A Real-World Retrospective Cohort Study Characterizing Patients with MMN in the United States

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INTRODUCTION

- Multifocal motor neuropathy (MMN) is a rare, acquired, immune-mediated, pure motor neuropathy characterized by slowly progressive, asymmetric muscle weakness in distal limbs unaccompanied by pain or sensory loss.[1]
- With a prevalence of <1 in 100,000, diagnosing MMN can be challenging due to overlapping signs and symptoms with other disorders.[1,2]
- Delay in diagnosis and thereby, treatment, leads to the accumulation of irreversible neurologic impairment and disability in patients with MMN.[3]

OBJECTIVE

- This retrospective, claims-based study was conducted to explore the diagnosis and identification of MMN in patients using a real-world dataset.

METHODS

- The Komodo Health claims database (January 2016 to March 2024), encompassing medical and prescription claims information from >150 payers across all geographic regions of the United States (US), was utilized for the analysis **(Figure 1)**.

Figure 1: Study design

Key patient selection criteria
- ≥2 claims with an MMN diagnosis (ICD 10: G61.82), ≥14 – ≤365 days apart[1]
- Continuous enrollment ±1 year pre- and post-index date
- ≥1 relevant test[2], i.e., electrophysiology, GM-1 serum evaluation, etc., is present before confirmatory or 2nd MMN diagnosis

Study variables
- Patient baseline characteristics for identified "Likely-MMN" patient cohort:
  - Misdiagnosis/other neuropathy conditions
  - Relevant procedures/tests that patients are undergoing
  - Relevant treatments (IVIG, SCIG, Plasma exchange etc.)

Study outcomes
- Characteristics of patients that can help to reduce the uncertainty in diagnosis

Statistical analysis
- Descriptive statistics were used to evaluate patient baseline characteristics

[1]First observed MMN diagnosis was considered as index date. [2]Relevant tests have been considered to increase the robustness and certainty of identifying patients with MMN diagnosis. Other relevant tests include Nerve Ultrasound, Nerve MRI, GM1-specific blood test, Brachial Plexus MRI, and CSF.
CSF, cerebrospinal fluid; GM1 specific blood test, monosialotetrahexosylganglioside; ICD, International Classification of Diseases; IVIG, intravenous immunoglobin; MMN, multifocal motor neuropathy; MRI, magnetic resonance imaging; SCIG, subcutaneous immunoglobin.

SUMMARY

Misdiagnosis and diagnostic delays are relatively common in MMN, with symptoms mimicking CIDP, ALS, or unspecified neuropathies.

Patients with MMN could face years of misdiagnosis before treatment, resulting in delayed access to treatment.

Improved diagnostic strategies are needed to reduce delays and optimize care for patients with MMN.

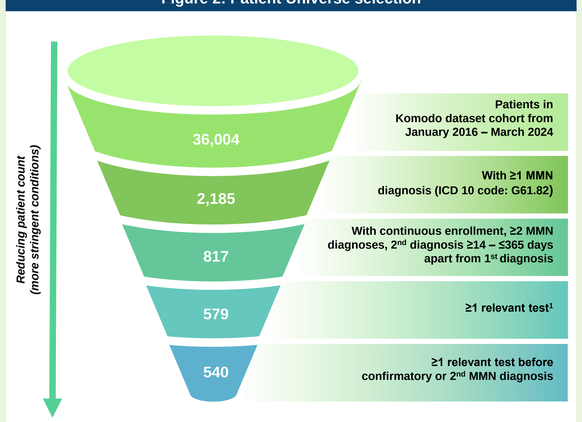
Limitations
- As the study population was identified from a US claims database, findings may not be generalizable to patients from other geographies.

RESULTS

Cohort selection

- A cohort of 540 patients with MMN were identified based on the inclusion criteria below **(Figure 2)**.

Figure 2: Patient Universe selection

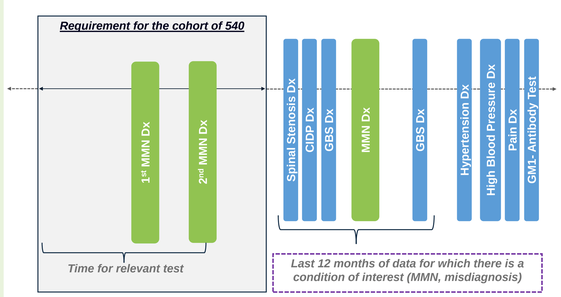


[1] Relevant tests include nerve ultrasound, NCT Test, GM1 specific blood test, brachial plexus MRI, CSF, nerve MRI.
CSF, cerebrospinal fluid; GM1, monosialotetrahexosylganglioside; ICD, International Classification of Diseases; MMN, multifocal motor neuropathy; MRI, magnetic resonance imaging; NCT, nerve conduction test.

Patient cohorts

- Most recent 12 months of available data for a patient was used to further dichotomize the patients into two different confidence buckets to eliminate cases of misdiagnosis **(Figure 3)**.
- Logic was applied to dichotomize patients **(Figure 4)**.

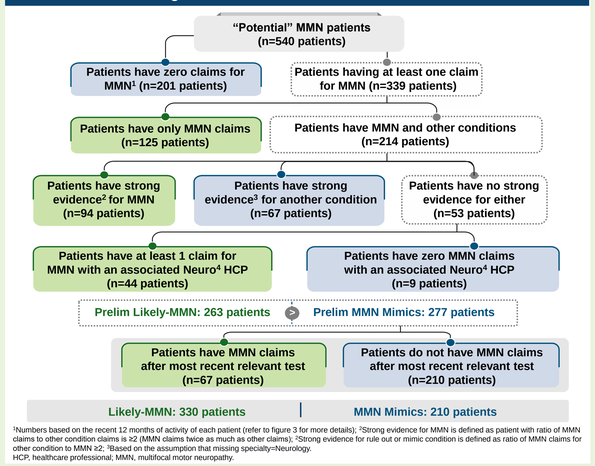
Figure 3: Definition for timeframe under consideration



CIDP, chronic inflammatory demyelinating polyneuropathy; Dx, diagnosis; GBS, Guillain-Barre syndrome; GM1, monosialotetrahexosylganglioside; MMN, multifocal motor neuropathy; Px, procedure.

- MMN cohort was dichotomized into 2 cohorts: 'Likely-MMN' and 'MMN Mimics', based on the recent diagnosis history, and specialty of the MMN diagnosing healthcare professional **(Figure 4)**.
- Grouping patients into Likely-MMN and MMN Mimics required a number of business rules, which is likely a reflection of the complex, lengthy and difficult diagnostic journey experienced by patients.
  - Misdiagnoses included chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), amyotrophic lateral sclerosis (ALS), Guillain-Barre syndrome, hereditary/entrapment neuropathy, distal hereditary motor neuropathy, motor neuron diseases, progressive muscular atrophy and many others.

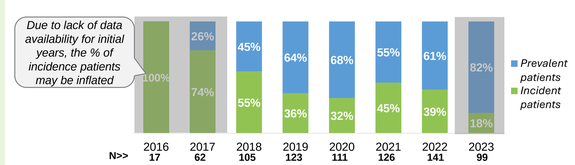
Figure 4: Identification of MMN cohort[1]



[1]Numbers based on the recent 12 months of activity of each patient (refer to figure 3 for more details); [2]Strong evidence for MMN is defined as patient with ratio of MMN claims to other condition claims is ≥2 (MMN claims twice as much as other claims); [3]Strong evidence for rule out or mimic condition is defined as ratio of MMN claims for other condition to MMN ≥2; [4]Based on the assumption that missing specialty=Neurology.
HCP, healthcare professional; MMN, multifocal motor neuropathy.

- In 2022, out of all MMN patients, 39% were newly diagnosed, and 61% were prevalent patients **(Figure 5)**.

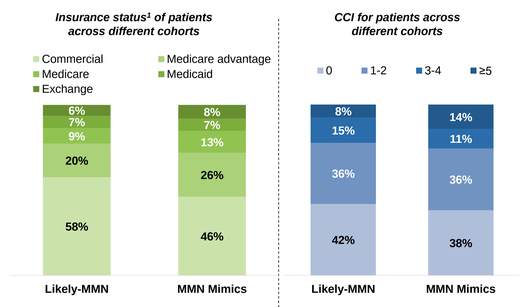
Figure 5: Incidence[1,2,3] and prevalence[2,3,4] for Likely-MMN patient cohort



[1]Number of Likely-MMN patients who had first MMN claim in that year; [2]Number of Likely-MMN patients who are active (≥1 MMN claim) in a particular year.
[3]Data considered: Continuously enrolled time-period for the all the Likely-MMN patient; [4]Only considers claims with primary diagnosis as MMN Diagnosis "G81.82".
MMN, multifocal motor neuropathy.

- Majority of patients in both cohorts were commercially insured, with an average Charlson Comorbidity Index score of 1.49 and 1.87 for Likely-MMN and MMN Mimics respectively **(Figure 6)**.

Figure 6: Insurance status and CCI index for patient cohorts



[1]Considers first MMN diagnosis date as the index date and time-period for analysis is one year lookback from index date.
CCI, Charlson Comorbidity Index; MMN, multifocal motor neuropathy.

MMN-related diagnoses

- Many patients had medical history of a plethora of other neuropathy-related diagnoses prior to the diagnosis of MMN.
- In the follow-up period (*one-year post MMN diagnosis*), both patient cohorts had frequent diagnosis of another condition such as CIDP and ALS **(Table 1)**.

Table 1: MMN-related diagnoses 1-year prior and post MMN diagnosis

Diagnosis	Events 1-year prior to MMN diagnosis		Events 1-year post MMN diagnosis	
	Likely-MMN (n=330) (%)	MMN Mimics (n=210) (%)	Likely-MMN (n=330) (%)	MMN Mimics (n=210) (%)
CIDP	16	16	23	25
ALS	5	10	7	19
Other neuropathies	64	71	64	69
Other motor diseases	76	82	65	80
Pain/ weakness/ evidence of other motor symptoms	85	86	76	81
Pain	55	60	49	60
Weakness	55	60	44	50
Evidence of motor symptoms (others)	38	40	33	41
Asymmetrical muscle weakness	35	42	27	36
Compression/ entrapment neuropathies	32	30	20	27
Monomelic amyotrophy	1	0	0	0
Muscle atrophy	15	13	12	11
Muscle disorder	9	22	12	28
Muscle fasciculation	7	5	4	2
Neuromuscular junction disorder	0	2	1	1
Peripheral neuropathy	53	63	57	62

ALS, amyotrophic lateral sclerosis; CIDP, chronic inflammatory demyelinating polyneuropathy; MMN, multifocal motor neuropathy.

- The Likely-MMN cohort had relatively fewer misdiagnoses in follow-up as compared to the MMN Mimics cohort.
- Peripheral neuropathy was commonly diagnosed in patients in both the cohorts during pre- and post-index time-period.
- In some cases, a patient's diagnosis could not be discerned due to MMN being interspersed in near-equal frequency with CIDP or unspecified codes **(Table 1)**.

MMN-related diagnostic tests

- A considerable decrease was noted in the proportion of testing in one-year post diagnosis as compared with prior to diagnosis **(Table 2)**.

Table 2: MMN-related diagnostic tests 1-year prior and post MMN diagnosis

Diagnostic tests	Events 1-year prior to MMN diagnosis		Events 1-year post MMN diagnosis	
	Likely-MMN (n=330) (%)	MMN Mimics (n=210) (%)	Likely-MMN (n=330) (%)	MMN Mimics (n=210) (%)
GM1 antibody	45	50	38	39
NCT	66	77	54	50
Nerve US or MRI	12	11	5	8
CSF analysis	18	21	12	12

CSF, cerebrospinal fluid; GM1, monosialotetrahexosylganglioside; MMN, multifocal motor neuropathy; MRI, magnetic resonance imaging; NCT, nerve conduction test; US, ultrasound.

MMN-related treatment

- In one-year post MMN diagnosis, IVIG was most frequently received in both Likely-MMN and MMN Mimics cohorts.
- Subcutaneous immunoglobin, steroids, rituximab, and plasma exchange were less likely to be received by patients in both prior to and post MMN diagnosis **(Table 3)**.

Table 3: MMN-related treatment 1-year prior and post MMN diagnosis

Treatment	Events 1-year prior to MMN diagnosis		Events 1-year post MMN diagnosis	
	Likely-MMN (n=330) (%)	MMN Mimics (n=210) (%)	Likely-MMN (n=330) (%)	MMN Mimics (n=210) (%)
IVIG	23	31	77	70
SCIG	0	0	3	1
Steroids	47	52	51	53
NSISTs	4	5	6	9
Rituximab	1	2	3	5
Plasma exchange	1	0	2	0
Conservative therapy[1]	48	61	49	69

[1]Includes Physiotherapy, Occupational Therapy and Chiro-Therapy.
IVIG, intravenous immunoglobin; MMN, multifocal motor neuropathy; NSISTs, non-steroidal immunosuppressants; SCIG, subcutaneous immunoglobin.

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DISCLOSURES:

Charlotte E. Ward, Divya Nagpal, and Kartik Wadhwa are employees of ZS Associates.

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