

## Introduction

- The National Health and Nutrition Examination Survey (NHANES) provides biometric and chemical exposure biomonitoring data that are statistically representative of the modern U.S. population.
- High-throughput toxicokinetics (HTTK) R package is open-source software which includes several toxicological models and supporting data.<sup>1</sup>
- HTTK-pop Monte Carlo (MC) simulator draws from the NHANES biometrics to simulate toxicokinetic variability but utilizes data only up to the 2011-12 NHANES cohort.<sup>2</sup>
- We updated HTTK-pop MC by obtaining the most recently available NHANES biometrics, up to the 2017-18 NHANES cohort.
- In addition to biometrics, we examined alternate model structures in the HTTK package to model excretion by the kidney.<sup>3</sup> Braun *et al.* (2017)<sup>4</sup> points out that race (as a social construct) was inappropriately considered as biological risk factor, causing sociological health inequalities.
- Equations describing glomerular filtration rate (GFR) were revised to more accurately represent physiology and population racial variability.

## Methods

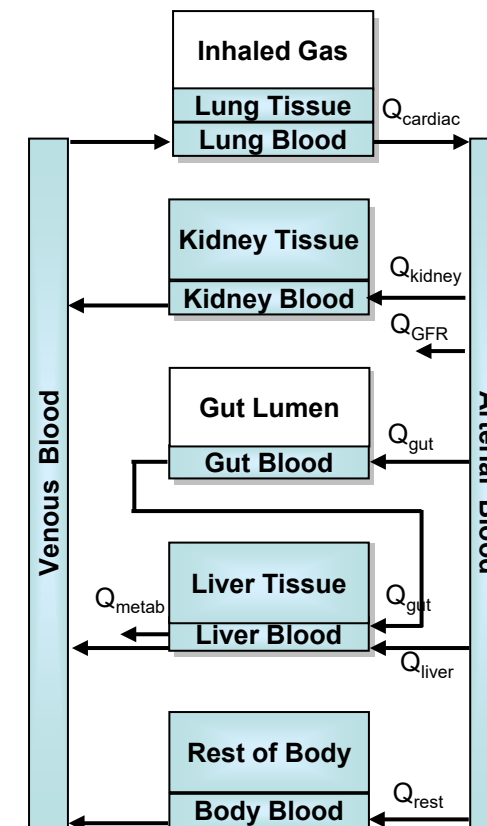


Figure 1. Representation of HTTK PBTK model structure

Corrected urinary clearance:

$$V_{ki} \frac{dC_{ki}}{dt} = Q_{ki} C_{art} - \frac{Q_{ki} R_{blood2plasma}}{K_{ki} f_{ub}} C_{ki} - \frac{Q_{gfr} f_{ub}}{R_{blood2plasma}} C_{art}$$

Original urinary clearance:

$$V_{ki} \frac{dC_{ki}}{dt} = Q_{ki} C_{art} - \frac{Q_{ki} R_{blood2plasma}}{K_{ki} f_{ub}} C_{ki} - \frac{Q_{gfr}}{K_{ki}} C_{ki}$$

where:

$$R_{blood2plasma} = \frac{\text{concentration in blood}}{\text{concentration in plasma}}$$

$$f_{ub} = \text{fraction unbound in plasma}$$

$$K_{ki} = \frac{\text{concentration in tissue}}{\text{concentration unbound in plasma}} = \frac{C_{ki}}{f_{ub} C_{plasma}}$$

$$Q_{gfr} = \text{glomerular filtration rate}$$

- Urinary Clearance correction based on concentration unbound in plasma leaving arterial blood, instead of leaving kidney**
- Removal of "race factor" in the equation used for GFR estimation**

## Conclusions

- Comparison of previous cohort (2007-12 NHANES cohort) and updated cohort (2013-18 NHANES cohort) indicates some increase in mean and median body weights for the updated cohort with no change or a slight decrease in body heights.
- The revised NHANES biometric data within HTTK-pop, GFR population prediction and variability, and the GFR physiological modeling structure produced refined estimates.
- Revised workflow to integrate new NHANES cohort data as they are published was developed, which also provides a template for analysis of other similar cohort biometric datasets.

*The views expressed here are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA.*

## Results

### NHANES biometrics and HTTK-pop MC simulator

	Total		Male		Female	
Weight (kg)	Median	Mean	Median	Mean	Median	Mean
NHANES 2007-2012	67.6	64.2	73	67.5	63	60.9
NHANES 2013-2018	67.8	65.2	72.9	68.2	63.5	62.4
Height (cm)	Median	Mean	Median	Mean	Median	Mean
NHANES 2007-2012	163	158	171	162	159	153
NHANES 2013-2018	162	157	170	162	158	153

Table 1. Comparison of mean/median weight and height of the previous cohort (2007-12 NHANES cohort) and updated cohort (2013-18 NHANES cohort) for three subgroups: Total, Male, Female.

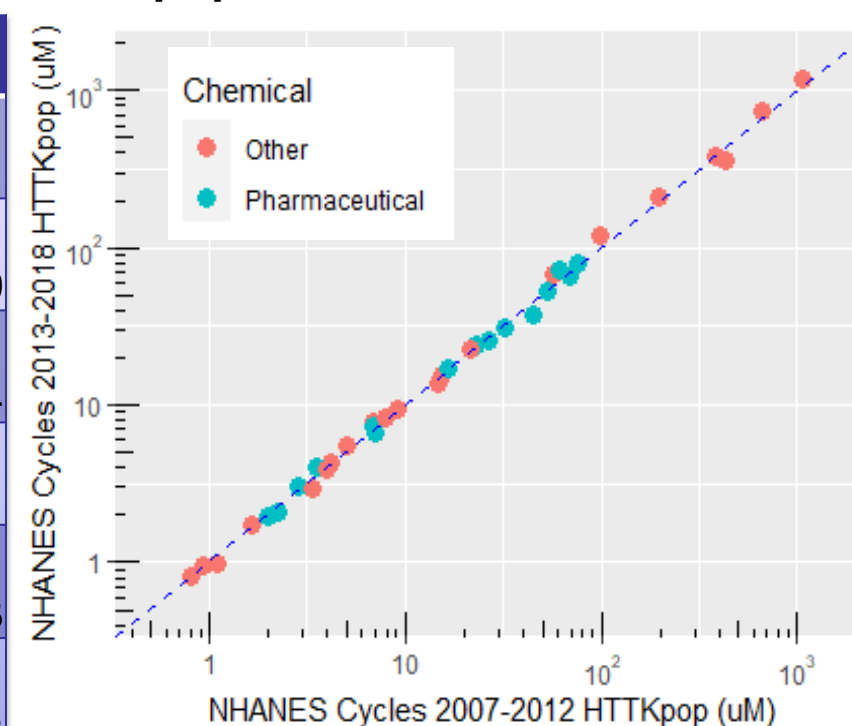


Figure 2. MC steady-state plasma concentration using the previous cohort (2007-12 NHANES cohort) versus updated cohort (2013-18 NHANES cohort) for 42 chemicals<sup>5</sup> with the HTTK PBTK model.

### HTTK PBTK GFR physiological modeling structure update

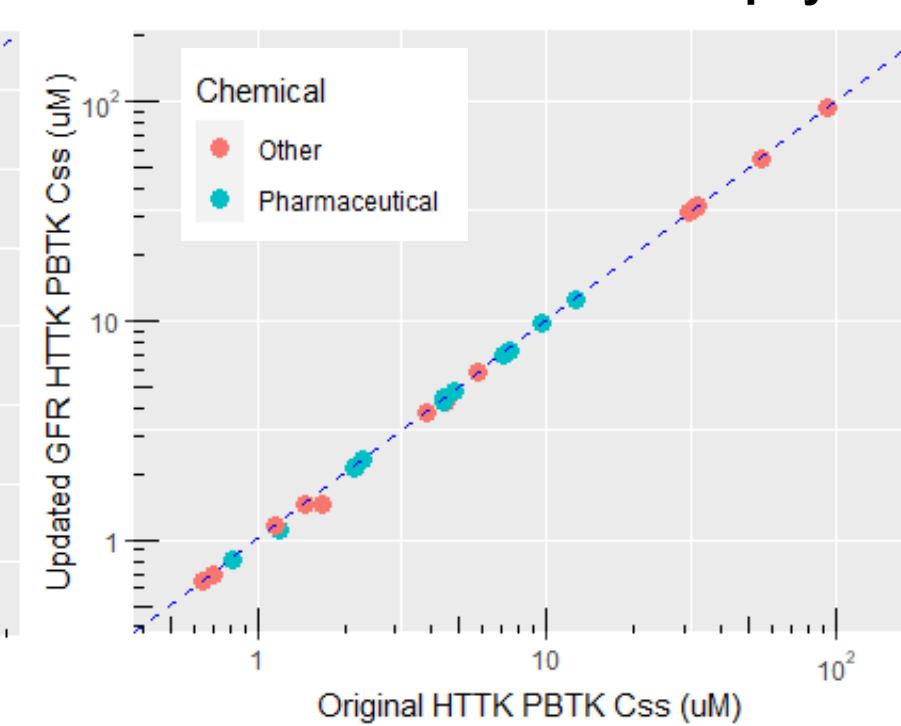


Figure 3. Steady-state plasma concentration using the original model versus updated GFR model for 42 chemicals<sup>5</sup> with the HTTK PBTK model.

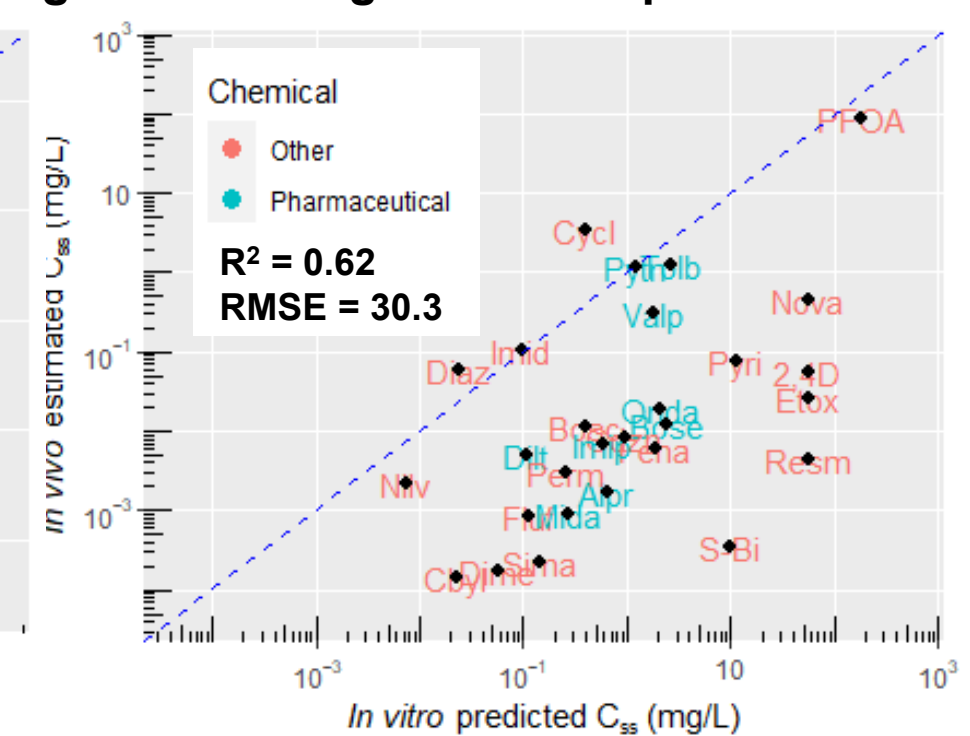


Figure 4. Steady-state plasma concentration using the updated GFR model with the HTTK PBTK model versus estimation based on *in vivo* data for 31 chemicals<sup>5</sup>.