**Author’s response to reviews**

**Title:** Effects of valproic acid on skeletal metabolism in children with epilepsy: a systematic evaluation and meta-analysis based on 14 studies

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BPED-D-19-00413R2

TI: “Effects of valproic acid on skeletal metabolism in children with epilepsy: a systematic evaluation and meta-analysis based on 14 studies.”

Dear Dr.:

Our manuscript has been carefully revised according to the reviewers’ suggestions and also revised according to the preferred format for the journal. The manuscript has been professionally edited for English language readability prior to resubmission to the journal. We have taken all of the comments of the two reviewers into account and wish to respond as follows:

Part A: COMMENTS OF REVIEWER #1

I think this is massively improved in terms of the language and clarity, nice work in getting that up to speed.

A couple of further corrections and suggestions;

On Page 4, under inclusion criteria: number 2) I would suggest instead "Children were under 18 years old and could participate in outdoor activities"

Answer: We thank the reviewer for his advice. The changes is showed on page 4, line 5-6, highlighted in blue.

Page 10, last paragraph starts with "The dual energy...." Remove "The", also in the next sentence, this

does not need a "the" in front of DEXA

Answer: The change is showed on page 10, line 17-18, highlighted in blue.

In the conclusion, in the very last part of the paragraph (and also in the conclusion section of the abstract), the use of bone damage may not really be accurate. As you have looked specifically at the parameters that are affected by long term use, and they are vitamin D and BMD, it might be more accurate to use osteopenia or osteoporosis?

Answer: We agree with the reviewer's suggestion, this will help us improve the quality of the
manuscript. We have made changes and this is shown on page 2, line 15, and page 11, line 19, highlighted in blue.

I think there needs to be a statistics review, as this is not my area of expertise, but the methods appear clear and data also clear
Answer: The statistical problems involved in our work are completed by a dedicated statistician. One of the authors, Wenlong Gao, is an expert in epidemiology and statistics.

Part B: COMMENTS OF REVIEWER #2
The authors are congratulated for a thorough revision and have addressed all the major concerns. Much more readable and only minor edits remain.

Background: page 3, line 2 ..... as it displays certain ...
Answer: We have revised it, which is showed on page 3, line 2, highlighted in blue.

Lit searching: page 3, line 20 ...... childhood epilepsy ..... indices ...
Answer: We have revised it, which is showed on page 3, line 21, highlighted in blue.

Inclusion criteria: 1 ..... epilepsy which met diagnostic ..... 
Answer: We have revised it, which is showed on page 4, line 4, highlighted in blue.

Results: 
25-OH-vitD paragraph: ..... in the valproic acid ....
Answer: We have revised it, which is showed on page 8, line 17, highlighted in blue.

Sensitivity: (Delete and) The funnel .......... was awarded
Answer: We have revised it, which is showed on page 9, line 15, highlighted in blue.

Discussion:
line 21 ...... control epileptic seizures ..... 
23 ..... and was followed ..... 
Answer: We have revised it, which is showed on page 9, line 22 and page 10, line 1, highlighted in blue.

2nd paragraph: 
Delete 2nd sentence - would not discuss non significant trends for PTH (figure 3B)
... showed that valproic ....
Answer: We have done it.

3rd: Dual ..... 
... and results indicated .... 
..... which implies that long .... 
... could help find changes .... 
Answer: We have revised it, which is showed on page 10, line 19, 21 and 22, highlighted in blue.

4th: Delete 'among the studies' line 8
Delete 'and the' line 9 and 'very'
Answer: We have removed it. The change is showed on page 11, line 4-6, highlighted in blue.
Figure 1 label: and (sp)
Answer: We have revised it. The change is showed on page 16, line 1, highlighted in blue.

We would like to extend thanks to all of the reviewers and to the editing staff at ‘BMC Pediatrics’ for this opportunity to resubmit a revised version of our work. We look forward to hearing from you, and, as before, please address all communications regarding this manuscript to myself as the corresponding author.

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