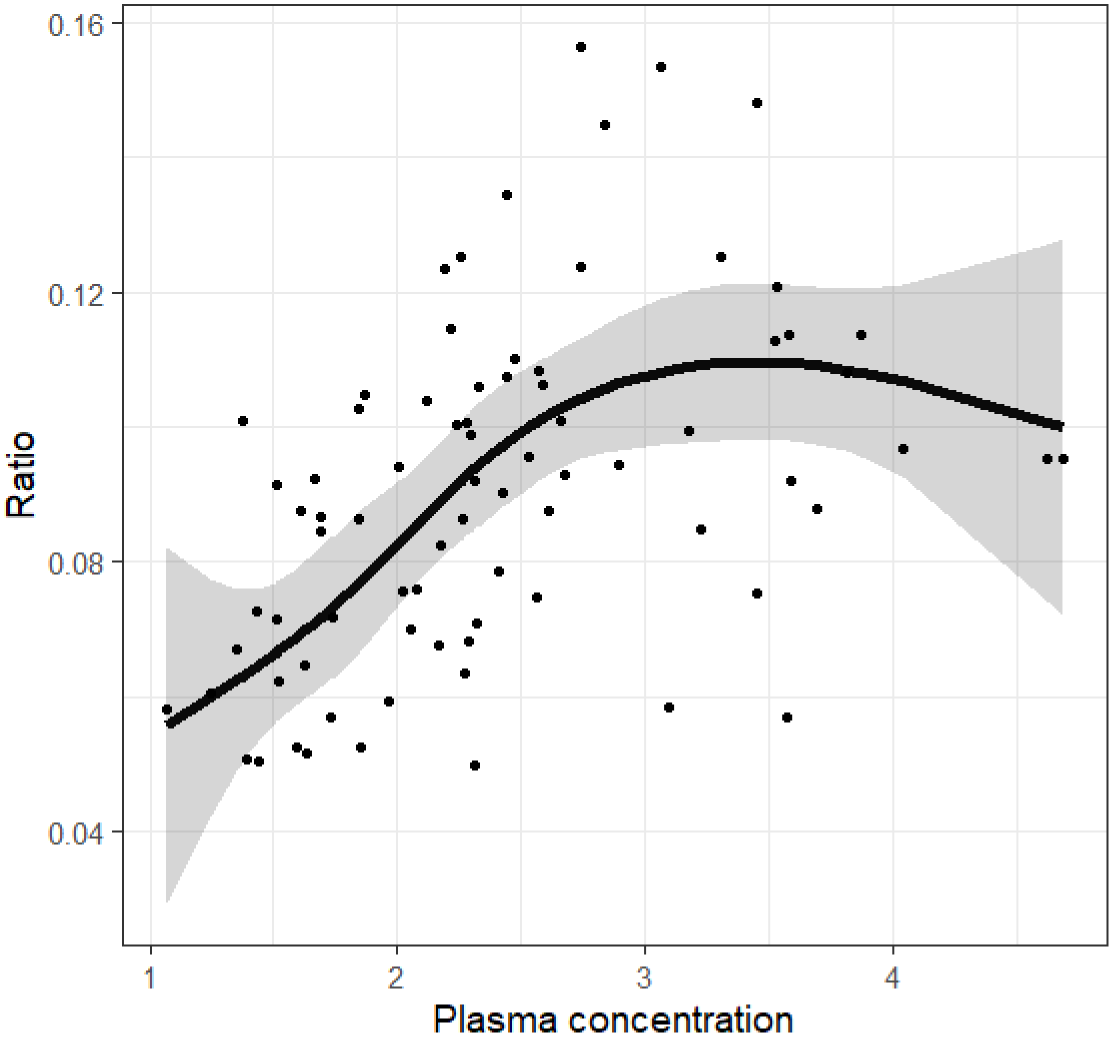
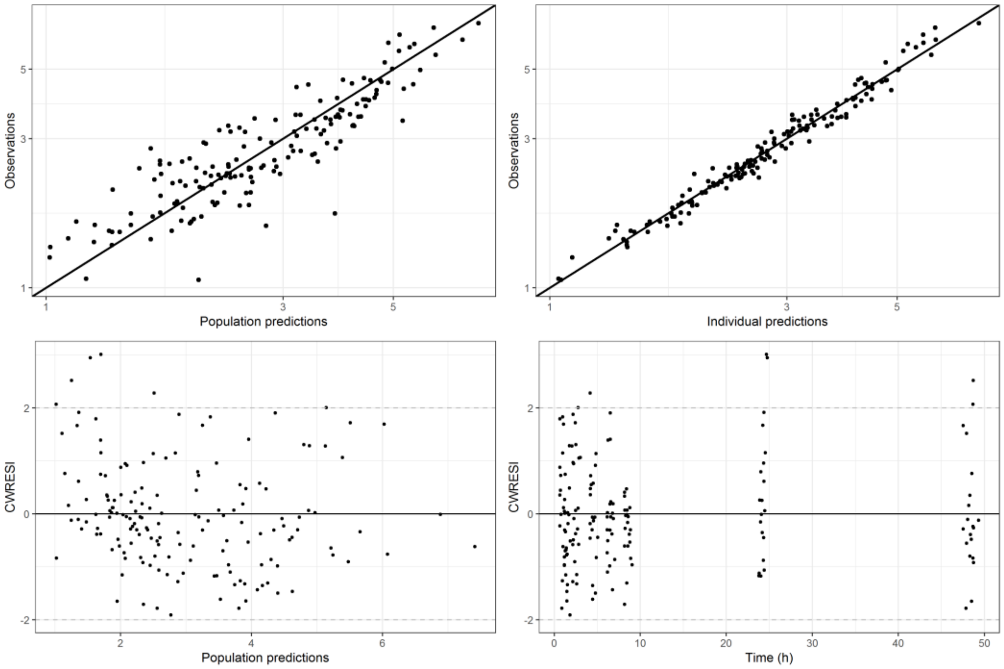
**Supplementary Figure S1. Nonlinear saliva:plasma ratio**



Relationship between saliva:plasma ratio (y axis) and plasma concentration (x-axis in ug/L). Each dot is an individual observation obtained later than 4h post-dose, the solid line and shaded area represents the estimated marginal mean (95% CI)

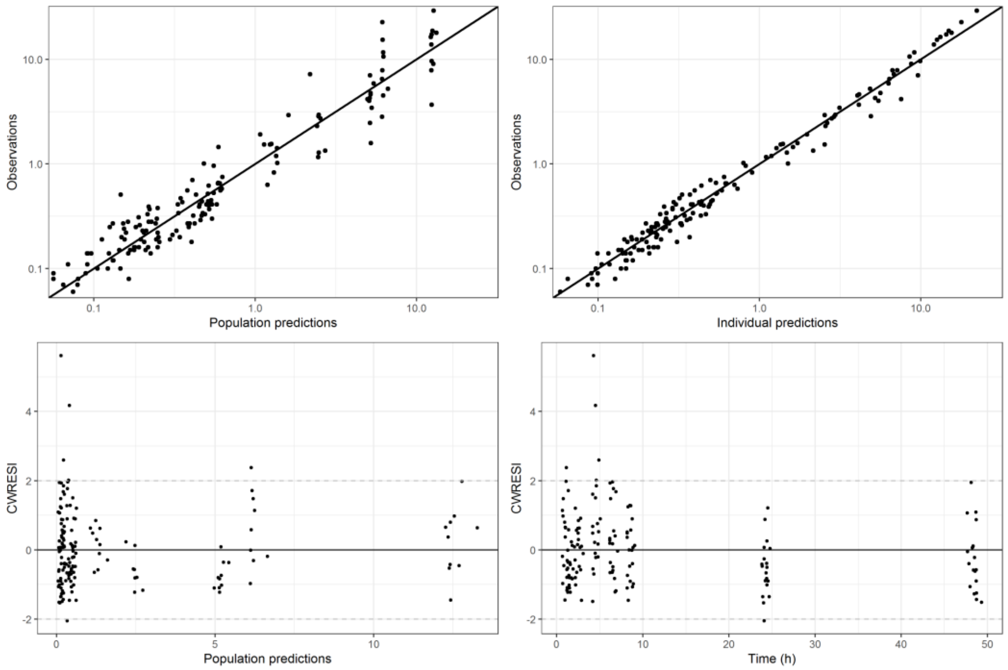
## Supplementary Figure S2. Goodness of fit plots

### A. Observation vs population prediction and individual prediction plasma observations



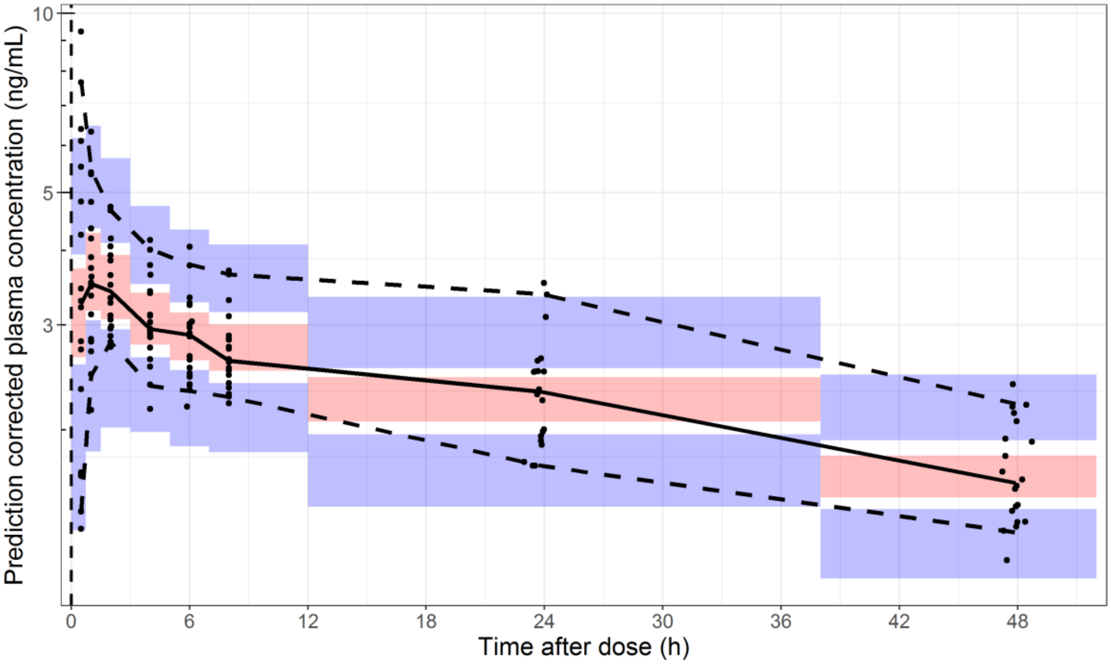
Upper left panel: plasma observations versus population prediction. Upper right panel: plasma observations versus individual predictions. Lower left panel: conditional weighted residuals with interaction (CWRESI) versus population prediction of plasma observations. Lower right panel: CWRESI versus time of plasma observations.

## B. Observation vs population prediction and individual prediction saliva observations



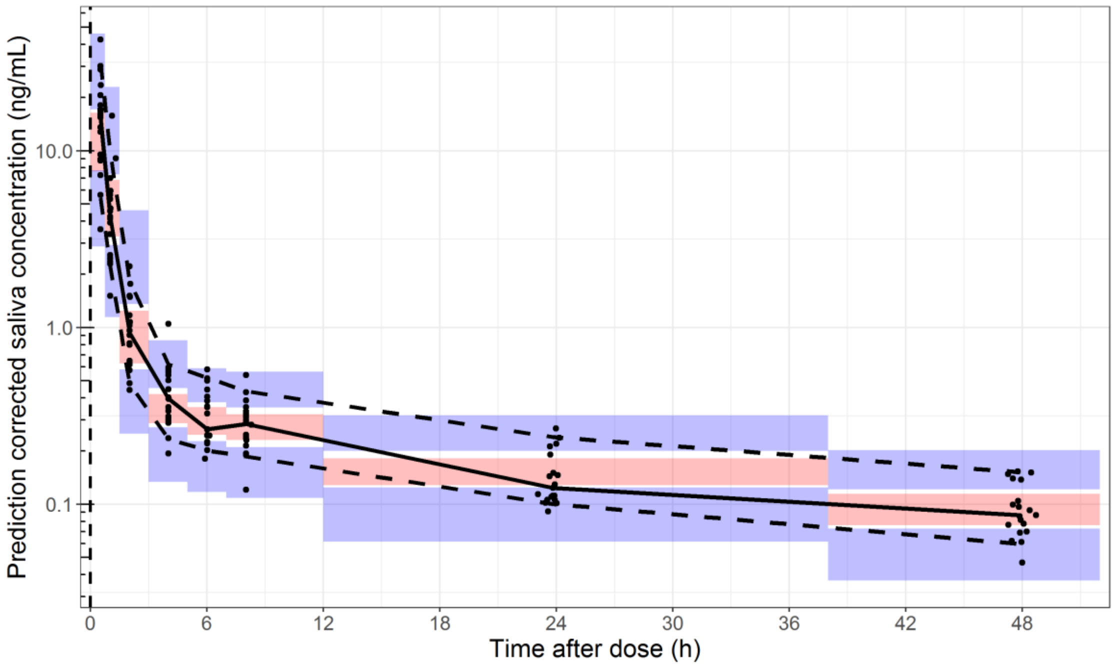
Upper left panel: saliva observations versus population prediction. Upper right panel: saliva observations versus individual predictions. Lower left panel: conditional weighted residuals with interaction (CWRESI) versus population prediction of saliva observations. Lower right panel: CWRESI versus time of saliva observations.

### C. pcVPC plasma observations



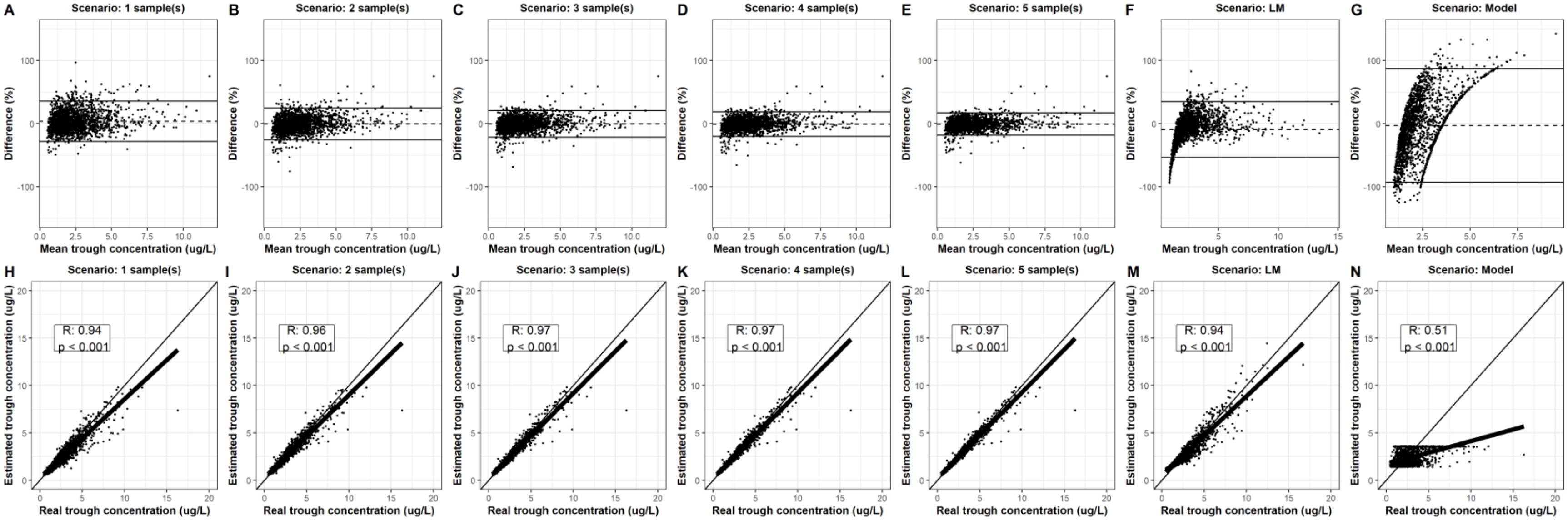
Prediction corrected visual predictive check of plasma observations. Black dots: prediction corrected observations; Black dashed lines: 80%-interval and median of the prediction corrected observations; Red shaded area: 95%-confidence interval (CI) of the median prediction; Blue shaded area: 95%-CI of the 10 and 90th prediction interval.

**pcVPC saliva observations**



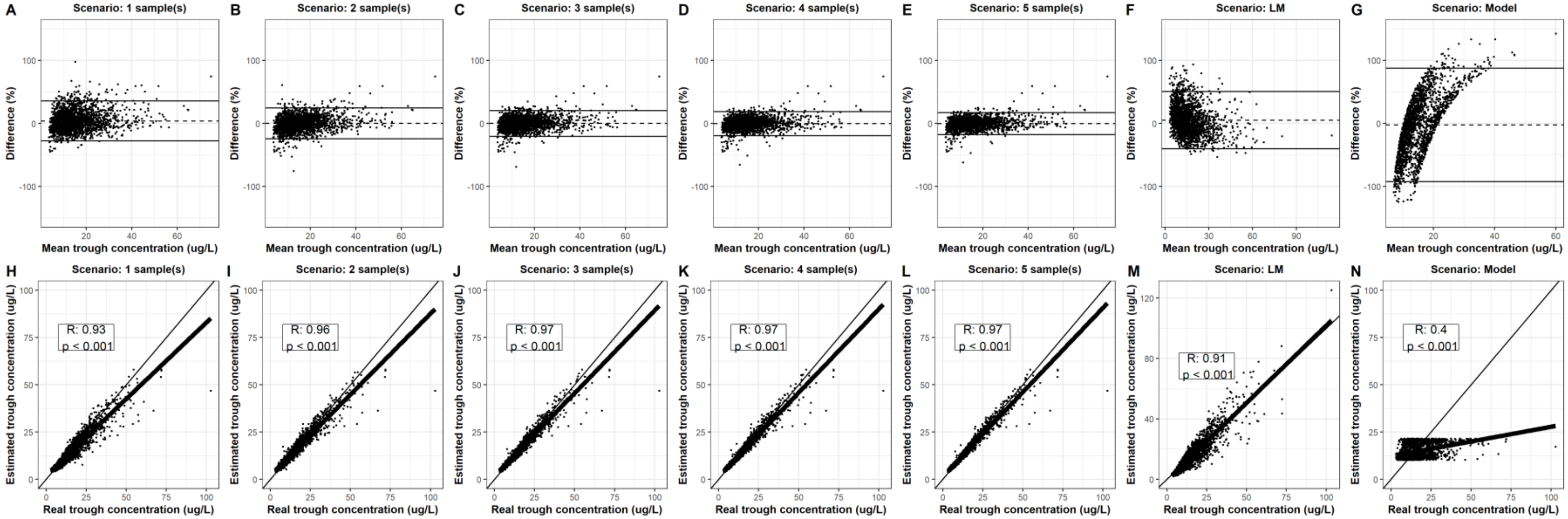
Prediction corrected visual predictive check of plasma observations. Black dots: prediction corrected observations; Black dashed lines: 80%-interval and median of the prediction corrected observations; Red shaded area: 95%-confidence interval (CI) of the median prediction; Blue shaded area: 95%-CI of the 10 and 90th prediction interval.

**Supplementary Figure S3. Relative bias, limits of agreement and correlation of predictions in different scenarios after dose 1**



A-G: relative bias (dotted line) and 95% limits of agreement (solid lines) of the model-based predictions of the $C_{trough}$ after dose 1 compared to the true saliva concentrations in the simulation cohort. Panel A-E represent Bayesian MAP-based predictions of an increasing number of samples. Panel F represents linear model-based predictions based on a single saliva sample, and panel G represents the individual predictions based on the population model without any saliva sampling. H-N: Pearson correlation between predicted $C_{trough}$ and true $C_{trough}$.

**Supplementary Figure S4. Relative bias, limits of agreement and correlation of predictions in different scenarios at steady state**



A-G: relative bias (dotted line) and 95% limits of agreement (solid lines) of the model-based predictions of the $C_{trough}$ at steady state compared to the true saliva concentrations in the simulation cohort. Panel A-E represent Bayesian MAP-based predictions of an increasing number of samples. Panel F represents linear model based predictions based on a single saliva sample, and panel G represents the individual predictions based on the population model and subject weight without any saliva sampling. H-N: Pearson correlation between predicted $C_{trough}$ and true $C_{trough}$.