A Bayesian Hidden Markov model to predict the dynamic evolution of disease severity in eczema

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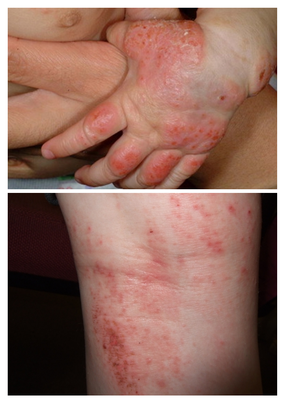
Introduction

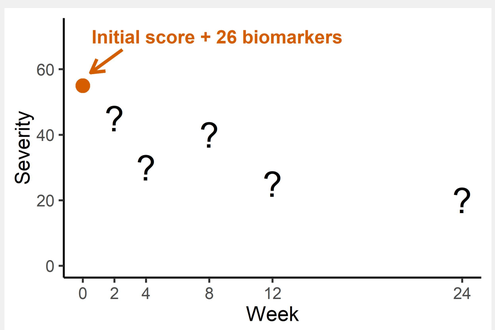
- **Atopic Dermatitis** (AD), aka eczema, is a most common chronic **skin disease** characterised by a dry, itchy skin.
- Treatment responses vary from patients to patients.
- Designing **personalised treatment strategies** is of high clinical relevance.
- Patient stratification requires the **prediction** of treatment effects.
- The disease **dynamic** and **measurement uncertainties** need to be considered for personalised medicine.



Eczema lesions

Objectives

- Predict the evolution of eczema severity in response to a systemic therapy.
- Identify potential biomarkers for patient stratification.



Methods

Data [1]

- **43 adults** with moderate to severe AD undergoing a systemic therapy.
- Severity score (EASI) assessed at **week 0, 2, 4, 8, 12, 24** (241 observations).
- **26 serum biomarkers** measured at week 0 (e.g. TARC, TNF-α, IL-8, IL-10).

Model

k-th patient

$$w_S^{(k)} \sim Beta(\mu_S \phi_S, (1-\mu_S)\phi_S)$$

$$S_l^{(k)}(t+1) \sim N(w_S^{(k)} S_l^{(k)}(t) + x_k^T \beta + b, \sigma_l^2)$$

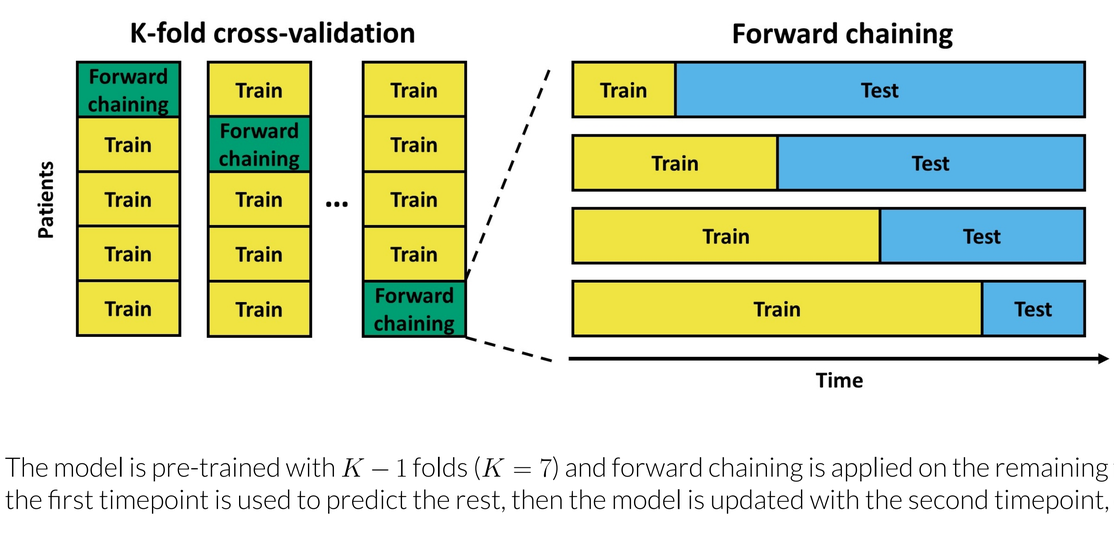
$$S_m^{(k)}(t) \sim N(S_l^{(k)}(t), \sigma_m^2)$$

Latent severity score: $S_l^{(k)}(t-1)$, $S_l^{(k)}(t)$, $S_l^{(k)}(t+1)$, $S_l^{(k)}(t+2)$

Measured severity score: $S_m^{(k)}(t-1)$, $S_m^{(k)}(t)$, $S_m^{(k)}(t+1)$, $S_m^{(k)}(t+2)$

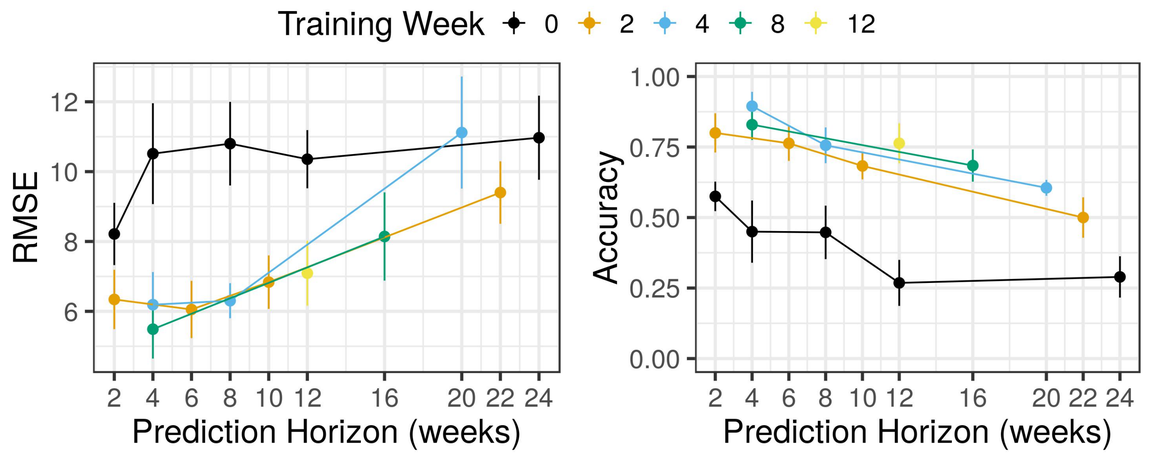
time

- The parameters of the model, θ, are probability distributions and updated with Bayes' theorem: $p(\theta|x) = \frac{p(x|\theta)p(\theta)}{p(x)}$.
- Feature selection is implemented with a **regularised horseshoe** prior [2].
- Weakly informative priors were used for the remaining parameters.
- Inference is performed with **Markov Chain Monte-Carlo** in Stan.
- Internal validation is conducted in a **K-fold cross-validation, forward chaining** setting.

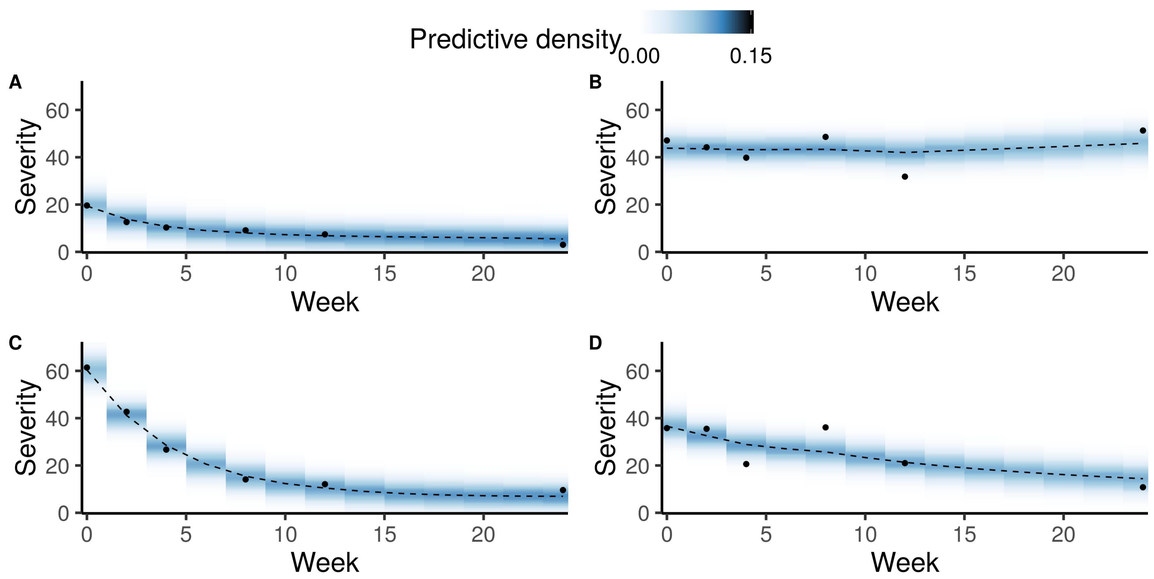


The model is pre-trained with $K-1$ folds ($K=7$) and forward chaining is applied on the remaining fold: the first timepoint is used to predict the rest, then the model is updated with the second timepoint, etc.

Results

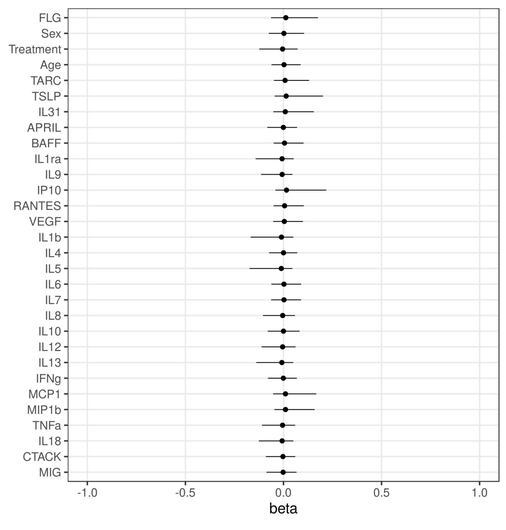


Predictive performance assessed by Root Mean Square Error (RMSE) or MCID Accuracy (proportion of predictions clinically similar to the true score)



Trajectory and posterior predictive distribution of four representative patients

- The model achieved **77.2% accuracy** for predictions one step-ahead.
- The model identified **no relevant biomarkers** to predict AD severity.
- We estimated the Minimal Detectable Change (MDC) to be 7.2 (95% CI: 6.1 - 8.2).
- The average autocorrelation was 0.66 with standard deviation 0.18



Parameters' value (β) after feature selection

Conclusion

- The evolution of eczema severity is described more by its dynamic evolution history, rather a single point measurement of biomarkers.
- Combining a Hidden Markov Model with the horsehoe prior enables to design complex yet interpretable prediction models while dealing with noisy and partially missing data.

Acknowledgements

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References

[1] M. E. Schram, E. Roekevisch, M. M. G. Leeflang, J. D. Bos, J. Schmitt, and P. I. Spuls, ``A randomized trial of methotrexate versus azathioprine for severe atopic eczema,'' *Journal of Allergy and Clinical Immunology*, vol. 128, no. 2, pp. 353--359, 2011.

[2] J. Piironen and A. Vehtari, ``Sparsity information and regularization in the horseshoe and other shrinkage priors,'' *Electronic Journal of Statistics*, vol. 11, no. 2, pp. 5018--5051, 2017.

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