Author’s response to reviews

Title: A comparison of treatment effectiveness between clear aligner and fixed appliance therapies

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Author’s response to reviews:

Responses to Queries:
Title: A comparison of treatment effectiveness between clear aligner and fixed appliance therapies
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Responses to Editor:

Q1: Please explain how your systematic review is different from the review by Zheng et al, 2017.
A1: First of all, the search items of this study are different from the ones of Zheng et al. 2017. The search items are listed as follow:

- ((orthodont* OR clear OR removable) AND aligner*) OR Invisalign (our study) VS clear aligners OR invisalign (Zheng).

- (conventional orthodontic treatment OR traditional orthodontic treatment OR brace* OR bracket* OR fixed appliance*) (our study) VS conventional bracket (Zheng).

We expanded the search range and identified 681 primary references, while only 239 primary references were found in Zheng et al. Our search strategy was more comprehensive than Zheng et al.

Second, Zheng et al conducted the search in Oct 2014 and only found one study concerning the treatment effectiveness. The other three included studies were about treatment duration. So they summarized little about treatment effectiveness and concluded that the evidence was generally lacking to verify the effectiveness of clear aligners in contrast to braces. We screened the literature published before Aug 2018 and found eight relevant studies. So the content of this study was totally different from the one of Zheng et al. We have added the following sentence to state the difference:
“While in terms of the comparison between clear aligners and braces, Zeng et al performed a review in 2014 and only found one relevant study. The authors concluded that the evidence was generally lacking to verify the effectiveness of clear aligners in contrast to braces [4].” (See Discussion, paragraph 1, line 14-19)

Responses to Reviewer 1:
Dear reviewer, thank you very much for your thorough and critical review of our study. We truly appreciate all of your comments, which have enabled us to greatly improve the quality of our manuscript. We have made the correction according to your comments. The revised portion were highlighted in yellow in the manuscript.

Q1: There are misspellings, statements that need to be cited, and numbers that need to be spelled out. Please see attachment.
A1: Thank you very much for your thorough review and we apologize for our oversight.
All the misspellings highlighted in attachment and numbers need to be spelled out have been correct except that we have not changed the search item “orthodont*” to “orthodontics” in Search strategies, because we think that the word “orthodont*” including “orthodontic”, “orthodontics”, “orthodontia”, and “orthodontist” would be more comprehensive in search strategies.

Citations for the highlighted statements have been added in Discussion. (See References 19, 20, 21, 23, and 25)
- Compared with conventional fixed braces, clear aligners allowed for improved esthetics, comfort and oral hygiene to patients [19, 20]. (See Discussion, paragraph 1, line 1-2)


- On the other hand, clear aligners had some shortages in controlling teeth tooth movement [21]. (See Discussion, paragraph 1, line 2-3)

- Then a recent systematic review published in 2015 concluded that clear aligners were effective in controlling anterior intrusion and posterior buccolingual inclination but not in anterior buccolingual inclination [23]. (See Discussion, paragraph 1, line 8-10)

- Alveolar bone resorption required 7–14 days with equal time needed for periodontal tissue regeneration. Thus, orthodontic appliances should not be reactivated more frequently than three weeks [25]. (See Discussion, paragraph 7, line 1-3)


Q2: In Results section and in 'Treatment effectiveness', paragraph 1, statement 11, the authors wrote that scores for occlusal relationships and overjet were lower in clear aligner group than braces group in
Another study (reference #15) did not show similar findings. The authors should address in the Discussion section why reference #15 did not show differences.

A2: Thank you very much for the helpful suggestion. We have added an explanation in the Discussion as follows:
“In terms of occlusal relationships and overjet, there was a discrepancy between the results of two included studies [10, 17]. In 2005, Djeu blamed the statistically lower scores of clear aligners on the relatively poor control of root torque [10]. While in 2015, Li’s study found no statistically significant difference between two groups [17]. The reason was probably that Li’ study included extraction cases while the previous study included non-extraction cases. Extraction space could be used to adjust overjet. And with the development of the materials, technology, and the application of optimized attachments, clear aligners had a better control of teeth movement compared with the previous ones.” (See Discussion, paragraph 6)

Q3: Regarding the last statement in paragraph three on clear aligners group had a significantly lower rate of receiving great improvement than braces group in Reference #10, but no difference in Reference #9, authors must write in Discussion why there are different results.

A3: The definitions of “great improvement” were not totally the same in these two studies, so there was a discrepancy between the results of the two included studies. We added a detailed description in Result-Treatment effectiveness as follows:

“Gu’s study defined the cases with a reduction of 22 PAR points and the cases with pretreatment PAR scores less than 22 points getting scores equal to 0 at the end of the treatment as great improvement and concluded that clear aligners group had a significantly lower rate of receiving great improvement than braces group [12]. Lanteri’s study expanded the range of great improvement. They defined great improvement as PAR score reduction > 70% or a reduction in PAR score > 22 or PAR score = 0 in the end and found no significant difference between two groups [11].” (See Results-Treatment effectiveness, paragraph 3, line 9-15)

Q4: Regarding treatment effectiveness on dental arches dimension, authors should correlate the changes in arch dimension with post-retention changes as reported in the classical literature.

A4: Thank you for the insightful suggestion. The included studies only reported the change of arch dimension between pretreatment and post-treatment and we failed to find the research which studied on the post-retention change of dental arch dimension after clear aligners treatment, so we were sorry that we could not analyze the post-retention changes of dental arch dimension in this systematic review.

Q5: Statement not clear: “The strength of the material manufacturing clear aligners was weaken compared with archwires”

A5: We have corrected this sentence to “The material strength of clear aligners was weaken compared with the one of archwires.” (See Discussion, paragraph 4, line 6-7)

Q6: Citations needed for risk of bias tools

A6: Citations have been added for risk of bias tools. (See References 5 and 6)
The Newcastle–Ottawa Scale was used to assess the quality of cohort studies [5]. (See Methods-Quality assessment, paragraph 1, line 1)

The recommendations by Cochrane were used to assess the quality of randomized controlled trials [6] (See Methods-Quality assessment, paragraph 2, line 1-2)


Responses to Reviewer 2:
Dear reviewer, thank you very much for your insightful and critical comments, we are very grateful for your valuable suggestions and truly appreciate all of your comments.

We have made the correction according to your comments. The revised portion were highlighted in yellow in the manuscript.

Abstract
Q1: Please add number and type of study (RCT, CCT).
A1: As you suggested, we have added a statement “Eight papers were included in this study. Two of the included papers were randomized controlled trials and six were cohort studies.” in the Abstract. (See Abstract, line 11)

Background
Q1: 1 Title; please remove "s" and ":".
A1: Thank very much for your suggestion. We have corrected the word “Backgrounds:” to “Background”.
Q2: 48 Please define "effectiveness".
A2: We have added a definition of “effectiveness” in the Methods-Focused question segment as follows: “the primary outcome was treatment effectiveness: the outcome assessment of the treatment, included arch width, occlusal contacts, alignment, derotation and inclination of teeth, et al”. (See Methods- Focused question, paragraph 1, line 8-10)

Methods
Q1: 59 Below "Search strategies": why did the authors not use effectiveness as a search term?
A1: “Effectiveness” was defined as the outcome assessment of the treatment, which could include alignment, change of arch width, improvement of occlusal contacts and rotation of teeth, inclination of teeth, and many kinds of grading system. It was difficult to include all the search terms relevant to “treatment effectiveness” without missing in search strategy. As the amount of primary references after searching without “effectiveness” was 681 which was within our ability to screen the literatures, we did not include “effectiveness” as a search term to avoid missing relevant studies. Instead, we screened the titles and abstracts or full-texts of the 681 primary references to identify the studies reporting the treatment effectiveness.
Q2: 42 Below "Study selection and data extraction": why was not gender included?
A2: Thank you very much for this helpful suggestion. We have added the gender ratio of each included study in Study selection and data extraction and Table 1. The following conclusion was added in the Results- Study characteristics: “The gender ratios of all included studies was balanced between two groups except one study not reporting the gender of patients [10].” (See Methods- Study selection and data extraction, paragraph 2, line 5; Table 1; Results- Study characteristics, paragraph 2, line 3-4)
Q3: 45 Below "Data analysis"; please add a reference after the sentence that ends with ... assess publication bias.
A3: We have added a reference as follows: (See References 9)
If more than 10 studies were included in the meta-analysis, funnel plots would be drawn to assess publication bias [9]. (See Methods- Data analysis, paragraph 1, line 8-9)

Results
Q1: 28 Minor comment. Below "Treatment efficiency", please read the sentence trough, the authors have to add "that" after found
A1: Thank you very much for the thorough review and we apologize for our oversight.
The word "that" has been added after “found” (See Results-Treatment effectiveness, paragraph 1, line 1)

Discussion
Q1: A major concern is that the authors did not discuss possible weaknesses. It is necessary to add some sentences about rating a CCT and RCT respectively. Is a moderate quality of a RCT stronger or weaker regarding scientific evidence compared to a CCT with low risk of bias and high quality???. It was just 2 RCT, one a prospectively Clinical comparative study, but 5 retrospective studies, how will this influence the results? Please add a comment about this.
A1: RCT is stronger than CCT and a RCT with high quality is stronger than a RCT with moderate quality regarding scientific evidence. But it is hard to compare a RCT with moderate quality to a CCT with high quality regarding scientific evidence. Different types of studies need to be rated by different tools. The Newcastle-Ottawa Scale is used to assess the quality of cohort studies. Cochrane’s recommendation is used to assess the quality of RCT. These two tools are composed of different items. Table 3 and 4 presented the bias of included studies item by item to provide the strength of evidence for readers.
The RCTs studying on the relevant topic of this review were rare, so we designed to include the cohort studies to get more evidence and this may result in bias. As the reviewer suggested, we added the following statement to discuss the possible weaknesses: “Second, the number of randomized controlled trials was so small that the cohort studies were also included in this systematic review which might result in a bias. Considering the high heterogeneity evident among studies, the outcome of meta-analysis estimating treatment effectiveness should be interpreted with caution. As few high-quality studies were found to extract data for a meta-analysis, a qualitative result was extracted from the included studies and the Newcastle-Ottawa Scale and Cochrane’s recommendation were used to assess the quality of two different types of studies respectively. More randomized controlled trials would be required in the provision of high-quality evidence.” (See Discussion, paragraph 9, line 9-17)

Q2: In addition: I think also that the authors should mention where the investigations were performed and by whom. Private practice/university; general practitioner/ specialists? If it is mentioned in the included studies. Otherwise the authors should discuss it.
A2: Thank you very much for this suggestion. We have added a “clinicians” column in Table 1 to present who performed the treatment and added the following statement in the Results- Study characteristics to mention where the investigations were performed: “All the investigations were performed in the universities. The treatments were conducted by clinicians specialized in orthodontics
in the included studies except one study not reporting who conducted the treatment [11].” (See Results-
Study characteristics, paragraph 1, line 7-9)

Q3: The authors should also discuss the present study in relation to the systematic review by Zheng et
al. 2017
A3: Zheng et al conducted the search in Oct 2014 and only found one study concerning the treatment
effectiveness. The other three included studies were about treatment duration. So they summarized little
about treatment effectiveness and concluded that evidence was generally lacking to verify the
effectiveness of clear aligners in contrast to braces. We screened the literature published before Aug
2018 and found 8 relevant studies. The content of this study was totally different from the one of Zheng
et al. As the reviewer suggested, we have added the following discussion: “Zeng et al performed a
review in 2014 and only found one relevant study. The authors concluded that evidence was generally
lacking to verify the effectiveness of clear aligners in contrast to braces [4]. As an increasing number of
relevant studies published in recent years, a systematic review was needed to update the knowledge of
the treatment effectiveness of clear aligners compared with braces.” (See Discussion, paragraph 1, line
14-19)