Peer Review File

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Reviewer A

Comment 1: All studies listed reported approximately the same magnitude of decentration. But there was no description of how the decentration was measured. This is critical to the point of the paper and should be described in detail:

Reply 1: Thank you very much for your reminder and we have fully realized that this is indeed indispensable information. The description of how the decentration was measured has been added to the Table1 (see Page 10, line 270).

Changes in the text:

Table 1. The basic characteristics of included seven studies.

Study	Definition of decentration** and the methods of decentration measurement
Gangyue Wu 2018[20]	A > 0.5mm Control≤0.5mm method：unclear
Guo Li 2021[21]	B > 0.5mm Control≤0.5mm method：displayed by corneal topography (TMS-4, Tomey, Nagoya, Japan)
Lu Sun 2022[22]	A > 0.5mm Control≤0.5mm method：inhouse developed computer program (Python)
Minfeng Chen 2022[23]	A > 0.5mm Control≤0.5mm method：Image software (National Institutes of Health, Bethesda, MD, USA)
Shuxian Zhang 2022[24]	A > 0.5mm Control≤0.5mm method：displayed by corneal topography (TMS-4, Tomey, Nagoya, Japan)
ZiYang Chen 2020[25]	C > 0.5mm Control≤0.5mm method ：displayed by corneal topography (the corneal front surface section) (Italy, CSO SIRIUS)
Anken Wang 2019[26]	A > 0.5mm Control≤0.5mm method：software (Photoshop 6.0)

Comment 2: The age of the subjects varied significantly in the various studies. This is a confounding factor in that the normal rate of axial elongation is quite different in an 8 year old vs a 14 year old (or in one study a 19 yr old). This factor can effect the reported degree of axial elongation. this should be explained and described as a limitation in the discussion.

Reply 2: Thank you for your professional advice. The age of the subjects included has now been explained and described as a limitation in the discussion (see Page 21, line 476).

Changes in the text: In general, smaller increases in AL are associated with older age according to previous studies [42,43]. So, the different age ranges of the subjects included in this study may affect the reported degree of axial elongation.

42. Wang B, Naidu RK, Qu X. Factors related to axial length elongation and myopia progression in orthokeratology practice. PLoS One. 2017;12(4): e0175913. Published 2017 Apr 18.

43. Qi Y, Liu L, Li Y, Zhang F. Factors associated with faster axial elongation after orthokeratology treatment. BMC Ophthalmol. 2022;22(1):62. Published 2022 Feb 8.

Comment 3: Also, there was no mention of the design of the lens (or lenses) used for the studies. Various designs may have different results relative to axial elongation based on overall diameter, optic zone diameter, width of the reverse curve, etc. If possible, this should be described and also listed as a study limitation. With these limitations, the stated conclusions in the paper may not be valid.

Reply 3: Thank you very much for reminding. The design of the lenses has been described in Table 1(see Page 10, line 270) and also listed as a study limitation now.

Changes in the text:

Table 1. The basic characteristics of included seven studies.

Study	Design and material of OK lenses
Gangyue Wu 2018[20]	**Brand：Unclear** **Four-zoned reverse-geometry design (diameter: 10.0-11.2 mm)** **Material: Boston XO**
Guo Li 2021[21]	**Brand：Hengtai** **Four-zoned reverse-geometry design (diameter: 10.2-11.0 mm)** **Material: Boston Equalens II**
Lu Sun 2022[22]	**Unclear**
Minfeng Chen 2022[23]	**Brand：Euclid**

	Four-zoned reverse-geometry design (diameter: 10.2-11.2 mm) **Material: Boston Equalens II**
Shuxian Zhang 2022[24]	**Brand：Euclid** **Four-zoned reverse-geometry design (diameter: 10.0-11.2 mm)** **Material: Boston Equalens II**
ZiYang Chen 2020[25]	**Brand：Euclid** **Four-zoned reverse-geometry design (diameter: 10.2-11.2 mm)** **Material: Boston Equalens II**
Anken Wang 2019[26]	**Brand：Lucid or Alpha** **Four-zoned reverse-geometry design (diameter: 10.0-11.0 mm)** **Material: Boston EN or Boston XO**

Based on current research, different lens designs may have an impact on the efficiency of myopia control [44,45], and the different lens designs involved in this study may affect the results. (see Page 21, line 479)

44. Pauné J, Fonts S, Rodríguez L, Queirós A. The Role of Back Optic Zone Diameter in Myopia Control with Orthokeratology Lenses. J Clin Med. 2021 Jan 18;10(2):336.

45. Guo B, Cheung SW, Kojima R, Cho P. One-year results of the Variation of Orthokeratology Lens Treatment Zone (VOLTZ) Study: a prospective randomised clinical trial. Ophthalmic Physiol Opt. 2021 Jul;41(4):702-714.

Comment 4: In light of the finding that subjects with a decentered treatment zone showed less axial elongation, there should be some discussion about how to intentionally create this effect in prospective patients.

Reply 4: The discussion about the attitude to creating the effect of decentration in prospective patients has been added (see Page 20, line 451). And indeed, this will bring this study closer to the clinic.

Changes in the text:

Attitude to the decentration (see Page 20, line 451)

Because of the unpredictability of the decentration itself, and the unpredictability of the resulting complications, the authors still insist that decentration should not be intentionally created. The conclusions of this study suggest that a decentration of less than or equal to 1.5 mm without relevant adverse consequences does not require clinicians to worry about the myopia control efficiency, and the continued wearing of OK lenses should be encouraged. As for the better myopia control efficiency caused by decentration, it can be applied to the modified lens design by further studies clarifing the mechanism of this phenomenon.

Comment 5: Line 7 – spelling of decentration

Reply 5: We sorry for all the wrong spelling and we have modified as advised (see Page 01, line 07)

Comment 6: Line 18 – should this be "patient" reports ?? Also in line 117
Reply 6: We confirm that the spelling is correct. In the Chinese platform, patents can be searched together and patent is a document that proving official right to be the only person to make, use or sell a product or an invention.

Comment 7: There is no section for conclusions, this needs to be added.
Reply 7: Section for conclusions has been added now (see Page 02, line 46).
Changes in the text:
Conclusion: Without decreased visual acuity (worse than 0.1 (logMar)), persistent corneal epithelial defects, glare or diplopia, orthokeratology with decentration (≤1.5mm) showed more efficacy in myopia control than orthokeratology with center-position in children within one year.

Comment 8: There is repeated us of the word "efficiency". The proper word for what you are describing is "efficacy"
Reply 8: Thank you for your advice and the same question in the full text have been modified.

Comment 9: The fact that there were multiple lens designs/brands may also reduce the validity of the results due to the different fitting and parameters of these brands.
Reply 9: Thank you for your professional advice and the relevant description has been added in section for limitations. (see Page 21, line 372)

Comment 10: In addition to the limitations you mentioned, one major one is the large age range of the subjects included in the Meta-analysis. Age is a significant factor in axial elongation and an 8 yr old can not be compared to that of a 15 or 18 yr old.
Reply 10: We quite agree with you and the relevant description has been added in section for limitations. (see Page 21, line 376)

Comment 11: Although the study has great interest, any conclusion from this study must be looked at very cautiously due to multiple and major limitations. Also, care must be taken on whether you are recommending that decentration should be encouraged to promote more slowing of axial elongation.
Reply 11: Thank you for your professional advice, and we very much agree with this view.
We still insist that decentration should not be intentionally created and relevant content can be seen in the section called Attitude to the decentration (see Page 20, line 351).

Reviewer B

Comment 1: Revise Abstract information. This Reviewer encourage authors to improve study description in Abstract. For example, describing study aim, wide description of the results, etc. Supported and registered of this meta-analysis could be not necessary in Abstract section.

Reply 1: Thank you for your professional advice and the abstract has been modified to better meet the requirements.

Changes in the text:

Background： Referring to the myopia control efficiency, the difference between the orthokeratology with dencentration (group OKD) and orthokeratology with center-position (group OKC) as control group is not clear currently. Therefore, the aim of this meta-analysis was to investigate the effect of decentration on myopia control efficiency based on existing studies. (see Page 01, line 09)

Results: Six retrospective case control studies and one retrospective self-control study with a total of 624 eyes for OKD group and 343 eyes for OKC group were included for analysis. Although all the include studies indicated that the axial elongation in the severe decentration group (1.0mm < decentration≤1.5mm) was less than that in the moderate group (0.5mm < decentration≤1.0mm), we still uniformly selected the moderate decentration group as the OKD group to improve the persuasiveness of the results. According to the heterogeneity results (I2=16%, p=0.31), fixed effect model was chosen to get the merged results. One years' MD in axial elongation were -0.06mm (95% [CI], -0.09 to -0.04, P < 0.01), indicating that orthokeratology with dencentration shows more efficiency in myopia control than orthokeratology with center-position. (see Page 02, line 28)

Comment 2: Please improve Introduction section with all myopia control strategies (defocus soft contact lenses and ophthalmic glasses) -Lines 51-62.

Reply 2: Thanks for reminding and all the myopia control strategies have been added in the introduction section.

Changes in the text: Different methods are used to slow the progression of myopia in children, including orthokeratology (OK), atropine, defocus soft contact lenses and ophthalmic glasses, rigid contact lenses, and outdoor light exposure [13-16]. (see Page 04, line 80)

Comment 3: Because main issue is related with literature review it is important that future readers understand how this was conducted. For example, how adverse consequences caused by decentration (line 106-107) were classified? Or how de degree of decentration in the test group was measured (line 134). Authors must clarify how extracted this information of the revised papers.

Reply 3: Thank you for your professional advice. The description of how adverse consequences caused by decentration were classified and how the decentration was measured has been added to the Table 1.

Changes in the text:

Studies were excluded if they were: (6) Including the case of adverse consequences caused by Orthokeratology (decreased visual acuity (worse than 0.1 (logMar)), persistent corneal epithelial defects, glare or diplopia). (see Page 06, line 140)

Table 1. The basic characteristics of included seven studies. (see Page 10, line 270)

Study	Definition of decentration** and the methods of decentration measurement
Gangyue Wu 2018[20]	A > 0.5mm Control≤0.5mm method：unclear
Guo Li 2021[21]	B > 0.5mm Control≤0.5mm method：displayed by corneal topography (TMS-4, Tomey, Nagoya, Japan)
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Comment 4: Also, it is relevant a deep discussion of the different criteria (in decentration magnitude and method to measure decentration) used in different revised papers and the impact in final conclusions of this meta-analysis. For

example, the absence of a "gold-standard" method to define lens decentration (that could be improved in future with further developing of image tools that assess fluorescein pattern for example, that will allow to measure lens position directedly and not use corneal topographic measurement to define decentration); or if lens decentration and topographic decentration could be of similar magnitude (this is not described in literature) to finally recommend future clinicians focus exam in fluorogram pattern assessment or in topographic change after lens wear, or may be in both to define an acceptable or not decentration in ortho-k practice.

Reply 4: Thank you very much for your perspicacity advice. Discussions about the affection of different standard to define decentration on the results have been added. In addition, exploration of potential consistent definitions of decentration has also been added.

Changes in the text:

At present, there is no unified measurement method for decentration, and it is mainly through the corneal topography at present. Finding the distance from the center of pupil to the center of the treatment zone through the tangential map is selected by more scholars [20,22,23,24,26]. It is expected that more accurate and unified automated decentration measurement software will emerge or that decentration can be measured directly and precisely by fluorescein pattern assessment in the future. Even if the measurement methods between each experimental group and the control group were the same for all the studies involved, it would still have an impact on the results of this meta-analysis. (see Page 17, line 364)

Comment 5: This Reviewer also encourage Authors to revise results and discussion section, because in lines 287-296 additional 13 studies (not described in Results) are discussed. So, it is unclear why these 13 studies without control group are relevant to be discussed without a description in results section of the decentration and statistical results that found. If Authors guess that these studies are relevant, they must be described in Results section because current presentation is unclear for future readers to understand what data are relevant of these papers (that are not cited).

Reply 5: Indeed, the previous statement would bring confusion to the readers. The additional 13 studies were discussed because the effect of decentration after orthokeratology on myopia control was mentioned, and the authors felt it was a bit regrettable to exclude them out without any mention. should be excluded because they do not meet the entry criteria for this study. The authors finally decided to remove the relevant discussion to avoid confusion. (see Page 19, line 406)

Changes in the text:

~~When scanning the full text, another 13 relevant studies without control group were found. In fact, many of them have done correlation analysis between the~~

~~decentration and axial elongation, but one part is single factor correlation analysis, one part is multi factor correlation analysis, and the other is multiple regression analysis, not to mention that most of them do not state whether it is Pearson correlation coefficient or Spearman correlation coefficient. Due to the above factors, it is not feasible for us to consider the integration of correlation coefficients to complete the Meta- analysis.~~

Comment 6: This Reviewer is not sure to understand the sentence in line 276-278, because the clinical hypothesis is that ortho-k wear induces mild-peripheral steepening in cornea that provokes a myopic defocus in peripheral retina, and this is supported with animal research results and clinical trials. This Reviewer recommend a deep rewritten of paragraph of lines 276-285.

Reply 6: We are sorry for our previous vague description about the mechanism of myopia control effect after orthokeratology and the relevant statements have been modified. (see Page 18, line 391)

Changes in the text:

The exact mechanism underlying the myopia control effect of orthokeratology is not fully understood and the main current hypothesis are the peripheral defocus provoked by mild-peripheral steepening in cornea and the higher-order aberrations that cannot be corrected with a conventional sphero-cylinder lens after orthokeratology [35,36].

35. Vincent SJ, Cho P, Chan KY, et al. CLEAR - Orthokeratology. Cont Lens Anterior Eye. 2021;44(2):240-269.

36. Nti AN, Berntsen DA. Optical changes and visual performance with orthokeratology. Clin Exp Optom. 2020;103(1):44-54.

Comment 7: This Reviewer also recommends avoid undefined or subjective terms that could have different meaning for different readers. For example, line 307 describe “obvious adverse consequences”, what is an obvious adverse consequence? This could be different for different readers and this Reviewer encourages Authors to be concrete and define these consequences. Same comment in study conclusions.

Reply 7: Indeed, the previous description was not rigorous enough and more detailed and accurate descriptions have been added.

Changes in the text:

Studies were excluded if they were: (6) Including the case of adverse consequences caused by Orthokeratology (decreased visual acuity (worse than 0.1 (logMar)), persistent corneal epithelial defects, glare or diplopia). (see Page 06, line 140)

So strictly speaking, the results of this meta-analysis was based on the absence of adverse consequences (decreased visual acuity (worse than 0.1 (logMar)), persistent corneal epithelial defects, glare or diplopia). (see Page 20, line 448)

In summary, without decreased visual acuity (worse than 0.1 (logMar)), persistent corneal epithelial defects, glare or diplopia, orthokeratology with decentration showed more efficiency in myopia control than orthokeratology with center-position in children after one year. (see Page 21, line 491)

Comment 8: Finally, please clarify in study conclusions that decentration must be slightly, because a high decentration could not be acceptable. This is not "obvious" because this is a subjective term that must be avoided in scientific literature. For this reason the expression "That is say, " (Line 331-332) must be deleted and this sentence rewritten.
Reply 8: Thank you very much for your reminding and we have realized that it is inappropriate to use the subjective term. All mentioned mistakes have been modified as required.
Changes in the text: In summary, without decreased visual acuity (worse than 0.1 (logMar)), persistent corneal epithelial defects, glare or diplopia, orthokeratology with decentration (≤1.5mm) showed more efficiency in myopia control than orthokeratology with center-position in children after one year. According to this result, a decentration of less than or equal to1.5 mm without relevant adverse consequences does not require clinicians to worry about the myopia control efficiency, and the continued wearing of OK lenses should be encouraged. More studies with long-term follow-up data are expected to draw a more precise conclusion. (see Page 21, line 491)

Comment 9: Please confirm that "patent" is not typing mistake and be patient (line 16, 102, 160, etc.).
Other possible typing mistake could be capital letter use in lines 101 to 106, or 112-113.
Revise random effect model description (lines 145-146), because a I2 is missing in line 145 and in both lines is described as I1>50%, could be >50% in one option and <50% in other?
Line 305 deviation could be decentration?
Line 311 could be clearest as "about a minimum decentration lower than 1.0 mm without impact in visual acuity and in ocular surface health after use orto-k lenses"?
Reply 9: We confirm that "patent" is not typing mistake because searching keywords in the Chinese platform will display all papers including the patents. We are very sorry for the rest carelessness and every mentioned mistake has been modified as required.
Changes in the text: If $I^2 > 50\%$, our meta-analysis would use a random-effects model, and a fixed-effects model would be used if $I^2 \leq 50\%$. (see Page 08, line 220)
This meta-analysis did not contain the adverse consequences of decentration. (see Page 19, line 414)
Attitude to the decentration

Because of the unpredictability of the decentration itself, and the unpredictability of the resulting complications, the authors still insist that decentration should not be intentionally created. The conclusions of this study suggest that a decentration of less than or equal to1.5 mm without relevant adverse consequences does not require clinicians to worry about the myopia control efficiency, and the continued wearing of OK lenses should be encouraged. As for the better myopia control efficiency caused by decentration, it can be applied to the modified lens design by further studies clarifing the mechanism of this phenomenon. (see Page 20, line 451)