

Computational tools for data-driven personalised medicine for atopic dermatitis

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Motivation

- Designing personalised treatment strategies is of high clinical relevance
- We develop computational tools to improve care for AD patients to
 - “assess” AD severity easily
 - “predict” the dynamic evolution of AD severity for each patient
 - “act”, i.e. suggest personalised treatment strategies

Computational tools to “assess” AD severity easily

Motivation

- Improve monitoring of AD severity by making data collection easier, at home, without the need to attend a clinic
- Help patients be better engaged in the management of their condition
- Reduce inter- and intra-observer variability in score evaluation

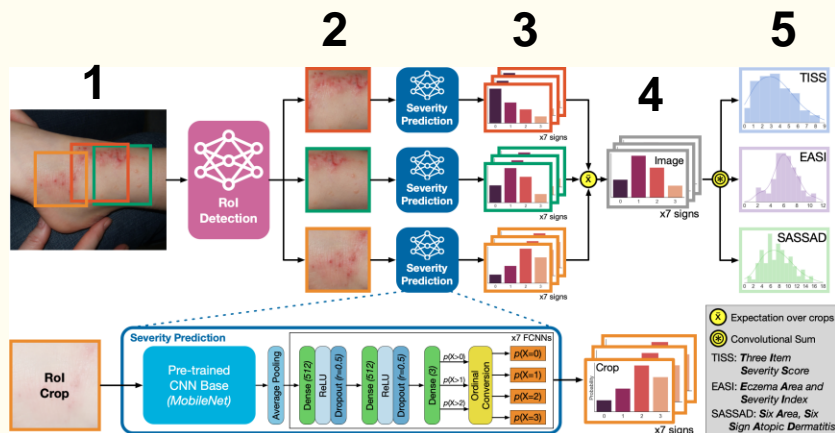
Objective

- Develop a method to detect and assess AD severity from camera images
-

EczemaNet: Automating Detection & Assessment of AD

- Training data from the SWET clinical trial (Thomas *et al.* 2008): 1393 images from 310 patients
- We developed EczemaNet, a deep learning computer vision pipeline to **detect eczema areas from camera images** and produce **probabilistic predictions of 7 disease signs**, which can be aggregated to produce predictions for regional severity score
- We demonstrated good performance for predicting regional EASI severity score (root mean squared error < 2)

EczemaNet pipeline



1. EczemaNet uses **camera images** as inputs, rather than already curated images
2. EczemaNet identifies eczema lesions in the image
3. EczemaNet makes probabilistic predictions of the severity of 7 disease signs for each lesion
4. Predictions for the image are obtained by averaging predictions from different lesions
5. Predictions for the 7 disease signs are aggregated into predictions for regional severity score

Computational tools to “predict” the dynamic evolution of AD severity

Motivation

- Predict severity dynamics to act on future worsening of the severity
- Better understand the disease dynamics

Objectives

- Provide personalised predictions using observational longitudinal data
 - Estimate responsiveness to treatment and the impact of environmental factors on predictions
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Proof of concept study – Prediction of AD severity

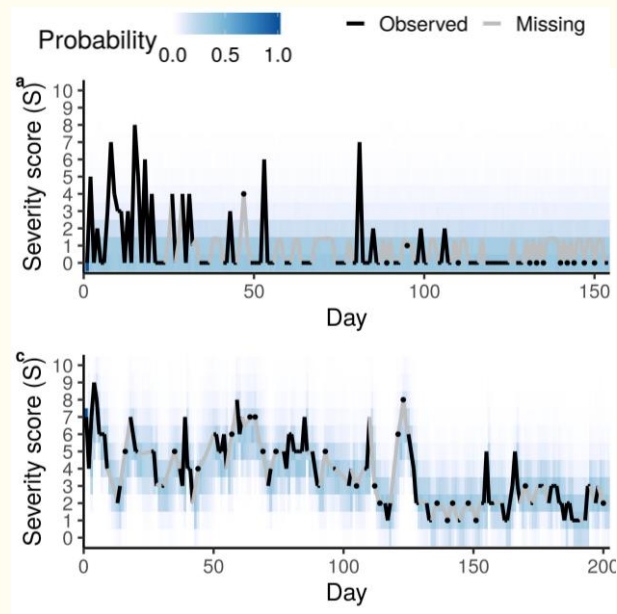
- We aim to show it is possible to predict the short-term evolution of AD severity
- We developed a mechanistically inspired Bayesian machine learning model
- We used two datasets which measured a daily “bother” score
 - 59 patients for 6-9 months (Langan *et al.* BJD 2009)
 - 334 patients for 16 weeks (SWET clinical trial, Thomas *et al.* 2008)

G. Hurault, E. Domínguez-Hüttinger, S. M. Langan, H. C. Williams, and R. J. Tanaka, “Personalized prediction of daily eczema severity scores using a mechanistic machine learning model,” Clin. Exp. Allergy, 2020.

Proof of concept study – Prediction of AD severity

- Our model was able to predict future severity scores at the individual level, and improved chance-level forecast by 60%.
- Our model was able to estimate patient-dependent responsiveness to corticosteroids, calcineurin inhibitors and emollients

Our model was able to capture different trajectory patterns.
Black lines: observed trajectory; Blue areas: model fit



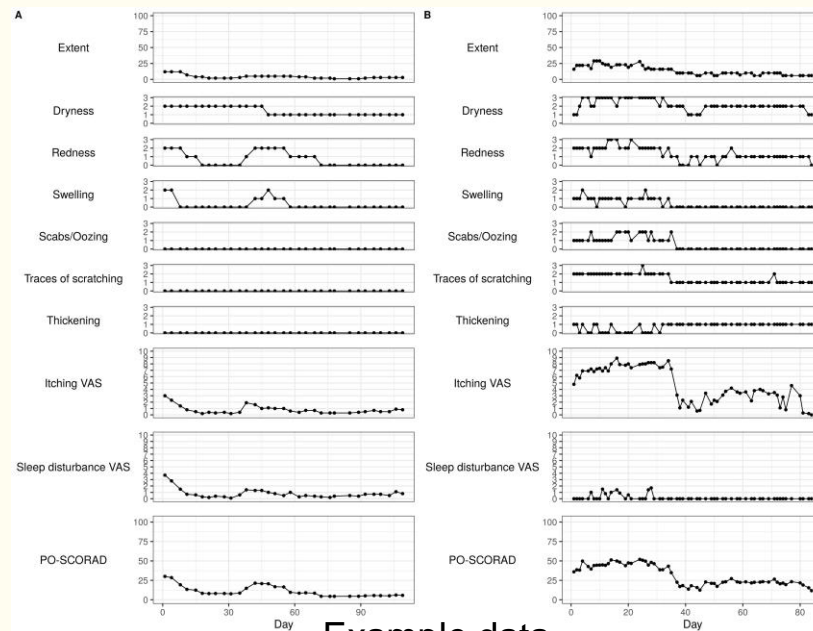
EczemaPred: a computational framework to predict the evolution AD severity

- We developed EczemaPred, a collection of statistical machine learning models to predict the evolution of eczema severity.
- EczemaPred models:
 - Are interpretable
 - Are tailored to individual severity items and can produce predictions for any severity scores
 - Quantifies uncertainty in measurements and predictions
 - Deal with missing values
 - Incorporate prior knowledge
 - Can deal with patient-dependence
- EczemaPred is available as a R package

EczemaPred for predicting PO-SCORAD

We used EczemaPred to predict **Patient-Oriented SCORAD** in two datasets:

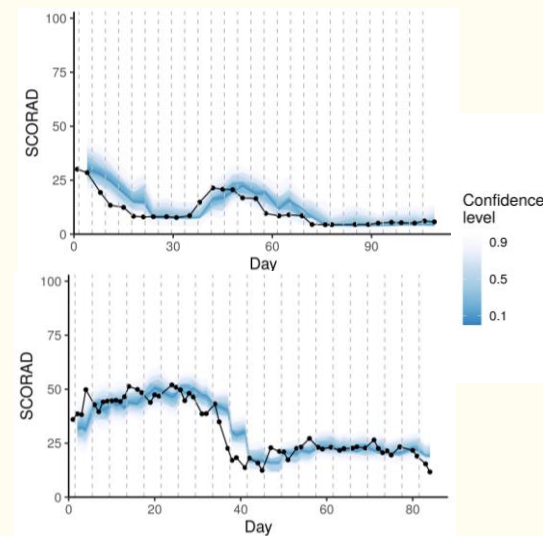
- Dataset 1 (*Tiplica et al., Pediatr. Dermatol. 2017*)
 - 347 children with mild to moderate AD
 - Twice weekly measurements for 17 weeks
- Dataset 2 (observational study)
 - 16 adults with moderate to severe AD
 - Daily measurements for 12 weeks



Example data

EczemaPred for predicting PO-SCORAD

- EczemaPred achieves 70-80% accuracy for 4-days-ahead forecasts.
- EczemaPred outperforms other off-the-shelf time-series forecasting models.
- We found that 75% of the uncertainty in predicting PO-SCORAD was attributed to uncertainty in predicting intensity signs.



Prediction intervals (blue shaded area) and observed trajectory (connected dots) for 2 representative patients

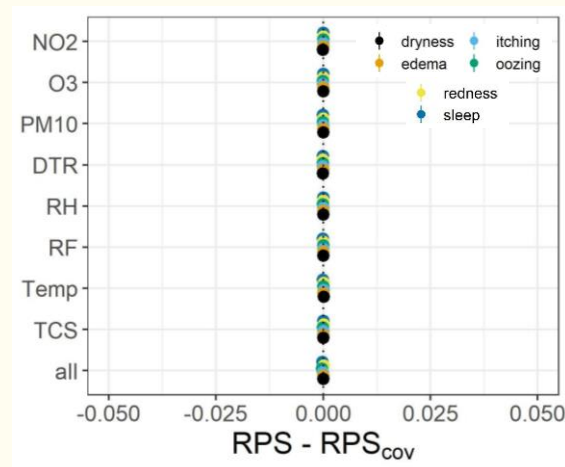
Can environmental factors predict future AD severity?

- Many prior studies investigated whether environmental factors were associated with the current AD severity. But they have failed to consider the dynamic nature of the severity nor investigated whether the future AD severity can be predicted by real time data on environmental factors.
- We aimed to assess the impact of environmental factors in predicting future AD severity scores
- We used the data from 177 Korean children with mild to severe AD (Kim *et al.* PLoS One, 2017)
 - Daily measurements of six AD signs
 - Daily record of air pollution (PM10, NO2, O3) and weather (temperature, humidity, rainfall)

G. Hurault, V. Delorieux, Y.-M. Kim, K. Ahn, H. C. Williams, and R. J. Tanaka, "Impact of environmental factors in predicting daily severity scores of atopic dermatitis," Clinical and Translational Allergy, in press

Can environmental factors predict future AD severity?

- Our model could accurately predict future AD severity without the information on environmental factors.
- Including environmental factors did not improve predictive performance.
- Using environmental factors without considering AD severity dynamics, as in previous studies, produces predictions not better than a historical forecast.



Difference in predictive performance for six signs when environmental factors are included as covariates

Summary

- We proposed a computational data-driven pipeline to foster personalised medicine for AD
 - EczemaNet automatically detects and assesses eczema lesions from camera images
 - EczemaPred predicts the evolution of AD severity
- We plan to extend EczemaPred to suggest personalised treatment strategies under uncertainty (“act”)

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