Efficiency, effectiveness and treatment stability of clear aligners: A systematic review and meta-analysis

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Structured Abstract

Objectives: The objective of this study was to perform a systematic review of the orthodontic literature with regard to efficiency, effectiveness and stability of treatment outcome with clear aligners compared with treatment with conventional brackets.

Methods: An electronic search without time or language restrictions was undertaken in October 2014 in the following electronic databases: Google Scholar, the Cochrane Oral Health Group’s Trials Register, Scopus, CENTRAL, MEDLINE via OVID, EMBASE via OVID and Web of Science. We also searched the reference lists of relevant articles. Quality assessment of the included articles was performed. Two authors were responsible for study selection, validity assessment and data extraction.

Results: Four controlled clinical trials including a total of 252 participants satisfied the inclusion criteria. We grouped the trials into four main comparisons. One randomized controlled trial was classified as level 1B evidence, and three cohort studies were classified as level 2B evidence. Clear aligners appear to have a significant advantage with regard to chair time and treatment duration in mild-to-moderate cases based on several cross-sectional studies. No other differences in stability and occlusal characteristics after treatment were found between the two systems.

Conclusions: Despite claims about the effectiveness of clear aligners, evidence is generally lacking. Shortened treatment duration and chair time in mild-to-moderate cases appear to be the only significant effectiveness of clear aligners over conventional systems that are supported by the current evidence.

Keywords
clear aligner, comparative effectiveness research, orthodontic appliances, systematic review, treatment outcome

1 INTRODUCTION

The first clear aligner was introduced by Kesling1 in the early 1940s. However, it did not gain much popularity because of scepticism and the lack of promotion at that time. With the development of dental materials and 3D technology, clear aligners became more popular.

Many advantages have been claimed of this type of appliance over conventional edgewise appliances. The greatest advantage of this appliance, compared to fixed orthodontic appliances, is improved aesthetics and comfort for the patient. For these reasons, patients who care about their appearance or their speech are good candidates for treatment with clear aligners. However, clear aligners have some disadvantages, including higher costs and the inability to treat certain types of malocclusion.2–4

Few clinical studies have been published that adequately assessed the effectiveness of treatment with clear aligners leaving uncertainty among clinicians about the effectiveness of the appliance. McNamara and others stated that more studies are needed to expand the understanding of the clinical applicability of clear aligners.2–4 Additionally, there is a paucity outcome studies in a case-controlled research design.
Published articles are mainly case reports and case series studies and descriptions of the use of the system. This made it difficult for clinicians to objectively compare the efficiency and effectiveness of clear aligners as well as treatment outcome relative to standard fixed appliances. Thus, clinicians who plan to use clear aligners on their patients have to rely on their clinical experience, the opinions of experts and limited published evidence.

The aim of this systematic review was to identify and review the orthodontic literature with regard to the efficiency (treatment time, chair time), effectiveness (occlusal indices) and long-term stability of treatment with clear aligners. If the data allowed, a meta-analysis would be performed.

2 MATERIAL AND METHODS

This systematic review and meta-analysis were conducted according to the guidelines of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and the Cochrane Handbook. A review protocol does not exist.

The inclusion and exclusion criteria for admittance in the systematic review are presented in Table 1.

An electronic search without time or language restrictions was undertake in October 2014 in the following electronic databases: Google Scholar, the Cochrane Oral Health Group’s Trials Register, Scopus, CENTRAL, MEDLINE via OVID, EMBASE via OVID and Web of Science. Detailed search strategies were developed for each database searched. These were based on the search strategy developed for MEDLINE (OVID) but revised appropriately for each database (Table 2).


We checked the bibliographies of included papers and relevant review articles for studies not identified by the search strategies above. We contacted the authors of identified and included studies to identify unpublished or ongoing trials.

At least two review authors independently scanned the list of titles and abstracts of potentially eligible studies. For studies appearing to meet the inclusion criteria, for which there were insufficient data in the title and/or abstract to make a clear decision, the full paper was obtained. Disagreements were resolved by discussion or judged by a third reviewer.

### TABLE 1 Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design: Prospective and retrospective original studies on human subjects with permanent dentition (minimum chronological age of 15 y).</td>
<td>(1) Animal studies; (2) studies with no comparison group; and (3) editorials, opinions, or treatment philosophy articles with no subjects.</td>
</tr>
<tr>
<td>Participants: Patients treated with clear aligners or conventional brackets.</td>
<td></td>
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<tr>
<td>Interventions: Treatment involving clear aligners or conventional brackets.</td>
<td></td>
</tr>
<tr>
<td>Outcome measures: Treatment duration, occlusal indices and stability of treatment related to both clear aligners and conventional brackets.</td>
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</tbody>
</table>

### TABLE 2 Search strategy

1. exp clear aligners
2. "conventional brackets".mp.
3. clear aligners or invisalign.mp.
4. "effect" or effic".mp.
5. (clear aligners adj3 clear aligners effect) or (conventional brackets adj3 conventional brackets effect*) or (clear aligners adj3 (clear aligners effic*)).mp.
6. Or/1-5

The above subject search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials in MEDLINE: sensitivity maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0 [updated March 2011]:

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/not humans.sh.
11. 9 not 10

Papers included in the final review were assessed using the following parameters: (i) study design; (ii) sample details; (iii) outcome measures; (iv) author’s conclusions; and (v) level of scientific evidence based on the criteria of the Oxford Centre for Evidence-based Medicine (see Table 3).

At least two review authors assessed all included studies, to confirm eligibility, assess risk of bias and extract data. The following data were extracted: study design, participants, intervention, outcome measure.

Meta-analyses would also be possible only on studies reporting the same outcome measures. A meta-analysis was performed to combine comparable results in each category using Review Manager (version 5.2.11, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2014). Heterogeneity was assessed among the included studies. Results with less heterogeneity ($I^2$ statistics<50%) were presented with a fixed-effects model, whereas results with $I^2>$50% utilized a random-effects model. Weighted mean differences were used to construct forest plots of continuous data.
<table>
<thead>
<tr>
<th>Level</th>
<th>Therapy/prevention, aetiology/harm</th>
<th>Prognosis</th>
<th>Diagnosis</th>
<th>Differential diagnosis/symptom prevalence study</th>
<th>Economic and decision analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>SR (with homogeneity) of RCTs</td>
<td>SR (with homogeneity) of inception cohort studies; validated in different populations</td>
<td>SR (with homogeneity) of Level 1 diagnostic studies; with 1b studies from different clinical centres</td>
<td>SR (with homogeneity) of prospective cohort studies</td>
<td>SR (with homogeneity) of Level 1 economic studies</td>
</tr>
<tr>
<td>1b</td>
<td>Individual RCT (with narrow Confidence Interval)</td>
<td>Individual inception cohort study with &gt; 80% follow-up; validated in a single population</td>
<td>Validating cohort study with good reference standards; or tested within one clinical centre</td>
<td>Prospective cohort study with good follow-up</td>
<td>Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses</td>
</tr>
<tr>
<td>1c</td>
<td>All or none</td>
<td>All or none case-series</td>
<td>All or none case-series</td>
<td>Absolute better-value or worse-value analyses</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>SR (with homogeneity) of cohort studies</td>
<td>SR (with homogeneity) of either retrospective cohort studies or untreated control groups in RCTs</td>
<td>SR (with homogeneity) of Level &gt;2 diagnostic studies</td>
<td>SR (with homogeneity) of 2b and better studies</td>
<td>SR (with homogeneity) of Level &gt;2 economic studies</td>
</tr>
<tr>
<td>2b</td>
<td>Individual cohort study (including low quality RCT; e.g., &lt;80% follow-up)</td>
<td>Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of RCT or validated on split-samples only</td>
<td>Exploratory cohort study with good reference standards; after derivation, or validated only on split-samples or databases</td>
<td>Retrospective cohort study, or poor follow-up</td>
<td>Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses</td>
</tr>
<tr>
<td>2c</td>
<td>&quot;Outcomes&quot; Research; Ecological studies</td>
<td>&quot;Outcomes&quot; Research</td>
<td>Ecological studies</td>
<td>Audit or outcomes research</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>SR (with homogeneity) of case-control studies</td>
<td>SR (with homogeneity) of 3b and better studies</td>
<td>SR (with homogeneity) of 3b and better studies</td>
<td>SR (with homogeneity) of 3b and better studies</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>Individual Case-Control Study</td>
<td>Non-consecutive study; or without consistently applied reference standards</td>
<td>Non-consecutive cohort study, or very limited population</td>
<td>Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Case-series (and poor quality cohort and case-control studies)</td>
<td>Case-series (and poor quality prognostic cohort studies)</td>
<td>Case-control study, poor or non-independent reference standard</td>
<td>Case-series or superseded reference standards</td>
<td>Analysis with no sensitivity analysis</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion without explicit critical appraisal, or based on physiology, bench research or &quot;first principles&quot;</td>
<td>Expert opinion without explicit critical appraisal, or based on physiology, bench research or &quot;first principles&quot;</td>
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</table>

Odds ratios were used for dichotomous data. If there were enough trials (more than 10) included in any meta-analysis, publication bias was to be assessed according to the recommendations on testing for funnel plot asymmetry as described in the Cochrane Handbook.

3 | RESULTS

3.1 | Description of studies

We initially identified a total of 239 references and 25 reports of trials as eligible according to the defined inclusion criteria for this review. The full text of 25 articles led to the exclusion of 21 because they did not meet the inclusion criteria (15 were case reports, four were not including a control group and two were laboratory studies). Additional handsearching of the reference lists of selected studies did not yield additional papers. Thus, a total of four studies were included in the review. The article selection process is illustrated in the PRISMA Flow Diagram (Figure 1). The details of each study are presented in Table 4.

3.2 | Quality analysis

Among the four included papers, three were cohort studies with a good follow-up and were classified as level 2B evidence according to the Oxford Centre for Evidence-Based Medicine criteria. One study was randomized and was judged as 1B evidence level due to the small sample size. Thus, conclusions with a limited level of evidence could be drawn from the review process.

3.3 | Effects of interventions

3.3.1 | Total treatment time

Three studies compared total treatment time. When analysing the average treatment duration for the two groups, Figure 2 shows the results of the meta-analysis from the three eligible studies. The treatment duration of the braces group was significantly longer than that of the Invisalign group.

3.3.2 | Chair time, appointments and emergency visits time

One study compared the time efficiency of aligner therapy and conventional edgewise braces based on a large sample of patients treated by the same highly experienced orthodontist, with the same treatment goals for both groups of patients. They found that treatment with conventional edgewise brackets required significantly more visits (approximately 4.0), more emergency visits (1.0), more emergency chair time (7.0 minutes) and a greater total chair time (93.4 minutes), compared to aligner therapy.
3.3.3 | Treatment outcomes

Only one study\(^{14}\) that included a control group assesses the treatment outcome of Invisalign relative to conventional braces. The American Board of Orthodontics Objective Grading System (OGS) was used to systematically grade post-treatment records in this study. It was found that the Invisalign group lost 13 OGS points more than the braces group on average. Invisalign scores were consistently lower than braces scores for buccolingual inclination, occlusal contacts, occlusal relationships and overjet. According to the OGS, Invisalign did not treat malocclusions as well as braces in this sample.

3.3.4 | Stability

Only one study\(^{15}\) compared the post-retention dental changes between patients treated with Invisalign and those treated with conventional fixed appliances. They found that the change in the total alignment score in the Invisalign group was significantly larger than that for the Braces group. There were significantly larger changes in maxillary anterior alignment in the Invisalign group than in the conventional bracket group.

4 | DISCUSSION

In this systematic review, we aimed to provide data on the efficiency (treatment time, chair time), effectiveness (occlusal indices) and stability of treatment with clear aligners compared with conventional brackets. We hoped to give clinicians a better understanding how well clear aligners work.

4.1 | Quality of the studies in this review

We identified three cohort studies with 2B evidence according to the Oxford Centre for Evidence-Based Medicine criteria and one randomized controlled trial with 1B evidence level. The evidence for each outcome of interest, however, was sparse, with only one analysis combining data from more than three studies. Many of the trials were small (mean number of participants 63, range 24-150) and may have had insufficient participants to determine a statistically significant difference between interventions, or between intervention and control, if in fact this was present. Furthermore, not any study reported a power analysis. We intended to assess publication bias, but only four studies for each outcome were too few to do so.

4.2 | Summary of main results

Four controlled clinical trials including a total of 252 participants satisfied the inclusion criteria for this review. We grouped the trials into four main comparisons.

4.2.1 | Total treatment time

Meta-analysis of the influence of bracket type on total treatment time confirmed that clear aligners have clinically significant shorter
treatment duration. Djeu\textsuperscript{14} found that the treatment time for the braces group (1.7 years) was significantly longer than that for the Invisalign group (1.4 years). Buschang\textsuperscript{13} found that Invisalign treatment duration was 67\% shorter than treatment with conventional edgewise braces. Aligner treatment lasted 11.5 months, whereas treatment with conventional edgewise braces required 17 months, but this could be the result of having more severe cases in the conventional appliance group. Baldwin\textsuperscript{12} found for premolar extraction cases that clear aligner therapy lasted 11.5 months, whereas treatment with conventional edgewise appliances required 17 months. Thus, on the basis of the existing literature, the duration of treatment was shorter in CAT only when applied to mild- to- moderate case.

4.2.2 | Chair time, appointments and emergency visits time

Only one study\textsuperscript{13} compared the time efficiency of aligner therapy and conventional edgewise braces. It was found that patients with aligner therapy spent 50\% less time in the chair, had 67\% fewer appointments and needed more emergency visits than patients treated with conventional edgewise appliances. This difference can be explained by the fact that aligner patients who had a good compliance were often seen at 10- to 12-week intervals, compared to a 6-week standard interval for conventional braces. The patients with conventional edgewise brackets required more appointment time due to the detailing and finishing phase of treatment. The total chair time for aligner patients was less due to fewer adjustment appointments during treatment. Patients with fixed appliances required adjustments of arch wires and/or brackets at each appointment, which significantly increased the total chair time.

Emergency visits are not common with aligner treatment because there are few auxiliary parts that are likely to break and there are no bands and brackets that could come loose. Also, the aligners are removed during eating, which eliminates the risk of breakage during mastication.

4.2.3 | Treatment outcomes

Only one trial\textsuperscript{15} assessed the treatment outcome between two groups. The comparison based on the American Board of Orthodontics Objective Grading System showed that aligner therapy did not correct malocclusions as well as conventional braces.\textsuperscript{15} Furthermore with aligner therapy, it was hard to correct severe malocclusions especially extraction cases. However, there is still much to learn regarding the biomechanics and efficacy of the aligner system.\textsuperscript{16} Kassas found similar results,\textsuperscript{17} but this study was excluded because it lacked a control group. Based on these small sample trials, there is insufficient evidence that clear aligner treatment is better or worse than conventional fixed appliances regarding treatment outcome.

4.2.4 | Stability

Only one study\textsuperscript{15} comparing the stability of treatment outcome with clear aligners to conventional brackets was identified. It was found that patients treated with Invisalign relapsed more than those treated with conventional fixed appliances. Both groups underwent a similar retention protocol, which means that gingival and periodontal fibres were equally reorganized. One difference in the treatment protocol of the two groups was that the patients treated with Invisalign inserted new aligners introducing new forces every 2 weeks. There is no research supporting the 2-week interval recommendation. The braces group, on the other hand, was adjusted usually every 4-6 weeks. Even under ideal orthodontic forces, some undermining resorption of the alveolar bone will occur. Undermining resorption requires 7-14 days, with equal time needed for periodontal ligament (PDL) regeneration and repair. Activating an appliance too frequently can produce damage to the teeth or bone by cutting short the repair process.\textsuperscript{18,19} It could be postulated that the 2-week interval of aligners in the Invisalign system is too short and is leading to poor bone formation and more relapse.

In addition, the current concept of an optimal force in orthodontics is based on the theory that a force of a certain magnitude and duration would be capable of producing a maximum rate of tooth movement without tissue damage.\textsuperscript{20,21} Tooth movement with the Invisalign system is distance-based, as opposed to forced-based with the fixed appliance systems. Due to static constraints, it is impossible to know exactly what forces are being created by continuous arch mechanics with fixed appliances, but material properties and stress/strain relationships of orthodontic wires and springs are known.\textsuperscript{19} Even though both fixed appliances and Invisalign can move teeth to clinically acceptable positions, there is no literature on the force magnitude that is being created by aligner therapy.

4.3 | Agreements and disagreements with other studies or reviews

Only two published systematic reviews were identified.\textsuperscript{10,22} These reviews only focused on treatment effects of the Invisalign system, while treatment duration, chair time and stability were also evaluated.
in our review. It should be noted that, due to a lack of homogeneity among the included studies, meta-analyses could not be undertaken in the earlier reviews,\textsuperscript{10,22} while by meta-analysis only one outcome parameter was included in this study. In similarity with our review, the earlier reviews also identified substantial bias, which reduced the quality of the evidence.

4.4 | Limitations

First, as in all systematic reviews we may have missed studies. We searched electronic databases and ongoing trials and performed a manual search, which could restrict this bias to some extent. Second, the sample size of the included studies was generally small. Therefore, statistical power was lacking. Third, only four studies were included, and funnel plots and the Begg’s rank correlation test were not conducted. Therefore, some publication bias might exist, such as funding support for published studies. Furthermore, the unexplained statistical heterogeneity and lack of randomized controlled trial studies limited the overall conclusions, which call for future high-quality studies to obtain more stable conclusions. Finally, none of the trials in this review reported both the benefits (periodontal status and/or quality of life) and the possible adverse effects (pain and/or root resorption) associated with the two systems.

5 | CONCLUSIONS

1. This review suggests that future studies in this field should include RCTs with rigorous methodology and proper sample size to increase the power of the studies for estimating the effects.
2. Aligner therapy appears to have a significant advantage with regard to efficiency (treatment time, chair time) in mild-to-moderate cases, based on several cross-sectional studies.
3. There is insufficient evidence with regard to the effectiveness and stability of treatment with clear aligners compared with conventional brackets.

ACKNOWLEDGEMENTS

We would like to acknowledge the assistance of Jerry Wood in developing the search strategy and also Jayne Cook in editing the review.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflict of interests in connection with this article.

REFERENCES

