Model predictive control with Bayesian updates (MPC) is more robust to model misspecification: investigation in a cohort of 315 patients receiving tacrolimus during the first 14d after renal transplantation. (I-49)

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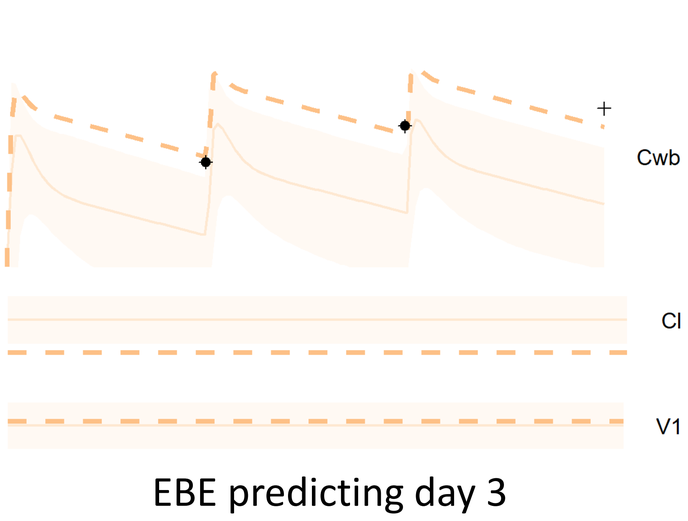
Introduction

- Empirical bayesian estimation (EBE) is the key algorithm behind model-informed precision dosing (MIPD). The technique is sensitive to model misspecification, especially in the presence of unaccounted trends. This is solved by downweighing earlier observations.
- When measurements are frequent, MIPD could be seen as a control problem instead. Model-predictive control (MPC) may offer robustness against misspecification and does not require downweighing earlier observations.
- We **compared the predictive performance of EBE vs MPC** for daily tacrolimus trough concentrations during the first 14 days post kidney transplant, a highly dynamic situation with unaccounted trends.

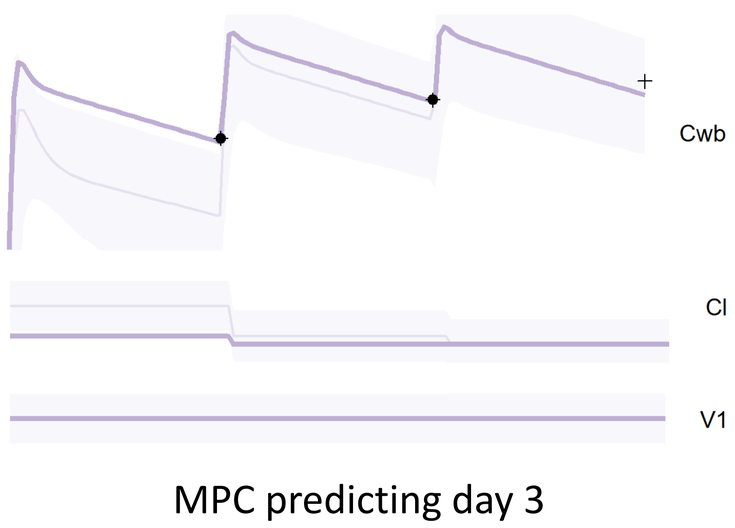
Methods

- Historic data of 315 patients having received tacrolimus during 14d after renal transplantation was used.
- 2 models were used as prior for both EBE and MPC
  - Model A: built from rich samples on d7 only (n=100, different cohort)
  - Model B: built from trough levels in the population to be evaluated (n=315)
- Prediction performance was evaluated as DV / IPRED. This measure has to be between 0.88 and 1.11 to attain the target (corresponding to levels of 12 – 15 ng/mL)
- Results are reported as empirical cumulative distribution curves, and as probability of target attainment.

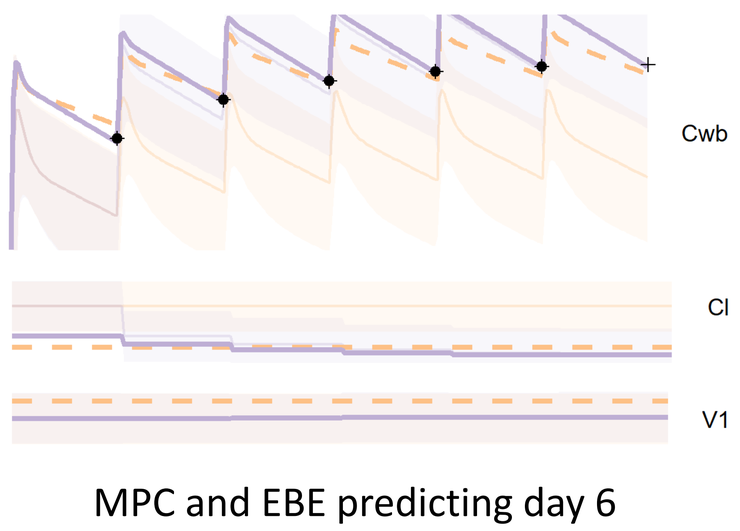
How does MPC work?



EBE predicting day 3

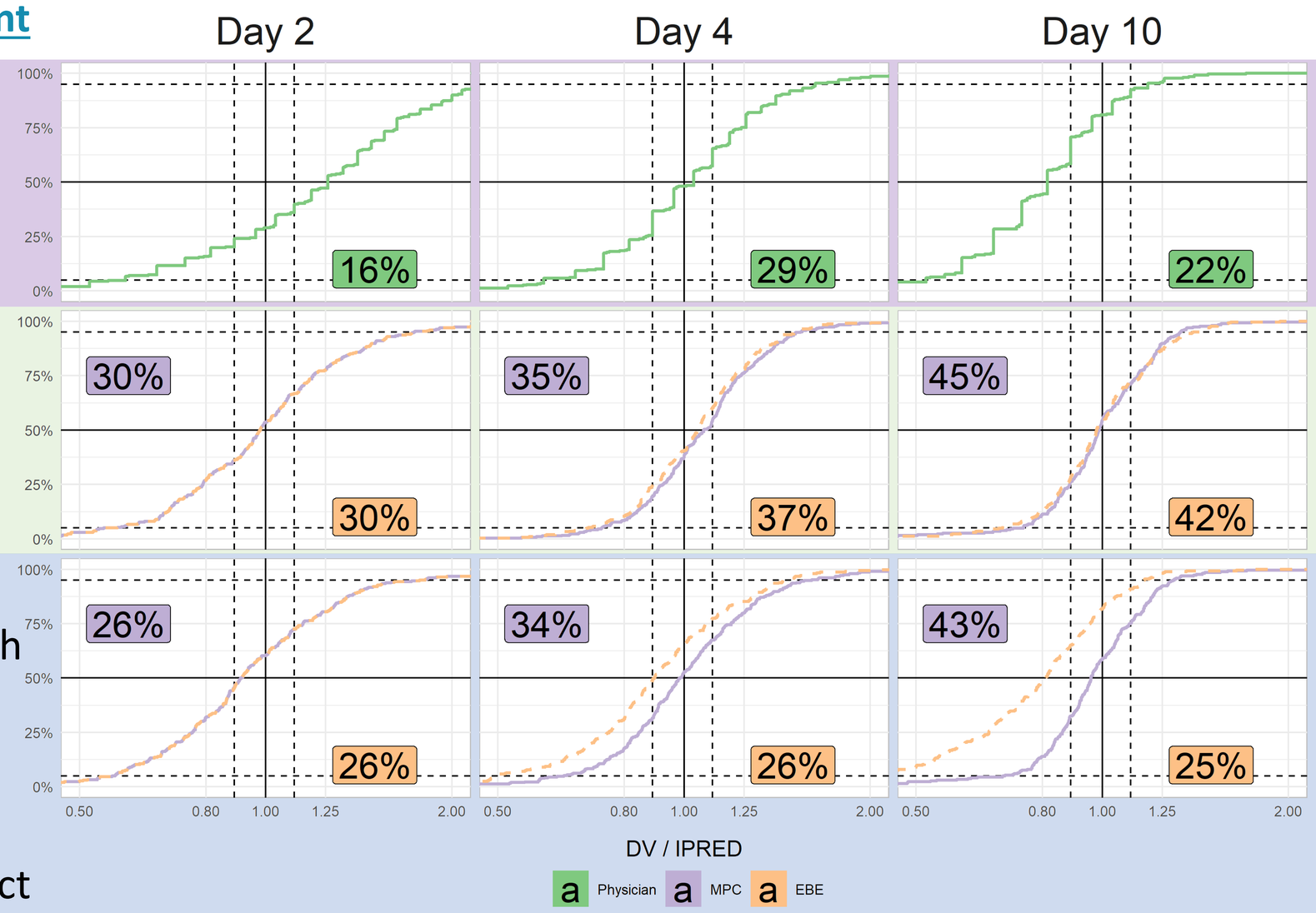


MPC predicting day 3



MPC and EBE predicting day 6

Comparison of target attainment



Conclusion

- MPC displays **superior predictive performance** vs. sEBE in tacrolimus d0-14 post renal transplant with a misspecified model. The technique handles trends not accounted for in the model used.
- In order to further assess MPC vs. EBE for dose adaptation, we advocate for *in silico* studies with diverse simulated and historical data sets. A head-to-head comparison with stochastic differential equations and weighted EBE should be performed, too.

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