

Optimizing vancomycin dosing in older adults: evaluating the predictive performance of nine pharmacometrics models

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Background

- Vancomycin is a broad-spectrum glycopeptide antibiotic, commonly prescribed to older patients (≥ 75 years).
- Vancomycin has a narrow therapeutic window and a high pharmacokinetic variability, complicating its clinical use.
- In the presence of >50 population pharmacokinetic models (popPK) for adults (≥ 18 years), model-informed precision dosing (MIPD) may help guide vancomycin dosing in older patients.
- However, the suitability of the popPK models for MIPD in older patients remains unclear.

Aim

- To evaluate the predictive performance of single-model and multi-model approaches using nine published popPK models to guide vancomycin dosing in older inpatients.

Methods

- Nine popPK models of vancomycin from the literature were encoded in NONMEM 7.5.¹⁻⁹
- The clinical dataset included 255 older inpatients, contributing each three consecutive therapeutic drug monitoring (TDM) concentrations.
- The predictive performance (accuracy and precision) for the third measured concentration was evaluated using single-model and multi-model approaches (model selection algorithm [MSA], and model averaging algorithm [MAA]).¹⁰
- Robustness analysis was performed to decrease the number of popPK models in the multi-model approach without compromising the predictive performance.
- Bland-Altman analysis was performed to assess the agreement between the predicted and measured vancomycin concentration across dosing intervals.

Results

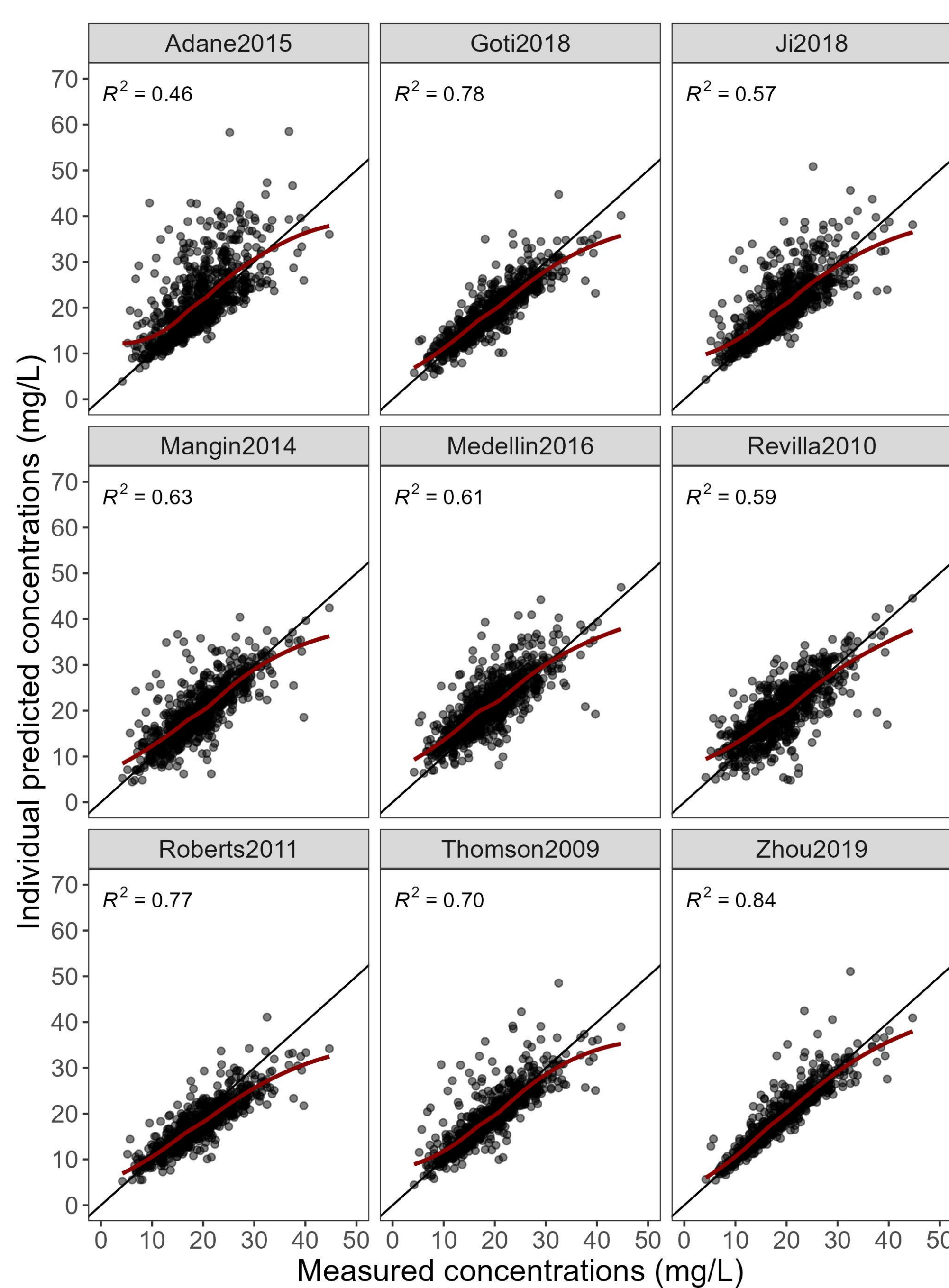


Figure 1. Goodness-of-fit plots

Robustness analysis

(inaccuracy -5%–6%, imprecision 26%–42%)

Adane2015, Ji2018, Roberts2011, Thomson2009, and Zhou2019 models

Abbreviations

C_{T0} , the most recent TDM concentration corresponding to the second measured concentration.

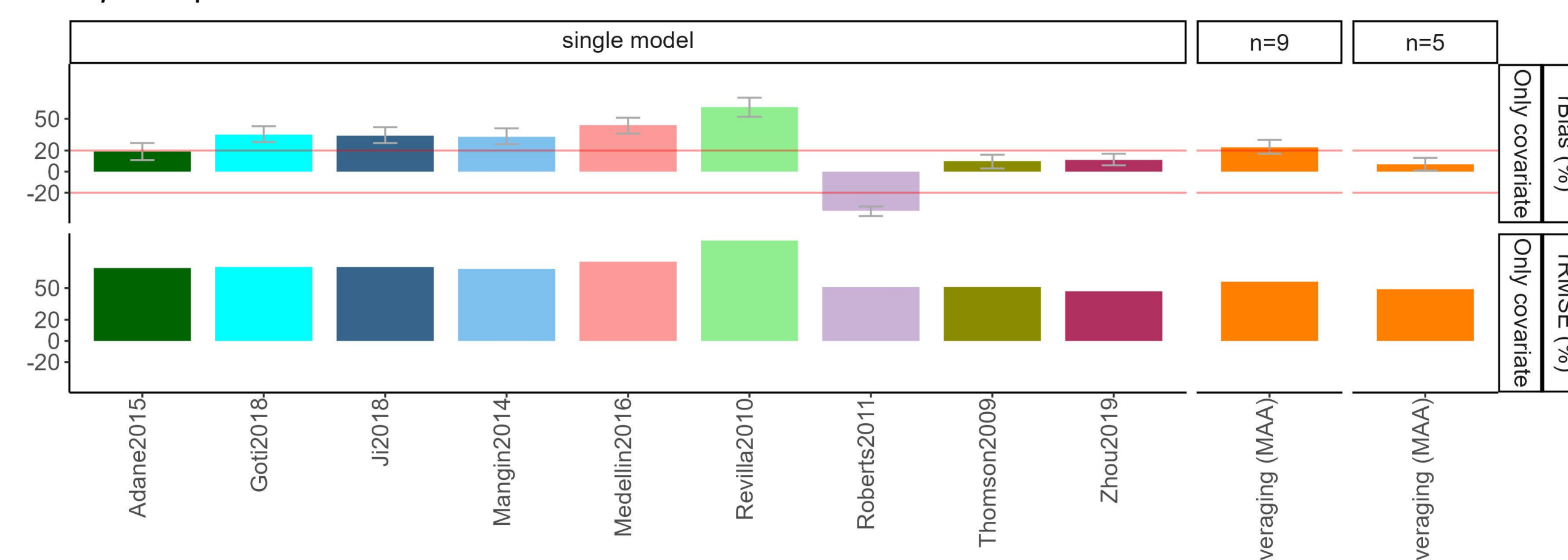
C_{T-1} , an earlier TDM concentration, corresponding to the first measured concentration.

C_{T1} , the third measured vancomycin concentration.

rBias, relative Bias.

rRMSE, relative root mean squared error.

a A priori predictions



b A posteriori predictions

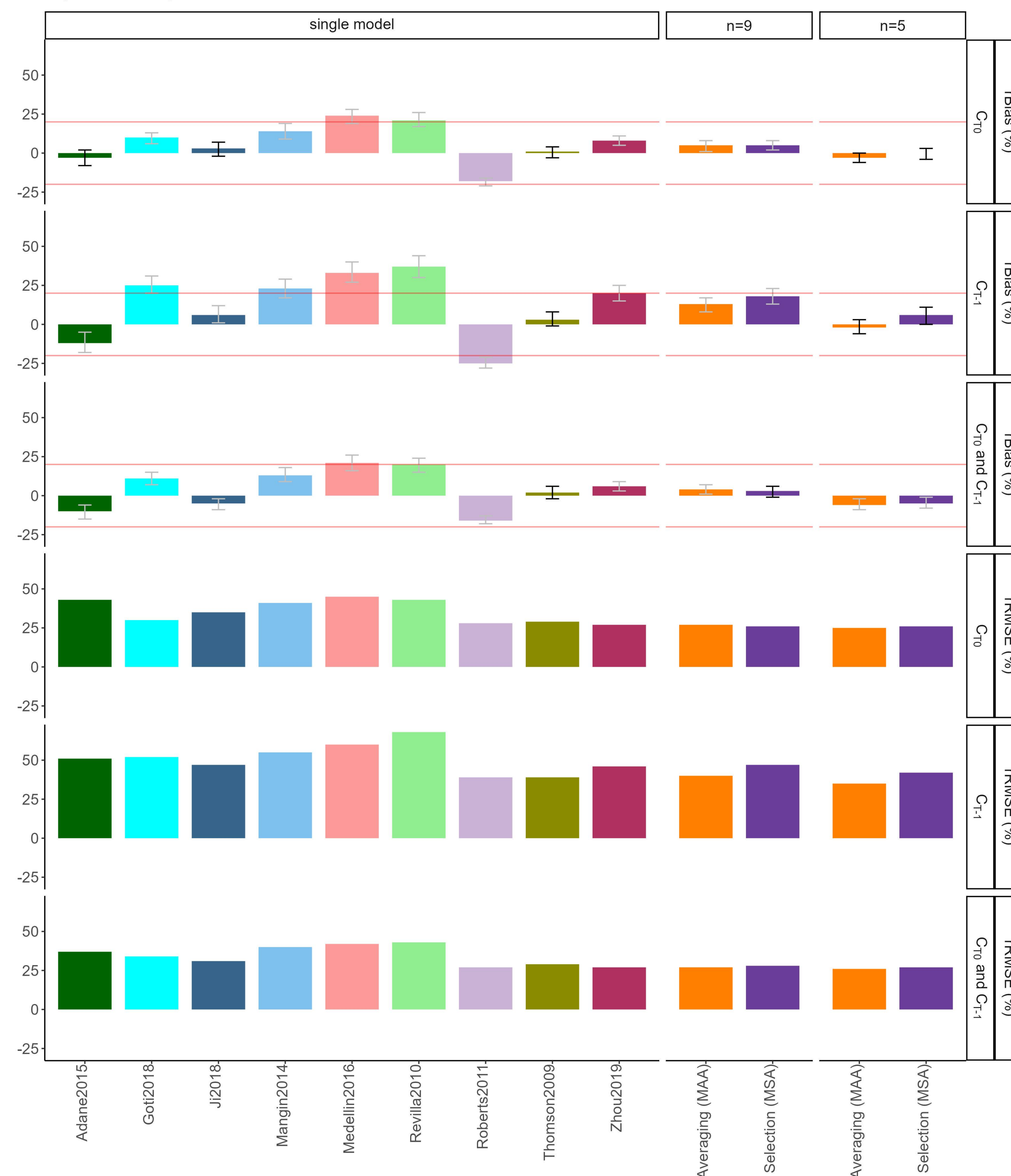


Figure 2. Predictive performance of single and multi-model approaches

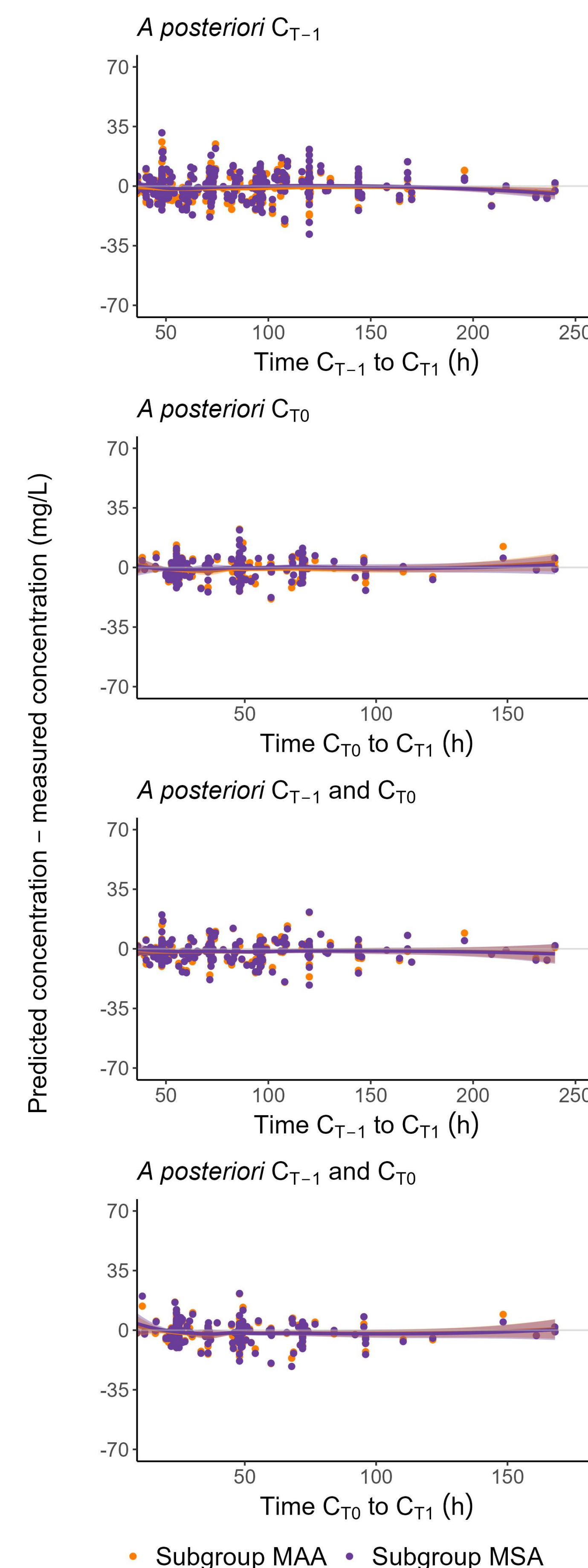


Figure 3. Bland-Altman plots

Conclusion

- We developed and validated a multi-model algorithm for MIPD of vancomycin in older adults.
- The MSA based on five models using the most recent TDM concentration had the best performance.
- This evidence-based algorithm rationalizes precision dosing of vancomycin, potentially improving safety and effectiveness in clinical practice.

