Subtyping Atopic Dermatitis Trajectories Using Digital Patient-Reported Outcomes and Machine Learning

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INTRODUCTION

Atopic dermatitis (AD) exhibits highly heterogeneous disease courses that are influenced by both biological and lifestyle factors. Traditional clinical measures often fail to reflect patients' lived experiences, while patient-reported outcomes (PROs) capture real-time perceptions of disease control, stress, and quality of life. However, conventional statistical approaches are limited in modeling the complex, multidimensional relationships among lifestyle and psychosocial domains. Recent advances in **machine learning** and **explainable AI (XAI)** provide new opportunities to extract meaningful insights from small yet information-dense datasets.

OBJECTIVE

To explore **short-term AD trajectories** among patients initiating JAK inhibitor therapy using digital PROs (dPROs), and to identify associations between **lifestyle and psychosocial factors** and distinct disease trajectory patterns through an interpretable AI framework.

METHOD

This exploratory single-center study enrolled **26 AD patients** treated with systemic JAK inhibitors (abrocitinib or upadacitinib) between 2023–2024. Each participant provided a rich dataset including:

- **90-day repeated ADCT (Atopic Dermatitis Control Tool)** scores
- **53 baseline lifestyle and psychosocial variables** covering stress, exercise, family, and occupation domains

Analytic workflow:

1. **Trajectory clustering:** Hierarchical clustering of 90-day ADCT scores to identify disease subtypes.
2. **Associative modeling**: A CatBoost multiclass model was used to examine associations between lifestyle factors and trajectory membership.
3. **Explainability:** SHAP values were applied to interpret the relative contribution and directionality of each variable.
4. **Semantic translation:** Large language model (LLM) converted SHAP findings into readable clinical narratives, reviewed by domain experts.

RESULTS

Trajectory Clustering (Figure 1):

Unsupervised hierarchical clustering of 90-day ADCT trajectories identified **three distinct subtypes**:

1. **Cluster 1 – Severe with Marked Improvement** (n = 11): greatest ADCT reduction (–16.4 points).
2. **Cluster 2 – Moderately Severe with Marked Improvement** (n = 10): intermediate ADCT reduction (–10.1 points).
3. **Cluster 3 – Moderately Severe with Modest Improvement** (n = 5): minimal ADCT reduction (–6.0 points).

All clusters showed overall improvement in ADCT scores, though the magnitude varied substantially, reflecting heterogeneous treatment responses.

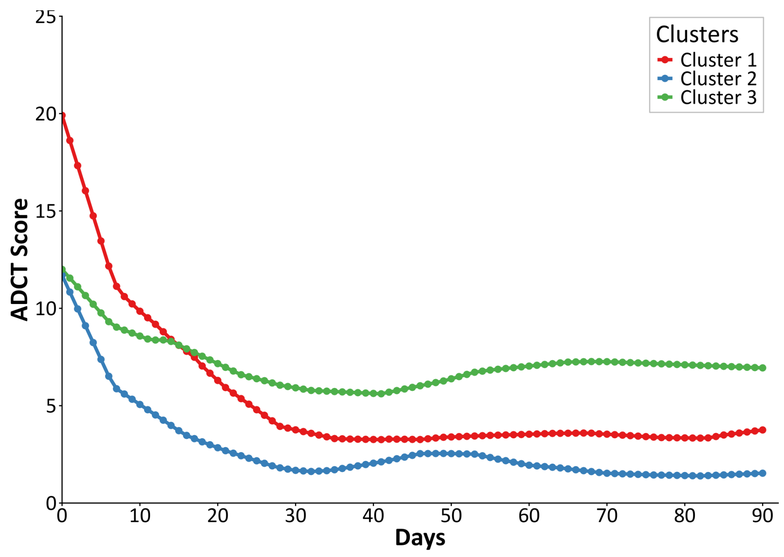

Figure 1. Longitudinal changes in ADCT scores across trajectory clusters.

Feature Attribution (Figure 2):

A CatBoost multiclass model incorporating 53 lifestyle and psychosocial variables achieved **75.0% classification accuracy** (AUC = 0.828).

SHAP analysis revealed that **stress perception, exercise frequency, family support,** and **weekly working hours** were the strongest contributors to cluster differentiation. Higher stress and longer working hours were associated with Cluster 1 (greater improvement but higher baseline severity), whereas lower exercise frequency and heavier family responsibilities characterized Cluster 3 (limited improvement). These findings demonstrate the feasibility of integrating digital PRO trajectories with explainable AI to uncover clinically interpretable lifestyle patterns linked to treatment response in AD.

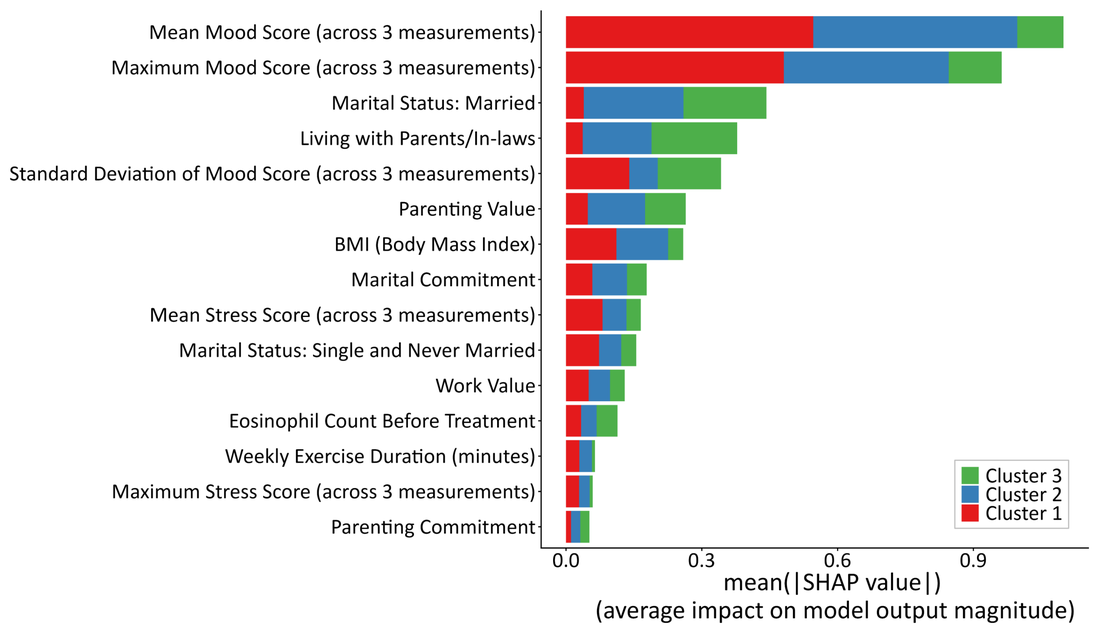

Figure 2. Top 15 features contributing to disease trajectory classification, ranked by SHAP values.

CONCLUSIONS

- Dense, high-frequency **digital PROs** enable meaningful "big-data" analysis even in small cohorts.
- The **CatBoost–SHAP–LLM** pipeline produced explainable insights that bridge quantitative outputs and clinical interpretation.
- Identifying **lifestyle-linked treatment response patterns** supports a shift toward **personalized, patient-centered care** in AD.
- External validation in larger, multi-center cohorts with longer follow-up is warranted.

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