Machine Learning–Based Identification of Moderate-to-Severe Atopic Dermatitis (AD) in US Patients Using the TARGET-DERM AD Registry

PO 73553

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Objectives

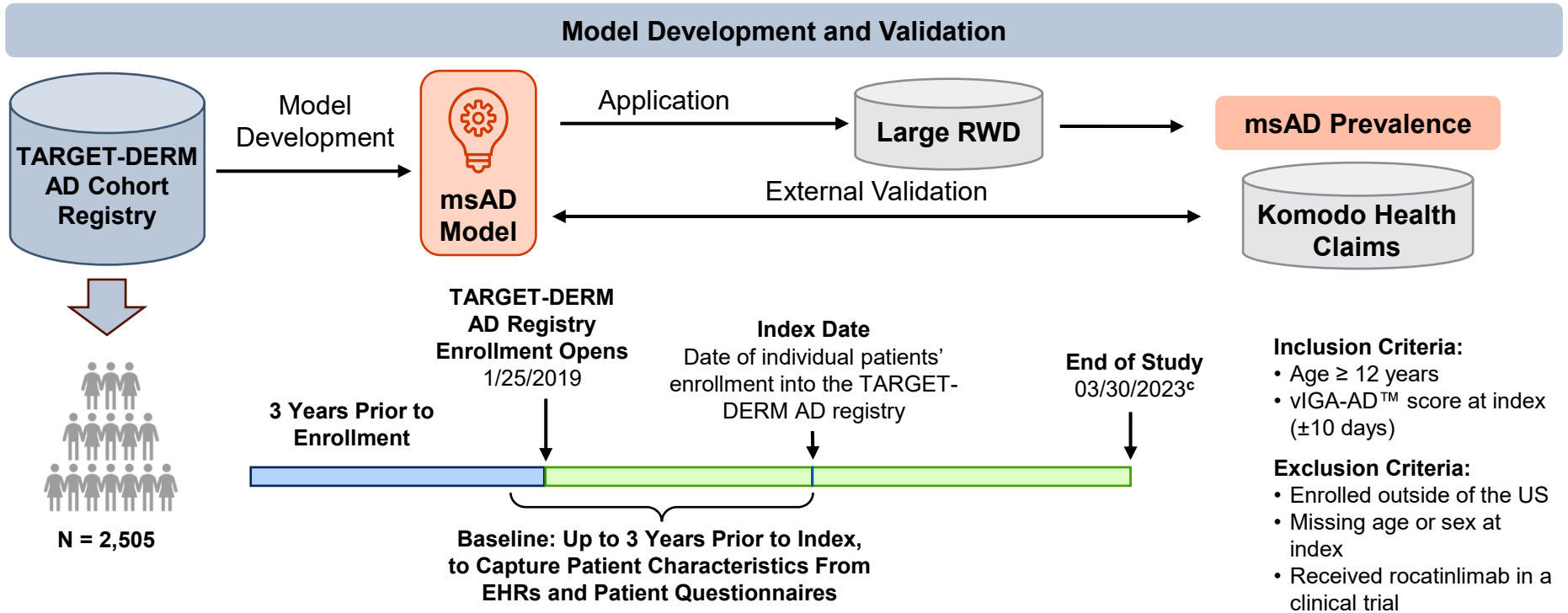
1. Develop a machine learning model to identify patients with msAD[a] using the TARGET-DERM AD registry and identify key predictors of msAD
2. Assess the generalizability of the model to claims data

Background

- msAD is associated with significant clinical burden and is often undertreated[1,2,b]
- Without clear records of disease severity across RWD, quantifying the burden of msAD remains challenging
- Published methods to predict AD severity rely on systemic therapy as a proxy[3,4] or were developed using highly curated and/or small datasets[5]

Model Development

- Data were modeled using US patients ≥ 12 years of age enrolled in the TARGET-DERM AD registry (N = 2,505), an international, longitudinal registry of patients with physician-diagnosed AD[6]
- Overall, 220 features were used to train the models (random training:holdout split, 7:3), including demographics, lifestyle factors, geographic region, comorbidities, and concomitant medications



[a]msAD is defined as a vIGA-AD™ score of 3 or 4. [b]Undertreatment is defined as not receiving an AST to adequately treat msAD. [c]Or most recent available data.

Abbreviations: AD, atopic dermatitis; AST, advanced systemic therapy; EHR, electronic health record; msAD, moderate-to-severe AD; RWD, real-world data; vIGA-AD™, validated Investigator Global Assessment for AD.

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Covariates & Modeling Results

Covariates	Examples	
Demographics, region, and lifestyle	• Age • Gender • Race • Region[a] • Site type[b] • Alcohol usage	• Tobacco usage • Marijuana usage • Insurance type (eg, private, Medicare, Medicaid)
AD history	• Age of AD onset	
Comorbidities (total = 110)	• Skin conditions (eg, erythema, acne, alopecia) • Allergies	• Chronic diseases (eg, asthma, high BP, hypercholesterolemia) • GERD
AD medication exposures (total = 21)	• Corticosteroids (topical or systemic) • Antibiotics • Antihistamines • Biologics	• JAK inhibitors • Antivirals • Topical calcineurin inhibitors
Other concomitant medications (total = 34)	• Acetylsalicylic acid • Statins • Cefalexin • Cetirizine • Ciclosporin • Fluticasone	• Influenza vaccine • Metformin • Pantoprazole • Paracetamol • Vitamins
Not available or not included	• Laboratory values • Family history of AD	• Pain-related scores (usually not in RWD)

Primary Model

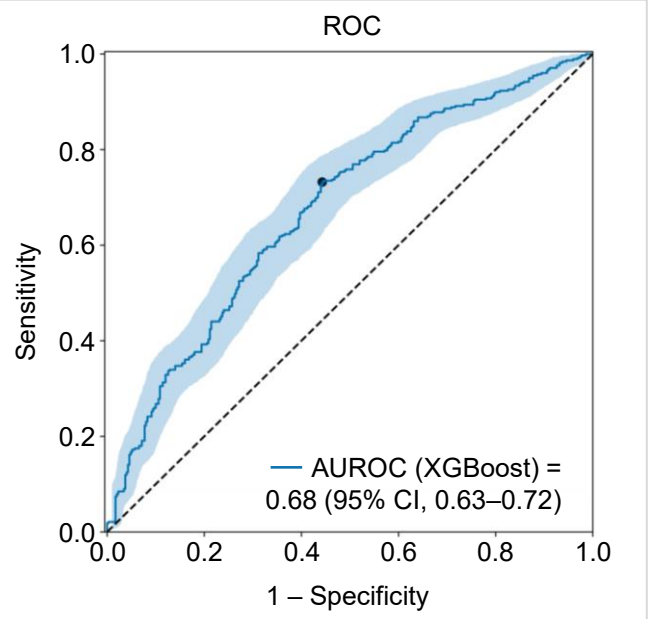
- Two machine learning models were explored, including logistic regression and XGBoost.
- The XGBoost model[7] performed better and was chosen as the primary model. This model is an ensemble of decision trees—where each successive tree is constructed to reduce the error in the prediction until there is no further room for substantial improvement.
- The ROC plot shown here presents the model's performance on the holdout set—comparing how often the model correctly identifies patients who truly have msAD (sensitivity) along the vertical axis versus how often it incorrectly flags patients who do not have msAD as having msAD (1 – specificity)[c] along the horizontal axis for various decision thresholds on the predicted probability for msAD.
- The probability threshold can be adjusted depending on the desired level of sensitivity at the cost of specificity, and vice versa.

- Max tree depth: 8
- Number of trees: 106

Training	Holdout
70%	30%

Internal holdout sample: n = 727

AUROC ≈ 0.68 (95% CI, 0.63–0.72)



Model Performance

For p_{thr} = 0.511,[d] at maximum J_{Youden}[e]

***Sensitivity* = 0.73**

***Specificity* = 0.56**

[a]US regions (Northeast, South, West, Midwest). [b]Community or academic. [c]Specificity is defined as how often the model correctly identifies patients as not having msAD when they truly do not have it. [d]p_{thr} is the threshold for the model's predicted probability, used for positive identification of msAD. [e]J_{Youden} (Youden's J statistic or the Youden's index) is maximum at the point on the ROC curve where the sum of sensitivity and specificity is maximum.

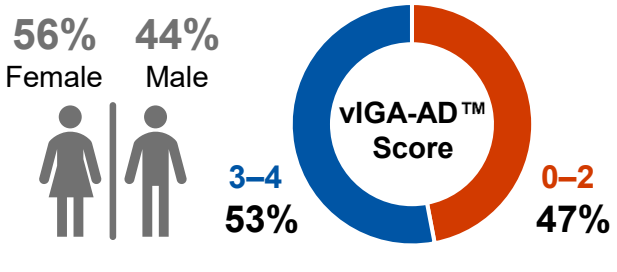
Abbreviations: AD, atopic dermatitis; AUROC, area under the ROC curve; BP, blood pressure; GERD, gastroesophageal reflux disease; JAK, Janus kinase; max, maximum; msAD, moderate-to-severe AD; ROC, receiver-operating characteristics; RWD, real-world data.

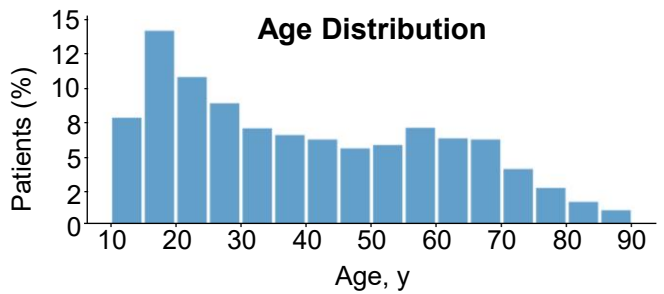
Top Predictors of msAD in Patients From the TARGET-DERM AD Registry Included AD Treatment Exposure, Region, Race, Age, Time of AD Onset, and Community Site

Study Cohort and Key Predictors of msAD

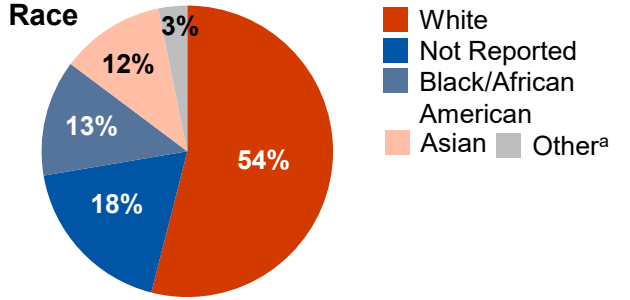
TARGET-DERM AD Registry

N = 2,505
met study eligibility criteria

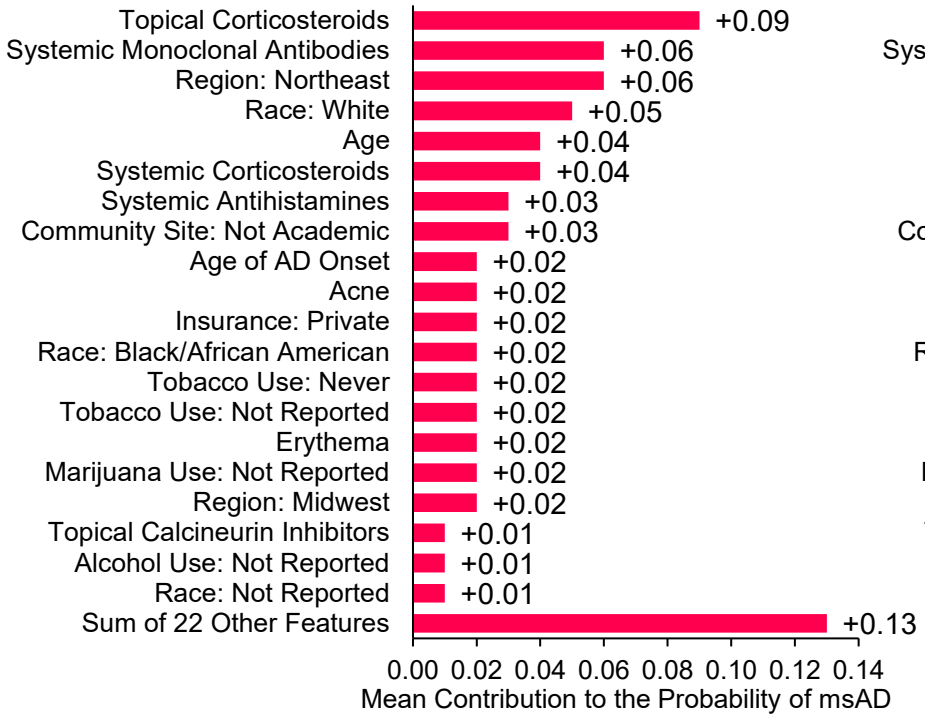




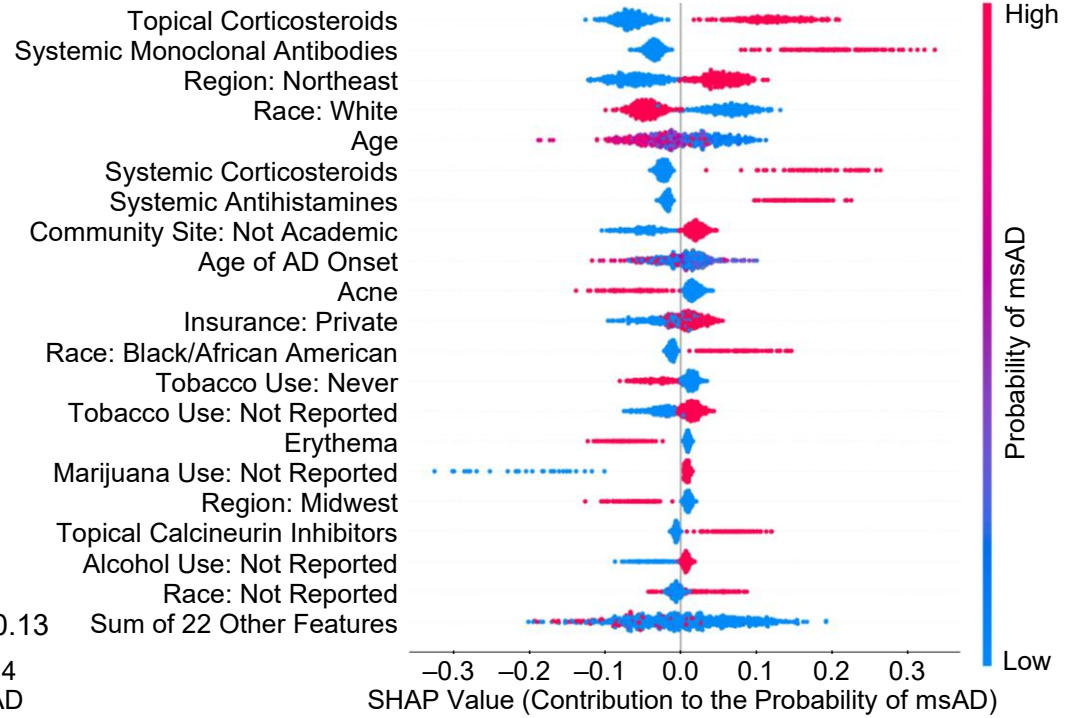
84%
Adults
(≥ 18 y)



SHAP Feature Importance



SHAP Feature Importance With Directionality



Higher probability of msAD:

- Use of any of the following medications within 4 months prior to index:
  - Topical corticosteroids
  - Systemic corticosteroids
  - Biologics
  - Systemic antihistamines
- Residence in the northeastern US
- Black/African American
- Younger age
- Younger age at AD onset
- Community site

Lower probability of msAD:

- Patients with acne
- Patients with erythema

[a]Other included other (2.4%), Native Hawaiian or other Pacific Islander (0.5%), and American Indian or Alaska Native (0.4%).

Abbreviations: AD, atopic dermatitis; msAD, moderate-to-severe AD; SHAP, Shapley Additive Explanations; vIGA-AD™, validated Investigator Global Assessment for AD.

Model Validation Using Linked Claims Data

Objectives

- Check the primary model's generalizability using linked Komodo Health claims data
- Develop a separate model on a subset of covariates that are consistently reproduced in Komodo Health and TARGET-DERM AD

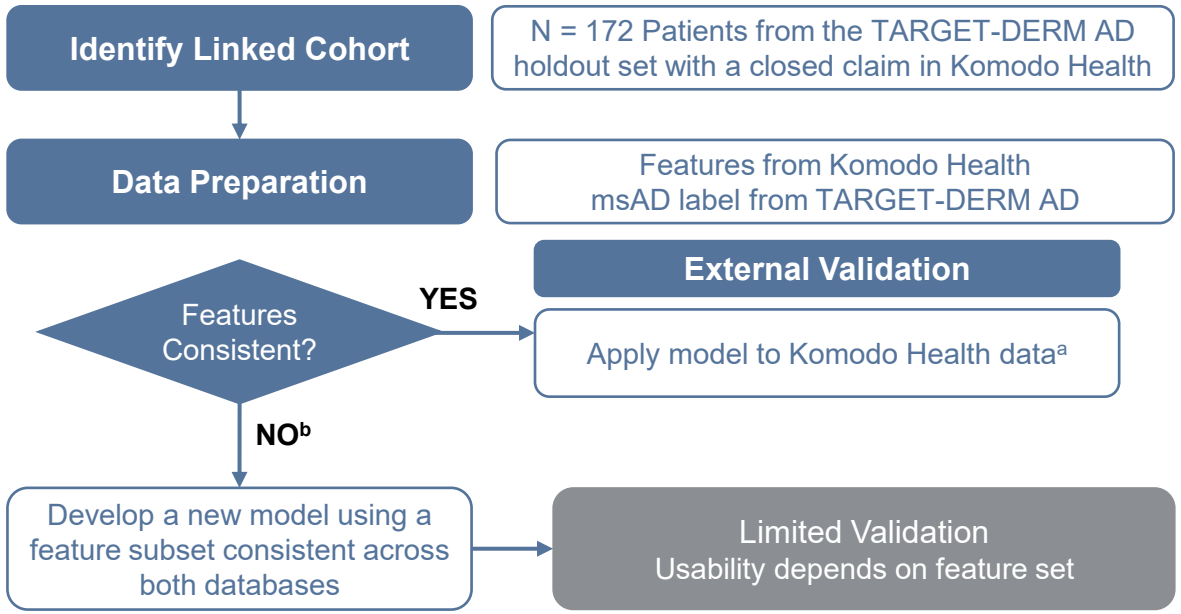
Results

- A parsimonious XGBoost model using the top 20 covariates was developed using the TARGET-DERM AD registry and applied to linked Komodo Health data. Some covariates had multiple categories, such that constructing one model feature for each category increased the total number of features to 42.
- Inconsistencies in key covariates (eg, AD medications) meant that a sensible validation of the model on the linked Komodo Health claims data was not possible.
- Alternate models obtained by removing inconsistent features only further reduced model performance. The only features remaining were basic demographics, including sex and age, which offer limited predictive power and clinical relevance.

Reasons for Inconsistencies

- Different data collection and recording methods across databases
  - **TARGET-DERM AD:** EHR data from specialty clinics were likely incomplete as GP EHRs were not included
  - **Komodo Health claims:** Excludes over-the-counter medications or medications obtained from physician samples

Methods



Exploratory Modeling

- Separate logistic regression and XGBoost models were developed after excluding AD medications
- The resulting models had reduced performance (AUROC range, 0.60–0.63) with larger uncertainty and were less interpretable due to the exclusion of clinically relevant features

[a]This step was not feasible in our work. [b]Implies that direct cross-validation is not feasible.
Abbreviations: AD, atopic dermatitis; AUROC, area under the receiver-operating characteristics curve; EHR, electronic health record; GP, general practitioner; msAD, moderate-to-severe AD.

Key Takeaways

A machine learning model leveraging diverse clinical and demographic characteristics was developed on a US cohort to infer moderate-to-severe AD (msAD). It does not rely solely on systemic therapy as a proxy for severity[3,4] and performed as well as, or better than, published models developed using highly curated and/or smaller datasets.[5]

The model indicated that patients were more likely to have msAD if they had recent use of corticosteroids, biologics, or systemic antihistamines in the prior 4 months, or if they were Black/African American, younger than approximately 25 years, or resided in the US Northeastern region.

Built using the TARGET-DERM AD registry data, primarily sourced from dermatologist-based practices, the model identifies clinically sensible predictors of AD severity and could potentially be applied to suitable specialty-derived EHR data to identify disease severity and infer treatment gaps (validation in external EHR data was out of scope).

Due to differences in data collection and recording methods in the different databases, the model could not be generalized to claims data.

Further development of a validated prediction model applicable to US claims data could better enable identification of the treatment needs among patients with msAD.

Abbreviations: AD, atopic dermatitis; EHR, electronic health record; msAD, moderate-to-severe AD.

References: 1. Langan SM, et al. *Lancet.* 2020;396:345-360. 2. Haft M, et al. Poster presented at: Fall Clinical Dermatology Conference; October 20-23, 2022; Las Vegas, NV, USA. 3. Paller AS, et al. *J Am Acad Dermatol.* 2020;82:651-660. 4. Chomistek AK, et al. *Br J Dermatol.* 2023;188:ii35-ii36. 5. Maintz L, et al. *JAMA Dermatol.* 2021;157:1414-1424. 6. Abuabara K, et al. *BMJ Open*. 2020;10:e039928. 7. Chen T, et al. Paper presented at: 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining; August 13-17, 2016; San Francisco, CA, USA.

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Disclosures

MC, KYC, JB, KG, and **JHP** are employees and stockholders of Amgen Inc. **BB** is an employee of Amgen Research (Munich) GmbH and a stockholder of Amgen Inc. **FY** and **JMC** are employees of Target RWE and may hold stock options. **FH** and **JQ** are employees of Kyowa Kirin, Inc. **ES** reports personal fees from AbbVie, Aclaris Therapeutics, Amgen Inc., Arcutis Biotherapeutics, Astria Therapeutics, Attovia Therapeutics, Bambusa Therapeutics, Castle Biosciences, CorEvitas, Dermira, Eli Lilly, Evommune, FIDE, Impetus Healthcare, Incyte, ImageneBio, Innovaderm Research/Indero, Janssen, LectureLinx, LEO Pharma, Numab Therapeutics, Pfizer, Recludix Pharma, Regeneron Pharmaceuticals, Roche, Sanofi, and Sitryx. ES also reports grants from (or serves as a principal investigator for) AbbVie, Acrotech Biopharma, Amgen Inc., Arcutis Biotherapeutics, ASLAN Pharmaceuticals, Castle Biosciences, CorEvitas, Dermavant Sciences, Dermira, Eli Lilly, Incyte, Pfizer, Regeneron Pharmaceuticals, Sanofi, Target RWE, and Veriskin.

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