Reviewer's report

Title: Covariates of intravenous paracetamol pharmacokinetics in adults

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Reviewer: Kashyap Patel

Reviewer's report:

This study develops a population pharmacokinetic model to assess the covariate effects of intravenous paracetamol disposition in adults. The authors then use the developed model to simulate the expected concentration-time profiles for a range of clinically-relevant patient sub-populations (healthy adult, intensive care, pregnant, postpartum and abdominal surgery).

The scientific rationale for the study is of clinical importance, and the procedures used for model development, evaluation and simulation are robust. I particularly wish to commend the authors for using allometry and a standardized body weight to estimate PK parameters (this is not surprising given that a senior author has extensively published in this area). The current study provides a real example of the application of weight standardization for covariate analysis and parameter comparison between- and within- studies.

Discretionary Revisions:

1. Abstract – The current “Background” section provides a statement of the study objective. I would recommend that the authors either change the sub-heading to “Objective” or provide a brief background.

2. Results – How much of the between-subject variability (BSV) in parameters were each of the covariates able to explain?

3. Table 2 – This table is probably not required for the general audience.

4. Figure 1 – The results of the VPC are acceptable. However, it may be clearer if the VPC were presented with the y-axis on a log scale. This is trivial, and I will leave it to the authors’ discretion.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests