**Open-Source Software for Vancomycin Therapeutic Drug Management in a Vietnamese hospital**

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**Introductions:** This study aims to assess and identify a suitable population pharmacokinetic (POP PK) model for vancomycin using concentration data from Vietnamese patients. The proper POP PK model was then utilized to construct a Bayesian tool to improve the quality of TDM service in Vietnam.

**Methods:** Reviewing literature in Pubmed and the sites of available Bayesian programs (InsightRX, DoseMe, TDMx), six POP PK models were selected with similar characteristics to Vietnamese patients. These POP PK models were then external validated by utilizing concentration data gathered from Vietnamese patients. For personalizing dose adjustment, the Bayesian forecasting was conducted with the support of Monolix version 2021 (Lixoft, France). The performance of the a priori prediction (using covariates information only) and Bayesian prediction (using the observed vancomycin concentrations) were evaluated by calculating MPE (mean prediction error) and MAPE (mean absolute prediction error). Model performance based on the MAPE values was classified as acceptable prediction (MAPE < 50%), good prediction (10% ≤ MAPE < 20%), and excellent prediction (MAPE < 10%) [1, 2]. Adopting the Bayesian approach, the most suitable POP PK model had been applied to develop a Vietnamese web-based TDM application. This application was then designed in R environment with a Mrgsolve package and an interactive graphical user interface (GUI) with Shiny. The AUC value predicted by this tool was compared with the value by the standard Sawchuk-Zaske method.

**Results:** The result demonstrated that the POP PK model published by Yamamoto 2009 was the best fit model with the excellent prediction level MAPE = 9.96% and MPE=0.217 mg/L (< 2.5 mg/L - limit of quantification) for the Bayesian forecasting. The POP PK model consists of a two-compartment structural model with linear elimination. Clearance creatinine was the only covariate that influenced the clearance of vancomycin. A Bayesian application was then designed with a Vietnamese interface and released at the address “[Chỉnh liều Vancomycin - Bayesian method (shinyapps.io)](https://hai-le-ba.shinyapps.io/VancoXP_Yamamoto2009/?_ga=2.174510242.1656690907.1640614991-1817234045.1620812527)”. The AUC anticipated by the new tool and the first-order method was 471 mg\*h/L (± 132) and 456 mg\*h/L (± 194), respectively. Therefore, there was no difference in clinical judgment based on the new tool and conventional first-order technique. Indeed, clinical pharmacists and doctors prefer using this web-based application rather than the conventional method because of its convenience and visual performance in their routine TDM practice.

**Conclusions:** The findings were convincing evidence of verifying a POP PK model's prediction performance before incorporating it into a Bayesian tool to improve the quality of TDM service. The Bayesian application can generate accurate and consistent AUC value in comparison with the classic peak-trough concentration technique. The existing open-source package offers the opportunity to implement the Bayesian approach into clinical practice in some low-income countries, including Viet Nam.

1. Lewis, C.D., *Industrial and business forecasting methods: a practical guide to exponential smoothing and curve fitting*. 1982, London; Boston: Butterworth Scientific.

2. Boger, E. and M. Fridén (2019), "Physiologically Based Pharmacokinetic/Pharmacodynamic Modeling Accurately Predicts the Better Bronchodilatory Effect of Inhaled Versus Oral Salbutamol Dosage Forms"*.* *J Aerosol Med Pulm Drug Deliv*. **32**(1): p. 1-12.