Testing a Claims-Based Algorithm to Identify Patients With Neuromyelitis Optica Spectrum Disorder

Alex Exuzides,[1] Irina Yermilov,[2] Hannah Dalglish,[2] Sarah N Gibbs,[2]
Michael S Broder,[2] Stanley Cohan,[3] Benjamin Greenberg,[4] Michael Levy[5]

[1]Genentech, Inc.; [2]Partnership for Health Analytic Research, LLC; [3]Providence Health; [4]University of Texas, Southwestern; [5]Massachusetts General Hospital, Harvard University

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Disclosures

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Introduction

- Neuromyelitis optica spectrum disorder (NMOSD) is a rare, inflammatory autoimmune disorder of the central nervous system (CNS) primarily characterized by acute attacks on the optic nerves, spinal cord, brain and brainstem[1]
  - These unpredictable attacks often lead to permanent neurological deficits and disability, including blindness and paralysis[2,3]
- In clinical practice, it can be difficult to distinguish patients with NMOSD from those with other demyelinating CNS disorders (e.g. multiple sclerosis [MS] and myelin oligodendrocyte glycoprotein antibody–associated disease [MOGAD])
- Further, we could find no validated algorithms for NMOSD for use in healthcare claims data sets

1. Wingerchuk DM, et al. *Lancet Neurol* 2007;6:805–815; 2. Oh J, Levy M. *Neurol Res Int* 2012;2012:460825; 3. Kessler RA, et al. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e269.

Objective

- Develop and test the performance of a healthcare claims–based algorithm to identify patients with NMOSD

Methods: diagnosis algorithm

We developed an algorithm to identify NMOSD through structured cognitive interviews with neurologists experienced in treating the condition[1]

The algorithm developed is as follows:

≥18 years old ***and*** ≥1 NMOSD diagnosis ***or*** (≥1 transverse myelitis ***and*** optic neuritis diagnosis) ***and*** ≥1 NMOSD drug

or

≥2 NMOSD diagnoses ≥90 days apart

And not any of the following exclusion criteria:

- MS diagnosis or MS-specific disease-modifying therapy after the last NMOSD diagnosis or NMOSD drug
- Sarcoidosis diagnosis after the last NMOSD diagnosis
- ≥1 immune checkpoint inhibitor

Disease	Drugs included in algorithm
NMOSD	Azathioprine, bortezomib, eculizumab, inebilizumab, mycophenolate mofetil, rituximab, satralizumab and tocilizumab
MS	Alemtuzumab, interferon-β, cladribine, daclizumab, dimethyl fumarate, fingolimod, glatiramer acetate, mitoxantrone, natalizumab, ocrelizumab, ofatumumab, ozanimod, siponimod and teriflunomide
Immune checkpoint inhibitors	Atezolizumab, avelumab, cemiplimab, durvalumab, ipilimumab, nivolumab and pembrolizumab

MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorder.

1. Exuzides A, et al. *ECTRIMS* 2021;Poster P049.

Methods: data and analysis

Data source and study cohort

- Data collected from three geographically dispersed US neurology care centers from 2016 to 2021 were used to test the algorithm
- A purposive sample of patients with NMOSD, MS or MOGAD was identified by physicians at the sites. These physician-identified diagnoses were considered the gold standard
- Demographics, clinical diagnoses (as recorded in physician notes/problem lists) and medications were collected from electronic health records. Billing data (ICD-10) were also collected for each patient

Analysis

- We confirmed the validity of the algorithm when used on the full data set (notes and medications)
- As a proxy for the algorithm's performance in insurance claims, we calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) in a subset of data containing only ICD-10 codes and medications
- We repeated these calculations on a subset that excluded patients with MOGAD, a rare condition that was oversampled in this study
- The study is ongoing with a goal of including 100 patients

ICD-10, *International Classification of Diseases, Tenth Revision*; MOGAD, myelin oligodendrocyte glycoprotein antibody–associated disease; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorder.

Results: patient demographics

- 55 adult patients with the following physician-identified diagnoses (gold-standard) were included:
  - 28 with NMOSD (22 AQP4-IgG+, 6 AQP4-IgG−/MOG-IgG−)
  - 17 with MS
  - 10 with MOGAD

	NMOSD			MS	MOGAD	All patients
	All NMOSD	AQP4-IgG+	AQP4-IgG−			
n (%)	28 (50.9)	22 (40.9)	6 (10.9)	17 (30.9)	10 (18.2)	55 (100)
Age, mean (SD)	47.7 (15.2)	48.0 (16.7)	46.8 (8.7)	47.0 (12.7)	46.0 (13.8)	47.2 (14.0)
Female, n (%)	22 (78.6)	18 (81.8)	4 (66.7)	11 (64.7)	4 (40.0)	37 (67.3)
Race, n (%)[a]						
White	17 (60.7)	12 (54.5)	5 (83.3)	17 (100.0)	8 (80.0)	42 (76.4)
Black or African American	8 (28.6)	8 (36.4)	0 (0)	0 (0)	2 (20.0)	10 (18.2)
Unclear or unknown	3 (10.7)	2 (9.1)	1 (16.7)	0 (0)	0 (0)	3 (5.5)
Hispanic, Latino or Spanish origin, n (%)	2 (7.1)	2 (9.1)	0 (0)	0 (0)	2 (20.0)	4 (7.3)

[a]No American Indian, Asian or Pacific Islander patients.
AQP4, aquaporin 4; MOGAD, myelin oligodendrocyte glycoprotein antibody–associated disease; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorder.

Results: prevalence of billing diagnoses

- Of 28 patients with a gold-standard NMOSD diagnosis:
  - 26 (92.9%)[a] had a billing diagnosis of NMOSD
  - 6 (21.4%) had a billing diagnosis of MS
- Of 17 patients with gold-standard MS diagnosis:
  - 15 (88.2%) had a billing diagnosis of MS
  - 1 (5.9%) had a billing diagnosis of NMOSD
- Of 10 patients with a gold-standard MOGAD diagnosis:
  - 9 (90.0%) had a billing diagnosis of NMOSD
  - 3 (30.0%) had a billing diagnosis of MS

[a]Percentages on this slide may sum to >100 because it is possible for both diagnoses to be present in patient billing records.
MOGAD, myelin oligodendrocyte glycoprotein antibody–associated disease; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorder.

Results: algorithm performance

- Of 28 patients with NMOSD, 24 true positives were identified by the algorithm, a **sensitivity of 85.7%**
- Of 27 patients without NMOSD, 19 true negatives were identified, a **specificity of 70.4%**
- In the test population, this would be a **PPV and NPV of 75% and 82.6%, respectively**

	Total patients	Sensitivity	Specificity	PPV	NPV
Billing and medication data for all patients	55	85.7%	70.4%	75.0%	82.6%
Billing and medication data excluding patients with MOGAD	45	85.7%	94.1%	96.0%	80.0%

- Excluding the oversampled patients with MOGAD, the algorithm's performance improved

MOGAD, myelin oligodendrocyte glycoprotein antibody–associated disease; NMOSD, neuromyelitis optica spectrum disorder; NPV, negative predictive value; PPV, positive predictive value.

Conclusions

This **clinically-derived algorithm performed very well** in a proxy insurance claims database derived from billing and medication records. When used in claims data, it is expected to have a PPV between 75.0% and 96.0% and an NPV of 80.0–82.6%, substantially higher than many published claims algorithms for uncommon conditions

We used a purposive sample to include patients with conditions that an ideal algorithm would screen out. However, even in clinical practice, **MOGAD cannot be differentiated from NMOSD without laboratory test results**. To mimic insurance claims data, our test data set did not include these results and **thus presented a very high bar for the algorithm**

In actual use, where MOGAD is far less common than the other included conditions, the algorithm test characteristics would likely fall between the values seen in the original and MOGAD-excluded analyses

This valid algorithm will **enable accurate estimation of the NMOSD disease burden** using insurance claims data

Limitations: (1) Medication data were derived from medical records, not pharmacy claims. If pharmacy claims are less comprehensive, accuracy could be overstated; (2) the care provided at the three centers from which our data were derived may not be representative of US practices broadly

MOGAD, myelin oligodendrocyte glycoprotein antibody–associated disease; NMOSD, neuromyelitis optica spectrum disorder; NPV, negative predictive value; PPV, positive predictive value.