Identifying Risk Profiles for Early Treatment Discontinuation in Geographic Atrophy Using Machine Learning and SHAP Clustering

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Ashwin Rai,[1] Ariel Berger,[1] Andre Ng,[2] Victoria Ikoro,[3] Devika Bhandary[2]

[1]Thermo Fisher Scientific, Waltham, MA, USA; [2]Thermo Fisher Scientific, London, UK; [3]Thermo Fisher Scientific, Ontario, Canada

Introduction

Geographic atrophy

- Geographic atrophy (GA) is an advanced form of age-related macular degeneration.
- Approximately 1 million US adults are affected in at least one eye.[1]
- Risk increases with age (~0.3% of persons aged 65–74 years; ~4% of persons aged ≥ 85 years).[2]
- It is a progressive disease that results in irreversible loss of vision over time.[3]

Treatment

- Frequency of administration depends on the drug and regimen selected, but the current mainstay of treatment is intravitreal injections directly into the eye every 25–60 days.[4]
- The main goal of this treatment is to delay GA progression.
- While effective, studies have shown 30%–40% of patients discontinue treatment within a year.[5]

Problem

- As treatment is only effective if maintained, relatively high rates of discontinuation reduce patient long-term quality of life.[6]
- However, healthcare professionals do not typically have the time or resources to intensively monitor their patients, and thus support their patients' decisions to adhere to treatment.[5]
- Early discontinuation also affects the accuracy and reliability of clinical studies of treatment for GA.[7]
- Therefore, decision rules/algorithms targeting patient profiles at elevated risk of discontinuation may represent an efficient means to improve adherence and subsequently optimize positive outcomes.
- Specifically, if these algorithms were built on electronic, real-world, health data, they could be automated at various points-of-care to maximize their impact on treatment adherence.

Objectives

- **The main objective of this study was to develop a machine learning algorithm to identify patients at risk of dropout.**
- **For each patient, the algorithm would produce a risk score for adherence based on their individual patient journey.**
- **By utilizing a data-driven approach, we sought to explore the clinical, behavioral, and psychosocial factors behind patients' decisions to be non-adherent.**
- **The ultimate goal was to subsequently create a toolkit for healthcare professionals to implement a tailored retention strategy.**

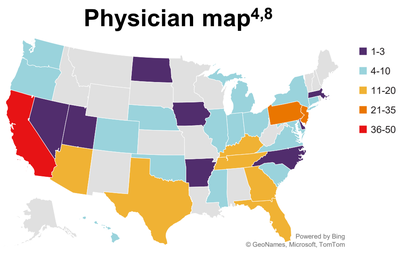
Methods

Data source – Vestrum retina database

Database overview[4,8]

Patient Visits (2015–Current)	18M
Patients (2015–Current)	2.4M
Sites (Current)	74
Retina Specialists (Current)	370
States (US) Represented (Current)	35

Physician map[4,8]



Patient follow-up time available[4,8]

Patients	2.4M
Total person years	4.1M
Mean follow-up time	1.7 Years

As of February 2024

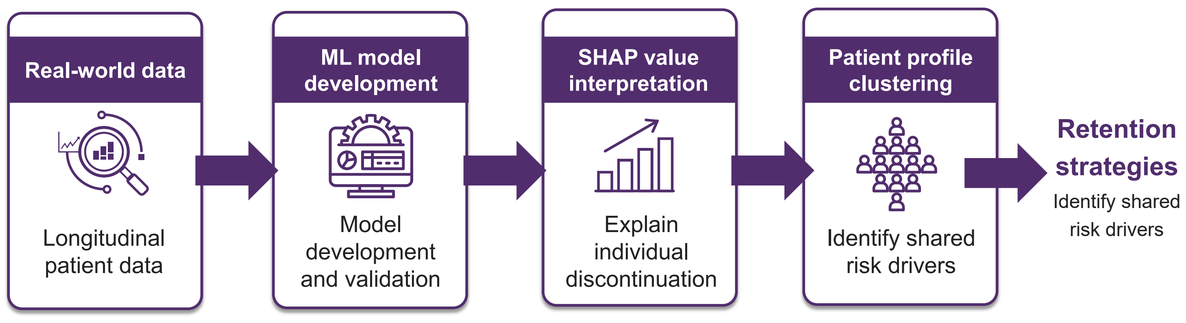
In addition, we can mine the free-text field within the electronic medical record (EMR) to discover further diagnostics and characteristics like subretinal fluid and vitreomacular traction (VMT)

- **Demographics:** Age, gender, smoking status, alcohol use
- Treatment history: Medications/treatment regimens (prior and present) and related procedures
- **Disease characteristics:** Relevant disease (e.g., GA) and comorbidities, year and severity of diagnosis, disease progression, adverse events
- **Patient-reported outcomes:** Visual acuity, central retinal thickness, fluid, surgery outcomes, change in therapy, lost to follow-up
- **Targeted adverse events:** infection (uveitis, endophthalmitis), retinal detachments, hemorrhaging, disease development, and progression

ML framework (Figure 1)

- We modelled early treatment discontinuation by training a supervised ML model based on 10,000+ GA patients; it was trained on 8,134 patients, tested on 2,034 patients (80–20% split)
- Model inputs included demographics, clinical history, and treatment patterns.
- We used SHapley Additive exPlanations (SHAP) to interpret patient-level risk drivers and applied K-means clustering on SHAP values to group similar patients. We identified five distinct patient profiles based on shared dropout risk factors.

Figure 1. Overview of risk profiling model and real-world impact



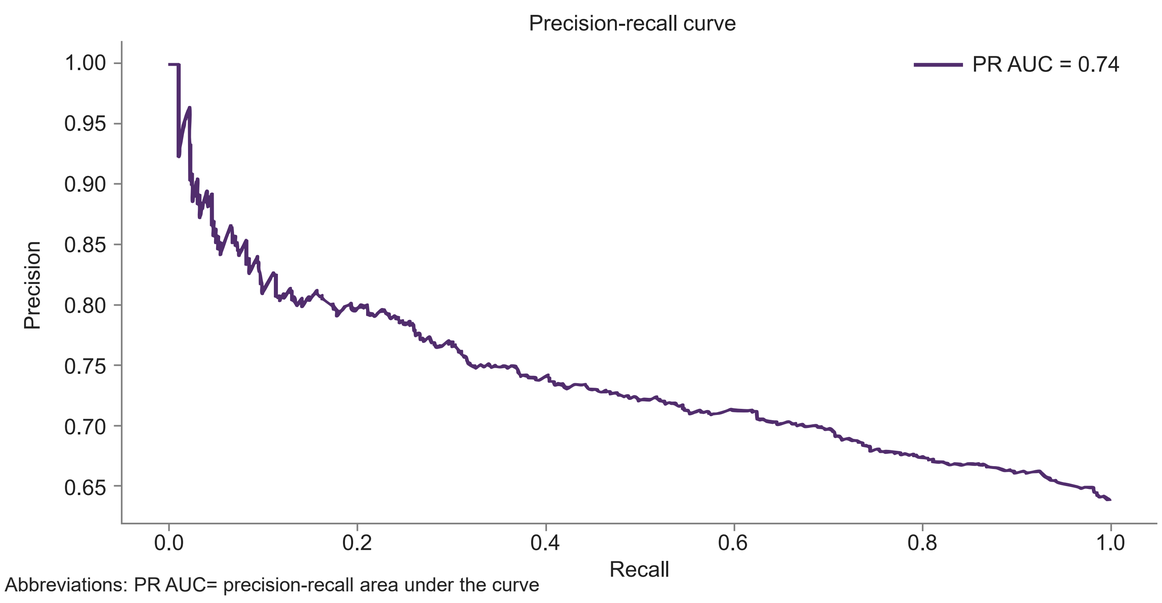
Abbreviations: ML = machine learning; SHAP = SHapley Additive exPlanations

Results

ML model results on patients at risk of GA treatment dropout (Figure 3)

- Prediction target was discontinuation within 120 days.
- The receiver operating characteristic (ROC) area under the curve (AUC) was 0.62; the precision-recall AUC was 0.74, with recall of 0.98 and precision of 0.64
- Overall accuracy was 64%.

Figure 3. Precision-recall curve by supervised machine learning model identifying patients at risk of GA treatment dropout



Abbreviations: PR AUC= precision-recall area under the curve

Patient profiles comparison (Figure 4)

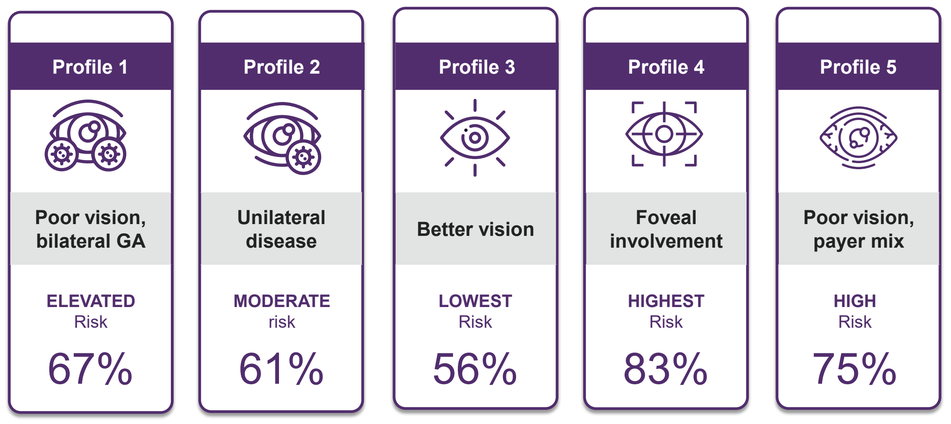
Profile 3—Lower GA treatment dropout

- 56% of patients in this cluster (which represents 26% of the total population) discontinued treatment within 120 days.
- They had relatively better initial vision, stable healthcare access, less severe disease (bilateral GA/fovea patterns), slower disease progression, and most were treatment naïve (i.e., first GA treatment ever).

Profile 5—Higher GA treatment dropout

- 75% of patients in this cluster (which represents 14% of the total population) discontinued treatment within 120 days.
- They had relatively poorer initial vision, limited/inadequate healthcare coverage, among other disease traits.

Figure 4. Patient profiles identified as at risk of GA treatment dropout



Conclusions

- **Patient profiles translated complex ML outputs and diverse real-world-data into clear, actionable subgroups.**
- **The profiles revealed both who is at risk or has a specific need, and why, enabling targeted strategies.**
- **The GA discontinuation example shows how prediction → explanation → segmentation can improve persistence and outcomes.**
- **Profiling is flexible—applicable to risk, engagement, value, and other use cases across the patient journey.**
- **Embedding profiles into workflows supports precision interventions, optimizes resources, and strengthens real-world evidence.**

References

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Disclosures

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