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

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Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) 2022 Forum
February 24–26, 2022 | West Palm Beach, FL, USA, and Virtual
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Disclosures

A Exuzides is an employee of Genentech, Inc., and shareholder of F. Hoffmann-La-Roche Ltd.

Irina Yermilov, **Cynthia Campos**, **Sarah N Gibbs** and **Michael S Broder** are employees of the Partnership for Health Analytic Research, LLC, which has received research funding from AbbVie, Akcea, ASPC, Amgen, AstraZeneca, BMS, Boston Scientific Corporation, Celgene, Eisai, Ethicon, GRAIL, Helsinn, Illumina, Innovation and Value Initiative, Ionis, Jazz, Kite, Novartis, Otsuka, Pathnostics, PhRMA, Prothena, Sage, Verde Technologies, Genentech, Inc., Greenwich Biosciences, Inc., Mirum Pharmaceuticals, Inc., Sanofi US Services, Inc., Sunovion Pharmaceuticals, Inc, BioMarin Pharmaceutical Inc, Takeda Pharmaceuticals U.S.A., Inc., and grants from Dompé US, Inc.

Stanley Cohan has served as a consultant or advisory board member for AbbVie, Biogen, Bristol Myer Squibb, Novartis, Sanofi Genzyme; and his institution has received research support from AbbVie, Adamas, Biogen, EMD Serono, Novartis, Roche Genentech, Sanofi Genzyme; and has received speaking honoraria from Biogen, Bristol Myers Squibb, Sanofi Genzyme.

Benjamin Greenberg has received consulting fees from Alexion, Novartis, EMD Serono, Viela Bio, Genentech/Roche, Greenwhich Biosciences, Axon Advisors, Rubin Anders, ABCAM, Signant, IQVIA, Sandoz, Druggability Technologies, Genzyme, Immunovant and PRIME Education; received grant funding from PCORI, NIH, NMSS, The Siegel Rare Neuroimmune Association, Clene Nanomedicine and the Guthy Jackson Charitable Foundation for NMO; receives royalties from UpToDate; and serves as an unpaid member of the board of the Siegel Rare Neuroimmune Association.

Michael Levy has received consulting fees from Alexion, Viela Bio, Genentech/Roche, UCB Pharmaceuticals, Mitsubishi Pharmaceuticals and Sanofi, and has received grant funding from NIH, Alexion, Bluerock, Siegel Rare Neuroimmune Association, Sumaira Foundation and Genentech.

This study was funded by Genentech, Inc., a member of the Roche Group. Editorial support, provided by Health Interactions, Inc, was funded by Genentech.

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.