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., South San Francisco, CA, USA; [2]Partnership for Health Analytic Research, LLC, Beverly Hills, CA, USA; [3]Providence Health, Portland, OR, USA; [4]University of Texas, Southwestern Medical Center, Dallas, TX, USA; [5]Massachusetts General Hospital, Harvard University, Boston, MA, USA

BACKGROUND

- 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

OBJECTIVE

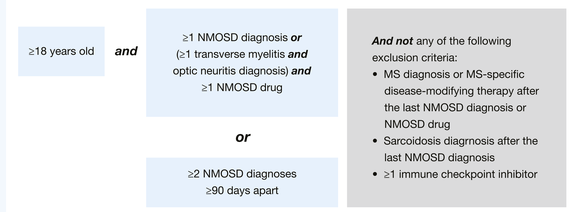
- Develop and test the performance of a healthcare claims–based algorithm to identify patients with NMOSD

METHODS

Diagnosis algorithm

- We developed an algorithm to identify NMOSD (**Figure 1** and **Table 1**) through structured cognitive interviews with neurologists experienced in treating the condition[4]

Figure 1. Algorithm to Identify NMOSD



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

Table 1. Drugs Included in Algorithm to Identify NMOSD

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.

Data source and study cohort

- Data collected from 3 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 (*International Classification of Diseases, Tenth Revision* [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

RESULTS

Patient Demographics

- 55 adult patients with the following physician-identified diagnoses (gold-standard) were included (**Table 2**):
  - 28 with NMOSD (22 AQP4-IgG+, 6 AQP4-IgG–/MOG-IgG–)
  - 17 with MS
  - 10 with MOGAD

Table 2. Patient Demographics

	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.

Prevalence of billing diagnoses

- Of 28 patients with a gold-standard NMOSD diagnosis:
  - 26 (92.9%) 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
- Percentages may sum to >100 because it is possible for both diagnoses to be present in patient billing records

Algorithm performance

- Of 28 patients with NMOSD, 24 true positives were identified by the algorithm, a sensitivity of 85.7% (**Table 3**)
- 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
- When the oversampled patients with MOGAD were excluded, the algorithm's performance improved

Table 3. Algorithm Performance

	Total patients, n	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

MOGAD, myelin oligodendrocyte glycoprotein antibody–associated disease; NPV, negative predictive value; PPV, positive predictive value.

LIMITATIONS

- Medication data were derived from medical records, not pharmacy claims. If pharmacy claims are less comprehensive, accuracy could be overstated
- The care provided at the 3 centers from which our data were derived may not be representative of US practices broadly

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 validated algorithm will enable accurate estimation of the NMOSD disease burden using insurance claims data

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DISCLOSURES

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