

# The treatment effects of Invisalign orthodontic aligners

## A systematic review

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**A**n orthodontic treatment method based on the usage of removable, clear semielastic polyurethane aligners known as Invisalign (Align Technology, Santa Clara, Calif.) has been available since 1997.<sup>1</sup> These aligners are made from a thin, transparent plastic that fits over the buccal, lingual/palatal and occlusal surfaces of the teeth. They conventionally are worn for a minimum of 20 hours per day and are changed sequentially every two weeks.<sup>2</sup>

**The authors found that no strong conclusions could be made regarding the treatment effects of Invisalign appliances.**

Invisalign has been indicated by its manufacturer to be used in adults and adolescents who have fully erupted permanent dentitions.<sup>3</sup> Although there seems to be a general agreement that it is not indicated for all types of patients receiving orthodontic treatment,<sup>4</sup> controversy exists about the extension of the aligners' treatment indications. Some indicate that they should be used in orthodontic cases without skeletal disharmonies with mild crowding,<sup>2</sup>

whereas others have suggested that Invisalign may be suitable for even moderately complex orthodontic cases.<sup>5,6</sup>

An evidence-based health care practice aims to provide the best possible treatment based on sound evidence.<sup>7</sup> It is clear that scientific evidence alone should not automatically dictate the selection of the treatment option. It is a combination of values (clinical, personal

**Background.** The authors conducted a systematic review of the literature to determine the treatment effects of the Invisalign orthodontic system (Align Technology), Santa Clara, Calif.).

**Types of Studies Reviewed.** The authors reviewed clinical trials that assessed Invisalign's treatment effects in nongrowing patients. They did not consider trials involving surgical or other simultaneous fixed or removable orthodontic treatment interventions.

**Results.** The authors searched electronic databases (PubMed, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, Evidence Based Medicine Reviews, EMBASE Excerpta Medica, Thomsen's ISI Web of Science and LILACS) with the help of a senior health sciences librarian. They used "Invisalign" as the sole search term, and 22 documents appeared in the combined search. Thereafter, they used "clinical trials," "humans" and "Invisalign treatment effects" as abstract selection criteria. Only two published articles met these inclusion criteria, though after reading the actual articles, the authors determined that they did not adequately evaluate Invisalign treatment effects. Both articles identified methodological issues.

**Clinical Implications.** The inadequately designed studies the authors found represented only a lower level of evidence (level II). Therefore, the authors found that no strong conclusions could be made regarding the treatment effects of Invisalign appliances. Future prospective randomized clinical trials are required to support, with sound scientific evidence, the claims about Invisalign's treatment effects. Clinicians will have to rely on their Invisalign clinical experience, the opinions of experts and the limited published evidence when using Invisalign appliances.

**Key Words.** Invisalign; treatment outcomes; orthodontics.



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and social) that the clinician analyzes before selecting the procedure, which determines if the intervention benefits are worth the cost.<sup>8</sup> Therefore, the application of evidence to clinical practice should be related to professional expertise and patients' values and needs. A systematic review evaluates the literature about a specific topic that has been prepared using a systematic approach to minimize biases and random errors.<sup>9</sup>

We conducted a systematic review to determine the magnitude of the reported treatment effects of Invisalign based on all available published scientific literature that met predetermined minimum criteria for study design. This information would help determine which Invisalign treatment indications are supported by the evidence.

## METHODS

We conducted a computerized search using PubMed (1966 to the second week of April 2005), MEDLINE (from 1966 to the first week of April 2005), MEDLINE In-Process & Other Non-Indexed Citations (from the first week of April 2005 to April 15, 2005), Evidence Based Medicine (EBM) Reviews Database (Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, Database of Abstracts of Reviews of Effects and Cochrane Central Register of Controlled Trials) (to the first quarter of 2005), EMBASE Excerpta Medica (from 1988 to the first week of April 2005), Thomsen's ISI Web of Science (1945 to the second week of April 2005) and LILACS (from 1982 to April 2005) databases. We made this literature search using "Invisalign" as the only term, as counseled by a senior librarian specializing in health sciences databases. We applied no language restrictions.

We determined the eligibility of the selected studies by reading the abstracts identified by the database searches. To select potentially appropriate articles from the published abstracts, we used human and clinical trials using Invisalign as a treatment option. We completed this initial selection process independently on the basis of the abstract information, then settled any discrepancies through discussion. We selected and collected all the articles that appeared to meet the initial inclusion criteria based on their abstracts.

In cases in which specific data were necessary for the discussion and was not specified in the abstract, we made efforts to contact the authors to obtain the required extra information. Before

making a final decision, we also obtained articles for which the abstract did not present enough relevant information to enable us to make a sound decision.

We arrived independently at our final conclusions about the appropriateness of the selected articles to meet our objective, reading the complete articles and then comparing and settling discrepancies by discussion. In addition, we hand-searched the reference lists of the selected articles for additional relevant publications that the database searches may have missed. In cases in which specific data were necessary for the discussion and were not specified in the article, we made efforts to contact the authors to obtain those data.

## RESULTS

We identified 22 abstracts after adding up the database results. From the total abstracts identified, MEDLINE and PubMed obtained the greatest diversity of abstracts, with 21 each (Table 1). From the other databases, EBM Reviews was the only one to present an abstract not included in either MEDLINE or PubMed.

Of the 22 abstracts, one<sup>10</sup> was a case report that also was included in the sample used in a later study by Vlaskalic and Boyd.<sup>6</sup> Two other studies<sup>11,12</sup> of Invisalign were published; one was published as an abstract<sup>12</sup> and the other was a study based on that abstract.<sup>11</sup> Finally, we determined that only two studies<sup>6,11</sup> satisfied the inclusion criteria (clinical trials in humans and evaluation of Invisalign treatment effects) (Table 2, page 1727). The figure (page 1728) is the flow diagram of the literature search.

**Study 1.** Vlaskalic and Boyd's study<sup>6</sup> reported results obtained on 38 patients (initial intended-treat sample of 40; dropout rate of 5 percent). The study's inclusion criteria were as follows: fully erupted permanent dentition not including third molars, dental health without immediate need for restorations, availability for evening appointments and a desire to comply with orthodontic treatment. The subjects' age range was 14 to 52 years, and some of them had been treated previously with fixed appliances. A \$200 incentive was offered to subjects, as well as a warranty that they would undergo a full fixed orthodontic treatment if they were not pleased with the results of the Invisalign treatment.

Patients with a Class I occlusion with mild crowding or spacing required an average of 20 months' treatment time. Nine of 10 patients (90

TABLE 1

SEARCH RESULTS FROM DIFFERENT INTERNET-ACCESSIBLE DATABASES.			
DATABASE	KEY WORD	RESULTS	ABSTRACTS NOT LISTED ON MEDLINE
PubMed	Invisalign (Align Technology, Santa Clara, Calif.)	21	0
MEDLINE	Invisalign	21	Not Applicable
MEDLINE In-Process & Other Non-Indexed Citations	Invisalign	0	0
EMBASE (Excerpta Medica)	Invisalign	1	0
All Evidence Based Medicine Reviews Database (Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, Database of Abstracts of Reviews of Effects and Cochrane Central Register of Controlled Trials)	Invisalign	2	1
Thomsen's ISI Web of Science	TS = (Invisalign)	7	0
LILACS	Invisalign	0	0

percent) completed their treatment. Several aligners made from different materials and of different thicknesses were used, and several new impressions were required in the process. At least 10 days were required for every aligner, and overcorrection of tooth positions was necessary. The only reported side effect was posterior open bite creation, though no specific incidence rates were reported.<sup>6</sup>

For subjects with a Class I occlusion, with moderate crowding, posterior crossbite and lingually impacted mandibular premolars, or subjects with a Class III occlusion, with mild to moderate crowding and anterior crossbite, an average of 27 months of treatment time was required. Only 10 patients of the 15 in this group (66.7 percent) completed their treatment. These types of cases required the addition of specific composite attachments to correct rotations, to extrude or rotate teeth and to obtain bodily movements. The authors suggested making an impression of the dentition before the removal of any tooth for the virtual set up.<sup>6</sup>

For subjects with Class I and Class II division 1 occlusion with severe crowding or class II division 2 occlusion with moderate crowding, an average of 32 months of treatment time was required. Only eight patients of the 13 in these groups (61.5 percent) completed their treatment.

These types of cases required long vertical attachments to maintain adequate root control in extraction cases with overcorrection in the virtual setup.<sup>6</sup>

As part of a survey, 100 percent of the subjects claimed that they would use Invisalign over fixed appliances and that oral hygiene was easy to maintain. Caries occurred in 5 percent of the total sample.<sup>6</sup>

**Study 2.** The study by Bollen and colleagues<sup>11</sup> was a clinical trial evaluating the effect of activation time and material stiffness in the ability to com-

plete use of a first set of prescribed aligners. A total of 51 subjects (mean age 34 years, range 19 to 55 years; 36 women and 15 men) were assigned randomly to a hard or soft appliance and a one-week or two-week activation time. Criteria for subjects' inclusion in the study were as follows: age older than 18 years, availability to attend the appointments and ability to pay for the services. Baseline characteristics were similar among the four groups. Only 15 subjects completed the full set of aligners (a dropout rate of 71 percent). Reasons the researchers offered as to why subjects did not complete the treatment were poor fit as judged by project orthodontists (23), refusal to proceed to the next appliance (three) or recommendation by Align Technology orthodontists to restart the process (10). The proportion of subjects who completed the treatment was similar in the four groups. The researchers found that the two-week interval was more likely to lead to completion of the treatment but that the stiffness of the aligners was not. They also found that more complex cases were less likely to be completed than were simpler cases, and subjects with premolar extractions had the largest rate of failure to complete treatment. All of the patients required a second set of aligners or fixed appliances to complete their initial treatment goals.

**Summary.** After reviewing both articles, we

TABLE 2

## STUDY TYPES AND SAMPLES FROM THE ABSTRACTS IDENTIFIED IN THE LITERATURE SEARCH.

AUTHOR	STUDY TYPE	NO. IN SAMPLE
Beers and colleagues <sup>21</sup>	Comment	N/A*
Bishop and colleagues <sup>14</sup>	Case report	2 (females, aged 17 and 34 years)
Bollen and colleagues <sup>11</sup>	Randomized clinical trial	51 (36 females, 15 males; average age 34 years)
Chenin and colleagues <sup>15</sup>	Case report	2 (both women, aged 41 and 42 years)
Christensen <sup>4</sup>	Comment	N/A
Clements and colleagues <sup>12</sup>	Abstract	N/A
Ellis <sup>19</sup>	Letter	N/A
Joffe <sup>2</sup>	Comment	N/A
McKenna <sup>5</sup>	Comment	N/A
Meier and colleagues <sup>1</sup>	Prospective survey (patient profiling)	89 (72 percent women aged 20-29 years; 28 percent men aged 30-39 years)
Miller and colleagues <sup>23</sup>	Case report	1 (woman, aged 24 years)
Miller and colleagues <sup>20</sup>	Validation study	N/A
Norris and colleagues <sup>13</sup>	Case report	1 (man, aged 39 years)
Owen <sup>24</sup>	Case report	1
Schuster and colleagues <sup>26</sup>	In vitro (Invisalign, Align Technology, Santa Clara, Calif, tray experiment)	10 patients (trays only)
Sheridan <sup>27</sup>	Comment	N/A
Turpin <sup>25</sup>	Comment	N/A
Vlaskalic and Boyd <sup>10</sup>	Case report	1 (male, aged 35 years)
Vlaskalic and Boyd <sup>6</sup>	Clinical trial	38 (aged 14-52 years)
Wheeler <sup>17</sup>	Letter	N/A
Whitehouse <sup>18</sup>	Comment	N/A
Wong <sup>22</sup>	Comment	N/A

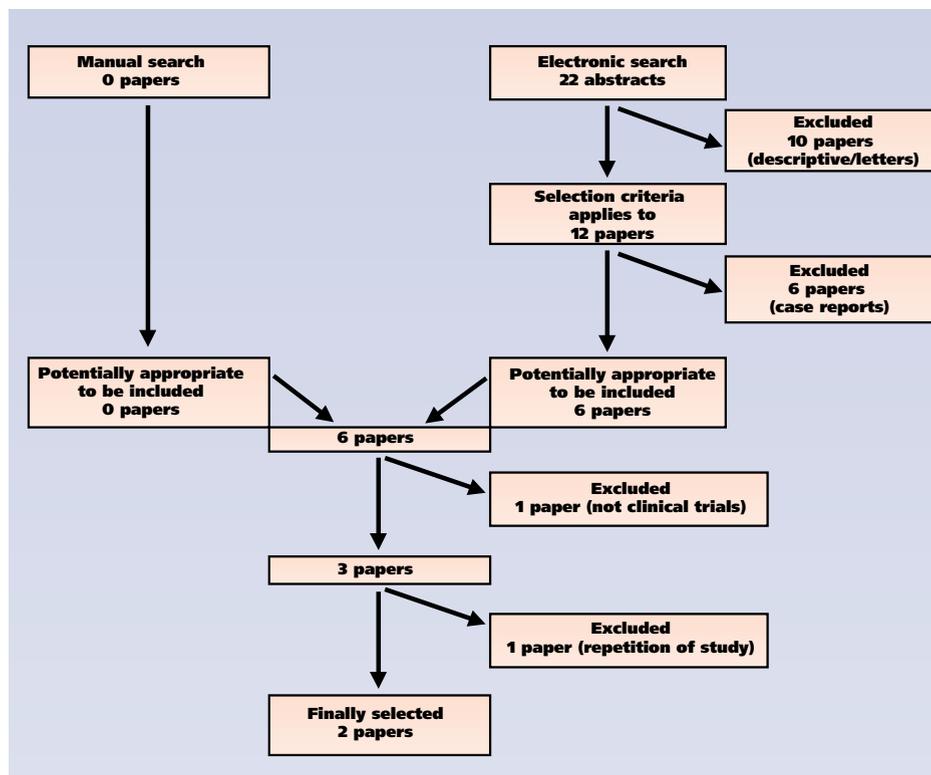
\* N/A: Not applicable.

determined that neither of them quantified the treatment effects of Invisalign. Both studies evaluated completion rates of Invisalign treatment under different malocclusion characteristics, material stiffness and interval between aligners. These rates were contradictory, ranging between 5 and 71 percent of dropout proportions. Randomization was used in only one of the studies,<sup>11</sup> but both<sup>6,11</sup> were published in peer-reviewed journals.

### DISCUSSION

Invisalign was developed to be used as an orthodontic treatment alternative for adults with a Class I malocclusion with mild-to-moderate crowding.<sup>5</sup> The company's Web site<sup>3</sup> claims that Invisalign "has been proven effective" and "can be

used to treat a vast majority of adults and adolescents," giving the impression that most of the orthodontic cases can benefit from this technology. However, Joffe<sup>2</sup> defined more specific selection criteria: caution should be taken when dealing with malocclusions that have more than 5 millimeters of spacing and crowding, skeletal anteroposterior discrepancies of greater than 2 mm, centric relation and occlusion discrepancies, teeth rotations of greater than 20 degrees, anterior and posterior open bites, teeth extrusion, teeth tipping of greater than 45 degrees, teeth with short clinical crowns and arches missing multiple teeth. As can be seen from these references, there is controversy about the complexity of orthodontic cases that can be treated success-



**Figure. Flow diagram of the literature search.**

fully with Invisalign. Therefore, a systematic review of the available evidence that may or may not support the possible dentoalveolar changes of this technology seemed warranted. We hoped to give clinicians a better understanding of the advantages and disadvantages of the technology.

Concerning the available literature, 18 percent of the published material was case reports.<sup>10,13-15</sup> In reviewing these, we found that all the subjects whose cases were reported were diagnosed with malocclusions not surpassing Joffe's<sup>2</sup> treatment criteria and were reported as having been treated successfully with Invisalign. Only two clinical trials have been published. The first trial<sup>6</sup> was a feasibility study with 38 patients. It had with methodological limitations concerning patient selection (nonrandomized and limited sample size per group). The researchers also failed to report precise malocclusion characteristics with respect to the amount of crowding and other parameters. Nevertheless, they concluded that patients whose permanent dentition has mild-to-moderate malocclusions may benefit from this treatment. They also suggested that prospective, controlled clinical trials with adequate sample sizes, increased record base and the use of objective assessment methods such as occlusal indexes should be used

to evaluate outcomes with Invisalign.

The other clinical trial only reported results from an initial alignment phase of treatment with respect to using different activation times and material stiffness.<sup>11</sup> This good-quality exploratory report followed most of the requirements of the Consolidated Standards of Reporting Trials (CONSORT) statement.<sup>16</sup> Although the sample of 51 subjects was categorized based on their occlusal characteristics (score on the Peer Assessment Rating [PAR] index), no quantification of the final treatment results after the use of the initial set of aligners was reported.

Future reports are expected regarding the magnitude of the achievement of treatment goals for occlusal change. A two-week activation regimen, no extractions and a low score on the PAR index were considered characteristics that increased the chances to complete a course of treatment with an initial set of aligners. All of these patients underwent a second set of aligners or comprehensive orthodontic treatment after completing treatment with these initial series of aligners.

On the basis of the limitations of the two studies we evaluated,<sup>6,11</sup> we could come to no conclusions regarding Invisalign treatment effects or, consequently, the system's treatment indications. Based on these two clinical trials, we can only conclude that stiffness of the material does not seem to affect the outcome, a two-week activation period seems to be more efficient and complexity of the malocclusion influences the chances to complete a set of aligners. Wheeler<sup>17</sup> commented that many orthodontic products are sent to the market without undergoing sufficient clinical trials, increasing the possibility for practitioners and patients to be frustrated by the outcomes. Considering this, it is clear that there is a need to develop well-designed clinical trials of Invisalign's treatment possibilities and limitations. So far, the

establishment of most of the indications has been determined by the personal experience of the clinicians using Invisalign. Research on Invisalign is reported to be conducted in diverse locations in the United States and Europe.<sup>2</sup> It is hoped that these studies will give us more sound evidence about Invisalign's treatment effects and indications.

A limitation that we can foresee is that Invisalign appliances used in future studies may not be the same. Invisalign aligners continue to evolve, including in terms of new material characteristics. This would make comparisons between future studies difficult.

Another important consideration is that most of the published reports about Invisalign are case reports, which are of interest for clinicians but do not present significant evidence to support treatments based on evidence. Also, reports that appear in non-peer-reviewed journals do not allow for the evaluation of the quantity and quality of the reported data by experts before been exposed to the public.

Because scientific evidence alone should not automatically dictate the selection of the treatment by the health professional, those making health care decisions should consider the values of not only the health care professional but also the patient. All these factors should be evaluated to determine whether the intervention benefits are worth the associated costs.<sup>8</sup>

## CONCLUSIONS

We could make no conclusion from this systematic review about the indications for, limitations of and outcomes of use of the Invisalign system because we found no study that quantified treatment effects or accomplishment of treatment goals using it.

Randomized clinical trials that follow the CONSORT statement are needed to evaluate the treatment effects of Invisalign.

No treatment indications for or limitations of Invisalign are supported with scientific evidence. Therefore, clinicians will have to rely on their clinical experience, the opinion of experts and the presented limited evidence when using Invisalign appliances. ■

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