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CONCLUSION

Current meropenem parametric models have bad population prediction ability and failed to predict the initial dose for ICU patients. For the TDM based dosing adjustment, more densely sampling (≥ 2 per dosing occasion) is necessary to predict the rest concentration. Model validation is always needed when using models from others.

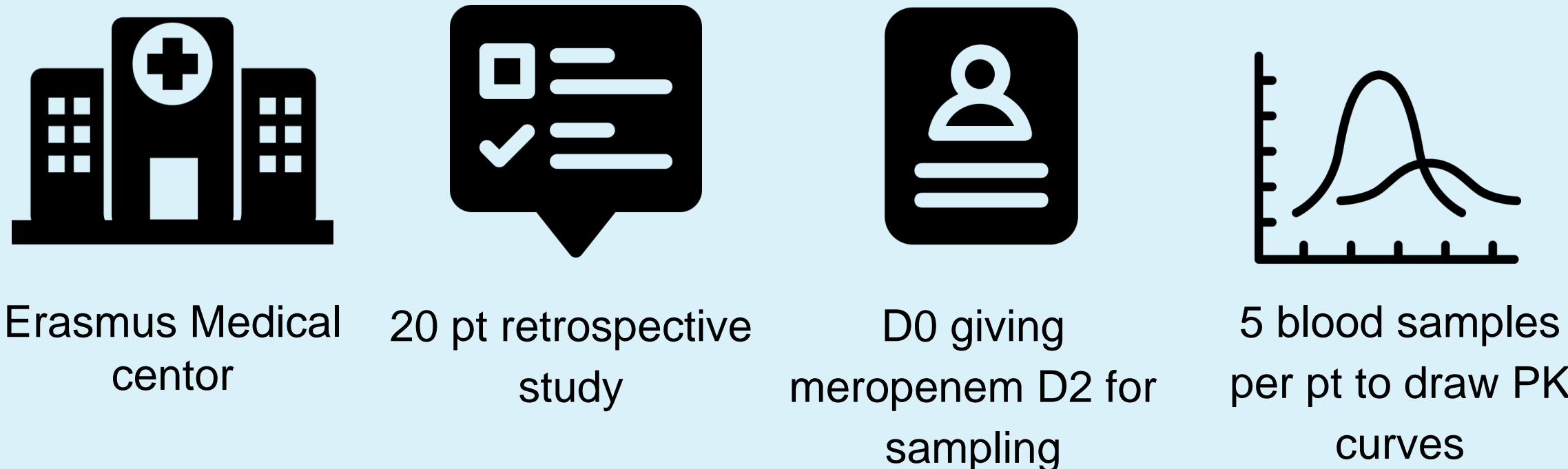
RATIONALE

Meropenem is an important beta-lactam antibiotic that is frequently used to treat serious infections in critically ill patients. Previous population pharmacokinetic (popPK) studies of meropenem in intensive care (ICU) patients have shown large differences in estimated PK parameters, making it difficult to select an appropriate model for clinical use. We perform external validation using real-world patient with EXAPT data to assess the suitability of these models for clinical application

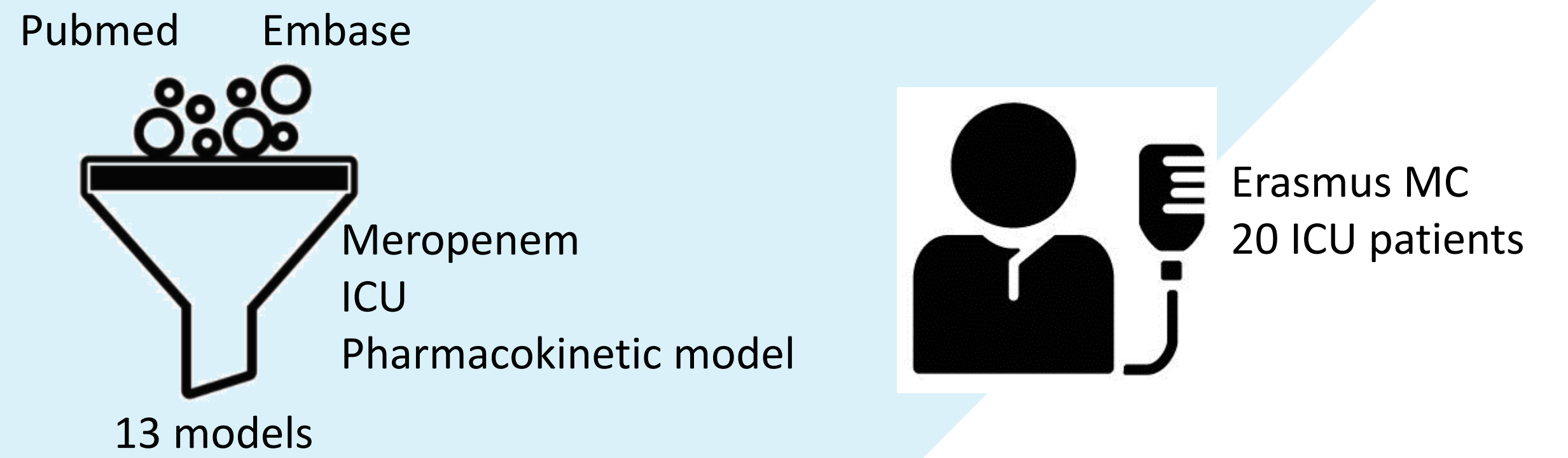
AIM

To evaluate the suitability and applicability of popPK models available in literature to be used for initial meropenem dosing and for TDM assisted dosing adjustments

PARTICIPANTS



METHODS

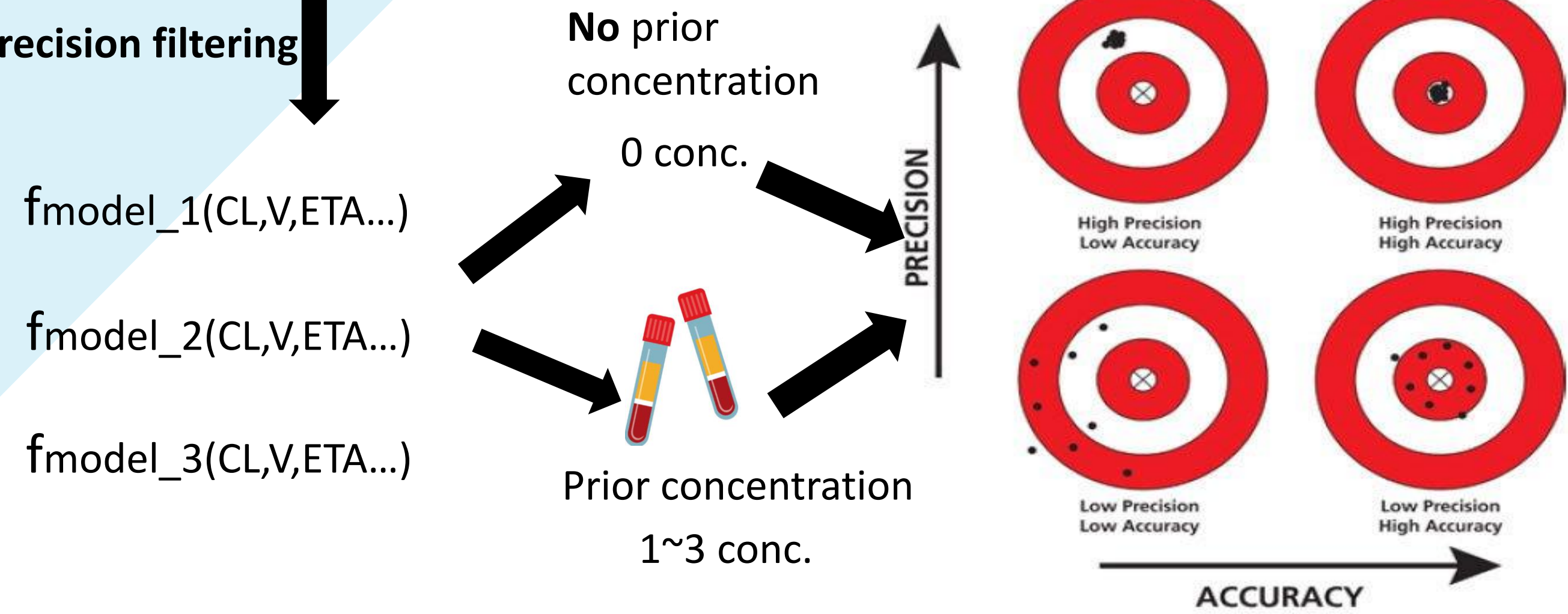


Precision evaluation

- fmodel_1(CL,V,ETA...)
- fmodel_2(CL,V1,V2,ETA...)
- fmodel_3(CL,V,ETA1...)
- ⋮
- fmodel_13(CL,V,ETA1,ETA2)

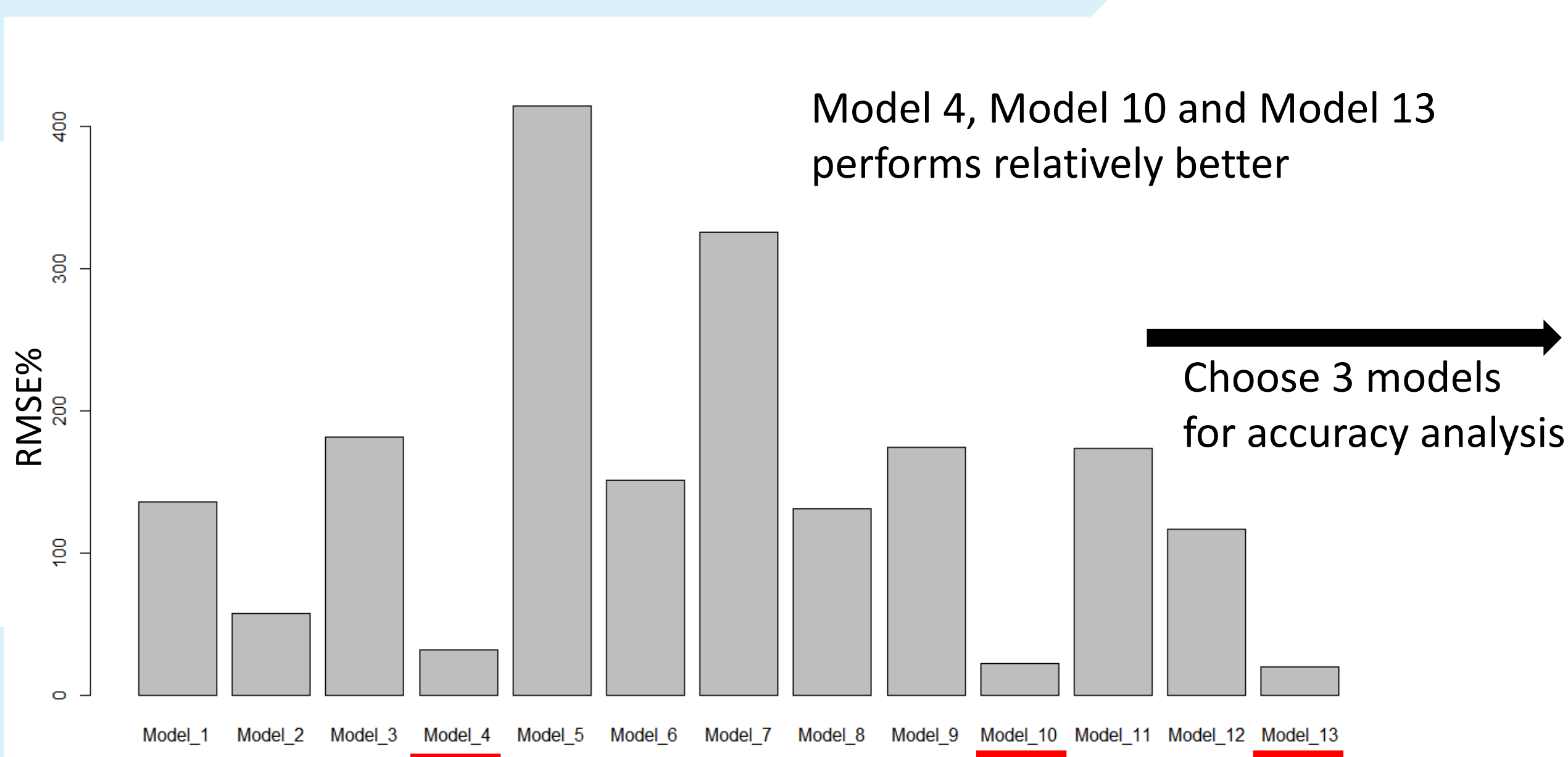
3~5 samples per patient
86 samples in total

Precision filtering

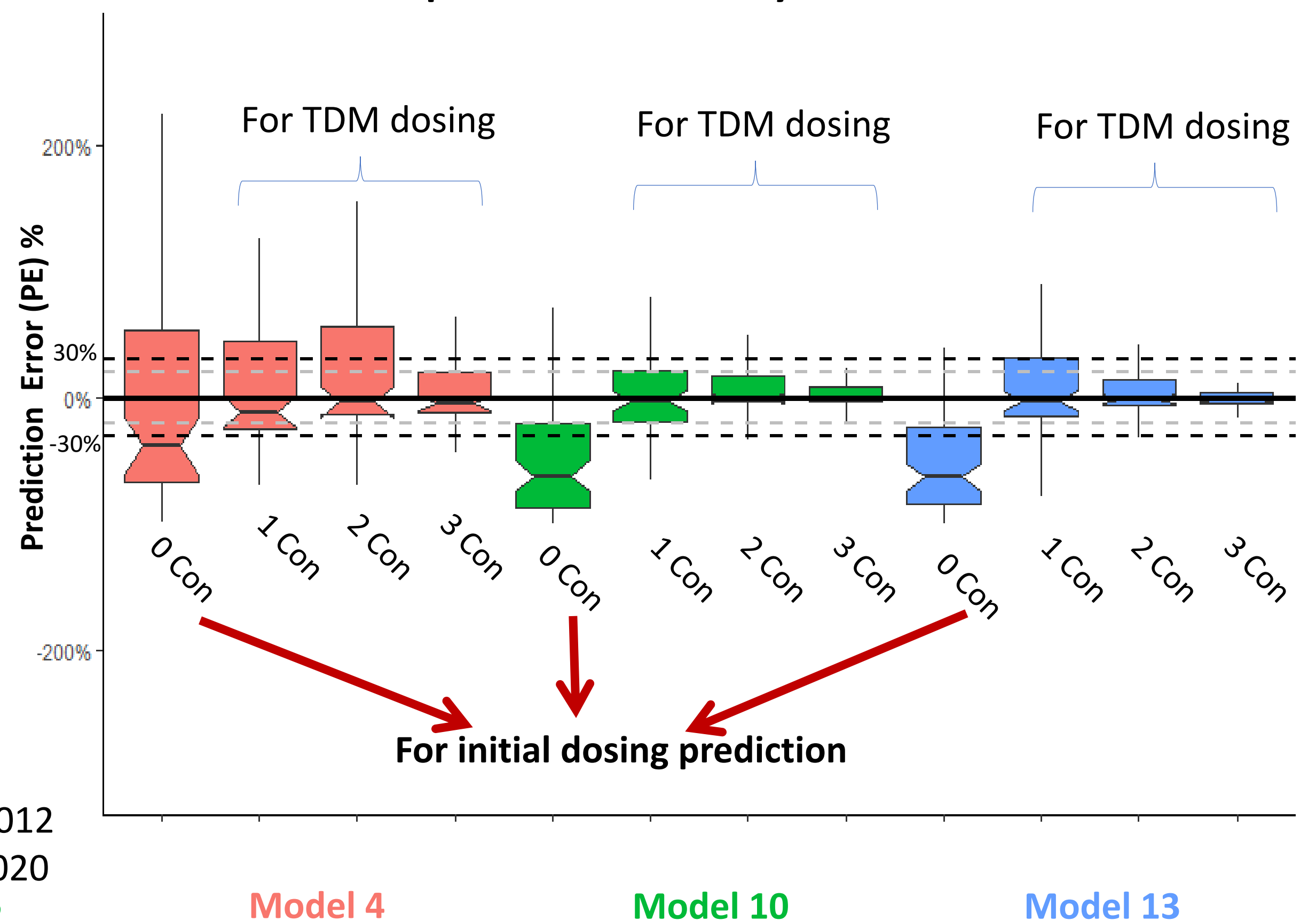


RESULTS

Evaluate the prediction preciseness of the 13 models



Evaluate the prediction accuracy of the 3 models



Model_1 Lisa Ehmann et al 2019
Model_2 Yong Kyun Kim et al 2018
Model_3 Muhammad Usman et al 2017
Model_4 Eun Kyoung Chung et al 2017
Model_5 Francesca Mattioli et al 2016
Model_6 Sutep Jaruratanasirikul et al 2015
Model_7 Yoko Niibe et al 2020

Model_8 Isabelle K.Delattre et al 2012
Model_9 Dagan O Lonsdale et al 2020
Model_10 Qing-tao Zhou et al 2012
Model_11 Jason A. Roberts et al 2009
Model_12 Frédéric Fripiat et al 2015
Model_13 Chonghua Li et al 2006

Conc.: Concentration
0-3 conc.: 0-3 Concentration incorporated into models
Prediction Error threshold is set within $\pm 30\%$

Cpred: model predicted concentration
PE: Predicted error
 $PE\% = (C_{pred} - C_{obs}) \div C_{obs} \times 100(\%)$

Cobs: observed drug concentration
RMSE: Root-mean-square error
 $RMSE = RMSE\% = \sqrt{[\sum (PE\%)^2 / n]}$