APPLICATION OF AN ARTIFICIAL INTELLIGENCE MODEL TO DETECT ALPHA-1 ANTITRYPSIN DEFICIENCY: CHARACTERIZING THE STUDY POPULATION

James K Stoller,[1]* Nikhil Khandelwal,[2†] Vahid Esmaeili,[3] Chris Blair,[2] Michelle Kirby,[2] Jimmy Hinson,[2] Lara Jehi,[1] Jingdi Shen,[1] Martin Beaussart,[3] David Castellano Falcon,[3] Leon van Wouwe,[3] Umur Hatipoğlu[1]

[1]Cleveland Clinic, Cleveland, OH, USA; [2]Takeda Pharmaceuticals USA, Inc., Lexington, MA, USA; [3]Volv Global SA, Epalinges, Switzerland

*Presenting author

†Corresponding author

INTRODUCTION

- Alpha-1 antitrypsin deficiency (AATD) is an autosomal codominant condition that predisposes patients to chronic obstructive pulmonary disease (COPD) and/or liver disease.[1]
- This condition is under-recognized globally; it is estimated that only 10% of patients with genotypes that are associated with severe AATD in the USA are diagnosed.[2]
- Optimal diagnostic tools are considered essential due to the similarity of the signs and symptoms of COPD and/or liver disease, irrespective of the presence of AATD.[3]
- Real-world data can be applied to machine learning models to aid patient identification; the application of an artificial intelligence (AI) model to a large Komodo US claims database to identify undiagnosed, symptomatic patients with AATD was previously reported.[4]
  - The model was subsequently calibrated to electronic medical record (EMR) data using a selected clinical cohort.
- To establish a robust machine learning model that can accurately identify and differentiate undiagnosed patients from diagnosed patients, it is critical to recognize the characteristics and clinical features of individuals diagnosed with AATD.

OBJECTIVE

- To characterize cohorts of patients with AATD using retrospective de-identified patients' data generated from the Cleveland Clinic EMR.

METHODS

- Retrospective, de-identified patient records from January 1, 1998, to August 15, 2024, were sourced from the Cleveland Clinic EMRs.
  - This study was processed under expedited review and approved by the Cleveland Clinic Institutional Review Board (#24-469).
- Patients were grouped into categories depending on how their diagnosis of AATD was confirmed, using either genotype information or serum alpha-1 antitrypsin (AAT) levels (**Table 1**).
- A subset of patients with mild deficiency (based on serum AAT levels) who received augmentation therapy (n = 13) were excluded *post hoc*. The true deficiency status of such patients may have been severe but potentially masked by either treatment received at the time of measurement or due to the absence of pre-treatment serum level values in the EMR.
- Clinical phenotypes in terms of symptoms, morbidities and treatment patterns for patients within these groups were analyzed using relevant medical codes from EMRs.

TABLE 1. PATIENTS WERE GROUPED BASED ON HOW THEIR DIAGNOSIS OF AATD WAS CONFIRMED

Category	AATD diagnosis
Genetic deficiency	Genotype information[a]
Severe deficiency	AAT serum level < 57 mg/dL
Mild deficiency	AAT serum level 57–90 mg/dL

[a]Diagnosis of AATD was based on the identification of biallelic pathogenic variants (SS, ZZ, II, FF or compound heterozygotes of these alleles) in *SERPINA1*.

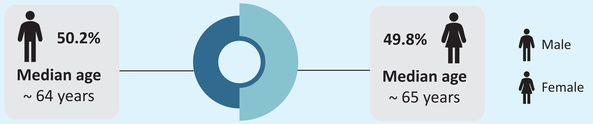
AAT, Alpha-1 antitrypsin; AATD, Alpha-1 antitrypsin deficiency.

RESULTS

Patient demographics

- Of the 781 patients with AATD, the majority were identified by serum AAT level, with 117 (15.0%) diagnosed with severe deficiency and 374 (47.9%) diagnosed with mild deficiency; the remaining 290 (37.1%) patients were identified by genotype.

FIGURE 1. REAL-WORLD DATA FROM THE CLEVELAND CLINIC EMR SHOWED A SIMILAR PROPORTION OF MALE AND FEMALE PATIENTS WITH AATD; THE MEDIAN AGE OF PATIENTS WAS ~ 64 YEARS

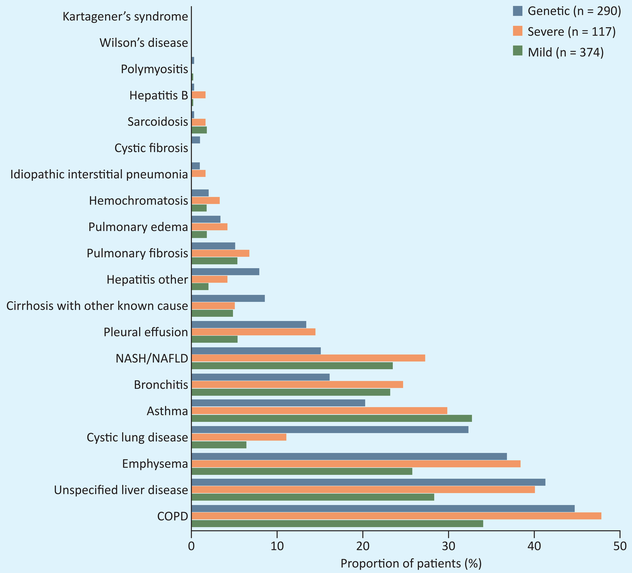


AATD, Alpha-1 antitrypsin deficiency; EMR, electronic medical record.

Symptoms and morbidities

- Overall, the most common morbidities identified for patients with AATD were COPD (39.2% [306/781]), unspecified liver disease (35.0% [273/781]) and emphysema (31.0% [242/781]) (**Figure 2**).

FIGURE 2. GENETIC AND SEVERE DEFICIENCY GROUPS HAVE A HIGHER PREVALENCE OF THE MOST COMMON MORBIDITIES THAN THE MILD DEFICIENCY GROUP



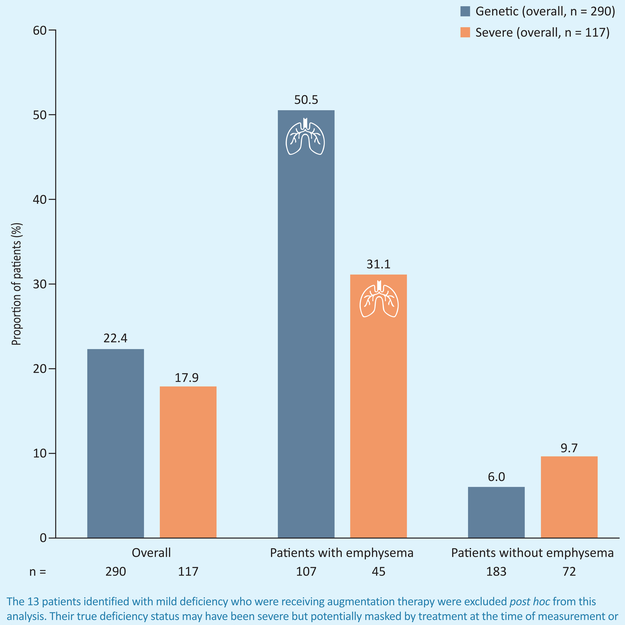
COPD, chronic obstructive pulmonary disease; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

- The prevalence of common morbidities was higher in the genetic and severe deficiency groups than in the mild deficiency group: COPD (genetic: 44.8%; severe: 47.9%; mild: 32.1%), unspecified liver disease (genetic: 41.4%; severe: 40.2%; mild: 28.3%) and emphysema (genetic: 36.9%; severe: 38.5%; mild: 24.1%).
- The prevalence of asthma, bronchitis and nonalcoholic steatohepatitis/nonalcoholic fatty liver disease was higher in the severe and mild deficiency groups than in the genetic deficiency group (**Figure 2**).

Treatment patterns

- In total, 22.4% of patients in the genetic deficiency group and 17.9% of patients in the severe deficiency group had AATD augmentation therapy noted in their EMRs (**Figure 3**).
- More patients with emphysema received augmentation therapy (genetic: 50.5%; severe: 31.1%) than patients without emphysema (genetic: 6.0%; severe: 9.7%) (**Figure 3**).

FIGURE 3. PATIENTS WITH EMPHYSEMA HAD HIGHER RATES OF RECEIVING AATD AUGMENTATION THERAPY THAN THOSE WITHOUT EMPHYSEMA



The 13 patients identified with mild deficiency who were receiving augmentation therapy were excluded *post hoc* from this analysis. Their true deficiency status may have been severe but potentially masked by treatment at the time of measurement or due to the absence of pre-treatment values in the EMR.

AATD, Alpha-1 antitrypsin deficiency; EMR, electronic medical record.

CONCLUSIONS

- Using de-identified data from the Cleveland Clinic EMR, this analysis demonstrated the phenotypic and treatment patterns among the different cohorts of patients confirmed to have AATD.
- Morbidities were more common in patients with severe deficiency AATD (based on either genetic or enzymatic diagnosis) than in those with a mild deficiency of AAT.
  - However, several of the common morbidities were observed in up to one-third of patients with mild deficiency AATD, highlighting that identification of patients with mild deficiency AATD remains important.
- Only half of the patients with genetically confirmed AATD and emphysema were receiving augmentation therapy. Future studies should seek to understand factors contributing to this finding.
- These findings, along with further AI model performance metrics and analyses presented in poster P41, suggest that AI could be used as an effective and generalizable tool to enhance the detection of AATD. Future studies should focus on validation work using real-time EMR.

REFERENCES

1. Stoller JK, Aboussouan LS. *Am J Respir Crit Care Med* 2012;185:246–59.
2. Ashenhurst JR *et al. Chest* 2022;161:373–81.
3. Craig TJ, Henao MP. *Allergy* 2018;73:2110–21.
4. Sharma R *et al. COPD* 2024;21:2393348.

DISCLOSURES

JKS has received royalties from Elsevier and UpToDate; has served as a consultant for 4DMT, 23andMe, Dicerna, Grifols, Insmed, Korro, Sanofi, Takeda and UpToDate; and serves on the Medical and Scientific Advisory Committee for the Alpha-1 Foundation. **NK**, **CB**, **MK** and **JH** are employees of Takeda Pharmaceuticals USA, Inc., and are Takeda shareholders. **VE**, **MB**, **DCF** and **LvW** are employees of Volv Global SA. **LJ** and **JS** have no relevant conflicts of interest to report. **UH** receives royalties from UpToDate as a section editor and author for COPD. He has provided *ad hoc* consulting services to CITI Pharma.

Scan this QR code to view a copy of this poster.

This poster is intended for healthcare professionals.

ACKNOWLEDGMENTS

This research was sponsored by Takeda Pharmaceuticals USA, Inc., Cambridge, MA, USA. Under the direction of the authors, medical writing services were provided by Jessica Boles, PhD, Oxford PharmaGenesis Inc., and were funded by Takeda Pharmaceuticals USA, Inc., Cambridge, MA, USA.

Presented at the American Thoracic Society International Conference, May 18–21, 2025, San Francisco, CA, USA