Author's response to reviews

Title: Clinical Decision Support of Therapeutic Drug Monitoring of Phenytoin: Measured Versus Adjusted Phenytoin Plasma Concentrations

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Author's response to reviews: see over
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To Editor, *BMC Medical Informatics and Decision Making*:

We submit a revised version of our manuscript entitled “Clinical Decision Support of Therapeutic Drug Monitoring of Phenytoin: Measured Versus Adjusted Phenytoin Plasma Concentrations” for consideration as a research article in *BMC Medical Informatics and Decision Making*. We have addressed the remaining concerns of the 2nd reviewer as detailed below.

The revised manuscript still has five figures and one table. The Additional File 1 now has seven figures, with one figure eliminated as recommended by the reviewer. A version of the manuscript that shows all changes made to the manuscript in Edit Tracking is submitted as supplemental data.

The authors attest that this is an original work and not in review at any other journal. The authors declare no conflicts of interest.

Thank you for your consideration.

Sincerely,

Matthew D. Krasowski, MD, PhD (for the authors)
Reviewer 2

Major Compulsory Revisions

This statement remains wrong: „... PTH\textsubscript{total} frequently is in a lower category than PHT\textsubscript{free} (e.g. PHT\textsubscript{total} below its therapeutic range but PHT\textsubscript{free} within or above its reference range), which could lead to clinical underdosing of the patient if PHT\textsubscript{total} and not PHT\textsubscript{free} were used as the basis to guide dosing.“

When PHT\textsubscript{total} is used for guiding of the treatment, these patients will be mistakenly supposed to be undertreated despite PHT\textsubscript{free} within or above its reference range and are in fact in a danger of toxicity when the dosage will be increased with the aim to reach PHT\textsubscript{total} reference range. The sentence should be rewritten or at least an adjective as „specious clinical underdosing …“ should be added.

This has been corrected to “...could lead to clinical overdosing of the patient...”

Discretionary revision
#1 As figure legend should be self-explanatory, it should be better to add the P value of statistical significance there.

Figure 5 legend now has P values of statistical significance.

#2 Additional figure 1 is superfluous as it contains the same data as Fig 1 but on logarithmic axes. Please use only one expression of data – preferably logarithmic axes. Consequently the logarithmic axes are recommended for the Additional fig 2.

Additional figure 1 has been eliminated. Additional fig 2 (Additional fig 1 in the revised manuscript) now has logarithmic axes.