Technical Performance Evaluation of a Deep Learning-based Vancomycin Therapeutic Drug Monitoring Model

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Introduction

We developed a deep-learning-based pharmacokinetic prediction model for vancomycin (PK-RNN-V) which takes the patient's real-time sparse and irregular observations from structured EHR and offers dynamic predictions. The main objective of this study is to evaluate the prediction accuracy of the PK-RNN-V model and its variants using standard benchmark measures and compare it with the Bayesian models.

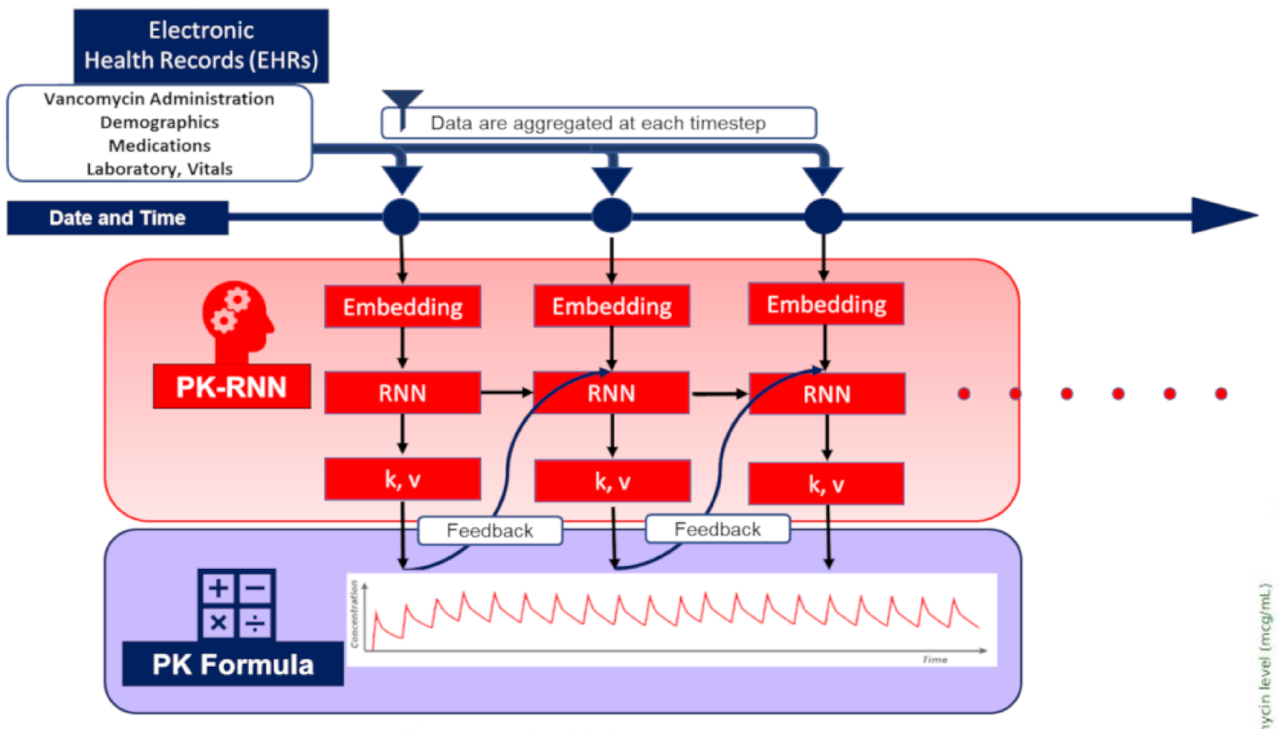

Figure 1: PK-RNN-V model architecture

Methods

The population-level Bayesian model VTDM[1] is our baseline. The original PK-RNN-V models predicted individual patient volume distribution (v) and vancomycin elimination (k) at each time step using an irregular timesteps GRU model. PK-RNN-V feedback uses the first measurement to adjust its hidden state. The variant that takes all measurements available as PK-RNN-V full feedback. Additionally, we use model ensembling (PK-RNN-V E) to get a posterior estimate of the vancomycin concentration.

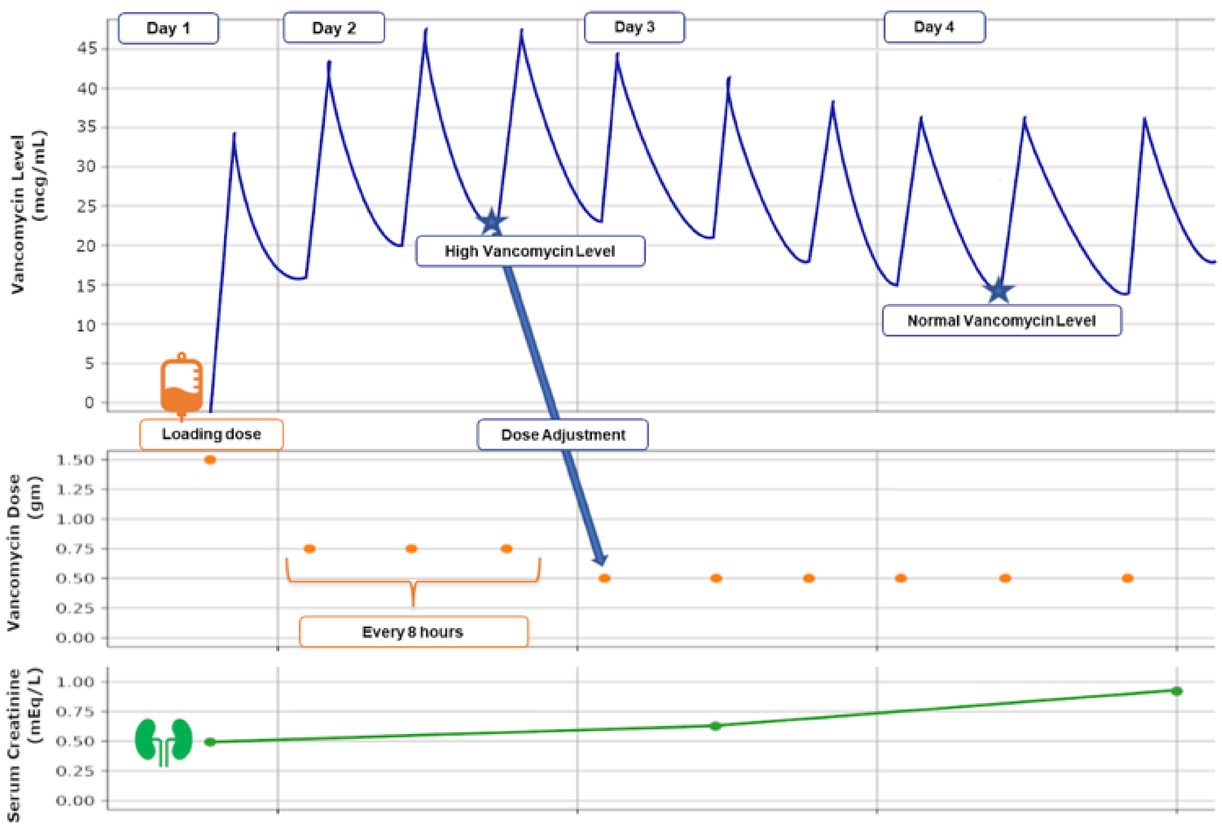

Figure 2: The simple schematic time sequence of an example patient from our cohort.

Results

All PK-RNN-V models exhibited better RMSE, MAE, and MAPE compared to any of the VTDM models. The baseline PK-RNN-V already shows good performance. The performance of the model was improved by ensembling and letting the model adjust its state based on the first measurement. PK-RNN-V E with full feedback uses all the available measurements to adjust its state and achieved the best result.

Model Name		RMSE (mg/L)	MAE (mg/L)	MAPE (%)
Bayesian Model	VTDM	8.58	6.54	41.81
	VTDM with Feedback	6.29	4.26	29.15
PK-RNN-V Model	PK-RNN-V	5.86	4.09	37.57
	PK-RNN-V E with Feedback	5.39	3.64	25.41
	PK-RNN-V E with Full Feedback	5.37	3.62	25.05

Table 1: Model performance comparing different types of PK-RNN-V and Bayesian Models

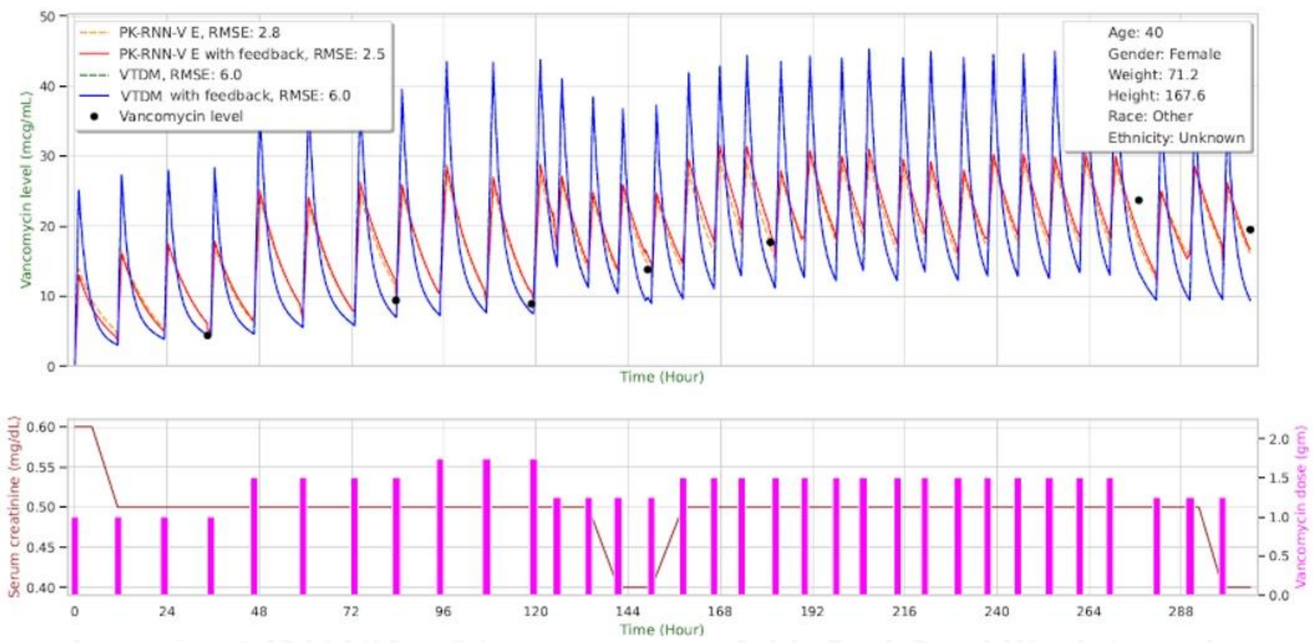

Figure 3: A sample patient in whom PK-RNN-V E with feedback model predicted vancomycin levels better than the VTDM model.

Conclusion

1. The evaluation results revealed the superior performance of PK-RNN-V models when compared with Bayesian VTDM models;

2. PK-RNN-V E model can integrate real-time patient-specific data from EHR, allowing real-time therapeutic drug monitoring and likely leading to precision dosing of vancomycin;

3. Potential biases due to the study design cannot be evitable; Additionally, we did not have access to commercially available Bayesian models for the comparison.

Acknowledgment & Reference

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Reference: 1. Lim HS, Chong YP, Noh YH, Jung JA, Kim, YS. Exploration of optimal dosing regimens of vancomycin in patients infected with methicillin-resistant Staphylococcus aureus by modeling and simulation. *J Clin Pharm Ther.* 2014; 39(2): 196–203. doi: 10.1111/jcpt.12123

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