

Population Pharmacokinetics-Pharmacogenetics of Efavirenz using Non-Linear Mixed Effects Modeling and Bayesian Estimation

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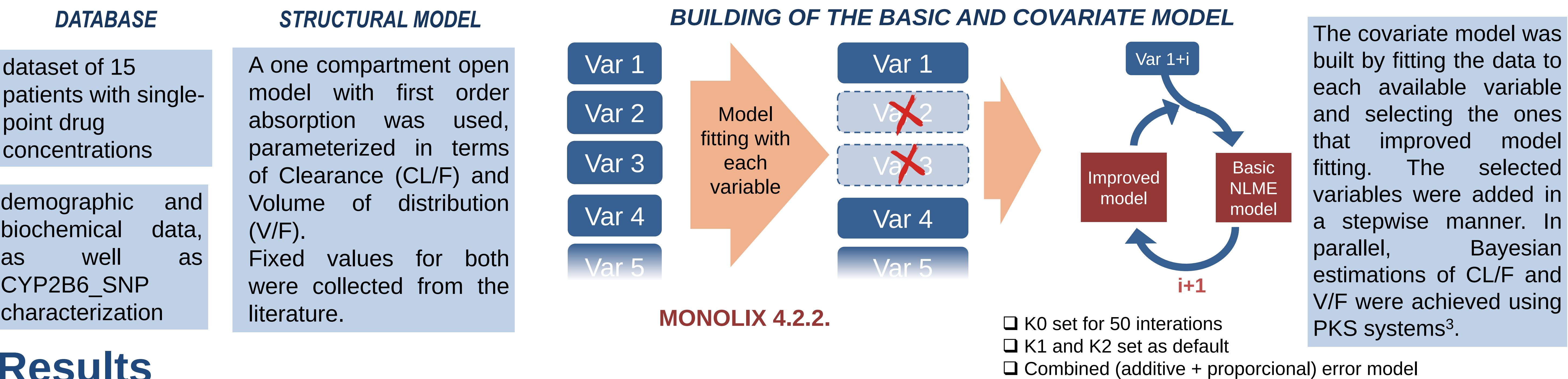
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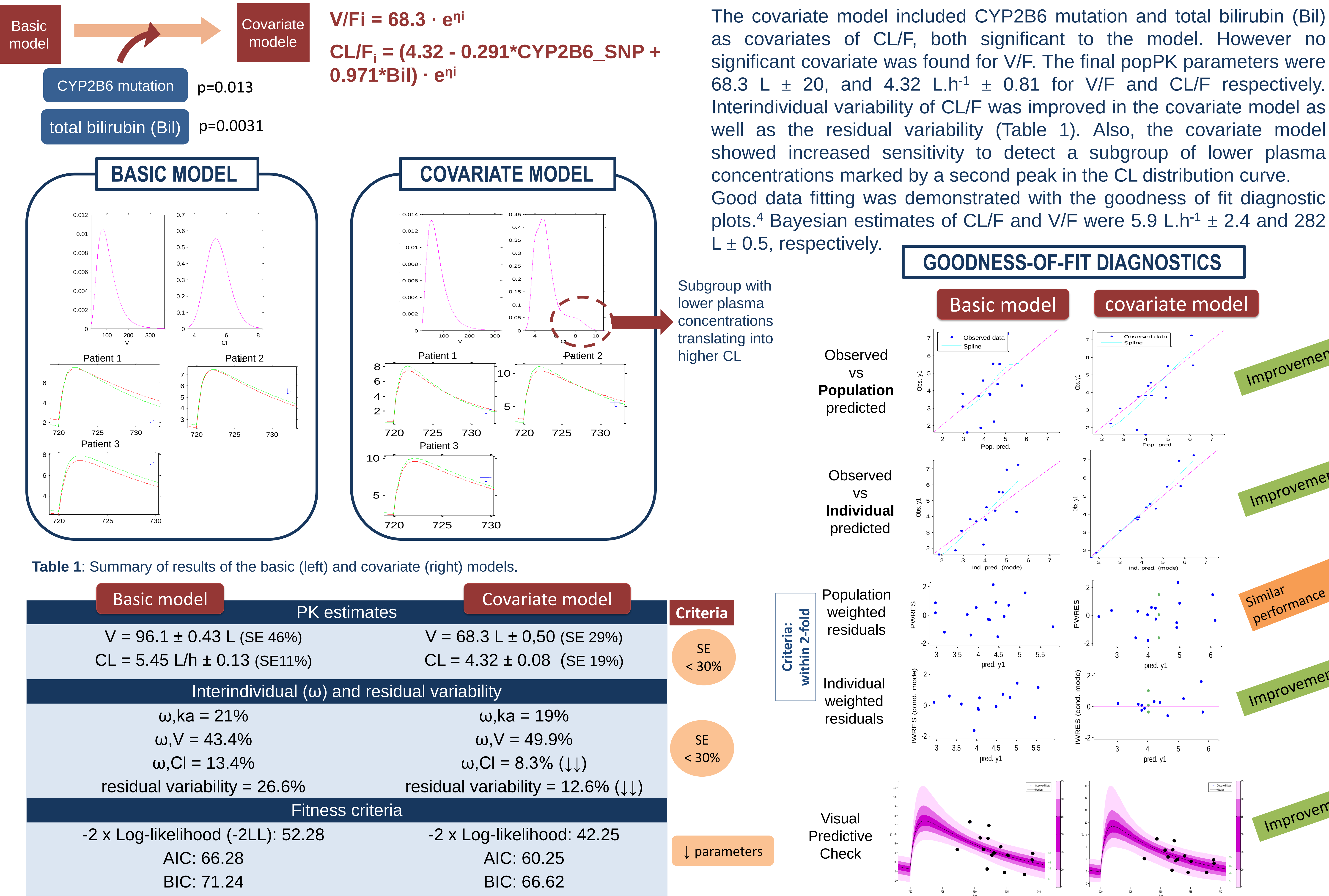
Objectives

Efavirenz, used in the treatment of HIV, belongs to the Non-Nucleoside Reverse Transcriptase Inhibitors class.¹ Currently, great variability is observed in the population pharmacokinetics (popPK) which hinders therapeutic management, and liver metabolism has been considered one of the main sources for this variability.² In order to establish the determining factors affecting popPK variability, we aim to construct a population pharmacokinetic-pharmacogenetic (PKPG) model by nonlinear mixed effects modeling (NLMEM) from sparse data, and accounting for CYP2B6 516G>T mutation (CYP2B6_SNP). Bayesian estimation of the popPK parameters was also performed.

Methods



Results



Conclusions

The model was improved with Bil and CYP2B6_SNP as covariates, demonstrating the important role of this protein in the pharmacokinetics of Efavirenz. The covariate model partially addressed the data variability. Bayesian estimation yielded similar CL/F values to those from the NLME basic model (5.45 L.h⁻¹). However, V/F values from the former and the latter (96.1 L) were very different, which could stem from the high impact of initial Bayesian estimates.

References

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