Comparison of Invisalign® Aligners versus Fixed Appliance Treatment in pain perception: a systematic review and meta-analysis

Dinis Pereira
Egas Moniz Cooperativa de Ensino Superior CRL
Vanessa Machado (vmachado@egasmoniz.edu.pt)
Egas Moniz Cooperativa de Ensino Superior CRL https://orcid.org/0000-0003-2503-260X
João Botelho
Egas Moniz Cooperativa de Ensino Superior CRL
José João Mendes
Egas Moniz Cooperativa de Ensino Superior CRL
Ana Sintra Delgado
Egas Moniz Cooperativa de Ensino Superior CRL

Research article

Keywords: Clear Aligners, Invisalign, Pain perception, VAS scale, Systematic review, Meta-analysis

Posted Date: May 31st, 2019

DOI: https://doi.org/10.21203/rs.2.9973/v1

Abstract

Background: This systematic review aimed to compare the pain discomfort levels between Invisalign® aligners comparing with traditional fixed appliances at multiple time points, through Pain Visual Analog Scale (VAS). Methods: Four electronic databases (Pubmed, Medline, CENTRAL and Scholar) were searched up to February 2019. There were no restrictions on year and publication status. Randomized clinical trials (RCTs) and case-control studies comparing pain perception through VAS in patients treated with Invisalign aligners and with labial appliances were included. Risk of bias within and across studies was assessed using Cochrane tool and Newcastle-Ottawa Scale (NOS) approach. Random-effects meta-analysis were conducted. VAS score at 1, 3 and 7 days, and analgesic consumption was collected. Pairwise and Binary Random-Effects Meta-analyses were used to synthesize available data. Results: At the initial search, a total of 87 articles were retrieved. Following the review protocol, 4 articles met the inclusion criteria and were included, with a total of 214 participants (139 females, 75 males). All studies were considered of high methodological quality. The results demonstrate that Invisalign aligners seems to be associated with significantly less pain than fixed appliances at 7 days after beginning the orthodontic treatment, although at 1 and 3 days the pain experience was similar in both orthodontics appliances. In regard to the type of material, SmartTrack® aligners appear to give significantly better comfort for orthodontic patients than previous standard material, being that 3 days after appliance's insertion this pain differential becomes significant, and this difference is more pronounced at 7 days. Conclusion: Patients treated with Invisalign experience less pain discomfort than those treated with fixed appliances and consume less analgesics. Overall, Invisalign promotes better pain and discomfort experience for the patient in the course of orthodontic treatment. Larger RCTs are needed to definitely demonstrate these findings throughout the orthodontic treatment.

Introduction

With the increase of esthetic requirements, facial's micro and macro-esthetic and smile have become a priority for adolescents and adults [1,2]. Consequently, patients lean to more esthetic and comfortable orthodontic treatments [3].

According to Kesling, clear aligners were predominantly to minor tooth movement, usually at the end of orthodontic treatment or to treat minor alignment relapse [4]. In 1998, Invisalign® aligners (Align Technology®, California, USA) were introduced into the orthodontic market [5]. Since then, clear aligners have been popularized and quickly became the preferred orthodontic appliances for patients with great esthetic demands [6]. In 2013, Invisalign introduced SmartTrack®, a new and highly elastic alignment material that allows a lower and more uniform force level. According to the brand, it offers patient better comfort, less pain and it is easier to handling. From that date, all patients were treated exclusively with this new material [7].

In fact, clear aligners, like Invisalign, have much more esthetic attractiveness than conventional fixed appliances with brackets and wires [1], and patients benefit by being able to have full access to remove clear aligners to eat and for oral hygiene. Still, patients treated with Invisalign have better periodontal health than those with conventional fixed appliances and there is better compliance with oral hygiene in teenagers [8–10].

Interestingly, pain experience research in orthodontic patients during treatment has been a research topic of interest . In fact, the pain experience progression after initial archwire placement in fixed orthodontic appliance is well established in the literature, comparing multistrand stainless steel and superelastic NiTi archwires [11–18]. However, overall pain perception during Invisalign aligners course of treatment and when compared with conventional fixed appliances are not well established.

Patients elect Invisalign aligners in hope that these appliances will have fewer negative impacts on their quality of life [19]. Therefore, it is essential to systematically evaluate whether there is a difference in pain perception between orthodontic fixed appliances and Invisalign aligners, and in this way, we can contribute to a more considered decision by the patient and the clinician about the following treatment.

Objectives

Given the increasing popularity of clear aligners, this systematic review aimed to compare the discomfort levels between traditional buccal fixed appliances with Invisalign aligners at multiple time points. The review PICO research question is "Does Invisalign have less pain discomfort impact than buccal fixed appliance treatment in orthodontic patients?", with the following statements: orthodontic patients (Patients – P); Invisalign treatment (Intervention/Exposure – I); Buccal fixed appliance treatment (Comparison – C); Pain discomfort (Outcome – O).

Methods

2.1. Protocol and registration

The present systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting studies that evaluate health care interventions [20] (Appendix S1) and its extension for abstracts [21]. The protocol was previously defined and have been registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42019124534). There were involved three researchers from the Orthodontics Department: DP, VM and ASD; and two researchers from the Clinical Research Unit: JB and JJM.

2.2. Eligibility criteria

Studies were eligible for inclusion based on the following criteria:

1. Invisalign aligners treatment comparing with buccal fixed orthodontic appliances and determined pain discomfort through Pain Visual Analog Scale (VAS) at multiple time points;
2. Observational studies (randomized and non-randomized study cohort/longitudinal study, cross-sectional study);
3. English language studies;
4. Human study population.

The exclusion criteria were:

1. Studies reporting results emerging from questionnaires;
2. Retrospective studies;
3. In vitro and animal studies;
4. Case reports/case series;
5. Editorials, opinions, narrative reviews, and technique description articles, without reported sample.

2.3. Search strategy

A total of four electronic databases (Pubmed, Medline, CENTRAL and Scholar) were searched systematically from inception to February 2019. The strategy used for the electronic search was the following: ("VAS"OR"Visual Analog Scale"OR"VAS scale"OR"pain perception"OR"pain")AND("Invisalign"OR"Invisalign aligner"OR"clear aligner")AND("orthodontic brackets"OR"bracket"OR"fixed appliance"). The reference lists of included articles and relevant reviews were manually searched. Gray literature was searched using the latter strategy in OpenGray.

2.4. Assessment of Validity

The eligibility of each study was assessed independently by two investigators (VM and DP), who screened the titles and/or abstracts of retrieved studies. Inclusion was dependent on the following eligibility criteria: randomized clinical trials and case-control studies who compare the discomfort level produced by traditional fixed appliances and Invisalign aligners at multiple

time points. Final selection of studies was performed by three authors independently (VM, DP, JB), and verified by a fourth and fifth author (JJM, ASD), by reviewing the full text based on inclusion criteria above. Discussion resolved any disagreements. Non-full papers, such as conference abstracts, thesis and letters to editors, were excluded.

2.5. Data extraction

Characteristics of the included studies and numerical data were extracted in duplicate by two authors (VM and DP) onto a predefined data extraction table: citation, publication status and year of publication, study design, setting, number of cases and characteristics of the participants (mean age, sex), VAS scores at multiple time points, type of fixed appliances, and analgesic consumption. Final data was reviewed by a third author (JB). Concerning additional data/clarifications, we tried to contact corresponding authors (on 10th of February 2019).

2.6. Quality assessment and Risk of Bias in Included Studies

The quality assessment of the eligible studies was performed by two independent reviewers (VM and JB). In areas of disagreements, a collective decision was obtained after a discussion between all authors to approach a consensus, with an opinion of a third reviewer (AD). Risk of bias of RCTs was assessed with the Cochrane Collaboration's tool. Case-control and cohort studies were appraised with the Newcastle-Ottawa Scale. "Stars" (points) were attributed for each methodologic quality criterion, and each study could achieve a maximum of 8 points. Studies with 7 to 8 points (80% or more of the domains satisfactorily fulfilled) were arbitrarily considered to be of high quality, studies with 5 to 6 stars were of medium quality, and studies with less than 5 stars were of low methodologic quality. Disagreements between the review authors over the risk of bias in particular studies were resolved by discussion, with the involvement of a third review author (DP) where necessary.

2.7. Summary Measures & Synthesis of Results

For the conversion of median and interquartile range VAS score values to mean and standard deviations, Hozo et al.[22] procedure was used, under the assumption of normal distribution. Firstly, pain discomfort through VAS score of Invisalign versus traditional fixed treatment at 1, 3 and 7 days following their initial treatment appointment was appraised through DerSimonian-Laird (DS) random-effect analysis. Secondly, Invisalign studies were subdivided according to the aligners materials, standard material and SmartTrack. Of the included studies, the percentage of analgesic consumption was also carried out at 1, 3 and 7 days after beginning orthodontic treatment through binary SD random-effects analysis. All random-effects meta-analysis and forest plots were performed using OpenMetaAnalyst (2016) software [23]. Quantity I^2 was used to measure to account for homogeneity and calculated through the $\chi 2$ test. Publication bias analysis was planned to be performed if, at least, we had 10 or more studies included [24]. All tests are two-tailed with alpha set at 0.05, except for the homogeneity test whose significance level cutoff will consider to be 0.10 due to the low power of the $\chi 2$ test with a limited amount of studies.

Results

3.1 Study Selection

From the databases and other sources, the initial electronic database search resulted in a total of 87 record, resulting in 60 after duplicates removal. Following title and abstract screening, 9 studies were selected for full-text evaluation. Nevertheless, after full-text eligibility assessment, 5 studies were excluded (in detail in Supplemental Table S2). Therefore, the meta-analysis was performed on the basis of 4 articles. The flow chart of study selection together with reasons for exclusion is provided in Figure 1.

3.2 Study characteristics

Four prospective studies evaluated the pain discomfort of Invisalign orthodontic treatment through the comparison with buccal fixed orthodontics appliance. A total of 214 participants (139 females, 75 males) were included. The characteristic of the participants is shown in Table 1.

3.3 Risk of bias within studies

Only one RCT was included and was assessed as unclear overall risk of bias [6]. Table 2 shows the summary of risk of bias assessment for the RCT study according to the Cochrane Risk of bias tool. Table 3 (NOS Scale scores) shows the risk of bias assessment for the included studies. All three studies were considered of low risk of bias and, therefore, of high quality [25–27].

3.4. Synthesis of results

Data from four studies including 165 patients reported pain discomfort through VAS score of Invisalign versus buccal fixed treatment [6,25,27]. All those studies provided data for pain discomfort at 1, 3 and 7 days following their initial treatment appointment, while two had data on a daily basis [6,25]. Heterogeneity exists between the three studies at all time points (Fig. 2). So, we opted for a random-effects model.

Although not significant, after 1 day of treatment, Invisalign patients experience in average 33.3% lower VAS score than patients with buccal fixed appliances (MD = 1.35, 95% CI: -0.04-2.74; Fig. 2). Similarly at 3 days after treatment, Invisalign patients experience in average 28.5% lower VAS score than patients with fixed appliances, but the difference is not statistically significant (MD = 1.56 , 95% CI: -0.16-3.29; Fig. 2). Meanwhile at 7 days follow-up, Invisalign patients experience in average 38.2% lower VAS score than patients with buccal fixed appliances, and the difference is statistically significant (MD =0.85 , 95% CI: 0.30-1.40; Fig.2).

In fact, although the difference in pain perception at 1 day after treatment beginning in patients treated with the Standard material of Invisalign (before 2013) versus SmartTrack (after 2013) is not significant (Fig. 3), on the 3 and 7 days patients treated with SmartTrack show a significant difference in mean VAS score of 53.7% and 50.1%, respectively (MD = 2.71, 95% CI: 0.49-4.93; Fig.4; and MD = 1.52, 95% CI: 0.34-2.70; Fig. 5). In the opposite, patients treated with Invisalign Standard material (before 2013) did not present significant differences in pain perception on any of the days evaluated. Thus, Invisalign's SmartTrack material appears to be more comfortable for patients than previously manufactured clear aligner materials.

3.5. Additional analysis

A detailed number analgesic consumption after beginning orthodontic treatment at 1, 3 and 7 days are reported in three studies [6,25,27]. Overall, patients treated with Invisalign have significantly less analgesic consumption compared with fixed orthodontic treatment group control one day and seven days after treatment beginning (Supplemental Fig. S1). Overall, patients with fixed appliances consume more analgesics at the beginning of treatment.

Discussion

4.1. Summary of Main Findings

This systematic review included one randomized and three case-control studies, with a total of 214 patients. The overall results demonstrate that Invisalign seems to be significantly associated with less discomfort rather than fixed appliances. Although at 1 and 3 days the results are not significant, at 7 days this difference is conclusive.

Notwithstanding, by accounting the type of material, SmartTrack appear to provide better comfort for orthodontic patients than the previous standard material. Notably, this differences becomes significant at 3 days after appliance insertion and turns more pronounced at 7 days. In fact, these results comply with a previous research where patients were transitioned to the aligners made with the SmartTrack material and experienced less pain intensity, pain duration, and less pressure upon insertion [7]. In addition, Invisalign patients reported less analgesics consumption compared to patients with fixed appliances, and present significant differences.

4.2. Quality of the Evidence, Limitations and Potential Biases in the Review Process

The strengths of this systematic review include the extensive unrestrictive literature search, with a rigorous and predetermined protocol implemented in each phase. However, there are limitations worth to mention among the included studies.

The included investigations were of small samples, and two of them lack sample size calculation [25,26]. As well, there are a diversity of buccal brackets description since one did not refer the type of fixed appliances [25], two used different self-ligated wire appliances [26] [27] and another used a traditional buccal fixed appliances [6]. Though passive self-ligating systems result in minor periodontal ligament ischemia and therefore less discomfort [28], literature evidences that pain experience in the beginning of treatment is independent of bracket type [29–32]. The type and size of archwires was only specified in two studies [6,26], which is also a limitation. However, previous studies have found no significant differences in the pain perception using different archwires types [29,33,34].

Moreover, only one study [6] performed allocation concealment, while the remaining three [25–27] did not randomly assigned the treatment modalities due to their cohort design nature. In fact, well-conducted and adequately informed “gold standard” RCTs are the epitome in clinical research [35,36]. The main advantage lies in the random allocation of patients minimizing patients selection bias [37]. However, randomizing adult patients is not simple, since some of whom are unwilling or unable to comply with the random assignment due to esthetic reasons [26]. This difficulty limits the ability to completely randomize the study. The fact that the patient has a choice demonstrates personality traits, which can impair the perception of pain.

Additionally, pain experience is a notoriously subjective response and there is a non-linear relationship upon multiple factors such as age, gender, individual pain threshold, the magnitude of the force applied, present emotional state and stress, cultural differences, and previous pain experiences [12,15,38–42]. A hypothetical limitation would be the fact that there is an unbalanced gender ratio. However, gender has no significant effect on orthodontic pain perception [12,15,41,43], except in adolescents, where females have less pain tolerance than males [44,45].

Finally, the placement of SmartForce attachments since the beginning of the treatment with Invisalign is relevant in pain perception, because they make more pressure during the insertion of the aligner. They were introduced by Align in September of 2009. In the included studies, Miller et al [25] in 2007 did not place attachments since it was not protocol, Shalish et al [26] do not describe the placement of attachments in the first set of aligners, White et al [6] placed attachments already in the first aligners, and Almasoud [27] delayed the attachments placement until the third set of aligners. The high heterogeneity among the studies prevent a definitive conclusion and, therefore, the influence of the attachments in pain perception and comfort should be considered in the future.

Conclusions

Within the limitations of this systematic review, the results show that patients treated with Invisalign experience less pain and discomfort than patients treated with traditional buccal fixed appliances. This becomes more significant since the SmartTrack introduction into the Invisalign aligners. This information may clarify patients about what to expect during the beginning of orthodontic treatment. In the future, larger randomized clinical trials are needed to definitely demonstrate Invisalign's better comfort over traditional fixed appliances throughout the orthodontic treatment.

5.1. Implications for Clinical Practice and Research

These findings may help both patients and clinicians in the treatment modality decision, concerning pain parameters and analgesic consultation, in the first phase of orthodontic treatment.

In the main, randomized clinical trials are needed to perform a robust comparison of Invisalign aligners and buccal orthodontic fixed appliances. Aspects concerning long-term outcomes appraisal, objective measurements of patient-centered reported outcomes (such as quality of life), and adverse effects (including allergies, periodontal damages and functional impairment) are important factors to consider.

Declarations

Conflict of interest statement

Nothing to declare.

Ethical committee information

Nothing to declare.

Acknowledgements

None to declare.

References

1. Ziuchkovski JP, Fields HW, Johnston WM, Lindsey DT. Assessment of perceived orthodontic appliance attractiveness. *Am. J. Orthod. Dentofacial Orthop.* 2008;133(4 Suppl):S68–78. Available at: http://dx.doi.org/10.1016/j.ajodo.2006.07.025.
2. Sarver DM. Interactions of hard tissues, soft tissues, and growth over time, and their impact on orthodontic diagnosis and treatment planning. *Am. J. Orthod. Dentofacial Orthop.* 2015;148(3):380–6. Available at: http://dx.doi.org/10.1016/j.ajodo.2015.04.030.
3. Rosvall MD, Fields HW, Ziuchkovski J, Rosenstiel SF, Johnston WM. Attractiveness, acceptability, and value of orthodontic appliances. *Am. J. Orthod. Dentofacial Orthop.* 2009;135(3):276.e1–12; discussion 276–7. Available at: http://dx.doi.org/10.1016/j.ajodo.2008.09.020.
4. Kesling HD. The philosophy of the tooth positioning appliance. *Am. J. Orthod. Oral Surg.* 1945;31(6):297–304. Available at: http://www.sciencedirect.com/science/article/pii/0096634745901013.
5. Wong BH. Invisalign a to z. *Am. J. Orthod. Dentofacial Orthop.* 2002;121(5):540–1. Available at: https://www.sciencedirect.com/science/article/pii/S0889540602539561.
6. White DW, Julien KC, Jacob H, Campbell PM, Buschang PH. Discomfort associated with Invisalign and traditional brackets: A randomized, prospective trial. *Angle Orthod.* 2017;87(6):801–8. Available at: http://dx.doi.org/10.2319/091416-687.1.

7. Bräscher A-K, Zuran D, Feldmann RE Jr, Benrath J. Patient survey on Invisalign® treatment comparen the SmartTrack® material to the previous aligner material. *J. Orofac. Orthop.* 2016;77(6):432–8. Available at: http://dx.doi.org/10.1007/s00056-016-0051-3.
8. Abbate GM, Caria MP, Montanari P, et al. Periodontal health in teenagers treated with removable aligners and fixed orthodontic appliances. *J. Orofac. Orthop.* 2015;76(3):240–50. Available at: http://dx.doi.org/10.1007/s00056-015-0285-5.
9. Azaripour A, Weusmann J, Mahmoodi B, et al. Braces versus Invisalign®: gingival parameters and patients' satisfaction during treatment: a cross-sectional study. *BMC Oral Health* 2015;15:69. Available at: http://dx.doi.org/10.1186/s12903-015-0060-4.
10. Lu H, Tang H, Zhou T, Kang N. Assessment of the periodontal health status in patients undergoing orthodontic treatment with fixed appliances and Invisalign system: A meta-analysis. *Medicine* 2018;97(13):e0248. Available at: http://dx.doi.org/10.1097/MD.0000000000010248.
11. Wang Y, Liu C, Jian F, et al. Initial arch wires used in orthodontic treatment with fixed appliances. *Cochrane Database Syst. Rev.* 2018;7:CD007859. Available at: http://dx.doi.org/10.1002/14651858.CD007859.pub4.
12. Ngan P, Kess B, Wilson S. Perception of discomfort by patients undergoing orthodontic treatment. *Am. J. Orthod. Dentofacial Orthop.* 1989;96(1):47–53. Available at: https://www.ncbi.nlm.nih.gov/pubmed/2750720.
13. Jones M, Chan C. The pain and discomfort experienced during orthodntic treatment: A randomized controlled clinical trial of two intial aligning arch wires. *Am. J. Orthod. Dentofacial Orthop.* 1992;102(4):373–81. Available at: http://www.sciencedirect.com/science/article/pii/088954069270054E.
14. Wilson S, Ngan P, Kess B. Time course of the discomfort in young patients undergoing orthodontic treatment. *Pediatr. Dent.* 1989;11(2):107–10. Available at: https://www.ncbi.nlm.nih.gov/pubmed/2762180.
15. Scheurer PA, Firestone AR, Bürgin WB. Perception of pain as a result of orthodontic treatment with fixed appliances. *Eur. J. Orthod.* 1996;18(4):349–57. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8921656.
16. Stewart FN, Kerr WJ, Taylor PJ. Appliance wear: the patient's point of view. *Eur. J. Orthod.* 1997;19(4):377–82. Available at: https://www.ncbi.nlm.nih.gov/pubmed/9308258.
17. Krishnan V, Davidovitch Z 'ev. Cellular, molecular, and tissue-level reactions to orthodontic force. *Am. J. Orthod. Dentofacial Orthop.* 2006;129(4):469.e1–32. Available at: http://dx.doi.org/10.1016/j.ajodo.2005.10.007.
18. Grieve WG 3rd, Johnson GK, Moore RN, Reinhardt RA, DuBois LM. Prostaglandin E (PGE) and interleukin-1 beta (IL-1 beta) levels in gingival crevicular fluid during human orthodontic tooth movement. *Am. J. Orthod. Dentofacial Orthop.* 1994;105(4):369–74. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8154462.
19. Flores-Mir C, Brandelli J, Pacheco-Pereira C. Patient satisfaction and quality of life status after 2 treatment modalities: Invisalign and conventional fixed appliances. *Am. J. Orthod. Dentofacial Orthop.* 2018;154(5):639–44. Available at: http://dx.doi.org/10.1016/j.ajodo.2018.01.013.
20. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;339:b2700. Available at: http://dx.doi.org/10.1136/bmj.b2700.
21. Beller EM, Glasziou PP, Altman DG, et al. PRISMA for Abstracts: reporting systematic reviews in journal and conference abstracts. *PLoS Med.* 2013;10(4):e1001419. Available at: http://dx.doi.org/10.1371/journal.pmed.1001419.
22. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med. Res. Methodol.* 2005;5:13. Available at: http://dx.doi.org/10.1186/1471-2288-5-13.
23. Wallace BC, Lajeunesse MJ, Dietz G. OpenMEE: Intuitive, open-source software for meta-analysis in ecology and evolutionary biology. *Methods Ecol. Evol.* 2017. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1111/2041-210X.12708.
24. Green S, Higgins J. Cochrane handbook for systematic reviews of interventions. 2005. Available at: http://www.rismes.it/pdf/Cochrane_handbook%202009.rtf.
25. Miller KB, McGorray SP, Womack R, et al. A comparison of treatment impacts between Invisalign aligner and fixed appliance therapy during the first week of treatment. *Am. J. Orthod. Dentofacial Orthop.* 2007;131(3):302.e1–9. Available at:

http://dx.doi.org/10.1016/j.ajodo.2006.05.031.

26. Shalish M, Cooper-Kazaz R, Ivgi I, et al. Adult patients' adjustability to orthodontic appliances. Part I: a comparison between Labial, Lingual, and Invisalign™. *Eur. J. Orthod.* 2012;34(6):724–30. Available at: http://dx.doi.org/10.1093/ejo/cjr086.
27. Almasoud NN. Pain perception among patients treated with passive self-ligating fixed appliances and Invisalign® aligners during the first week of orthodontic treatment. *Korean J. Orthod.* 2018;48(5):326–32. Available at: http://dx.doi.org/10.4041/kjod.2018.48.5.326.
28. Wright N, Modarai F, Cobourne MT, DiBiase AT. Do You do Damon®? What is the Current Evidence Base Underlying the Philosophy of this Appliance System? *J. Orthod.* 2011;38(3):222–30. Available at: https://journals.sagepub.com/doi/abs/10.1179/14653121141479.
29. Fleming PS, DiBiase AT, Sarri G, Lee RT. Pain Experience during Initial Alignment with a Self-Ligating and a Conventional Fixed Orthodontic Appliance System. *The Angle Orthodontist* 2009;79(1):46–50. Available at: http://dx.doi.org/10.2319/121007-579.1.
30. Fleming PS, Johal A. Self-ligating brackets in orthodontics. A systematic review. *Angle Orthod.* 2010;80(3):575–84. Available at: http://dx.doi.org/10.2319/081009-454.1.
31. Miles PG, Weyant RJ, Rustveld L. A clinical trial of Damon 2 vs conventional twin brackets during initial alignment. *Angle Orthod.* 2006;76(3):480–5. Available at: http://dx.doi.org/10.1043/0003-3219(2006)076[0480:ACTODV]2.0.CO;2.
32. Miles PG. Self-ligating brackets in orthodontics: Do they deliver what they claim? *Aust. Dent. J.* 2009;54(1):9–11. Available at: http://dx.doi.org/10.1111/j.1834-7819.2008.01081.x.
33. Rahman S, Spencer RJ, Littlewood SJ, O'Dywer L, Barber SK, Russell JS. A multicenter randomized controlled trial to compare a self-ligating bracket with a conventional bracket in a UK population: Part 2: Pain perception. *Angle Orthod.* 2016;86(1):149–56. Available at: http://dx.doi.org/10.2319/112414-838.1.
34. Scott P, Sherriff M, Dibiase AT, Cobourne MT. Perception of discomfort during initial orthodontic tooth alignment using a self-ligating or conventional bracket system: a randomized clinical trial. *Eur. J. Orthod.* 2008;30(3):227–32. Available at: http://dx.doi.org/10.1093/ejo/cjm131.
35. Egger M, Davey-Smith G, Altman D. *Systematic Reviews in Health Care: Meta-Analysis in Context*. John Wiley & Sons; 2008. Available at: https://market.android.com/details?id=book-ErhNdafPCrQC.
36. Meikle MC. Guest editorial: what do prospective randomized clinical trials tell us about the treatment of class II malocclusions? A personal viewpoint. *Eur. J. Orthod.* 2005;27(2):105–14. Available at: http://dx.doi.org/10.1093/ejo/cji038.
37. Kunz R, Vist G, Oxman AD. Randomisation to protect against selection bias in healthcare trials. *Cochrane Database Syst. Rev.* 2007;(2):MR000012. Available at: http://dx.doi.org/10.1002/14651858.MR000012.pub2.
38. Bergius M, Kiliaridis S, Berggren U. Pain in orthodontics. A review and discussion of the literature. *J. Orofac. Orthop.* 2000;61(2):125–37. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10783564.
39. Firestone AR, Scheurer PA, Bürgin WB. Patients' anticipation of pain and pain-related side effects, and their perception of pain as a result of orthodontic treatment with fixed appliances. *Eur. J. Orthod.* 1999;21(4):387–96. Available at: https://www.ncbi.nlm.nih.gov/pubmed/10502901.
40. Brown DF, Moerenhout RG. The pain experience and psychological adjustment to orthodontic treatment of preadolescents, adolescents, and adults. *Am. J. Orthod. Dentofacial Orthop.* 1991;100(4):349–56. Available at: http://dx.doi.org/10.1016/0889-5406(91)70073-6.
41. Krishnan V. Orthodontic pain: from causes to management—a review. *Eur. J. Orthod.* 2007;29(2):170–9. Available at: https://academic.oup.com/ejo/article-abstract/29/2/170/522873. Accessed March 5, 2019.
42. Chow J, Cioffi I. Pain and orthodontic patient compliance: A clinical perspective. *Semin. Orthod.* 2018;24(2):242–7. Available at: http://www.sciencedirect.com/science/article/pii/S1073874618300306.
43. Erdinç AME, Dinçer B. Perception of pain during orthodontic treatment with fixed appliances. *Eur. J. Orthod.* 2004;26(1):79–85. Available at: https://www.ncbi.nlm.nih.gov/pubmed/14994886.

44. Sandhu SS, Sandhu J. Orthodontic pain: an interaction between age and sex in early and middle adolescence. *Angle Orthod.* 2013;83(6):966–72. Available at: http://dx.doi.org/10.2319/030113-174.1.

45. Abu Alhaija ES, Aldaikki A, Al-Omairi MK, Al-Khateeb SN. The relationship between personality traits, pain perception and attitude toward orthodontic treatment. *Angle Orthod.* 2010;80(6):1141–9. Available at: http://dx.doi.org/10.2319/012710-59.1.

46. Bowling A. Mode of questionnaire administration can have serious effects on data quality. *J. Public Health* 2005;27(3):281–91. Available at: http://dx.doi.org/10.1093/pubmed/fdi031.

47. Noll D, Mahon B, Shroff B, Carrico C, Lindauer SJ. Twitter analysis of the orthodontic patient experience with braces vs Invisalign. *Angle Orthod.* 2017;87(3):377–83. Available at: http://dx.doi.org/10.2319/062816-508.1.

48. Noll D, Mahon B, Shroff B, Carrico C, Lindauer SJ. Twitter analysis of the orthodontic patient experience with braces vs Invisalign. *Angle Orthod.* 2017;87(3):377–83. Available at: http://dx.doi.org/10.2319/062816-508.1.

Tables

Table 1: Characteristic of included studies and participants.

Author, year (ref.)	Country	Study Type	Participants (N)		Gender (F/M)		Mean age (years)	
			Invisalign	Fixed appliance	Invisalign	Fixed appliance	Invisalign	Fixed appliance
Almasoud (2018)	Saudi Arabia	Prospective study	32	32	22/10	20/12	28,47± 8,17	23,56 ± 5,44
Shalish (2011)	Israel	Prospective study	21	28	16/5	14/14	Not available	Not available
White (2017)	USA	A randomized, prospective trial	23	18	12/11	12/6	Not stated	Not stated
Miller (2007)	USA	Longitudinal, Prospective study	33	27	22/11	21/6	38,0 ± 12,4	28,6 ± 8,7

Table 2: Quality Assessment Tool for RCT Studies according to the Cochrane Risk.

COCHRANE TOOL							
Author (Year)	Random Sequence Generation	Allocation Concealment	Blinding participants and personnel	Blinding outcome assessment	Incomplete outcome data	Selective reporting	Other bias
White 2017	+	+	-	+	+	+	+

Table 3: Newcastle-Ottawa Scale (NOS) for Case-Control Studies

The Newcastle-Ottawa Scale (NOS) - Case-Control Studies										
	Selection				Comparability	Outcome			TOTAL	
	Is the case definition adequate?	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cohorts on the basis of the design or analysis	Ascertainment of outcome	Save method of ascertainment for cases and controls	Non-response rate		Quality
Miller 2007	a	a	a	a	a	a	a	a	□□□□□□□□	High
Shalish 2011	a	a	a	a	a	a	a	a	□□□□□□□□	High
Almasoud 2018	c	a	a	a	a	a	a	a	□□□□□□□	High

Figures

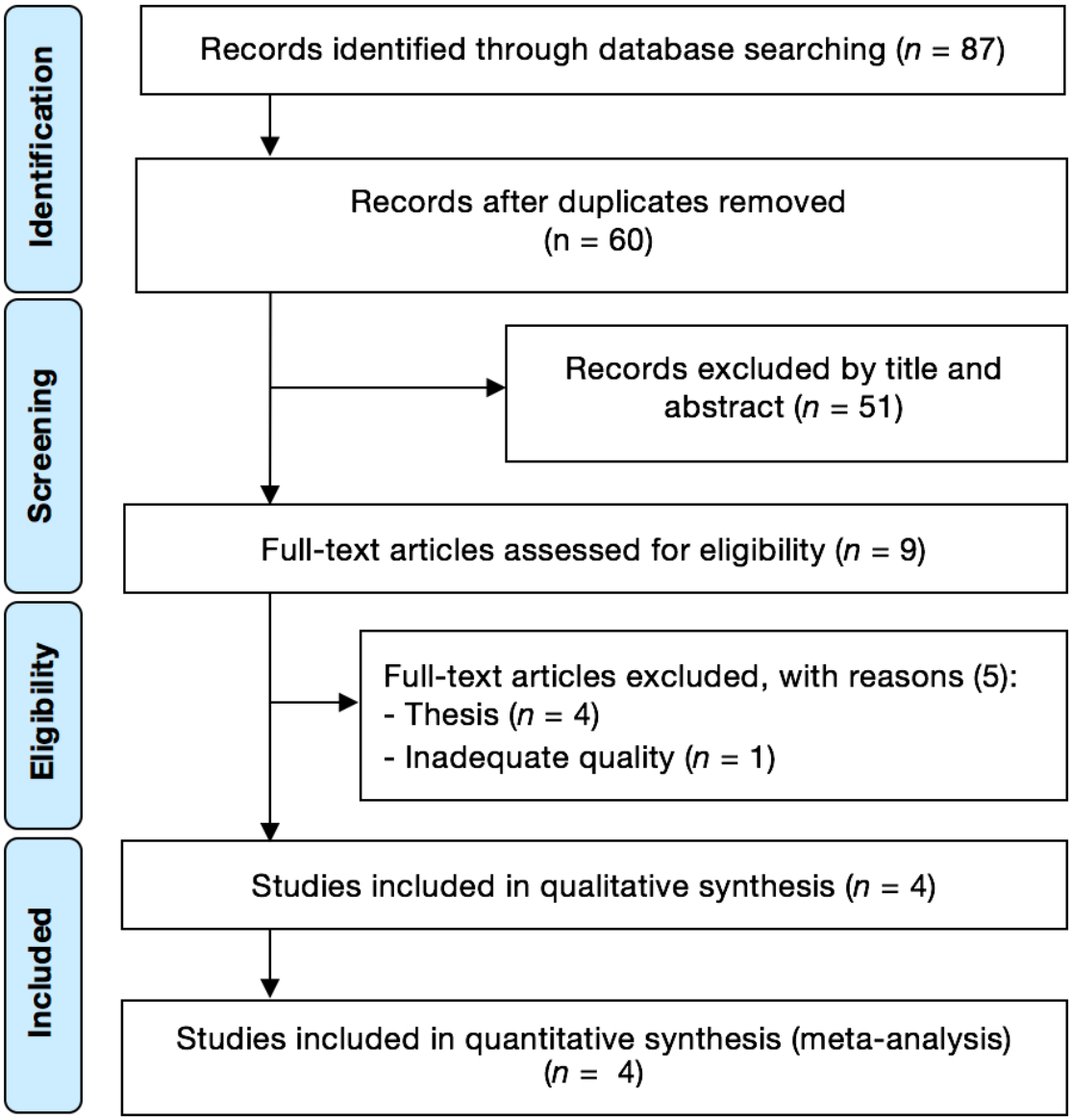

Figure 1

PRISMA flow-chart representing the results of the workflow to identify eligible studies.

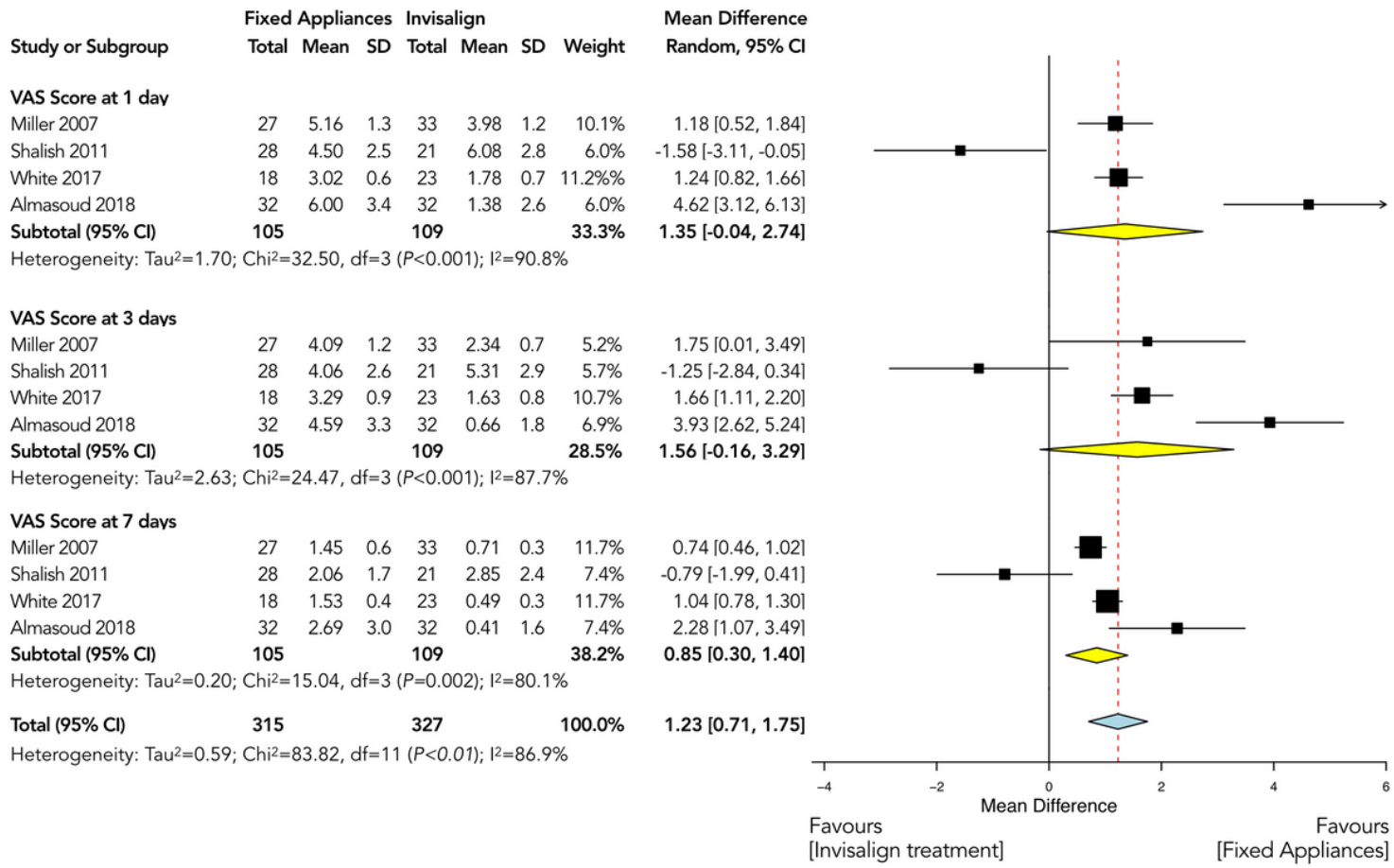

Figure 2

Forest plot diagram showing VAS scores at day 1, 3 and 7 of Invisalign treatment versus Fixed appliances. Mean effect size estimates have been calculated with 95% confidence intervals and are shown in the figure. Area of squares represents sample size, continuous horizontal lines and diamonds width represents 95% confidence interval. Blue diamond center and the vertical red dotted line represent the overall pooled estimate.

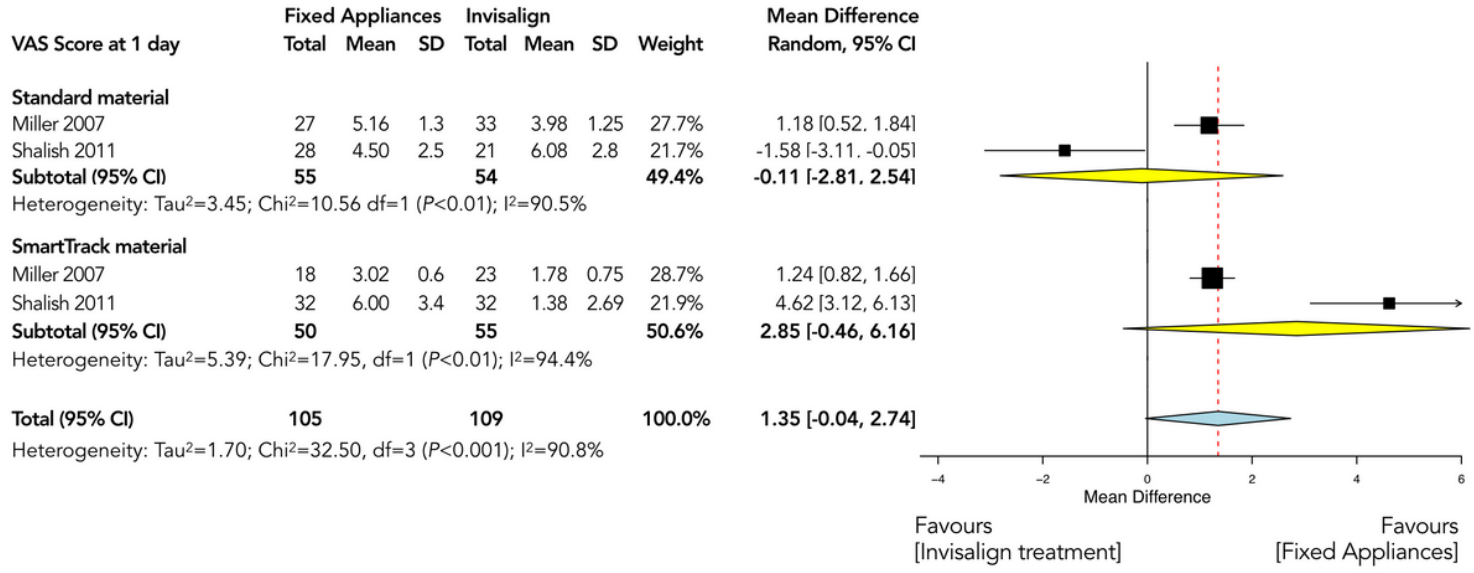

Figure 3

Forest plot diagram showing VAS scores at 1 day of Invisalign with Standard material (before 2013) and with SmartTrack (after 2013) treatment versus Fixed appliances. Mean effect size estimates have been calculated with 95% confidence intervals and are shown in the figure. Area of squares represents sample size, continuous horizontal lines and diamonds width represents 95% confidence interval. Blue diamond center and the vertical red dotted line represent the overall pooled estimate.

	Fixed Appliances			Invisalign				Mean Difference
VAS Score at 3 days	**Total**	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Weight**	**Random, 95% CI**
Standard material								
Miller 2007	27	4.09	1.2	33	2.34	0.77	5.2%	1.75 [0.01, 3.49]
Shalish 2011	28	4.06	2.6	21	5.31	2.90	5.7%	-1.25 [-2.84, 0.34]
Subtotal (95% CI)	**55**			**54**			**46.3%**	**0.23 [-2.71, 3.17]**
Heterogeneity: Tau²=3.78; Chi²=6.25 df=1 (*P*=0.012); I²=84.0%								
SmartTrack material								
White 2017	18	3.29	0.9	23	1.63	0.87	10.7%	1.66 [1.11, 2.20]
Almasoud 2018	32	4.59	3.3	32	0.66	1.80	6.9%	3.93 [2.62, 5.24]
Subtotal (95% CI)	**50**			**55**			**53.7%**	**2.71 [0.49, 4.93]**
Heterogeneity: Tau²=2.32; Chi²=9.88, df=1 (*P*=0.002); I²=89.9%								
Total (95% CI)	**105**			**109**			**100.0%**	**1.56 [-0.16, 3.29]**
Heterogeneity: Tau²=2.63; Chi²=24.47, df=3 (*P*<0.001); I²=87.7%								

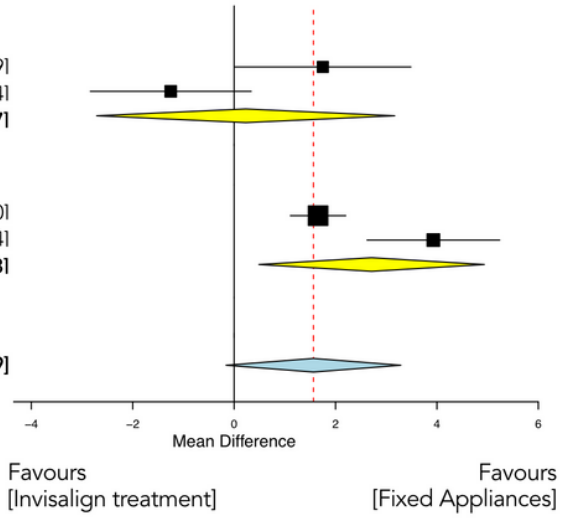

Figure 4

Forest plot diagram showing VAS scores at 3 day of Invisalign with Standard material (before 2013) and with SmartTrack (after 2013) treatment versus Fixed appliances. Mean effect size estimates have been calculated with 95% confidence intervals and are shown in the figure. Area of squares represents sample size, continuous horizontal lines and diamonds width represents 95% confidence interval. Blue diamond center and the vertical red dotted line represent the overall pooled estimate.

	Fixed Appliances			Invisalign				Mean Difference
VAS Score at 7 days	**Total**	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Weight**	**Random, 95% CI**
Standard material								
Miller 2007	27	1.45	0.6	33	0.71	0.33	36.1%	0.74 [0.46, 1.02]
Shalish 2011	28	2.06	1.7	21	2.85	2.4	13.8%	-0.79 [-1.99, 0.41]
Subtotal (95% CI)	**55**			**54**			**49.9%**	**0.09 [-1.39, 1.57]**
Heterogeneity: Tau²=0.97; Chi²=5.93 df=1 (*P*=0.015); I²=83.1%								
SmartTrack material								
White 2017	18	1.53	0.4	23	0.49	0.33	36.4%	1.04 [0.78, 1.30]
Almasoud 2018	32	2.69	3.0	32	0.41	1.60	13.7%	2.28 [1.07, 3.49]
Subtotal (95% CI)	**50**			**55**			**50.1%**	**1.52 [0.34, 2.70]**
Heterogeneity: Tau²=0.57; Chi²=3.87, df=1 (*P*=0.049); I²=74.19%								
Total (95% CI)	**105**			**109**			**100.0%**	**0.85 [0.30, 1.40]**
Heterogeneity: Tau²=0.20; Chi²=15.04, df=3 (*P*=0.002); I²=80.1%								

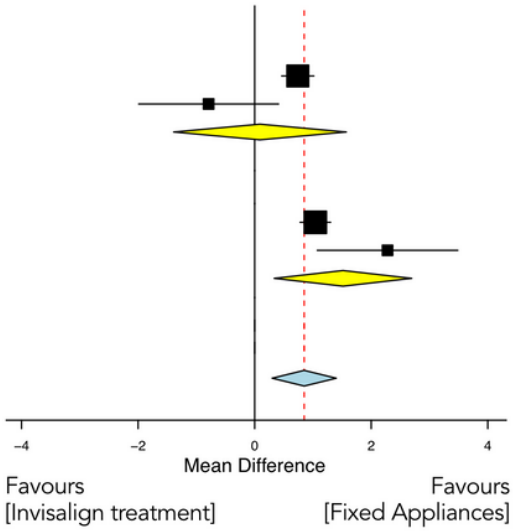

Figure 5

Forest plot diagram showing VAS scores at 7 day of Invisalign with Standard material (before 2013) and with SmartTrack (after 2013) treatment versus Fixed appliances. Mean effect size estimates have been calculated with 95% confidence intervals and are shown in the figure. Area of squares represents sample size, continuous horizontal lines and diamonds width represents 95% confidence interval. Blue diamond center and the vertical red dotted line represent the overall pooled estimate.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- PRISMA2009Checklist.docx
- Supplemental.docx