

1 **Ms. Ref. No.: World Journal of Orthopedics-72695**

2 **Title:** Fragility of statistically significant findings from randomized clinical trials of surgical  
3 treatment of humeral shaft fractures: a systematic review

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5 Dear Reviewers and Editors,

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7 The authors of this team thank you for your time spent in evaluation of this manuscript. We hope  
8 that you found this article valuable to the readership of *World Journal of Orthopedics*. The  
9 reviewers have provided excellent feedback to increase the impact of our article. We have  
10 revised the manuscript per the reviewer comments and feel that this has substantially increased  
11 the quality of this paper. Please find these revisions below. For ease of viewing, these revisions  
12 have been uploaded as a separate file as well with specific changes are highlighted. The  
13 reviewers will find that the manuscript also reflects the same highlighted changes. We hope that  
14 all comments were sufficiently addressed. If there are any additional concerns with this  
15 manuscript, please do not hesitate to contact our office.

16  
17 Sincerely,

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19 Joseph N. Liu, MD

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Reviewer/Editor Comment	Author Response
<i>Reviewer 1</i>	
Very well written manuscript and quite an innovational way of applying the concept of FI in interpreting the review's findings to understand the application of available evidence beyond the p-value to clinical application. Consider the comments below 1. Minor grammatical error	Thank you for your kind words. There were no references by the reviewer to minor grammatical errors. However, the authors went through the manuscript and changed all grammatical errors as identified by the word processing system. If there are any additional grammatical errors, the authors are more than willing to make these changes if they are pointed out by the reviewer/editor.
2. The assessment of the quality of evidence was missing- i.e. assessment of heterogeneity, assessment of the risk of bias	Thank you for this comment. The author is provided the JADAD score which assesses the quality of evidence of a particular study in Table 1.
<i>Reviewer 2</i>	
Several points need to be addressed before this article is ready for publication. In the part of Keywords: Humerus fracture, open reduction internal fixation, intramedullary nail, fragility index, complications, fragility index) fragility index is repeated.	Thank you for the comment. The repeated keyword was removed.
In the introduction you emphasized how: While the vast majority may be managed nonoperatively[1-5], surgical treatment is generally indicated for open fractures, polytrauma patients, ipsilateral humeral shaft and forearm fractures (floating elbow), segmental fractures, and cases of failed treatment in functional brace[3]. Maybe you should change: Currently, there are no defined gold standards for the treatment of humeral shaft fractures. 1.Ouyang H, Xiong J, Xiang P, Cui Z, Chen L, Yu B. Plate versus intramedullary nail fixation in the treatment of humeral shaft fractures: an updated meta-analysis. J Shoulder Elb Surg. 2013;22(3):387-9. 2. Gosler MW, Testroote M, Morrenhof JW, Janzing HM. Surgical versus non-surgical interventions for treating humeral shaft fractures in adults. Cochrane Database Syst Rev. 2012;1:CD008832.	Thank you for this comment. The authors decided to not remove the section from the introduction that is highlighted by the reviewer. However, the authors have addended the statement to highlight that there is currently no goal standards of humeral shaft fracture management as highlighted by the reviewer (lines 7-8).  "However, it is important to note that there are currently no defined gold standards for the treatment of humeral shaft fractures[6,7]."

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