. FAT)

**Treatment outcomes**

Leveling and aligning	It has been found that CAT is effective (as FAT) for aligning and leveling of dental arches of non-growing patients with mild to moderate malocclusions, especially when no extractions are required [24, 27, 29].
Anterior teeth intrusion and inclination	Both CAT and FAT were found to be comparable (with no significant differences) for anterior intrusion [29] and, with a low level of evidence, for buccolingual inclination (torque) of maxillary incisors, and proclination of mandibular incisors (in mild to moderate malocclusions) [28].
Overbite	Invisalign® can maintain normal overbite, but can only partially correct deep bite and open bite by mandibular incisor proclination and incisor extrusion, respectively [24].
Molar distalization	When molar distalization is required with Invisalign® treatment, it was found to be effective in controlling maxillary molar bodily movement of about 1.5 mm or $\leq \frac{1}{2}$ cusp [24, 29, 30]
Arch dimension	<b>Galan-Lopez et al.</b> [30]assessed the accuracy and efficiency of Invisalign® and found that Invisalign®, just like FAT, was capable of increasing intercanine, interpremolar, and intermolar dentoalveolar widths in the presence of crowding. While, [25]reported that CAT tended to increase mandibular intercanine width greater than FAT, and FAT was found to increase maxillary intercanine and interpremolar widths greater than CAT. Intermolar width and maxillary arch depth were changed similarly by both appliances
Relief of crowding	When treating severe crowding (greater than 6 mm), CAT is inferior to FAT as it results in significant incisor proclination and protrusion [24, 30]. CAT was also reported to increase tipping of mandibular canines and produce less proclination of mandibular incisors than FAT, however this was not statistically significant [25].

**Table 4** (continued)

## Treatment outcome indices

- Treatment outcome indices have been used to compare the two treatment techniques and reported by several systematic reviews. **Zheng et al.** [23] reported lower quality of treatment outcomes with CAT when compared to FAT using the American Board of Orthodontics Cast-Radiograph Evaluation (ABO CR-EVAL), however the authors highlighted that these results were not supported by sufficient evidence. Treatment effectiveness and efficiency was also evaluated in the meta-analysis by **Ke et al.** [25]. The authors reported that the quality of the treatment outcome did not significantly differ between CAT and FAT when using Peer Assessment Rating index (PAR) and the American Board of Orthodontics Cast-Radiograph Evaluation (ABO CR-EVAL). The meta-analysis of ABO CR-EVAL scores showed a mean difference of 8.38 points (95% CI: -0.17 to 16.93 points;  $P=0.05$ ) in favor of the FAT. Moreover, it has been found that the CAT scores were consistently lower than that of FAT scores in the buccolingual inclination and occlusal contact components of the ABO CR-EVAL, and the proportion of cases that score below 30 points (passing level of ABO phase III examination) were less with CAT. On the other hand, the meta-analysis by **Papageorgiou et al.** [26] revealed that five of the eight components of the ABO CR-EVAL were finished significantly worse with CAT than with FAT: buccolingual inclination (mean difference: 0.78 points; 95% CI: 0.47 to 1.09 points), occlusal contacts (mean difference: 3.07 points; 95% CI: 0.56 to 5.58 points), occlusal relationship (mean difference: 0.99 points; 95% CI: 0.58 to 1.40 points), overjet (mean difference: 1.81 points; 95% CI: 0.63 to 2.99 points), and root angulation (mean difference: 0.79 points; 95% CI: 0.48 to 1.10 points). Additionally, the overall ABO scores were significantly worse with CAT than that with FAT (mean difference 9.91 points; 95% CI: 3.62 to 16.21 points), and patients who were treated with aligners were significantly more likely to be finished to an unacceptable quality according to the ABO standards and fail the ABO examination criteria (ABO CR-EVAL score > 30 points) compared to those treated with fixed appliances
- However, when the PAR index was used, no significant differences were reported between CAT and FAT in terms of post-treatment scores, PAR reduction, or proportions of patients that received great improvement in PAR scores (PAR score reduction of at least 22 points or PAR score of 0 post-treatment) [26]. In the systematic review by **Pithon et al.** [27], regarding the ABO CR-EVAL scores, both the CAT and FAT passed according to this index for treating class I malocclusion, however CAT group was worse at achieving proper buccolingual inclination and occlusal contact of teeth with some limitations in terms of anteroposterior and vertical tooth movement

**Table 4** (continued)

## Outcomes in general

- In general, CAT was less effective and inferior to FAT in the following: vertical tooth movements (especially extrusion), rotational movements (especially of rounded teeth, hence IPR is recommended, especially in canines and when there is crowding), controlling root movement/buccolingual inclination, achieving adequate occlusal contacts, expansion of the arch by bodily tooth movement, and expression of the fully programmed tooth movement [24, 27, 29, 30].
- The accuracy of Invisalign® (evaluated as the deviation between the achieved and the planned tooth movements) showed conflicting results from sufficient to insufficient and this could be related to a varying ability of this appliance to achieve different types of tooth movements [24, 30]. The systematic review by Robertson et al. [28] compared *predicted* versus *achieved* tooth movements with CAT and found that most of the predicted tooth movements may not be achieved as planned, with some exception of minor horizontal tooth movement. Koletsi et al. [43] found (with the use of simulation programs) inaccurate prediction of rotational tooth movements especially for canines (maxillary canines: 47.9%, mandibular canines: 49.9%)

**Treatment duration**

- Zheng et al. [23] concluded that the main advantage of CAT over FAT was in treatment time in mild to moderate cases; CAT required significantly less appointments by approximately 4 appointments, less emergency appointments by 1 appointment, less emergency chair time by 7 min, less total chair time by 93.4 min, and shorter overall treatment duration (mean difference 0.5 months; 95% CI: 0.26 to 1.29). However, these findings were based on several cross-sectional studies. The systematic review by Papadimitriou et al. [24] showed that treatment duration tended to be shorter with Invisalign® unless where extractions are indicated (complex cases) which required longer duration. The meta-analysis by Ke et al. [25] revealed that CAT was associated with statistically significant shorter treatment duration compared to FAT (mean difference 6.31 months, 95% CI: 4.24 to 8.37 months)
- Three systematic reviews (one with meta-analysis) found that the results comparing treatment duration with CAT and that with FAT were insignificant, unclear, and conflicting [26, 27, 30]. The majority of tooth movements with Invisalign® occur during the first week of each aligner wear, and affecting factors such as age, gender, bone quality, tooth length, location of center of resistance, and systemic factors should be considered [30].

**Treatment stability**

- All the systematic reviews that evaluated post-treatment stability (1–3 years post-treatment) ended up with finding greater relapse and a higher tendency of recurrence of crowding with CAT than that with FAT [23–25, 27, 29, 30]. However, Zheng et al. [23] downgraded the level of evidence regarding this finding
- Galan-Lopez et al. [30] concluded that although it is possible to treat complex malocclusions with clear aligners, the results are still less accurate and less stable than those achieved with fixed appliances. The meta-analysis by [25] evaluated post-retention dental changes of treated patients with ABO CR-EVAL and found non-significant results but there was more relapse in alignment for patients who were treated with clear aligners

**Periodontal health (CAT vs. FAT)**

- It has been found that periodontal health, the quantity and quality of plaque were more favorable during CAT than during FAT, with a significant decrease of periodontal indices (plaque index, gingival index, bleeding on probing, papillary bleeding index, probing pocket depth, sulcus probing depth) [33]
- The meta-analysis by Jiang et al. [32] revealed that CAT is associated with significantly better periodontal health when compared to FAT in terms of; significantly lower plaque index scores (mean difference 0.53, 95% CI: 0.20 to 0.85), significantly lower gingival index scores (mean difference 0.27, 95% CI: 0.17 to 0.37), and significantly lower probing depth values (mean difference 0.35, 95% CI: 0.03 to 0.67). Lu et al. [35], in their meta-analysis, also found that Invisalign® patients have better periodontal health than fixed appliance patients. Their results for the gingival index and sulcus probing depth were comparable to the former meta-analysis but were not statistically significant. However, subgroup analysis revealed a significant lower level of sulcus probing depth at six months in the Invisalign® group when measured using the Ramfjord index (mean difference 0.74, 95% CI: 0.12 to 1.35). For the plaque index the results were significantly lower in the Invisalign® group at one month (mean difference 0.53, 95% CI: 0.18 to 0.89), three months (mean difference 0.69, 95% CI: 0.27 to 1.12), and six months (mean difference 0.91, 95% CI: 0.35 to 1.47). Additionally, there was a significantly lower sulcus bleeding index for patients treated with Invisalign® at one month (mean difference 0.44, 95% CI: 0.19 to 0.70), three months (mean difference 0.49, 95% CI: 0.05 to 0.93), and six months (mean difference 0.40, 95% CI: 0.07 to 0.73)
- Papageorgiou et al. [26] reported, with limited evidence, that there were no significant differences between CAT and FAT in the development of gingival recession (two years after treatment), periodontal probing depth, and alveolar bone level

**Table 4** (continued)**Root resorption (CAT vs. FAT)**

- The incidence and severity of root resorption were found to be lower with aligners than with fixed appliances and to be comparable to the resorption with light forces of fixed appliances [37]. The meta-analysis by **Fang et al.** [38] reported that generally for all incisors there was significantly less root resorption with CAT than with FAT (mean difference 0.65 mm, 95% CI: 0.55 to 0.74 mm). Similarly, the difference for each incisor showed also significantly less root resorption with CAT compared to FAT (maxillary central incisor: mean difference 0.61 mm, 95% CI: 0.27 to 0.95 mm; maxillary lateral incisor: mean difference 0.61 mm, 95% CI: 0.44 to 0.79 mm; mandibular central incisor: mean difference 0.53 mm, 95% CI: 0.18 to 0.89 mm; and mandibular lateral incisor: mean difference 1.06 mm, 95% CI: 0.86 to 1.26 mm). On the other hand, **Gandhi et al.** [39] could not find a significant difference between the two types of appliances in terms of overall amount of root resorption for the four maxillary incisors (CAT: 0.44 mm, 95% CI: 0.00 to 0.89 mm; FAT: 0.52 mm; 95% CI: 0.20 to 0.83 mm; mean difference 0.19 mm, 95% CI: 0.39 to 0.77 mm). Nonetheless, there was only significantly less root resorption with CAT than with FAT for the maxillary right lateral incisor (mean difference 0.41 mm, 95% CI: 0.15 to 0.67 mm), but not for the other maxillary incisors
- **Papageorgiou et al.** [26] also reported a significantly smaller percentage of incisor root resorption with CAT compared to FAT, but this was from a single study (mean difference 1.8%, 95% CI 1.3% to 2.4%)

**Oral health-related quality of life (CAT vs. FAT)**

- Generally, it has been found that orthodontic patients treated with Invisalign® tend to report lower pain levels than those treated with fixed appliances especially during the first week of treatment. Later during treatment, the differences seem to disappear. Furthermore, analgesic consumption, soft tissue irritation, and eating disturbances were found to be lower for patients treated with Invisalign®, and those patients also presented a better response in terms of eating and chewing. However, in the above finding no evaluation was carried out regarding the complexity of malocclusion and its relation to pain [40]. The meta-analysis by **Pereira et al.** [41] also found that there was a significant difference between CAT and FAT, where patients with CAT experienced less pain and consumed less analgesics than those with FAT, especially during the first week of treatment
- **Zhang et al.** [42] reported (with weak evidence) that CAT might be associated with significantly less negative impact on eating disturbance (difficulties in eating and chewing, reduced enjoyment of food and change of taste) than FAT. However, there were no significant differences between the two groups in pain, psychosocial improvement, general and social performance. Oral discomfort (oral symptoms on the tongue, cheek, or lip, bad tastes/smells, and food accumulation) tended to be lower with CAT compared to FAT

Jadad et al. (1997) [47] has been applied, indicating that the evidence of the inferior buccolingual inclination control by CAT which was supported by a greater number of systematic reviews which included studies with higher levels of evidence should be accepted.

According to the ABO CR-EVAL index, treatment outcomes were worse with CAT than with FAT, especially when treatment included extractions. This is due to difficulty in achieving complex tooth movements with aligners. However, **Zheng et al.** (2017) [23] in their meta-analysis could not reach a clear conclusion regarding which technique is better because of insufficient evidence. On the other hand, the meta-analysis by **Ke et al.** (2019) [25] found that both CAT and FAT did not show statistically significant differences in the quality of treatment outcomes measured with the ABO CR-EVAL and PAR indices. Nevertheless, by looking at the mean difference of the ABO CR-EVAL index, which is 8.38 points (95% CI –0.17 to 16.93), in favor of FAT, this could be of clinical significance as it has been determined that a score difference of five points can be considered to be of clinical importance [48]. Moreover, the consistently lower scores in the buccolingual inclination and occlusal contact with CAT may highlight the limitation of CAT in achieving root control and extrusion movement as noted above, agreeing with other reviews [24, 26, 27, 30]. The meta-analysis by **Papageorgiou et al.** (2019) [26] found a mean difference of 9.91 points when using ABO CR-EVAL in favor of FAT,

which is comparable to that of **Ke et al.** (2019) [25]. This was considered of statistical and clinical significance. It is worth noting that the meta-analysis by **Papageorgiou et al.** (2019) [26] included 11 studies (including four RCTs), while that by **Ke et al.** (2019) [25] included five studies (including two RCTs). Therefore, the evidence of the **Papageorgiou et al.** (2019) [26] study can be deemed to be of a higher level. The lower quality of finish with CAT compared to FAT in terms of unacceptably finished cases (score > 30 points) or with significantly worse occlusal outcomes (with the ABO CR-EVAL index) is in line with other reviews regarding the limitations of CAT. On the other hand, the non-significant difference between CAT and FAT in the PAR scores may be attributed to several reasons. The ABO index included greater and more objective components that provide a detailed assessment of tooth relationship in all three planes (first, second, and third order), while the PAR index provides a less detailed assessment of occlusion and neglects some important aspects such as buccolingual inclination, root angulation, occlusal contacts, interproximal contacts, and leveling of posterior teeth [26]. Therefore, it would not be expected to find the same result for these indices as it has been noted that they are not significantly correlated [49, 50]. The systematic review by **Pithon et al.** (2019) [27] reported from one RCT that both CAT and FAT groups were successful with the ABO CR-EVAL scores (achieved scores below 30 points), but this was only for class I malocclusion

cases, and also noted the CAT group had worse scores in the buccolingual inclination and occlusal contact components, and to some extent in the overjet and occlusal relationship components.

It should be kept in mind that patient's motivation and compliance with wearing aligners could have an impact on the treatment outcome and explain in part the comparison with the FAT.

All the above findings can also explain the variation in the accuracy of CAT (i.e., the amount of deviation between the achieved and the planned tooth movements) [24, 30]. Many of the predicted tooth movements are not achieved as planned with CAT, with some exceptions, notably minor horizontal tooth movement [28]. Koletsi et al. (2021) [43] found that prediction of rotational tooth movements with CAT did not appear accurate, especially for canines and for rotational movement of more than 15°. However, Galan-Lopez et al. (2019) [30] mentioned that the precision of tooth movement and malocclusion correction have improved with the development of new generations of aligners (for example those launched after Invisalign G5 in 2014), although these still do not reach the accuracy of FAT yet. Future further improvement in aligner design, materials, computer programming, and attachments could enhance the ability to perform difficult tooth movement and overcome these limitations.

### Treatment duration

Total treatment duration was reported to be shorter with CAT, but this was mainly for mild to moderate cases, as any extractions can render treatment with aligners longer than that with FAT. This can be explained by the difficulties in achieving bodily or root movement with aligners as most extraction or complex cases require root torquing or uprighting movement which was found to be limited with aligners [23–25]. Similarly, it would be expected that CAT is associated with significantly less chair time, fewer appointments, and less emergency visits than FAT. From the initial appointment, aligners need reduced chair time for insertion compared to direct bracket bonding. Moreover, aligners usually require less adjustment than fixed appliances which require adjustment of archwires and/or brackets at each appointment. The regular interval between appointments with CAT is 10–12 weeks, while with FAT it is 4–8 weeks and this explains the difference in the appointment number. Regarding emergency visits, it is uncommon to experience emergencies with CAT due to the flexibility of the material with a relatively short wear time for each set of aligners, and adding fewer auxiliaries that are prone to breakage. This compares with FAT with brackets and tubes/bands that can become debonded. Also, the removal of aligners during

eating reduces the risk of breakage when compared to fixed appliances [23].

The conflicting findings regarding treatment duration between CAT and FAT, from three reviews [26, 27, 30], was due to heterogenous results from different study designs. Therefore, the appliance alone may not be the key influence on treatment duration but this could also be due to different patient- and treatment-related factors that were not investigated in the available studies. For example, severity of malocclusion, extractions, patient age, gender, and compliance. These factors can influence treatment duration even when the appliance is not a variable [30, 51].

### Treatment stability

Despite the ability to align teeth with mild to moderate crowding effectively, the tendency for relapse was shown to be higher with CAT than with FAT. This may be related to the limitation of CAT in obtaining solid occlusal contact and controlling root movement which in turn could increase the tendency of teeth to return to their original position. Therefore, the full sequence of tooth tipping and root uprighting that usually occurs with FAT does not occur with CAT [23–25, 27, 29, 30]. In addition to the above, the tendency of aligners to increase proclination of mandibular canines and mandibular intercanine width is greater than with FAT [25] and produces significant proclination of incisors when severe crowding cases are treated [24, 30]. Therefore, this may position the canines and incisors in a less stable zone and increase the probability of relapse. As alveolar bone resorption requires 7–14 days and almost an equal time is needed for periodontal tissue regeneration, Zheng et al. (2017) [23] and Ke et al. (2019) [25] postulated that this higher tendency of relapse with CAT could be related to the relatively short time for progressing aligners every 2 weeks. This frequent activation produces undermining resorption, root and bone resorption by truncating the repair process which leads to poor bone formation and greater relapse than with fixed appliances which are usually adjusted every 4–8 weeks. This postulation should be considered in detail, but it can also be refuted when other findings regarding orthodontically induced inflammatory root resorption (OIIRR) is regarded in the current overview. CAT was found to deliver a force comparable to that of the light forces with fixed appliances and a lower risk of root resorption.

The recent decision by Align Technology for weekly aligner changes is not to be recommended due to the problems of inadequate tooth adaptation, recovery from the force applied, and consequently reduced stability. Overcorrection is therefore recommended to decrease the relapse with CAT [30].

## Periodontal health (CAT vs. FAT)

The majority of periodontal health problems with orthodontic treatment are related to plaque retention and inadequate oral hygiene measures. The finding that CAT was associated with lower scores of periodontal indices, more favorable quality and quantities of plaque which overall result in better periodontal health as compared to FAT can be explained as follows. The removable nature of aligners allows adequate tooth brushing, dental flossing, and extra-oral appliance cleansing. The smooth surfaces of aligners also play an important role in reducing plaque retention. In contrast, plaque retention with fixed appliance components is greater and these components can decrease natural self-cleansing by the saliva and tongue and impede toothbrushing and maintaining adequate oral hygiene [33–35]. The longer the time of plaque retention, the greater the possibility of more harmful plaque quality, and hence periodontal breakdown [33]. It is worth mentioning that in both treatment modalities good oral health is required to maintain periodontal health; moreover, periodontitis is a contraindication to start orthodontic treatment, irrespective of the type of appliance used.

The outcome of the systematic review by Rossini et al. (2015b) [33] (CAT is associated with better periodontal health outcomes than FAT) was further confirmed in two meta-analyses [34, 35]. The quality of evidence of these reviews was considered to be of moderate level. On the other hand, the meta-analysis by Papageorgiou et al. (2019) [26] reported no significant differences between these two treatment techniques in terms of gingival recession (2 years after treatment) and periodontal health. However, the evidence regarding these findings was limited as each was derived from a single study. Generally, gingival recessions do not result from orthodontic treatment, as long as correct biomechanics considering individual anatomical borders are applied.

An important point raised by Jiang et al. (2018) [34] is the need to measure periodontal health status before and after treatment in order to ensure adequate blinding without any chance of identifying the identity of the appliance used as well as assessing the periodontal health status over a long-term follow-up.

The effect of orthodontic appliances on periodontal health depends on the forces that are applied. This is influenced by the magnitude of tooth movement and in the case of aligners that are not constructed by the clinician, the level of forces is unknown. Variability in FAT due to labial or lingual appliances, use of the 0.018 or 0.022-inch slot and other factors can influence force levels.

## Root resorption (CAT vs. FAT)

The evidence related to OIIRR with aligners is scarce, however all of the available studies have revealed that aligners are associated with a lower risk of OIIRR when compared to fixed appliances [26, 37, 38, 52, 53], and this may be due to the nature of intermittent (due to occasional removal during food consumption and hygiene maintenance) and relatively light forces with aligners, as well as the simpler types of tooth movement which result in smaller amounts of tooth movement/apical displacement (approximate velocity 0.5 mm/month for CAT and 1 mm/month for FAT). Hence, there is a greater chance of root healing by promoting the cementum repair process. Moreover, aligners are usually indicated for cases with minor crowding where no extractions are indicated and with shorter treatment duration [38, 39, 54]. Aligners are also subject to patient compliance, and any lack of compliance results in more intermittent force delivery with shorter duration of force application resulting in reduced OIIRR [55], but this may also produce jiggling forces which may increase the risk of OIIRR [38]. This may not be easily determined and hence is not readily reported [53]. The most recent systematic review and meta-analysis could not find a significant difference between preadjusted edgewise fixed appliance and aligners in terms of OIIRR, except for the maxillary right lateral incisor which showed reduced OIIRR with aligners. However, the level of incisor root resorption was not of clinical significance (less than 1 mm) [39]. It has been highlighted that the variation in the detection methods of OIIRR (such as periapical radiographs, orthopantomogram, cephalometric radiographs, microscopic investigation, and CBCT) could influence the results of the available studies among other factors that could produce risk of bias to the outcomes [37–39].

In light of the above, the comparison between CAT and FAT regarding OIIRR should be interpreted with caution [38, 53], especially because these two treatment techniques differ in their indications, treatment duration, and mechanism of action [26].

## Oral health-related quality of life (CAT vs. FAT)

Pain and discomfort represent two important aspects that can affect quality of life [56], and fear of pain is one of the reasons for rejection or discontinuation of treatment [57]. The highest level of pain perception is usually felt during the initial phase/days of treatment, due to release of inflammatory mediators such as prostaglandin E and interleukin 1 $\beta$  as a result of the initial orthodontic forces that compress the periodontal ligament and lead to ischemia, edema, and release of these mediators (which sensitize nociceptors of the periodontal ligament). The level of these mediators reaches their peak during the first 24 h after the onset of orthodontic

force and returns to normal level after about 7 days [58–60]. Patients who have been treated with aligners reported lower levels of pain during the first few days of treatment than those who were treated with fixed appliances [40, 41]. This can be attributed to several reasons. The lower level of pain associated with aligners may be related to the removable nature of the appliance and therefore the intermittent forces which produce less pressure, tension, and sensitivity than the continuous forces with fixed appliances [61]. Additionally, aligners can be removed by patients when they feel pain in order to relieve it, thus reducing pain experience by patients [40]. Consequently, this may explain the lower consumption of analgesics by patients treated with aligners.

The systematic review by Zhang et al. (2020) [42] found no significant differences in pain perception between CAT and FAT, but their results were only obtained from one cohort and one cross-sectional study and this could explain the minor differences, if present, between the two appliances. Interestingly, the meta-analysis by Pereira et al. (2020) [41] reported that placing attachments at the beginning of CAT is associated with higher pain perception due to greater pressure applied at the insertion of an aligner. Generally, pain perception is a subjective process and the difference between CAT and FAT was not noted in the medium or longer term (after the first month). Moreover, pain is influenced by several factors, such as age, gender, pain threshold, magnitude of force applied, emotional status, cultural differences, and individual's personality [40, 41].

Zhang et al. (2020) [42] concluded that the difference between CAT and FAT on the overall OHRQoL was not conclusive due to lack of evidence. However, their results, from two studies, regarding eating and chewing disturbance and discomfort during treatment was in favor of CAT. This can be related to the difference in the design of two appliances, where the aligners can be removed during eating and allow normal function without the possibility of food accumulation around the appliance or fear from appliance breakage. Similarly, the smooth surfaces and margins of aligners can allow lower oral symptoms on the tongue, cheek, and lips compared to fixed appliances.

It is worth noting that in addition to different sources of bias, variation in types of appliances, sequence of archwires, type of malocclusion, and consumption of analgesics could have influenced the results of individual studies [40, 41].

### Strengths and limitations

The protocol of this overview has been registered a priori [62]. This overview has been conducted following the PRISMA guidelines and using the AMSTAR 2 quality assessment tool to evaluate the published systematic reviews concerning the comparison of CAT with FAT. The number of the included systematic reviews in this

discussion was considerable (18 systematic reviews). These were only of moderate- and high-quality level reviews in order to keep the level of evidence as high as possible.

Several limitations have been identified by the included systematic reviews as follows:

1. There are few prospective RCTs that investigated the difference between CAT and FAT. With many of the available studies are retrospective in design or case reports.
2. The available studies are influenced by different types of bias due to the followings:
  - Lack of randomization and allocation concealment (selection bias).
  - Lack of blinding (detection bias).
  - Lack of adequate experience with CAT and lack of standardized treatment protocol (performance bias).
  - Several potential confounders were not considered in the available studies and could bias their results. For example, severity of malocclusion, oral hygiene, patient's compliance, number of aligners, aligner change frequency, psychosocial status, and other patient and treatment-related factors.
  - Inadequate power (due to small sample size) and lack of method of error analysis of the clinical studies.
  - The majority of studies with CAT investigated mild to moderate malocclusion only.
  - Heterogeneity in terms of methodology, outcome reporting, types of fixed appliances, and types aligners used (like Invisalign®, Smart Track®, ClearSmile®, F22 aligner, and Nuvola system). However, most of them investigated Invisalign® only and this might cause some bias as only a specific material and planning software were used.
  - The continuous improvement of the aligners may hamper the direct comparison between older studies with the most recent ones. Robertson et al. (2020) [28] stated that the difference in aligner production processes and material properties can affect the force levels and thus, the predictability of tooth movements.
  - Variation in the detection methods of OIIRR.
  - Few validated OHRQoL instruments used, in addition to their heterogeneity in terms of types and time of assessment
3. The comparison of cost effectiveness was not undertaken yet between CAT and FAT.

Therefore, owing to the above limitations, the results should be considered with caution as further studies may alter the findings.

## Suggestions for future studies

The following suggestions can be made. Further high-quality RCTs that follow the CONSORT statement with rigorous methodology and appropriate sample sizes are needed to further evaluate the treatment effectiveness of CAT with FAT. These trials should assess the most recent aligners, include different types of malocclusion, control confounding variables, use ABO CR-EVAL (to evaluate treatment outcomes and post-treatment retention), measure periodontal health status before and after treatment, use CBCT (to evaluate root resorption where appropriate), and use a validated tool to assess OHRQoL.

## Clinical recommendations

1. Based on to the available evidence, aligners are indicated in the following cases:
  - Patients with mild-to-moderate malocclusion (especially in non-extraction cases or where extrusive, severe rotation, bodily, and root movements are not required).
  - Minor relapse post-orthodontic treatment.
  - Patients with compromised periodontal health.
  - Patients who have social or emotional problems with fixed appliances.
2. The orthodontist should have sufficient knowledge and clinical experience before practicing CAT.
3. The use of precision attachments, IPR, and reduction of the amount of activation/aligner are important and should be used to achieve adequate control of tooth movement.
4. Overcorrection should be considered when using CAT to reduce the impact of relapse.

## Conclusions

According to the available evidence, the following conclusions can be drawn:

1. The level of evidence regarding CAT is moderate.
2. Aligners can be a successful alternative to fixed appliances to treat patients with mild to moderate malocclusion.
3. The quality of treatment with CAT is inferior to that of FAT in the following clinical conditions:
  - Severe malocclusion cases (including extraction cases)

- When extrusion, severe rotation, bodily tooth movement including expansion, and root movements are required
4. The accuracy of CAT can be improved with the utilization of advanced computer programming, improvement in aligner design and materials, reduced amount of activation of each aligner, and use of precision attachments and IPR.
  5. There is inconclusive evidence regarding treatment duration with CAT; however, it tends to be shorter than that with FAT in mild to moderate cases and longer in severe cases.
  6. The tendency of relapse is greater with CAT.
  7. Aligners can allow better maintenance of oral hygiene and hence better periodontal health status compared to FAT.
  8. Due to the intermittent force and mild-to-moderate malocclusions that can be treated with CAT, the risk of OIIRR tends to be lower with CAT and is comparable to that of light forces in FAT.
  9. Due to the nature of aligners, CAT can be considered more comfortable for patients and with minimal impact on eating, chewing, and OHRQoL compared to FAT.

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## Declarations

**Conflict of interest** The authors declare no competing.

## References

1. Bollen A-M, Cunha-Cruz J, Bakko DW, Huang GJ, Hujoel PP (2008) The effects of orthodontic therapy on periodontal health: a systematic review of controlled evidence. *J Am Dent Assoc* 139(4):413–422. <https://doi.org/10.14219/jada.archive.2008.0184>
2. Ren Y, Jongsma MA, Mei L, van der Mei HC, Busscher HJ (2014) Orthodontic treatment with fixed appliances and biofilm formation: a potential public health threat? *Clin Oral Investig* 18(7):1711–1718. <https://doi.org/10.1007/s00784-014-1240-3>
3. Sandić MZ, Popović B, Carkić J, Nikolić N, Glišić B (2014) Changes in subgingival microflora after placement and removal of fixed orthodontic appliances. *Srp Arh Celok Lek* 142(5–6):301–305. <https://doi.org/10.2298/SARH1406301Z>
4. Fujiyama K, Honjo T, Suzuki M, Matsuoka S, Deguchi T (2014) Analysis of pain level in cases treated with Invisalign aligner: comparison with fixed edgewise appliance therapy. *Prog Orthod* 15(1):64. <https://doi.org/10.1186/s40510-014-0064-7>
5. Azaripour A, Weusmann J, Mahmoodi B, Peppas D, Gerhold-Ay A, Van Noorden CJF, Willershausen B (2015) Braces versus Invisalign®: gingival parameters and patient's satisfaction during treatment: a cross-sectional study. *BMC Oral Health* 15(1):69. <https://doi.org/10.1186/s12903-015-0060-4>



6. White DW, Julien KC, Jacob H, Campbell PM, Buschang PH (2017) Discomfort associated with Invisalign and traditional brackets: a randomized, prospective trial. *Angle Orthod* 87(6):801–808. <https://doi.org/10.2319/091416-687.1>
7. Kesling HD (1945) The philosophy of the tooth positioning appliance. *Am J Orthod Oral Surg* 31(6):297–304. [https://doi.org/10.1016/0096-6347\(45\)90101-3](https://doi.org/10.1016/0096-6347(45)90101-3)
8. Sheridan JJ, LeDoux W, McMinn R (1993) Essix retainers: fabrication and supervision for permanent retention. *J Clin Orthod* 27(1):37–45. <https://doi.org/10.5005/jp-journals-10021-1138>
9. Meier B, Wiemer KB, Miethke RR (2003) Invisalign: patient profiling-analysis of a prospective survey. *J Orofac Orthop* 64(5):352–358. <https://doi.org/10.1007/s00056-003-0301-z>
10. Kuo E, Miller RJ (2003) Automated custom-manufacturing technology in orthodontics. *Am J Orthod Dentofacial Orthop* 123(5):578–581. <https://doi.org/10.1067/mod.2003.S0889540603000519>
11. Buschang PH, Shaw SG, Ross M, Crosby D, Campbell PM (2014) Comparative time efficiency of aligner therapy and conventional edgewise braces. *Angle Orthod* 84(3):391–396. <https://doi.org/10.2319/062113-466>
12. Kravitz ND, Kusnoto B, BeGole E, Obrez A, Agran B (2009) How well does Invisalign work? A prospective clinical study evaluating the efficacy of tooth movement with Invisalign®. *Am J Orthod Dentofacial Orthop* 135(1):27–35. <https://doi.org/10.1016/j.ajodo.2007.05.018>
13. Krieger E, Seiferth J, Saric I, Jung BA, Wehrbein H (2011) Accuracy of Invisalign® treatments in the anterior tooth region. First results *J Orofac Orthop* 72(2):141–149. <https://doi.org/10.1007/s00056-011-0017-4>
14. Krieger E, Seiferth J, Marinello I, Jung BA, Wriedt S, Jacobs C, Wehrbein H (2012) Invisalign® treatment in the anterior region: were the predicted tooth movements achieved? *J Orofac Orthop* 73(5):365–376. <https://doi.org/10.1007/s00056-012-0097-9>
15. Flores-Mir C, Brandelli J, Pacheco-Pereira C (2018) Patient satisfaction and quality of life status after 2 treatment modalities: Invisalign and conventional fixed appliances. *Am J Orthod Dentofacial Orthop* 154(5):639–644. <https://doi.org/10.1016/j.ajodo.2018.01.013>
16. Abbate GM, Caria MP, Montanari P, Mannu C, Orrù G, Caprioglio A, Levrini L (2015) Periodontal health in teenagers treated with removable aligners and fixed orthodontic appliances. *J Orofac Orthop* 76(3):240–250. <https://doi.org/10.1007/s00056-015-0285-5>
17. Djeu G, Shelton C, Maganzini A (2005) Outcome assessment of Invisalign and traditional orthodontic treatment compared with the American Board of Orthodontics objective grading system. *Am J Orthod Dentofacial Orthop* 128(3):292–298. <https://doi.org/10.1016/j.ajodo.2005.06.002>
18. Giancotti A, Greco M, Mampieri G (2006) Extraction treatment using invisalign technique. *Prog Orthod* 7(1):32–43
19. Phan X, Ling PH (2007) Clinical limitations of Invisalign. *J Can Dent Assoc* 73(3):263–266
20. Pavoni C, Lione R, Laganà G, Cozza P (2011) Self-ligating versus Invisalign: analysis of dento-alveolar effects. *Ann Stomatol (Roma)* 2(1–2):23–27
21. Aligntech Institute: Tooth movement assessment. Available at: <https://s3.amazonaws.com/learn-invisalign/docs/us/ToothAssesment.pdf>. Accessed on 16<sup>th</sup> February, 2021.
22. Lagravere MO, Flores-Mir CF (2005) The treatment effects of invisalign orthodontic aligners. *J Am Dent Assoc* 136(12):1724–1729. <https://doi.org/10.14219/jada.archive.2005.0117>
23. Zheng M, Liu R, Ni Z, Yu Z (2017) Efficiency, effectiveness and treatment stability of clear aligners: a systematic review and meta-analysis. *Orthod Craniofac Res* 20(3):127–133. <https://doi.org/10.1111/ocr.12177>
24. Papadimitriou A, Mousoulea S, Gkantis N, Kloukos D (2018) Clinical effectiveness of Invisalign® orthodontic treatment: a systematic review. *Prog Orthod* 19(1):37. <https://doi.org/10.1186/s40510-018-0235-z>
25. Ke Y, Zhu Y, Zhu M (2019) A comparison of treatment effectiveness between clear aligner and fixed appliance therapies. *BMC Oral Health* 19(1):24. <https://doi.org/10.1186/s12903-018-0695-z>
26. Papageorgiou SN, Koletsi D, Iliadi A, Peltomaki T, Eliades T (2020) Treatment outcome with orthodontic aligners and fixed appliances: a systematic review with meta-analyses. *Eur J Orthod* 42(3):331–343. <https://doi.org/10.1093/ejo/cjz094>
27. Pithon MM, Baião FCS, Sant Anna LIDA, Paranhos LR, Cople Maia L (2019) Assessment of the effectiveness of invisible aligners compared with conventional appliance in aesthetic and functional orthodontic treatment: a systematic review. *J Investig Clin Dent* 10(4):e12455. <https://doi.org/10.1111/jicd.12455>
28. Robertson L, Kaur H, Fagundes NCF, Romanyk D, Major P, Flores Mir C (2020) Effectiveness of clear aligner therapy for orthodontic treatment: a systematic review. *Orthod Craniofac Res* 23(2):133–142. <https://doi.org/10.1111/ocr.12353>
29. Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi CL (2015) Efficacy of clear aligners in controlling orthodontic tooth movement: a systematic review. *Angle Orthod* 85(5):881–889. <https://doi.org/10.2319/061614-436.1>
30. Galan-Lopez LG, Barcia-Gonzalez JB, Plasencia E (2005) A systematic review of the accuracy and efficiency of dental movements with Invisalign. *Korean J Orthod* 49(3):140–149. <https://doi.org/10.4041/kjod.2019.49.3.140>
31. Mortazavi M, Naeim M, Badri A, Sharifi R, Hasheminasab M (2020) An updated systematic review on the effectivity of clear aligner therapy: a review. *J Craniomax Res* 7(4):165–177. <https://doi.org/10.18502/jcr.v7i4.5552>
32. Koletsi D, Iliadi A, Eliades T (2021) Predictability of rotational tooth movement with orthodontic aligners comparing software-based and achieved data: a systematic review and meta-analysis of observational studies. *J Orthod DOI*: <https://doi.org/10.1177/14653125211027266>.
33. Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi CL (2015) Periodontal health during clear aligners treatment: a systematic review. *Eur J Orthod* 37(5):539–543. <https://doi.org/10.1093/ejo/cju083>
34. Jiang Q, Li J, Mei L, Du J, Levrini L, Abbate GM, Li H (2018) Periodontal health during orthodontic treatment with clear aligners and fixed appliances. *J Am Dent Assoc* 149(8):712–720.e12. <https://doi.org/10.1016/j.adaj.2018.04.010>
35. Lu H, Tang H, Zhou T, Kang N (2018) Assessment of the periodontal health status in patients undergoing orthodontic treatment with fixed appliances and Invisalign system. *Medicine (Baltimore)* 97(13):e0248. <https://doi.org/10.1097/MD.00000000000010248>
36. Elhaddaoui R, Qoraich HS, Bahije L, Zaoui F (2017) Orthodontic aligners and root resorption: a systematic review. *Int Orthod* 15(1):1–12. <https://doi.org/10.1016/j.ortho.2016.12.019>
37. Aldeeri A, Alhammad L, Alduham A, Ghassan W, Shafshak S, Fatani E (2018) Association of orthodontic clear aligners with root resorption using three-dimension measurements: a systematic review. *J Contemp Dent Pract* 19(12):1558–1564. <https://doi.org/10.1016/j.ajodo.2014.12.026>
38. Fang X, Qi R, Liu C (2019) Root resorption in orthodontic treatment with clear aligners: a systematic review and meta-analysis. *Orthod Craniofac Res* 22(4):259–269. <https://doi.org/10.1111/ocr.12337>
39. Gandhi V, Mehta S, Gauthier M, Mu J, Kuo C, Nanda R, Yadav S (2021) Comparison of external apical root resorption with clear aligners and pre-adjusted edgewise appliances in non-extraction cases: a systematic review and meta-analysis. *Eur J Orthod* 43(1):15–24. <https://doi.org/10.1093/ejo/cjaa013>

40. Cardoso PC, Espinosa DG, Mecenas P, Flores-Mir CF, Normando D (2020) Pain level between clear aligners and fixed appliances: a systematic review. *Prog Orthod* 21(1):3. <https://doi.org/10.1186/s40510-019-0303-z>
41. Pereira D, Machado V, Botelho J, Proença L, Mendes JJ, Delgado AS (2020) Comparison of pain perception between clear aligners and fixed appliances: a systematic review and meta-analysis. *Appl Sci* 10:4276. <https://doi.org/10.3390/app10124276>
42. Zhang B, Huang X, Huo S, Zhang C, Zhao S, Cen X, Zhao Z (2020) Effect of clear aligners on oral health-related quality of life: a systematic review. *Orthod Craniofac Res* 23(4):363–370. <https://doi.org/10.1111/ocr.12382>
43. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group (2010) Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Int J Surg* 8(5):336–341. <https://doi.org/10.1016/j.ijsu.2010.02.007>
44. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA (2017) AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 358:j4008. <https://doi.org/10.1136/bmj.j4008>
45. Kravitz ND, Kusnoto B, Agran B, Viana G (2008) Influence of attachments and interproximal reduction on the accuracy of canine rotation with Invisalign. A prospective clinical study *Angle Orthod* 78(4):682–687. [https://doi.org/10.2319/0003-3219\(2008\)078\[0682:IOAAIR\]2.0.CO;2](https://doi.org/10.2319/0003-3219(2008)078[0682:IOAAIR]2.0.CO;2)
46. Hennessy J, Al-Awadhi EA (2016) Clear aligners generations and orthodontic tooth movement. *J Orthod* 43(1):68–76. <https://doi.org/10.1179/1465313315Y.0000000004>
47. Jadad AR, Cook DJ, Browman GP (1997) A guide to interpreting discordant systematic reviews. *CMAJ* 156(10):1411–1416
48. Yassir YA, El-Angbawi AM, McIntyre GT, Revie GF, Bearn DR (2019a) A randomized clinical trial of the effectiveness of 0.018-inch and 0.022-inch slot orthodontic bracket systems: part 2-quality of treatment. *Eur J Orthod* 41(2):143–153. DOI: <https://doi.org/10.1093/ejo/cjy038>.
49. Deguchi T, Honjo T, Fukunaga T, Miyawaki S, Roberts WE, Takano-Yamamoto T (2005) Clinical assessment of orthodontic outcomes with the peer assessment rating, discrepancy index, objective grading system, and comprehensive clinical assessment. *Am J Orthod Dentofacial Orthop* 127(4):434–443. <https://doi.org/10.1016/j.ajodo.2004.03.030>
50. Hong M, Kook YA, Baek SH, Kim MK (2014) Comparison of treatment outcome assessment for class I malocclusion patients: peer assessment rating versus American Board of Orthodontics-Objective Grading System. *J Korean Dent Sci* 7(1):6–15. <https://doi.org/10.4041/kjod.2016.46.4.199>
51. Yassir YA, El-Angbawi AM, McIntyre GT, Revie GF, Bearn DR (2019b) A randomized clinical trial of the effectiveness of 0.018-inch and 0.022-inch slot orthodontic bracket systems: part 1-duration of treatment. *Eur J Orthod* 41(2):133–142. DOI: <https://doi.org/10.1093/ejo/cjy037>.
52. Weltman B, Vig KWL, Fields HW, Shanker S, Kaizar EE (2010) Root resorption associated with orthodontic tooth movement: a systematic review. *Am J Orthod Dentofacial Orthop* 137(4):462–476. <https://doi.org/10.1016/j.ajodo.2009.06.021>
53. Roscoe MG, Meira JB, Cattaneo PM (2015) Association of orthodontic force system and root resorption: a systematic review. *Am J Orthod Dentofacial Orthop* 147(5):610–626. <https://doi.org/10.1016/j.ajodo.2014.12.026>
54. Yassir YA, McIntyre GT, Bearn DR (2020) Orthodontic treatment and root resorption: an overview of systematic reviews. *Eur J Orthod* cjaa058. DOI: <https://doi.org/10.1093/ejo/cjaa058>.
55. Currell SD, Liaw A, Blackmore Grant PD, Esterman A, Nimmo A (2019) Orthodontic mechanotherapies and their influence on external root resorption: a systematic review. *Am J Orthod Dentofacial Orthop* 155(3):313–329. <https://doi.org/10.1016/j.ajodo.2018.10.015>
56. Krukemeyer AM, Arruda AO, Inglehart MR (2009) Pain and orthodontic treatment patient experiences and provider assessments. *Angle Orthod* 79(6):1175–1181. <https://doi.org/10.2319/121308-632R.1>
57. Oliver RG, Knapman YM (2019) Attitudes to orthodontic treatment. *Brit J Orthod* 12(4):179–188. <https://doi.org/10.1179/bjo.12.4.179>
58. Furstman L, Bernick S (1970) Clinical considerations of the periodontium. *Am J Orthod* 61(2):138–155. [https://doi.org/10.1016/0002-9416\(72\)90092-9](https://doi.org/10.1016/0002-9416(72)90092-9)
59. Grieve WG III, Johnson GK, Moore RN, Reinhardt RA, Dubois LM (1994) Levels in gingival crevicular fluid during human orthodontic tooth movement. *Am J Orthod Dentofacial Orthop* 105(4):369–374. [https://doi.org/10.1016/s0889-5406\(94\)70131-8](https://doi.org/10.1016/s0889-5406(94)70131-8)
60. Dray A (1995) Inflammatory mediators of pain. *Brit J Anaesth* 75(2):125–131. <https://doi.org/10.1093/bja/75.2.125>
61. Seroglou HG, Klages U, Zentner A (1998) Pain and discomfort during orthodontic treatment: causative factors and effects on compliance. *Am J Orthod Dentofacial Orthop* 114(6):684–691. [https://doi.org/10.1016/s0889-5406\(98\)70201-x](https://doi.org/10.1016/s0889-5406(98)70201-x)
62. Sideri S, Papageorgiou SN, Eliades T (2008) Registration in the international prospective register of systematic reviews (PROSPERO) of systematic review protocols was associated with increased review quality. *J Clin Epidemiol* 100:103–110. <https://doi.org/10.1016/j.jclinepi.2018.01.003>

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