Historical individual Bayesian estimates improve model predictions in repeat vancomycin courses Hughes, JH Keizer, RJ. *InsightRX, San Francisco, CA*

Background Model-informed precision dosing (MIPD) employs pharmacokinetic (PK) models to aid clinicians in determining doses that optimize therapeutic effectiveness while minimizing adverse effects. Bayesian methods enhance the precision of PK model predictions by updating population-based parameters using individual-specific data, such as therapeutic drug monitoring (TDM) samples. Often, patients receive multiple courses of the same medication. Intuitively, the use of individualized PK parameter estimates from prior courses instead of population parameters for adjusting initial doses for subsequent courses of therapy should be more accurate, however no study has yet confirmed this hypothesis.

Methods Routine clinical care data entered into the InsightRX Nova MIPD software tool formed the basis of this study. Patients were included if they received at least two courses of vancomycin with at least one TDM sample per course. Using samples collected from the *n*th course, individual PK parameters were estimated using maximum *a posteriori* Bayesian estimation, and these parameters were used to predict the first level drawn during the *(n+1)*th treatment course. Predictive performance was quantified using accuracy (defined as a prediction with 15% or 2.5 mg/mL of the measured value) and root mean square error (RMSE). For patients with a BMI above 40, predictions were made with two obese-specific models (Hughes 2024, Carreno 2017) while for other patients three general population models were used (Colin 2019, Tong 2021, Thomson 2009). An XGBoost model was developed to predict when prior parameters should be used in place of population parameters based on patient covariates, time since last course, and number of TDM samples.

Results Using individual parameter estimates from prior courses reduced RMSE by an average of 15.7% and improved accuracy by an average of 26%, with prior parameter estimates producing more precise predictions in 58-65% of patients, compared to population estimates. The XGBoost model achieved an AUC of 0.59 and a balanced accuracy of 55% on a hold-out test set, but did not statistically reduce RMSE or accuracy.

Conclusions For patients resuming a therapy for which they have previously provided TDM levels, using prior Bayesian estimates improves model predictions for most patients.

Key Words clinical decision support, model-informed precision dosing, vancomycin, obese, Bayesian, pharmacometrics

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