

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Hallux Valgus Orthosis Characteristics and Effectiveness: A Systematic Review with Meta-analysis
<b>AUTHORS</b>	Kwan, Mei-Ying; Yick, Kit-Lun; Yip, Joanne; Tse, Chi-Yung

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Reina-Bueno, María University of Seville
<b>REVIEW RETURNED</b>	17-Jan-2021

<b>GENERAL COMMENTS</b>	<p>The article is very interesting, but for its publication you need to make some changes. The inclusion of the PICO question is essential.</p> <p>The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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<b>REVIEWER</b>	Chang, Min Cheol Yeungnam University Medical Center
<b>REVIEW RETURNED</b>	21-Jan-2021

<b>GENERAL COMMENTS</b>	<p>The authors evaluated the effectiveness of hallux valgus orthosis with meta-analysis.</p> <p>This is a very interesting study. However, there is no pooled analysis of the included studies after the classification of studies following the types of orthoses. Also, there are no results on publication bias. I think the authors did not follow a general rule for meta-analysis.</p>
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<b>REVIEWER</b>	XIN, Binjie Shanghai University of Engineering Science
<b>REVIEW RETURNED</b>	02-Apr-2021

<b>GENERAL COMMENTS</b>	<p>This paper presents a systematic review and meta analysis is to determine whether current foot orthoses are effective in treating HV, and to investigate the associated orthosis characteristics. This systematic review demonstrates a positive relationship between HVA reduction and pain level with orthoses that offer a toe separator. The length of the orthosis could also be a critical factor in HV treatment. Therefore, it is important to include these two elements in the conservative treatment of HV deformity, as well as the future development of HV orthoses. It is recommended that a full-length orthosis with a fixed toe separator or a dynamic orthosis is used to maintain the anatomic alignment of the big toe for those who suffer from HV. The results of this study provide patients, practitioners and physicians with important information to help</p>
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	them better understand the characteristics of various HV orthoses and their performance in reducing HV deformity, and contribute to decisions around optimal treatment for patients. Generally, this paper is well written with detailed data and result analysis. It is a review of the related works. I suggest this paper could be accepted for the publication.
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<b>REVIEWER</b>	Sachiko, SUKIGARA Kyoto Institute of Technology, Fibre Science and Engineering
<b>REVIEW RETURNED</b>	06-Apr-2021

<b>GENERAL COMMENTS</b>	<p>A systematic review with Meta-analysis is the new approach for this particular topic, that is the design of orthoses for hallux valgus. It is very interesting approach. But following points to be considered to make strength of this paper.</p> <p>1. P2-3. ABSTRACT [Objective: ] Please make clearly mention the advantage using the meta-analysis for this hallux valgus orthosis effectiveness. [Strengths and limitations] P3, L22 I have doubt “the results can highlight the design features” based on this data. Consider the expression.</p> <p>2. P8 L17 Assessment of the study eligibility was performed by one investigator. Please mention the background of investigator and reliability of one investigator.</p> <p>3. Discussion 9 papers were chosen and analyzed. Unfortunately, experimental design in Table II is not well compatible, therefore author explained the individual case. The quality of data may be discussed based on authors expert knowledge to find the more sophisticated future trials.</p>
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<b>REVIEWER</b>	Joo, LiJin National Cancer Institute, Biostatistics Branch, Division of Cancer Epidemiology and Genetics
<b>REVIEW RETURNED</b>	10-May-2021

<b>GENERAL COMMENTS</b>	<p>To Authors,</p> <p>Authors of “Hallux Valgus Orthosis Characteristics and Effectiveness: A Systematic Review with Meta-analysis” attempted to propose the unique usage of meta-analysis on a topic rarely discussed. As a statistician, I am a bit concerned about the validity of extended interpretation of meta-analysis, however, this study possesses the strength in two aspects, 1) finding nine high quality papers on a very specific topic, 2) through comparison of each orthosis item and outcome.</p>
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To be more easily accepted by potential readers who may not be familiar topic or meta-analysis, I would like to encourage authors to work more on distinguishing which findings are more important and which are about details in the manuscript and making the presentation to be more effective.

For the better usage of meta-analysis  
Currently, the message or objective of manuscript is not clear, and I suspect this confusion is rooted from authors' misunderstanding of the purpose of meta-analysis based on certain statements of their findings.

Meta-analysis is not a tool of exploration but a way of confirmation of certain hypothesis. Based on the secondary information, findings of meta-analysis have limited implications only. For this reason, I suggest to re-write the objective and the conclusion in the abstract.

I think the better description of objective or finding is to confirm "current foot orthoses are effective in treating HV", not to "investigate the associated orthosis characteristics". Accordingly, some descriptions of result and conclusion need to be updated.

Based on your result, the better conclusion is that "orthoses with a toe separator are effective for reducing the HAV and foot pain."  
You are currently describing full-length and ¾ length design separately. Since there is no significant difference (estimated SMD is too small and 95 CI of two are overlapping) between the two, you cannot claim that the full length is better.

For better description of result  
Need some emphases on findings in "Overview of results from meta-analyses". One of the main complaints about writing is no clear unified message. It was confusing whether you want to talk about differences between different options (in this case, meta-analysis is not an ideal study method), or existing orthoses, regardless of types, are effective.

I suggest focusing on one key message, such as "toe-separators are effective on HVA" in the first part. A statement that toe-separator is effective treating HV is your interpretation of this. I'd suggest to be more careful to describe what you are observing from the data and what you can learn from the observations. You may also need to adjust descriptions, stating HVA as primary outcome and result in other outcomes supporting the findings in HVA.

For improving presentations

Transform the Table 4 and 5 to forest plots using a software package, such as R [3].

1) Tables may be kept, but a graph can emphasize findings more effectively.

2) Also, the pooled estimates from all available studies can justify your conclusion despite relatively small effect size of individual studies.

Please check if your labeling for Table 5 is correct. There is no label indicating which values are for treatment group versus control group currently.

You should consider a forest plot focused on HVA only and comparing pre and post-operative in both “treatment” and “control” arms.

1) You may treat HVA as your primary outcome and the efficacy of “toe separator” or other accessories can be better supported if the post and pre difference is greater in treatment arms than in control arms.

2) All other findings seem secondary to me. Please re-organize the plots/tables and the result section to emphasize “how certain the efficacy of toe separator is” or any other key message.

Correct Table 3.

1) Consider each cell to have 0/1/2 so that each column (paper) has a numeric score.

2) I'd suggest putting the forest plots first followed by Table 3. Though qualitative evaluation of reliability/validity for nine selected studies provides the rich information, these are only secondary information as the reliability info is not used for adjusting meta-analysis result.

Reference

	1.Wolfgang Viechtbauer, "The metaphor package: A Meta-Analysis Package for R.", Metaphor Project, 08 Feb 2021, <a href="https://www.metafor-project.org/doku.php/">https://www.metafor-project.org/doku.php/</a>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. María Reina-Bueno, University of Seville

Comments:

The article is very interesting, but for its publication you need to make some changes. The inclusion of the PICO question is essential.

Response: Taking the advice of Reviewer 1, the PICO question has been added to the section of "Search methods for identification of studies" that details of the search strategy has been addressed.

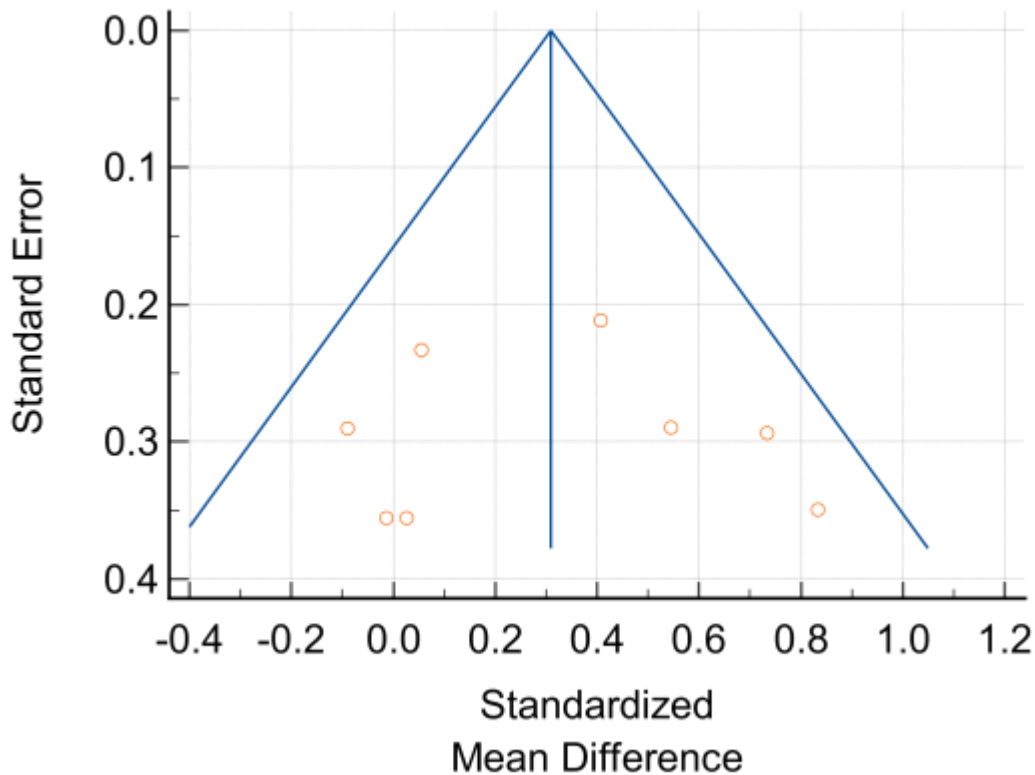
Reviewer: 2

Prof. Min Cheol Chang, Yeungnam University Medical Center

Comments:

The authors evaluated the effectiveness of hallux valgus orthosis with meta-analysis. This is a very interesting study. However, there is no pooled analysis of the included studies after the classification of studies following the types of orthoses. Also, there are no results on publication bias. I think the authors did not follow a general rule for meta- analysis.

Response: Thank you. Following your suggestion, the results of pooled estimation have been added and shown in Figure IV. The analysis follows the instructions of Cochrane training and complies with PRISMA. The funnel plot below illustrates the potential publication bias of studies focusing on HVA evaluation. No asymmetry was reported, nor indication of possible publication bias. Egger's test for asymmetry is not significant ( $p= 0.9427$ ).



Reviewer: 3  
 Dr. Binjie XIN, Shanghai University of Engineering Science  
 Comments:

□ This paper presents a systematic review and meta-analysis is to determine whether current foot orthoses are effective in treating HV, and to investigate the associated orthosis characteristics. This systematic review demonstrates a positive relationship between HVA reduction and pain level with orthoses that offer a toe separator. The length of the orthosis could also be a critical factor in HV treatment. Therefore, it is important to include these two elements in the conservative treatment of HV deformity, as well as the future development of HV orthoses. It is recommended that a full-length orthosis with a fixed toe separator or a dynamic orthosis is used to maintain the anatomic alignment of the big toe for those who suffer from HV. The results of this study provide patients, practitioners and physicians with important information to help them better understand the characteristics of various HV orthoses and their performance in reducing HV deformity, and contribute to decisions around optimal treatment for patients. Generally, this paper is well written with detailed data and result analysis. It is a review of the related works. I suggest this paper could be accepted for the publication.

Response: Thank you very much for your appreciation.

Reviewer: 4  
 Prof. SUKIGARA Sachiko, Kyoto Institute of Technology

Comments:

A systematic review with Meta-analysis is the new approach for this particular topic, that is the design of orthoses for hallux valgus. It is very interesting approach. But following points to be considered to make strength of this paper.

P2-3. ABSTRACT

□ [Objective: ]

Please make clearly mention the advantage using the meta-analysis for this hallux valgus orthosis effectiveness.

Response: Thank you very much for your comment. The objective is modified with focus on exploring the HV orthotic treatment effect. With the use of systematic review and meta-analysis, previous literatures on evaluation of the functionality of HV orthosis has been screened out. Hence, the therapeutic effect of HV orthoses can be evaluated, with particular attention on the outcome of angle correction. The treatment effectiveness of different types and features of orthoses can also be estimated, providing a clear direction and evidence on the choice of orthoses.

□ [Strengths and limitations]

P3, L22 I have doubt “the results can highlight the design features” based on this data. Consider the expression.

Response: Taking the advice of Reviewer 2, the pooled estimation comparing different orthoses designs in terms of angle correction was conducted. Based on the results, the statement above has been revised. It is found that “the orthoses with a toe separator had better treatment effects”.

□ P8 L17 Assessment of the study eligibility was performed by one investigator. Please mention the background of investigator and reliability of one investigator.

Response: In this study, an experienced researcher who has been intensively trained by a registered prosthetist-and-orthotist with more than 20 years of clinical experiences on foot orthoses was invited to perform the assessment twice. The results were compared with excellent repeatability.

□ [Discussion] 9 papers were chosen and analyzed. Unfortunately, experimental design in Table II is not well compatible, therefore author explained the individual case. The quality of data may be discussed based on authors expert knowledge to find the more sophisticated future trials.

Response: Thank you very much for your comment. Table II has been revised, and pooled estimation has been given to advance the analysis and confirm the findings.

Reviewer: 5

Dr. LiJin Joo, National Cancer Institute

Comments:

Authors of “Hallux Valgus Orthosis Characteristics and Effectiveness: A Systematic Review with Meta-analysis” attempted to propose the unique usage of meta-analysis on a topic rarely discussed. As a statistician, I am a bit concerned about the validity of extended interpretation of meta-analysis, however, this study possesses the strength in two aspects, 1) finding nine high quality papers on a very specific topic, 2) through comparison of each orthosis item and outcome.

To be more easily accepted by potential readers who may not be familiar topic or meta-analysis, I would like to encourage authors to work more on distinguishing which findings are more important and which are about details in the manuscript and making the presentation to be more effective.

#### 1. For the better usage of meta-analysis

□ Currently, the message or objective of manuscript is not clear, and I suspect this confusion is rooted from authors’ misunderstanding of the purpose of meta-analysis based on certain statements of their findings.

Meta-analysis is not a tool of exploration but a way of confirmation of certain hypothesis. Based on the secondary information, findings of meta-analysis have limited implications only. For this reason, I suggest to re-write the objective and the conclusion in the abstract. I think the better description of objective or finding is to confirm “current foot orthoses are effective in treating HV”, not to “investigate the associated orthosis characteristics”.

Accordingly, some descriptions of result and conclusion need to be updated.

Based on your result, the better conclusion is that “orthoses with a toe separator are effective for reducing the HAV and foot pain.” You are currently describing full-length and  $\frac{3}{4}$  length design separately. Since there is no significant difference (estimated SMD is too small and 95 CI of two are overlapping) between the two, you cannot claim that the full length is better.

Response: Thank you very much for your suggestions. The objectives and conclusion of this study have been revised to confirm the effectiveness of HV orthoses treatment. The results and conclusions have also been updated. Concerns about the length of the orthoses have been minimized to avoid confusion.

#### □ 2. For better description of result



Need some emphases on findings in “Overview of results from meta-analyses”. One of the main complaints about writing is no clear unified message. It was confusing whether you want to talk about differences between different options (in this case, meta-analysis is not an ideal study method), or existing orthoses, regardless of types, are effective.

I suggest focusing on one key message, such as “toe-separators are effective on HVA” in the first part. A statement that toe-separator is effective treating HV is your interpretation of this. I’d suggest to be more careful to describe what you are observing from the data and what you can learn from the observations. You may also need to adjust descriptions, stating HVA as primary outcome and result in other outcomes supporting the findings in HVA.

Response: Thank you. The description of result has been substantially changed, focusing on the main effect of HV orthoses, which is HVA correction. The treatment effectiveness of different types and features of orthoses is now clearly presented, by using the approach of meta-analysis.

□ 3. For improving presentations

1. Transform the Table 4 and 5 to forest plots using a software package, such as R [3].

1) Tables may be kept, but a graph can emphasize findings more effectively.

2) Also, the pooled estimates from all available studies can justify your conclusion despite relatively small effect size of individual studies.

Response: Thank you for your suggestions, forest plots were generated for improve visualization of results. They are combined with the result table and shown in Figure IV. Results of pooled estimation are also added.

2. Please check if your labeling for Table 5 is correct. There is no label indicating which values are for treatment group versus control group currently.

Response: Thank you very much for checking. However, in order to make the objective of the article clearer, the comparison between treatment and control group is removed in the revised manuscript.

3. You should consider a forest plot focused on HVA only and comparing pre and postoperative in both “treatment” and “control” arms.

1) You may treat HVA as your primary outcome and the efficacy of “toe separator” or other accessories can be better supported if the post and pre difference is greater in treatment arms than in control arms.

2) All other findings seem secondary to me. Please re-organize the plots/tables and the result section to emphasize “how certain the efficacy of toe separator is” or any other key message.

Response: Thank you for your suggestion. The pooled estimation on HVA has been completed, and the result is described in the text in the section “Overview of results from meta-analyses” as “The

pooled estimation for orthoses with a toe separator was further investigated that the effect is medium with SMDs 0.50 (0.189,0.803), with I2 statistics 14.52%.....The pooled estimation for dynamic orthoses showed small effect in HVA correction with SMDs 0.27 (-0.211,0.751), I2 42.29%.” In the discussion, the advantages of including toe separator was emphasized with “The treatment effect of orthoses with a toe separator are larger than tht of dynamic orthoses”. The result table is combined with the forest plots.

□ 4. Correct Table 3.

1) Consider each cell to have 0/1/2 so that each column (paper) has a numeric score.

2) I'd suggest putting the forest plots first followed by Table 3. Though qualitative evaluation of reliability/validity for nine selected studies provides the rich information, these are only secondary information as the reliability info is not used for adjusting meta-analysis result.

Reference

1.Wolfgang Viechtbauer,“The metaphor package: A Meta-Analysis Package for R.”, Metaphor Project, 08 Feb 2021, <https://www.metafor-project.org/doku.php/>

Response: Based on your suggestion that the sequence of result tables and figures are reviewed. Taking your advice, numbers are given for clear demonstration. The order of operation is prior to the meta-analysis. The forest plots and the table shown in Figure IV are important, and are discussed in several connected sections at the end of the manuscript, namely “Overview of results from meta-analyses”, “Observation of key design features”, and “Discussion”.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Joo, LiJin National Cancer Institute, Biostatistics Branch, Division of Cancer Epidemiology and Genetics
<b>REVIEW RETURNED</b>	11-Jul-2021

<b>GENERAL COMMENTS</b>	<p>I am impressed by the improvements in the revised manuscript. Though your work made many progresses, your new attempts created a few issues. I hope the authors put extra hours on them to make the manuscript immaculate:</p> <ol style="list-style-type: none"> <li>1. Please include a few lines of descriptions about random effect model and I<sup>2</sup> in the method section, if you want to include these statistics. The two concepts may not be known to all readers.</li> <li>2. Your interpretation about random effect model is a bit problematic.</li> </ol> <p>It is unclear why random effect is introduced and how the statistics is related to your result. An estimated random effect from multiple studies gives the better sense of uncertainty.</p>
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	<p>For instance, if your fixed effect estimate (i.e., overall SMD) is greater than a random estimate, you may feel more confident that the intervention of interest is more likely meaningful. You may revise the result descriptions how the overall SMD is relative to the size of a random effect.</p> <p>Or, you may drop the first sentence in "Overview of results from meta-analysis" but add the color legend descriptions for random effects in the figure description of Figure IV only.</p> <p>3. Overall, the "Overview of results from meta-analysis" section is not easy to follow. My suggestion to improve the radiality of the section is to unify the format.</p> <p>Currently, you use at least three formats: 1) SMD (CI), I<sup>2</sup>, 2) (SMD, CI), I<sup>2</sup>, 3) SMD, CI, no I<sup>2</sup>. This makes it difficult to spot your findings at the first sight. Please consider report all result in one format: your verbal description of result (SMD, CI, I<sup>2</sup>) or (SMD, CI: ) with I<sup>2</sup>: (if available).</p> <p>4. I found two typos, i) the second sentence of "Result" section in page 2, "The major bias are ...", you may use the same phrase in page 12 "the main causes of potential bias"; ii) adhered ==&gt; adhere in Results/Search Results selection, in page 9.</p> <p>Though my comments get a bit longer, these are to improve the quality rather than to address the inadequacy of your work. Hope this long comment would not discourage you to put a few more hours for even better result.</p>
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## VERSION 2 – AUTHOR RESPONSE

Reviewer: 5

Dr. LiJin Joo, National Cancer Institute

Comments:

I am impressed by the improvements in the revised manuscript. Though your work made many progresses, your new attempts created a few issues. I hope the authors put extra hours on them to make the manuscript immaculate:

1. Please include a few lines of descriptions about random effect model and  $I^2$  in the method section, if you want to include these statistics. The two concepts may not be known to all readers.

Response: Thank you for your suggestion. An explanation of  $I^2$  has been added to the "Data Management" section.

2. Your interpretation about random effect model is a bit problematic.

It is unclear why random effect is introduced and how the statistics is related to your result. An estimated random effect from multiple studies gives the better sense of uncertainty.

For instance, if your fixed effect estimate (i.e., overall SMD) is greater than a random estimate, you may feel more confident that the intervention of interest is more likely meaningful. You may revise the result descriptions how the overall SMD is relative to the size of a random effect.

Or, you may drop the first sentence in "Overview of results from meta-analysis" but add the color legend descriptions for random effects in the figure description of Figure IV only.

Response: Thank you for your suggestions. Based on your suggestion, the description of the color legend has been moved to Figure IV.

3. Overall, the "Overview of results from meta-analysis" section is not easy to follow.

My suggestion to improve the readability of the section is to unify the format.

Currently, you use at least three formats: 1) SMD (CI),  $I^2$ , 2) (SMD, CI),  $I^2$ , 3) SMD, CI, no  $I^2$ . This makes it difficult to spot your findings at the first sight.

Please consider report all result in one format: your verbal description of result (SMD, CI:,  $I^2$ ) or (SMD, CI: ) with  $I^2$ : (if available).

Response: Thank you for your careful review. The format is corrected to (SMD, CI: ) with  $I^2$ : (if available).

4. I found two typos, i) the second sentence of "Result" section in page 2, "The major bias are ...", you may use the same phrase in page 12 "the main causes of potential bias";  
ii) adhered ==> adhere in Results/Search Results selection, in page 9.

Though my comments get a bit longer, these are to improve the quality rather than to address the inadequacy of your work. Hope this long comment would not discourage you to put a few more hours for even better result.

Response: The typo has been corrected. Thank you for your comment. These comments are very detailed and constructive, which are of great help in improving the quality of the manuscript. We express our heartfelt thanks to you.