Cost of Neuromyelitis Optica Spectrum Disorder Misdiagnosis

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BACKGROUND

- Misdiagnosis of neuromyelitis optica spectrum disorders (NMOSD) as other demyelinating central nervous system (CNS) disorders, such as multiple sclerosis (MS), is common
- Previous studies have reported MS misdiagnosis rates ranging from 29% to 42.5% in NMOSD,[1] and >70% of participants carried an initial diagnosis other than NMOSD, including MS[2]
  - Some immunomodulatory treatments that are effective for MS have been shown to exacerbate disease in NMOSD[3]
- Real-world studies examining the economic and clinical burden of NMOSD are limited[2, 4-7]

OBJECTIVE

- To study the clinical and economic burden associated with misdiagnosis of NMOSD as MS in the United States

METHODS

- This retrospective cohort study used IBM® MarketScan® Commercial and Medicare Supplemental databases
- Inclusion criteria
  - Patients with NMOSD were identified in 2016–2019 and were those who met at least one of two criteria below:
    - ≥1 claim of NMOSD drug with either
      - ≥1 claim with an *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* diagnosis for neuromyelitis optica (NMO) (G36.0), *or*
      - ≥1 claim with a diagnosis for transverse myelitis (G37.3) and ≥1 claim with a diagnosis for optic neuritis (H46.1x, H46.8, H46.9)
    - ≥2 NMO diagnosis claims ≥90 days apart
  - Newly diagnosed patients required ≥1 diagnosis in 2016–2018 (first diagnosis was defined as the index date) and lacked an NMOSD diagnosis during the 1-year pre-index (baseline) period
- Exclusion criteria
  - Disenrollment during the baseline or 1-year post-index (follow-up) period
  - MS diagnosis/drug or sarcoidosis diagnosis after the last NMO diagnosis/drug
  - ≥1 immune checkpoint inhibitor during the baseline period (i.e. evidence of secondary NMO)
- With the patients identified above, we created two study groups for comparison:
  - 1) Patients with NMOSD who previously were misdiagnosed with MS, defined as having ≥2 claims with a diagnosis for MS or ≥1 claim for an MS drug during the baseline period vs
  - 2) All other identified patients with NMOSD
- Patient clinical characteristics, utilization and costs were described for the two groups
  - An exploratory analysis of the misdiagnosed patients was performed during the period of misdiagnosis (i.e. from the first MS diagnosis in baseline until the index NMOSD diagnosis)

RESULTS

- 163 patients with NMOSD were identified
  - 24 (14.7%) were misdiagnosed with MS during baseline
- Misdiagnosed patients (vs not) had a mean (SD) age of 42.9 (13.1) vs 49.5 (13.6) years (*P*=0.028) and Charlson Comorbidity Index of 0.9 (1.1) vs 1.3 (2.1) (*P*=0.221); 79.2% vs 76.3% (*P*=0.756) were female (**Table 1**)
- High utilization and costs, often higher in those misdiagnosed, were observed in both groups (**Tables 2 and 3; Figures 1 and 2**):
  - Baseline period key results:
    - Hospitalization (41.7% vs 30.9%; *P*=0.300)
    - Magnetic resonance imaging (MRI) use (79.2% vs 49.6%; *P*=0.007)
    - Mean (SD) number of office visits (22.3 [18.6] vs 12.7 [13.1]; *P*=0.005)
    - High-dose intravenous (IV) steroid use (33.3% vs 15.1%; *P*=0.031)
    - Mean (SD) total costs ($64,831 [$72,294] vs $37,827 [$65,536]; *P*=0.068)
  - Follow-up period key results:
    - Hospitalization (33.3% vs 46.0%; *P*=0.247)
    - MRI use (70.8% vs 66.9%; *P*=0.705)
    - Mean (SD) number of office visits (23.8 [21.9] vs 19.6 [18.6]; *P*=0.274)
    - High-dose IV steroid use (50.0% vs 37.4%; *P*=0.243)
    - Mean (SD) total costs ($74,275 [$53,919] vs $98,514 [$137,708]; *P*=0.135)
- In the 24 misdiagnosed patients (results not displayed):
  - The mean (SD) number of days from the first MS diagnosis to the index diagnosis was 192.0 (119.8) days
  - 41.7% received MS medication before receiving a correct NMOSD diagnosis
- An exploratory analysis of the 24 misdiagnosed patients during the period of misdiagnosis (from the first MS diagnosis until the index NMOSD diagnosis) showed utilization and costs related to MS that were non-negligible
  - On average, the total MS-related costs were $5,357 (SD, $5,046) per month (result not displayed), translating to roughly $32,000 over a period of 6 months of being misdiagnosed. Such costs may reflect excess expenditure associated with the MS misdiagnosis

Table 1. Patient demographics and clinical characteristics

	Misdiagnosed with MS: Yes	Misdiagnosed with MS: No	All	*P* value
N (%)	24 (14.7)	139 (85.3)	163 (100)	
Age, mean (SD)	42.9 (13.1)	49.5 (13.6)	48.5 (13.7)	0.028
Female, n (%)	19 (79.2)	106 (76.3)	125 (76.7)	0.756
Region, n (%)				0.030
Midwest	2 (8.3)	29 (20.9)	31 (19.0)	
Northeast	11 (45.8)	33 (23.7)	44 (27.0)	
South	6 (25.0)	62 (44.6)	68 (41.7)	
West	5 (20.8)	15 (10.8)	20 (12.3)	
Usual physician specialty, n (%)				<0.001
Neurologist	13 (54.2)	16 (11.5)	29 (17.8)	
Ophthalmologist	1 (4.2)	2 (1.4)	3 (1.8)	
Primary care physician (including physician assistant and nurse practitioner)	6 (25.0)	40 (28.8)	46 (28.2)	
Internist	1 (4.2)	30 (21.6)	31 (19.0)	
Other/unknown specialty	3 (12.5)	51 (36.7)	54 (33.2)	
Charlson Comorbidity Index, mean (SD)	0.9 (1.1)	1.3 (2.1)	1.2 (2.0)	0.221
No. of chronic conditions, mean (SD)	4.2 (2.2)	4.1 (2.4)	4.1 (2.4)	0.767

MS, multiple sclerosis.

Table 2. Healthcare utilization

	Baseline				Follow-up			
	Misdiagnosed with MS: Yes	Misdiagnosed with MS: No	All	*P* value	Misdiagnosed with MS: Yes	Misdiagnosed with MS: No	All	*P* value
N	24	139	163		24	139	163	
Inpatient hospitalization, n (%)	10 (41.7)	43 (30.9)	53 (32.5)	0.300	8 (33.3)	64 (46.0)	72 (44.2)	0.247
ED visit, n (%)	9 (37.5)	51 (36.7)	60 (36.8)	0.939	5 (20.8)	45 (32.4)	50 (30.7)	0.258
No. of office visits, mean (SD)	22.3 (18.6)	12.7 (13.1)	14.1 (14.4)	0.005	23.8 (21.9)	19.6 (18.6)	20.2 (19.1)	0.274
MRI, n (%)	19 (79.2)	69 (49.6)	88 (54.0)	0.007	17 (70.8)	93 (66.9)	110 (67.5)	0.705
MOG antibody disease test, n (%)	7 (29.2)	25 (18.0)	32 (19.6)	0.203	6 (25.0)	42 (30.2)	48 (29.4)	0.605
Received high-dose IV methylprednisolone, n (%)	8 (33.3)	21 (15.1)	29 (17.8)	0.031	12 (50.0)	52 (37.4)	64 (39.3)	0.243
Oral steroid use, n (%)	12 (50.0)	52 (37.4)	64 (39.3)	0.243	13 (54.2)	75 (54.0)	88 (54.0)	0.985
NMOSD medication use, n (%)[a]	3 (12.5)	12 (8.6)	15 (9.2)	0.466	6 (25.0)	51 (36.7)	57 (35.0)	0.267

[a]Pre-index medication use was limited to azathioprine and mycophenolate mofetil in both cohorts. Bortezomib, eculizumab, rituximab and tocilizumab had no observed use during baseline. Note that inebilizumab and satralizumab were approved by the US Food and Drug Administration (FDA) in 2020 (after the study ended). Post-index medication use was limited to azathioprine, mycophenolate mofetil and rituximab in both cohorts, and tocilizumab in the non-misdiagnosed cohort. Bortezomib and eculizumab had no observed use during baseline in either cohort. Note that inebilizumab and satralizumab were approved by the FDA in 2020 (after the study ended).

ED, emergency department; IV, intravenous; MOG, myelin oligodendrocyte glycoprotein; MRI, magnetic resonance imaging; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorders.

Table 3. Healthcare costs

	Baseline				Follow-up			
	Misdiagnosed with MS: Yes	Misdiagnosed with MS: No	All	*P* value	Misdiagnosed with MS: Yes	Misdiagnosed with MS: No	All	*P* value
N	24	139	163		24	139	163	
Total healthcare costs, mean (SD), $	64,831 (72,294)	37,827 (65,536)	41,803 (67,028)	0.068	74,275 (53,919)	98,514 (137,708)	94,945 (129,000)	0.135
Inpatient services	19,408 (33,708)	17,055 (46,144)	17,401 (44,450)	0.812	11,726 (21,752)	41,532 (107,579)	37,144 (100,191)	0.004
Outpatient services	28,139 (37,788)	15,891 (35,888)	17,695 (36,316)	0.127	51,481 (41,033)	50,070 (62,807)	50,277 (59,997)	0.888
Outpatient pharmacy	17,284 (23,269)	4,881 (15,999)	6,707 (17,730)	0.018	11,068 (19,076)	6,912 (17,909)	7,524 (18,085)	0.300

Figure 1. Baseline healthcare costs: misdiagnosed with MS (yes vs no)

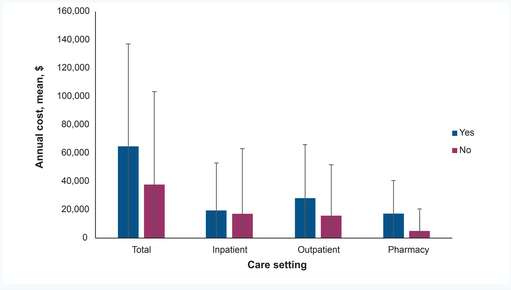
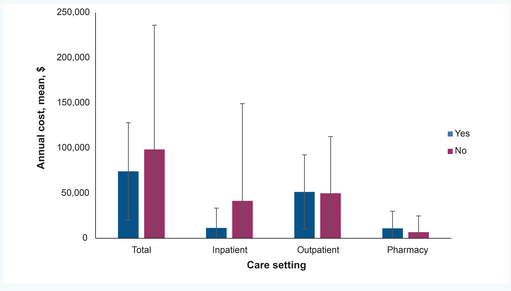


Figure 2. Follow-up healthcare costs: misdiagnosed with MS (yes vs no)



LIMITATIONS

- Patients diagnosed with NMOSD may have been misclassified due to coding error in claims data (e.g. a diagnosis code that was incorrectly coded or included as a rule-out criterion). However, our patient identification was based on an algorithm that was developed using clinical input and validated using medical charts in an unpublished analysis
- Results of this study are only descriptive. Due to the small sample size of the misdiagnosed cohort, adjustments through matching or multivariable analysis were not conducted, thereby limiting our ability to make comparisons between cohorts
- This study population was limited to those with commercial and Medicare supplemental insurance and cannot be generalized to other populations

CONCLUSIONS

- Patients with NMOSD experience substantial burden, which may be worsened by prior MS misdiagnosis
- Patients with NMOSD and a MS misdiagnosis incur healthcare utilization and costs during the period of misdiagnosis, including, for some, use of MS medication which is linked to NMOSD treatment ineffectiveness and even disease exacerbation[3, 8-10]
  - Such disease and cost burden may be potentially avoidable with an earlier, accurate diagnosis

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DISCLOSURES

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