Estimating the Costs of Emergency Room Visits and Inpatient Hospitalizations for Patients With Neuromyelitis Optica Spectrum Disorder in the United States from Commercial Claims

A Exuzides,[1] D Sheinson,[1] P Sidiropoulos,[1] A Surinach,[2] L Cook,[3] C Meyer,[1] M Yeaman,[4]

[1]Genentech, Inc., South San Francisco, CA; [2]Genesis Research, Hoboken, NJ; [3]Department of Pediatrics, University of Utah, Salt Lake City, UT; [4]University of California, Los Angeles (UCLA), and Division of Molecular Medicine, Harbor-UCLA Medical Center, Torrance, CA

BACKGROUND

- Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease of the central nervous system characterized by inflammatory lesions that mainly affect the optic nerves and spinal cord[1,2]
- Core clinical manifestations contributing to a diagnosis of NMOSD include acute optic neuritis (ON) and/or longitudinally extensive transverse myelitis (TM); in some cases area postrema syndrome is observed[2]
- Diagnosis can be challenging as NMOSD exhibits multiple phenotypes (e.g. positive serostatus for anti-aquaporin-4 [AQP4] immunoglobulin G [IgG] vs. anti-myelin oligodendrocyte glycoprotein [MOG] IgG), and can parallel clinical presentation in multiple sclerosis (MS)[1]
- Although the prevalence may be higher due to misdiagnosis or lack of access to diagnostic AQP4-IgG or MOG-IgG biomarker testing,[1] approximately 15,000 patients in the US have an NMOSD diagnosis based on current estimates, with a disproportionate female-to-male ratio of 7:1[3]
- Patients with NMOSD frequently experience a relapsing disease course, with repeated relapses leading to accumulating neurological disability, including vision loss[4]
  - These relapses often require outpatient care, hospitalization and/or treatment, resulting in costs that are ≥4-times higher than those incurred by patients without relapses[5]
- Patients with highly active NMOSD, defined as patients with at least two relapses in the previous 12 months, have a roughly 10-times higher hospital inpatient admission rate compared with patients without NMOSD[5]
- Data on the economic burden of NMOSD, including cost of illness related to emergency room (ER) and inpatient hospital settings, are limited; additional studies evaluating the real-world healthcare utilization and cost of illness are needed

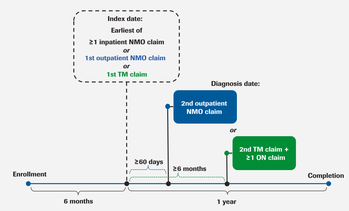
OBJECTIVE

- To evaluate the cost of illness of patients with NMOSD during a ≥1-year postindex follow-up period compared with controls without an NMOSD diagnosis (non-NMOSD) in US commercial claims databases

METHODS

- This study analyzed claims data from the Truven Health MarketScan Commercial and Medicare Supplemental Databases between January 1, 2014, and December 31, 2018
- Patients meeting the following diagnostic criteria, based on a previously published algorithm,[6] were included in the analysis (**Figure 1**, **Table 1**):
  - ≥1 inpatient or ≥2 outpatient claims ≥60 days apart for NMO diagnosis **or**
  - ≥2 claims for TM diagnosis ≥6 months apart in combination with ≥1 claim for ON diagnosis
- The date of the first claim was considered the index date
- Continuous enrollment for ≥6 months before and ≥1 year after the index date was required
- Patients were excluded from the NMOSD cohort if they had an MS diagnosis on or after the index date or any claim for treatment with a disease-modifying therapy approved for use in MS (e.g. glatiramer acetate, natalizumab, dimethyl fumarate, teriflunomide, fingolimod, interferon β-1a, interferon β-1b, ocrelizumab or alemtuzumab) any time in the study period

Figure 1. Study design and NMOSD diagnostic criteria



NMO, neuromyelitis optica; NMOSD, neuromyelitis optica spectrum disorder; ON, optic neuritis; TM, transverse myelitis.

Table 1. Diagnosis codes accepted as NMO, TM or ON claim

Diagnosis code	*ICD* version	Description	Classification
341.0	9	Neuromyelitis optica (Devic)	NMO
G36.0	10	Neuromyelitis optica (Devic)	NMO
323.82	9	Other causes of myelitis	TM
341.2	9	Acute (transverse) myelitis	TM
341.20	9	Acute (transverse) myelitis (NOS)	TM
341.21	9	Acute (transverse) myelitis in conditions classified elsewhere	TM
341.22	9	Idiopathic transverse myelitis	TM
G37.3	10	Acute transverse myelitis in demyelinating disease of CNS	TM
377.3	9	Optic neuritis	ON
377.30	9	Optic neuritis, unspecified	ON
377.31	9	Optic papillitis	ON
377.32	9	Retrobulbar neuritis (acute)	ON
377.33	9	Nutritional optic neuropathy	ON
377.34	9	Toxic optic neuropathy	ON
377.39	9	Other optic neuritis	ON
H46	10	Optic neuritis	ON
H46.0	10	Optic papillitis	ON
H46.00	10	Optic papillitis unspecified eye	ON
H46.01	10	Optic papillitis right eye	ON
H46.02	10	Optic papillitis left eye	ON
H46.03	10	Optic papillitis bilateral	ON
H46.1	10	Retrobulbar neuritis	ON
H46.10	10	Retrobulbar neuritis unspecified	ON
H46.11	10	Retrobulbar neuritis right eye	ON
H46.12	10	Retrobulbar neuritis left eye	ON
H46.13	10	Retrobulbar neuritis bilateral	ON
H46.2	10	Nutritional optic neuropathy	ON
H46.3	10	Toxic optic neuropathy	ON
H46.8	10	Other optic neuritis	ON
H46.9	10	Unspecified optic neuritis	ON

CNS, central nervous system; ICD (version 9), *International Classification of Diseases, Ninth Revision*; *ICD* (version 10), *International Statistical Classification of Diseases, Tenth Revision*; NMO, neuromyelitis optica; NOS, not otherwise specified; ON, optic neuritis; TM, transverse myelitis.

- Non-NMOSD controls were patients with no medical encounter suggesting NMO or NMOSD, TM or ON based on diagnostic codes in **Table 1**
  - Control patients were matched 5:1 to the NMOSD cohort based on characteristics described in **Table 2**
  - Qualified non-NMOSD control patients were assigned the same index date as their respective matched patient with NMOSD

Table 2. Criteria used to match the non-NMOSD controls and NMOSD cohorts

Characteristic	Criteria
Age	±5 Years of matched patient with NMOSD
Sex	Female or male
Insurance	Commercial or Medicare
Plan type	HMO, PPO, POS, etc.
Geographic location	Based on US census region: North Central, Northeast, South or West
Continuous enrollment period	≥6 months before and ≥1 year after the index date

HMO, health maintenance organization; NMOSD, neuromyelitis optica spectrum disorder; POS, point of service; PPO, preferred provider organization.

Statistical Analysis

- Patient demographic characteristics were described for each group
- Metrics related to hospital admissions and ER visits within 12 months after the index date were assessed
- Total cost of healthcare services in consumer price index–adjusted 2019 US dollars during the postindex follow-up period was calculated for each patient and included the following costs:
  - Outpatient services
  - Outpatient services attributed to the ER
  - Inpatient services (hospital admission)
  - Pharmacy costs (inpatient and/or outpatient)
  - Total costs (e.g. outpatient [in and out of the ER], inpatient and pharmacy)
- Average annual costs were calculated for each cost component and for total costs
- Wilcoxon-rank sum tests were used to evaluate significant differences in costs between patients with NMOSD and the non-NMOSD controls

RESULTS

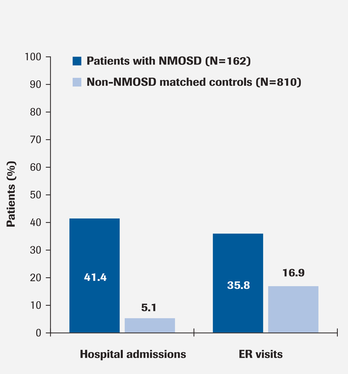
- Of the 1,817 patients in the Truven Health MarketScan Commercial and Medicare Supplemental Databases meeting the inclusion criteria, 162 patients with NMOSD and 810 non-NMOSD controls were evaluated
- Baseline characteristics were comparable between the NMOSD and the non-NMOSD control cohorts (**Table 3**)
  - The majority of patients in both cohorts had commercial insurance (89.5%) and a preferred provider organization plan (63.0%)
- Significantly more patients with NMOSD visited the ER and/or were admitted to the hospital within 12 months after the index date compared with non-NMOSD controls ($p<0.001$; **Figure 2**)
  - Mean [SD] total number of days in hospital was significantly higher for patients with NMOSD (21.2 [32.7]) compared with non-NMOSD controls (5.2 [6.5]; $p<0.001$)
- The mean healthcare resource utilization costs per patient during the postindex follow-up period were significantly higher for the NMOSD group than the non-NMOSD controls overall ($62,685 vs $8,270, respectively) and across all categories ($p<0.001$ for all; **Figure 3**)

Table 3. Baseline characteristics of patients with NMOSD and non-NMOSD controls

	Patients with NMOSD (N=162)	Non-NMOSD controls (N=810)
Age at index, years		
Mean (SD)	43.31 (18)	43.31 (18)
Median (Q1–Q3)	45 (33–58)	45 (33–58)
Female, n (%)	119 (73.5)	595 (73.5)
Geographic region, n (%)		
North Central	28 (17.3)	140 (17.3)
Northeast	31 (19.1)	155 (19.1)
South	78 (48.2)	390 (48.2)
West	25 (15.4)	125 (15.4)
Insurance, n (%)		
CCAE	145 (89.5)	725 (89.5)
MDCR	17 (10.5)	85 (10.5)
Insurance plan type, n (%)		
CDHP	15 (9.3)	75 (9.3)
Comprehensive	10 (6.2)	50 (6.2)
EPO	2 (1.2)	10 (1.2)
HDHP	6 (3.7)	30 (3.7)
HMO	15 (9.3)	75 (9.3)
Missing	2 (1.2)	10 (1.2)
POS	9 (5.6)	45 (5.6)
POS with capitation	1 (0.6)	5 (0.6)
PPO	102 (63.0)	510 (63.0)
Follow-up time, months		
Mean (SD)	27.12 (11.09)	28.46 (11.15)
Median (IQR)	23.7 (18.2–35.3)	25.72 (19.0–37.1)

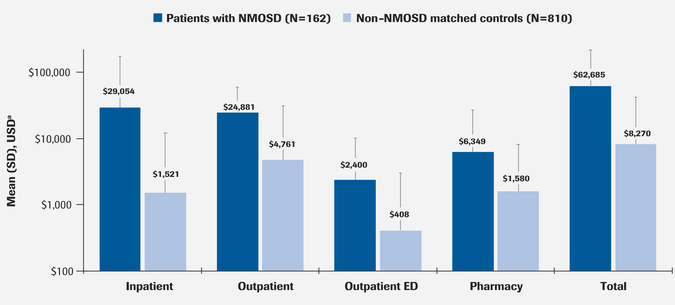
CCAE, Commercial Claims and Encounters Data; CDHP, consumer-driven health plans; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; IQR, interquartile range; MDCR, Medicare; NMOSD, neuromyelitis spectrum disorder; POS, point of service; PPO, preferred provider organization.

Figure 2. Number of hospital admissions and ER visits within 12 months after index date



All comparisons were significant at $p<0.001$ level. ER, emergency room; NMOSD, neuromyelitis optica spectrum disorder.

Figure 3. Annual healthcare costs incurred by patients with NMOSD vs non-NMOSD controls in the follow-up period



[a]Data is plotted on $\log_{10}$ scale. All comparisons were significant at $p<0.001$ level.
ER, emergency room; NMOSD, neuromyelitis optica spectrum disorder; USD, US dollar.

LIMITATIONS

- Although the results presented here provide real-world healthcare utilization and cost of illness associated with NMOSD, this analysis is limited by claims available in the Truven MarketScan US database
  - Inclusion of cases as NMOSD despite lack of International Panel for NMO Diagnosis (IPND) diagnostic criteria
  - Patients with NMOSD may be inaccurately identified by claims entered as rule-out codes for MS or NMO instead of a confirmed diagnosis
  - Patients with NMOSD may potentially be misclassified based solely on using the *International Classification of Diseases, Ninth Revision,* and *International Statistical Classification of Diseases, Tenth Revision*, diagnostic codes

CONCLUSIONS

- Using a US claims database, patients with NMOSD, as qualified in this study, compared with non-NMOSD matched controls, had:
  - Significantly more ER visits and hospital admissions
  - Significantly longer hospital stays
  - Significantly higher costs across all services evaluated (e.g. outpatient services in and out of the ER, inpatient services and inpatient/outpatient pharmacy costs)
- Overall, these results highlight the significant cost burden associated with the clinical management of patients with NMOSD and the need for more efficacious and regulatory-approved treatments that reduce cost burden to patients

REFERENCES

1. Kim SM, et al. *Ther Adv Neurol Disord* 2017;10:265–289.
2. Huda S, et al. *Clin Med (Lond)* 2019;19:169–176.
3. Cook LJ, et al. *Neurol Neuroimmunol Neuroinflamm* 2019;6:e583.
4. Kessler RA, et al. *Curr Treat Options Neurol* 2016;18:2.
5. Stafkey-Mailey D, et al. *Neurology* 2016;86(16 suppl) [abstract P6.161].
6. Ajmera MR, et al. *J Neurol Sci* 2018;384:96–103.

SPONSORSHIP

This study was funded by Genentech, Inc. Writing and editorial assistance for this presentation was provided by Health Interactions, Inc, USA, and funded by Genentech, Inc.

DISCLOSURES

A Exuzides, D Sheinson, P Sidiropoulos and C Meyer are employees of Genentech, Inc., and shareholders of F Hoffmann-La Roche Ltd.

A Surinach is an employee of Genesis Research, which receives fees for consulting with Genentech, Inc.

L Cook has nothing to disclose.

M Yeaman is founder and shareholder of NovaDigm Therapeutics, Inc., and Metacin, Inc., and advisor to the Guthy-Jackson Charitable Foundation; he is a member of the Genentech, Inc., Scientific Advisory Committee for NMOSD.

Presented at the International Society for Pharmacoeconomics and Outcomes (ISPOR) Virtual Meeting 2020; May 18–20, 2020