

External evaluation of selected infliximab population pharmacokinetic models on patients with fistulizing Crohn's disease

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Introduction

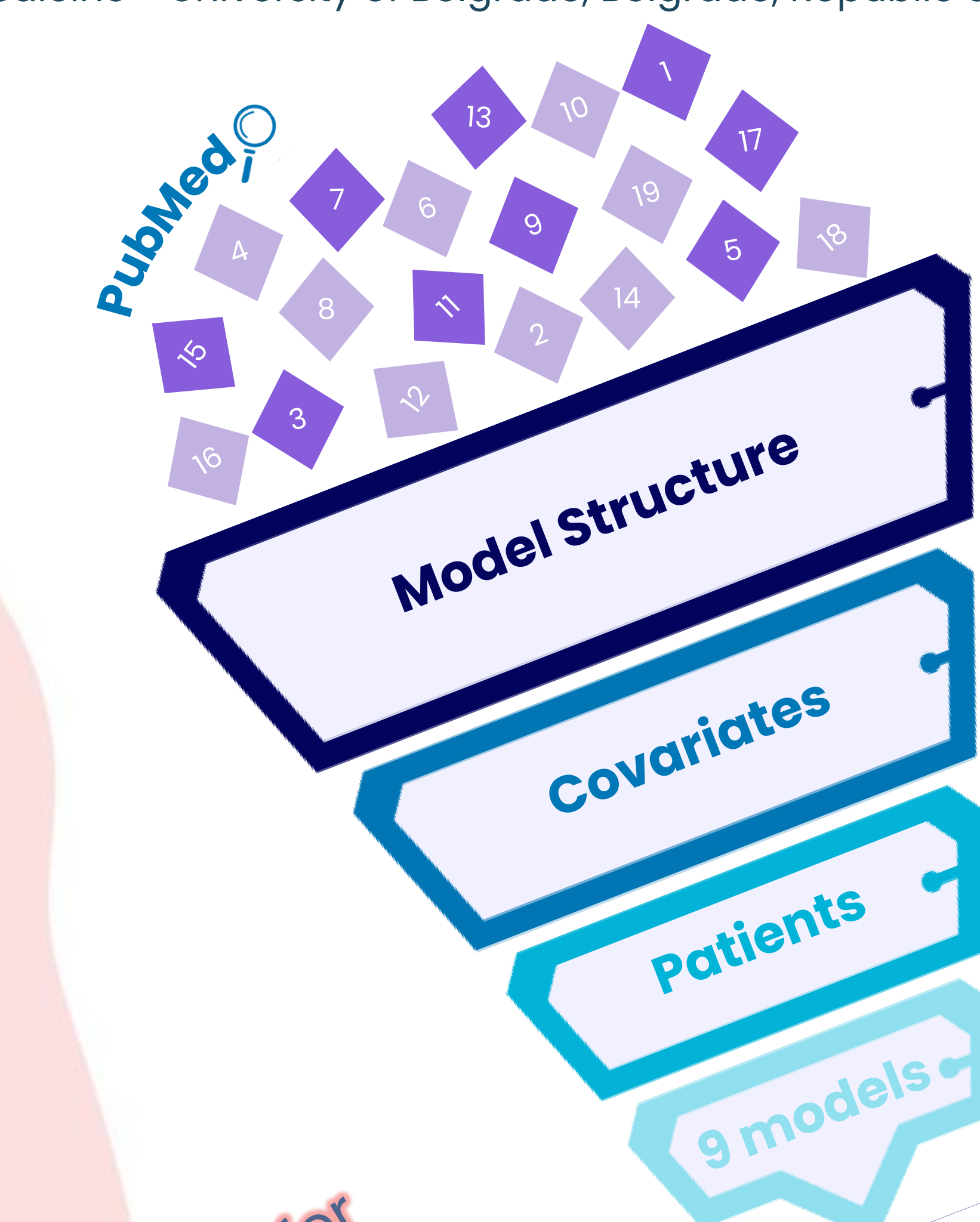
The development of fistulas in patients with Crohn's disease is a recognised complication of this chronic disorder, posing challenges for both patients and gastroenterologists. While infliximab (IFX), an anti-tumour necrosis factor alpha antibody, has demonstrated efficacy in treating this form of the disease [1], numerous challenges persist in ensuring optimal patient care and achieving disease remission.

Objectives

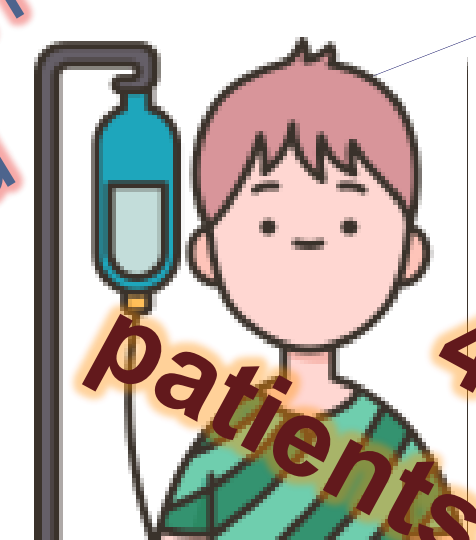
- to evaluate existing IFX population pharmacokinetic models
- to assess their predictive capabilities within this population
- to evaluate the alignment of population pharmacokinetic model parameters with the individual therapeutic drug monitoring data
- to determine their suitability for everyday clinical practice

Conclusions

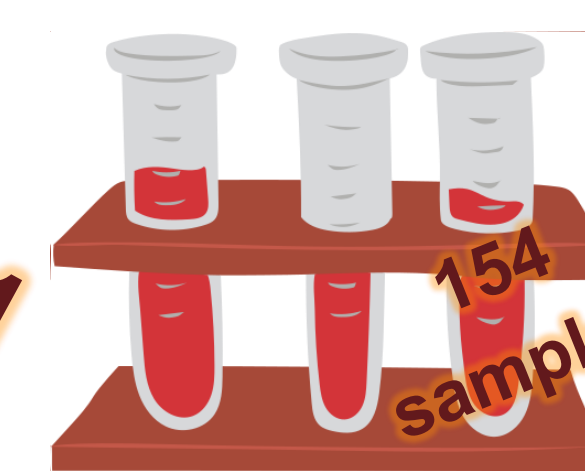
Although some models performed better predictions than others, **none** of them met all criteria assessed in this evaluation. The inconclusive nature of the results suggests that none of the models fully suited our patient population. Considering that this **specific** patient population has not been included during the development of any tested models, there is a clear need to **develop a new model** that accounts for fistulizing Crohn's disease characteristics. Doing so would improve predictions of IFX trough concentrations for this disease form and, therefore, facilitate a more **individualised** approach to treatment.



Dataset for evaluation included



41



154

samples

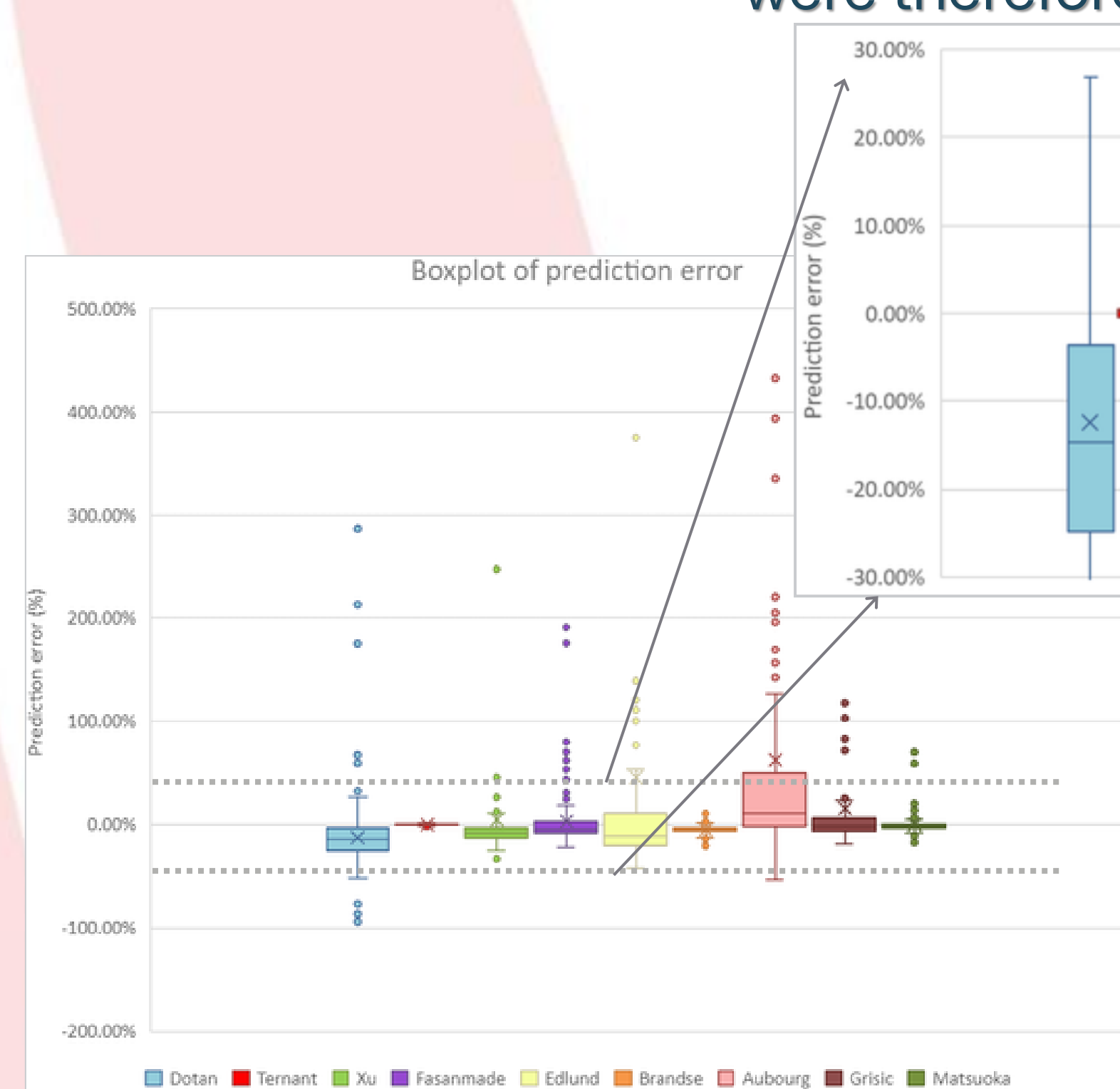


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Based on the calculated MPEs, three models [3, 6, 9] exhibited confidence intervals that included zero, and were therefore selected as the more accurate ones.



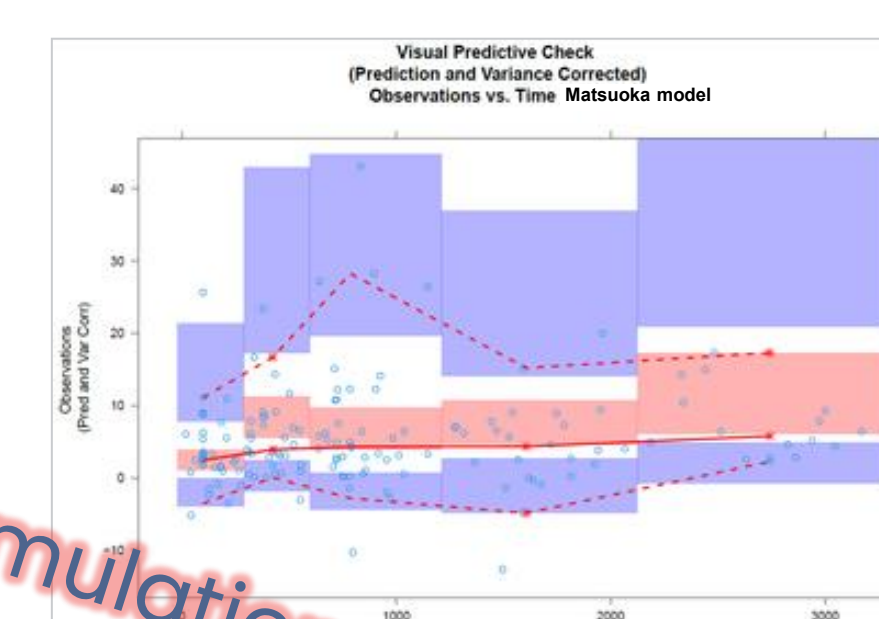
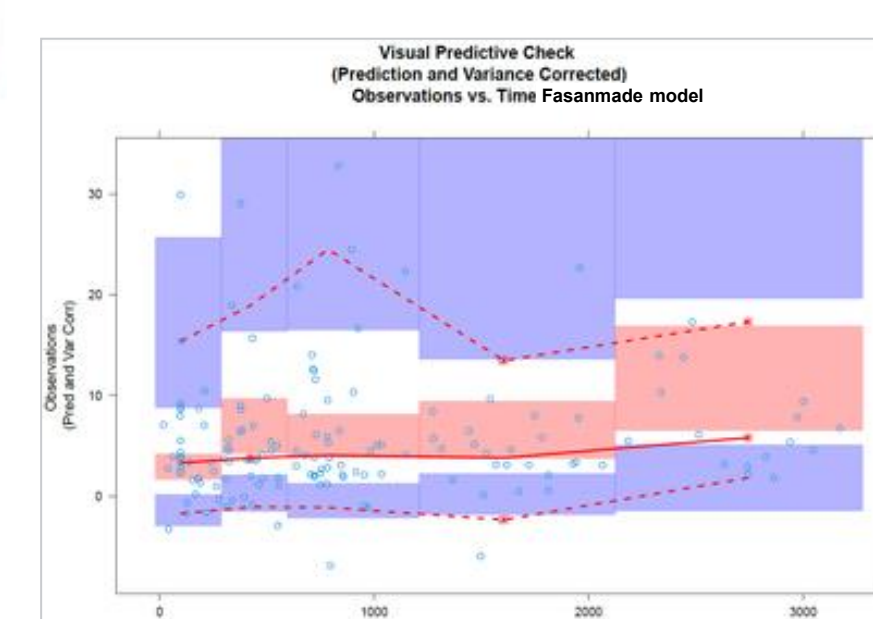
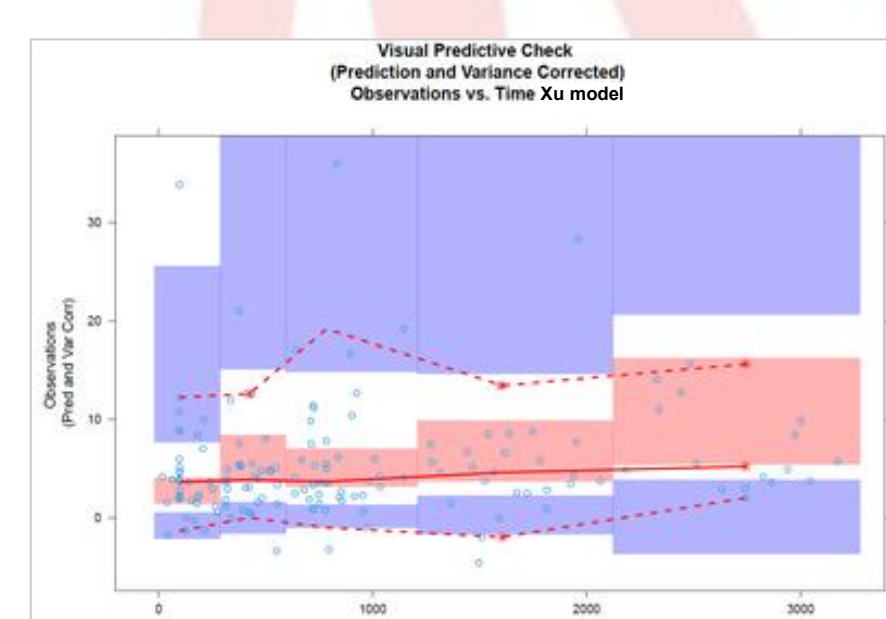
Prediction-based analysis
Ternant model
the most accurate and precise

Additionally, rMPEs of Ternant [3] and Matsuoka [10] models were notably low. Also, the most precise models according to rRMSE were the same ones [3, 10].

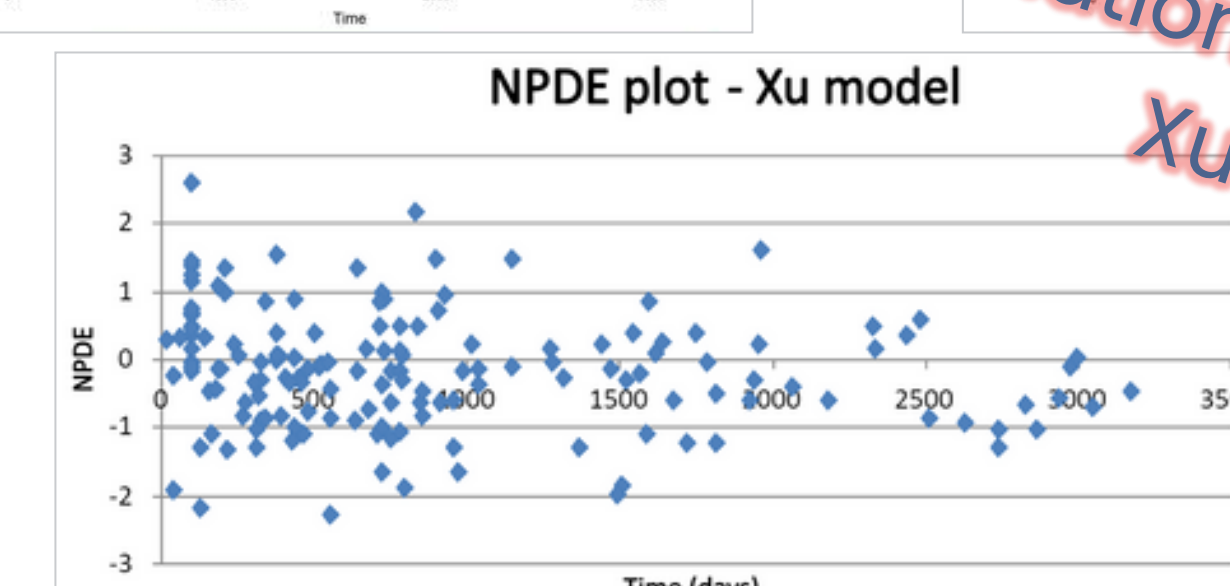
Parameter/Model	rMPE	rRMSE	R2
Dotan	-12.4825	46.2729	0.9701
Ternant	0.0851	0.6051	0.9999
Xu	4.7156	136.4762	0.8987
Fasanmade	2.2850	26.7507	0.9916
Edlund	44.6060	304.5693	0.6781
Brandse	-5.1301	6.3190	0.9975
Aubourg	62.4153	159.8419	0.9765
Griscic	15.6459	90.4442	0.8379
Matsuoka	-0.1975	9.4007	0.9975

Regression analysis revealed that the Ternant model [3] exhibited the strongest correlation between measured concentrations and IPRED.

Upon reviewing VPCs, three models [4, 5, 10] outperformed others. Notably, the NPDE plots highlighted the superiority of the Xu model [4] according to simulation-based methods.



Simulation-based analysis
Xu model



References

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