To the Editorial Board,

We are grateful for your consideration of our manuscript entitled, 'Effect of NSAIDs on Fracture Healing in Children: A Systematic Review' as an invited systematic review. We appreciate your comments for improvement and have addressed these changes in our manuscript. Please see our responses below.

1. The language of the article should be reviewed by a native speaker.

Each of the authors is a native English speaker, and we have each reviewed the manuscript carefully for grammatical and typographical errors. We have corrected any such errors where we encountered them. If the editors have any further concerns about the language of the paper, we would be grateful to learn of these and to incorporate any desired changes.

2. The discussion section should be written in more elaborately. The effects of COX-1 and COX-2 on wound healing should be mentioned in detail.

We agree that surgeons may be concerned about the potential wound-healing effects of COX-1 and -2 inhibiting drugs. There is no current evidence, including in the six studies contained within the review, that NSAIDs adversely affect wound healing in children. To better emphasize this finding, we have briefly expounded upon our existing discussion point in line 164-165.

3. A statistics section does not appear in the study. Didn't the authors do any statistics?

With respect to the reviewer's final query regarding a statistical analysis section, the authors agree that this manuscript does not have a statistical analysis section, as no statistical analysis was done. Rather, this invited article was a systematic review of the existing literature. As detailed in the methods section, we utilized a clearly defined, systematic method to gather all available empirical research and answer a specific, predefined question in a narrative format. In contrast, a meta-analysis is the statistical

Pediatric NSAIDs Systematic Review

process of analyzing and combining results from several similar studies. Given the

limited available evidence and broad disparity in published data, this type of

methodology would not be feasible for the specific question posed in this systematic

review. Therefore, the authors do not feel that we can add a statistical analysis section

and defer further changes to the discretion of the editor.

This manuscript has not been previously published and is not under consideration in

the same or substantially similar form in any other peer-reviewed media. As

corresponding author, I take full responsibility for all aspects of this paper. We have no

conflicts of interest to disclose.

Re-reviewer comment: I have no further comments.

Thanks for your comments.

Sincerely,

Ashaan Swarup

Ishaan Swarup, MD

Assistant Professor of Clinical Orthopaedic Surgery

Associate Fellowship Director, Pediatric Orthopaedic

Surgery University of California, San Francisco

UCSF Benioff Children's Hospital Oakland

747 52nd Street

Oakland, CA 94609

Re-reviewer comment:

I have no further comments.

Pesponse: Thanks for your comments.