deciphehr™

connecting the dots of rare disease

SUPPORTING SUSPECT PATIENT RECOGNITION
FOR FURTHER CLINICAL EVALUATION

NMOSD Program Implementation Guide

NMOSD=neuromyelitis optica spectrum disorder.

deciphEHR™ provides educational resources to help health systems, hospitals, and specialty practices leverage their electronic health record (EHR) systems. Data from the EHR system may help triage suspect patients for further clinician evaluation.

ALEXION®
AstraZeneca Rare Disease

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, autoimmune disease of the central nervous system characterized by recurrent attacks that can result in cumulative disability with potentially devastating consequences including blindness, paralysis, or premature death.[1-4] Due to the rare nature of the disease combined with the heterogeneity of NMOSD symptoms,[1,5,6] and the similarity of many NMOSD symptoms with those of more common neurological conditions, such as MS, diagnoses are often delayed or missed.[7] This can be particularly harmful in underrepresented populations as NMOSD has a higher prevalence and disproportionately impacts patients of Asian and African descent who may already have a lack of access to the healthcare system.[8-11] The objective of this guide is to help HCPs understand the clinical presentation of NMOSD in adults and triage patients who may be suspected of having NMOSD for further HCP evaluation to diagnose or rule out the disease. Specifically, deciphEHR™ will help HCPs make use of relevant patient history data, disease codes, suspect patient lists, order sets, and best practice alerts (BPAs).

Key Sections

HCP=healthcare provider; MS=multiple sclerosis.

Clinical Criteria for NMOSD in Adults

1

NMOSD is a serious, deadly, and rare autoimmune disease of the central nervous system where approximately 75% of cases are associated with aquaporin-4 antibodies (AQP4-IgG) and complement-mediated damage to astrocytes.[12,13]* NMOSD is a **heterogenous disease, which makes easy recognition of NMOSD difficult.**[7] Additionally, many symptoms of NMOSD overlap with those of other neurological conditions such as multiple sclerosis (MS),[14,15] myelin oligodendrocyte-glycoprotein antibody-associated disease (MOGAD),[14,16] acute disseminated encephalomyelitis (ADEM),[14] and sarcoidosis.[14] Misdiagnosis has become less common as the technology available for diagnostics has become more commercially available, but there is still much room to grow in improving NMOSD diagnostics.[1] **Diagnostic delays can be exacerbated by inaccurate testing.**[17] For example, while both ELISA and live cell-based assays can test for AQP4 to identify NMOSD, ELISA testing could confuse the identification of seropositive patients through both false negative and false positive results.[18]

Accurate diagnosis requires patient recognition, validated testing procedures, and disease differentiation. The following diagnostic criteria can be used by HCPs to understand the clinical presentation of NMOSD, how to triage patients who may be suspected of having NMOSD, and how to complete further clinical evaluation to diagnose or rule out the disease.

Check with your laboratory to ensure you have access to sensitive cell-based assays, the gold standard for AQP4 testing.[17,18,19]

Diagnostic Criteria for Adults With Anti-AQP4 Antibody Positive NMOSD[19]

Approximately three-quarters (75%) of all patients with NMOSD have anti-AQP4 autoantibodies.[12] Diagnosing NMOSD in these patients requires the following criteria:

- ✓ **At least 1 core clinical characteristic**

- ✓ **Positive test for AQP4-IgG (immunoglobulin G) using best available detection method (cell-based assay is strongly recommended)**†

- ✓ **Exclusion of alternative diagnoses**

*A cross sectional study to determine the prevalence of AQP4-IgG negative NMOSD patients (N=132) who were seropositive for MOG-IgG.

†Note: Accurately assessing AQP4 serostatus can be complicated, leading to misdiagnosis. The type of test run (ELISA vs live cell-based assay) can impact the validity of test results. Additionally, patients receiving immunosuppressant therapies or those already recovering from an attack may experience inaccurate seronegative results. In this case, if clinical suspicion remains for patients who received a false negative test, retesting can occur at least 3 to 6 months after a negative result.[18] For diagnostic criteria for NMOSD without AQP4 or unknown AQP4 status, see here.

1. Core clinical characteristics[19]

NMOSD is thought to have 6 core clinical characteristics that can present with unique symptoms. Optic neuritis, transverse myelitis, and area postrema syndrome are the most common presenting clinical characteristics. For additional, rare, presenting characteristics, see Appendix B.

Optic neuritis*
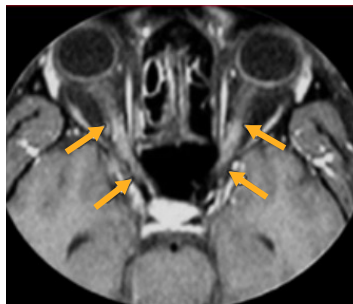
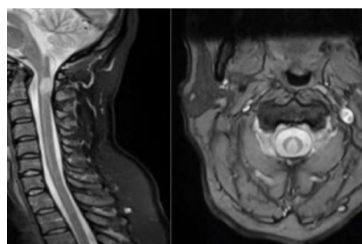MRI image[20]

Presenting Symptoms

Typically presents as acute, unilateral, painful vision loss that can worsen with eye movements.[21]

Bilateral optic neuritis can be found in patients with AQP4-IgG.[21]

Considerations for Differential Diagnosis

- More common in NMOSD relative to MS patients.[22]
- Severity of vision loss tends to be more severe in patients with NMOSD (20/400) relative to patients with MS (20/200).[21]
- Bilateral optic neuritis is more common in NMOSD relative to MS.[21]

Transverse myelitis*

MRI images[23]

Presenting Symptoms

Weakness of the legs and arms; pain in the lower back; or sharp, shooting sensations that radiate down the legs or arms or around the torso; sensory alterations; bowel and bladder dysfunction.[24]

Considerations for Differential Diagnosis

- Detection of a Longitudinally Extensive Transverse Myelitis (LETM) spinal cord lesion associated with acute myelitis is a specific neuroimaging characteristic of NMOSD, which is uncommon in adult MS.[19]
- NMOSD-related myelitis is often observed to be longitudinally extensive, involving three or more vertebral segments.[25]

Area postrema syndrome

MRI images demonstrating bilateral lesions in area postrema in A) sagittal and B) transverse planes.[26]

Presenting Symptoms

Intractable nausea, vomiting, and hiccups.[6]

Considerations for Differential Diagnosis

- Intractable vomiting and hiccups due to area postrema involvement are essentially pathognomonic and can be a key differentiator of NMOSD relative to other neurological diseases.[27]
- Triaging patients with an "inverted V" sign on the axial medulla oblongata and a linear medullary lesion upon MRI examination can help to quickly triage APS patients and avoid diagnostic delays.[28]
- These symptoms may precede the development of optic neuritis or transverse myelitis, making the identification of these symptoms paramount in diagnosing NMOSD prior to a debilitating attack.[29]

> ▶ **Neuroimaging** is key in helping to confirm core clinical characteristics.

For additional information on using MRI images for disease differentiation, see MRI findings.

*Most common core clinical presentations in patients with NMOSD. Of initial NMOSD events, ~35% of patients will experience optic neuritis, ~50% will experience transverse myelitis, and ~10% will experience optic neuritis and transverse myelitis.[30†]

†Based on a retrospective review of medical records of 187 patients with NMOSD based on Wingerchuk DM, et al. *Neurology.* 2006;66(10):1485-1489 NMO Diagnostic Criteria.

2. Positive test for AQP4-IgG

- **It is estimated that ~75% of NMOSD patients are AQP4-positive**[12]*
  - A negative AQP4 test result cannot rule out NMOSD[17,18]; for diagnostic guidelines for AQP4 negative patients, see [here](#)

- **Cell-based assays (CBAs) are the preferred method of testing due to high sensitivity and specificity (>80%, >99%) compared to ELISA (60%-65%, 99%-100%)**[18,19,31,32]
  - Likelihood of false-negative results is **1.5–15 times greater** with ELISA vs CBA[18]

- **False negatives are possible and are more likely to happen if:**
  - A patient is recovering from relapse[19]
  - A patient is currently on B-cell or antibody-targeted therapies (plasma exchange, immunosuppressive drugs)[19]
  - A less accurate method of testing was used (eg, ELISA)[19]
  - Retesting is recommended during acute attacks and during treatment-free intervals, possibly 3-6 months after a previous test and with a more sensitive method[18]
    - » Repeat testing in genuinely seronegative patients increases the risk of false-positive results, "sero-conversion" in previously seronegative patients should ideally be confirmed by testing of a follow-up sample using a cell-based assay[18]

- **AQP4 tests are not included in the MS panel and must be ordered separately to help confirm an NMOSD diagnosis**[33]

3. Exclusion of alternative diagnoses

While clinical observations and testing are important, they alone are not enough to confirm an NMOSD diagnosis. It is important to differentiate among similar neurological conditions through additional tests, disease probability, and individual patient demographics and history.

High-level clinical and epidemiological comparison between AQP4-antibody-seropositive NMOSD, MOG-antibody disease, and MS[11]

	MS	AQP4-antibody disease	MOG-antibody disease
Mean age at onset	30 years	40 years	More common in children than in adults
Prevalence by sex Female : Male	2-4:1[34]	9:1	Around 1:1
Prevalence by race	Up to 100–200/100,000 in White populations, but <5–50/100,000 in many Asian and African countries rising in most parts of the world	East Asians: 3.5/100,000 Whites: 1/100,000 Blacks: range from 1.8 to 10/100,000	More common in children than in adults
Optic neuritis	Unilateral, short	Bilateral[35] or unilateral/chiasmal, long (>1/2 of optic nerve)	Unilateral/simultaneous bilateral, long; frequent optic disc swelling
Myelitis	Non-transverse, short; peripheral/dorsolateral	Long (>3 vertebral segments) in 85%; centrally located; affects cervical or thoracic cord	Often long, but may be <3 vertebral segments; gadolinium enhancement less common than AQP4-antibody disease; relatively more common in the lumbosacral region
Attack severity	Mild to moderate	Moderate to severe	Mild to moderate
Disability	Mainly due to progression	Attack related	Attack related

*A cross sectional study to determine the prevalence of AQP4-IgG negative NMOSD patients (N=132) who were seropositive for MOG-IgG.

Symptomatology

While many symptoms are shared across NMOSD and other neurological conditions, **it is key to look beyond shared symptomatology to differentiate NMOSD from conditions such as MS.**[14] Often, symptoms caused by impacts from lesions to the area postrema are quite unique to NMOSD relative to other neurological conditions.[19]

Disease Impact	NMOSD[15,36-38]	MS[39]
Vision loss	✓	✓
Blindness	✓	✗
Spasms	✓	✓
Limb weakness	✓	✓
Sensation loss	✓	✓
Paralysis	✓	✓
Loss of bowel/bladder function	✓	✓
Hiccups*	✓	✗
Nausea*	✓	✗
Vomiting*	✓	✗

*Impact due to lesions in the area postrema.
Not all symptoms must be present for disease differentiation.

MRI findings

MRI results can be key for NMOSD disease differentiation. Many MRI findings indicative of NMOSD are highlighted in the clinical characteristics table. Below you will find a few examples of MRI differentials for NMOSD relative to MS.[20]

Normal[40]

Axial T1-weighted image showing normal optic nerve

NMOSD[20]

Extensive bilateral gadolinium-enhancing lesions at the posterior portion of the optic nerves (arrows)

MS[20]

Unilateral and short-length involvement of the right intraorbital optic nerve (arrows) showing the typical pattern of MS

Normal[41]

Sagital T2-weighted image of normal cervical spine

NMOSD[20]

Longitudinally extensive transverse myelitis, characteristic of NMOSD, extending into the area postrema

MS[20]

Ovoid and longitudinally short lesions typical of MS myelitis

Normal[40]

Axial T1-weighted image of a normal brain

NMOSD[20]

Hyperintense lesions compromising periependymal surfaces of the ventricles (arrows) and the right corticospinal tract (dotted circle)

MS[20]

Focal acute lesion in the right posterior limb of the internal capsule

Recently, 5 validated imaging predictors for the differentiation of NMOSD and MS, named Cacciaguerra's criteria, were described.[42] These imaging criteria included the absence of combined juxtacortical/cortical lesions, the absence of ovoid periventricular lesions, the absence of Dawson's fingers, the presence of LETM, and the presence of periependymal lesions along the lateral ventricles. Fulfillment of at least 2 of the 5 criteria distinguished NMOSD from MS with 92% sensitivity and 91% specificity in training samples, and 82% sensitivity and 91% specificity in validation samples.[42] Images above are only illustrative and do not represent all NMOSD patients.

Myelin oligodendrocyte glycoprotein (MOG) antibody serologic testing

- The lack of coexistence of AQP4-IgG and MOG-IgG in the serum of the same patient suggests that AQP4-IgG NMOSD and anti-MOG syndromes are distinct diseases[7]

- MOG antibody tests may be performed in seronegative NMOSD patients to rule out MOGAD[43]

Cerebrospinal fluid (CSF)[19,44]

- CSF oligoclonal bands are rare in AQP4-IgG-NMOSD but common in MS

- CSF pleocytosis >50 leukocytes/μL (incidence approximately 35% in NMOSD) or the presence of neutrophils or eosinophils (either >5/μL; incidence 44% and 10%, respectively, in attack-associated samples) is particularly useful in distinguishing NMOSD from MS

Vision and function[19,45]

- Visual evoked potentials (VEPs) may be used to differentiate between NMOSD and MS. MS patients with optic neuritis had normal amplitude and delayed VEPs whereas NMOSD patients with optic neuritis displayed reduced amplitude and preserved latency

- Optical coherence tomography (OCT) may also be useful in disease differentiation

Comorbidities[19]

Comorbidities in NMOSD patients have been reported for autoimmune diseases. For common comorbid conditions, see Appendix B. While these findings alone are not enough for a clinical differentiation between disease states, they can be early indicators for further assessment of suspect NMOSD patients.

Diagnostic Criteria for NMOSD Without AQP4 or Unknown AQP4 Status[19]

Diagnostic requirements are more stringent for patients in whom AQP4-IgG is not detected or for whom testing is unavailable. The following criteria can be used in the absence of AQP4-IgG:

✓ **At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:**

    1. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome

    2. Dissemination in space (2 or more different core clinical characteristics)

    3. Fulfillment of additional MRI requirements, as applicable

✓ **Negative tests for AQP4-IgG using best available detection method, or testing unavailable**

✓ **Exclusion of alternative diagnoses**

Additional MRI Requirements for NMOSD Without AQP4-IgG or Unknown AQP4-IgG Status[19]

1. Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over greater than 1/2 optic nerve length or involving optic chiasm

2. Acute myelitis: requires associated intramedullary MRI lesion extending over greater than or equal to 3 contiguous segments (LETM) OR greater than or equal to 3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis

3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions

4. Acute brain stem syndrome: requires associated periependymal brain stem lesions

→

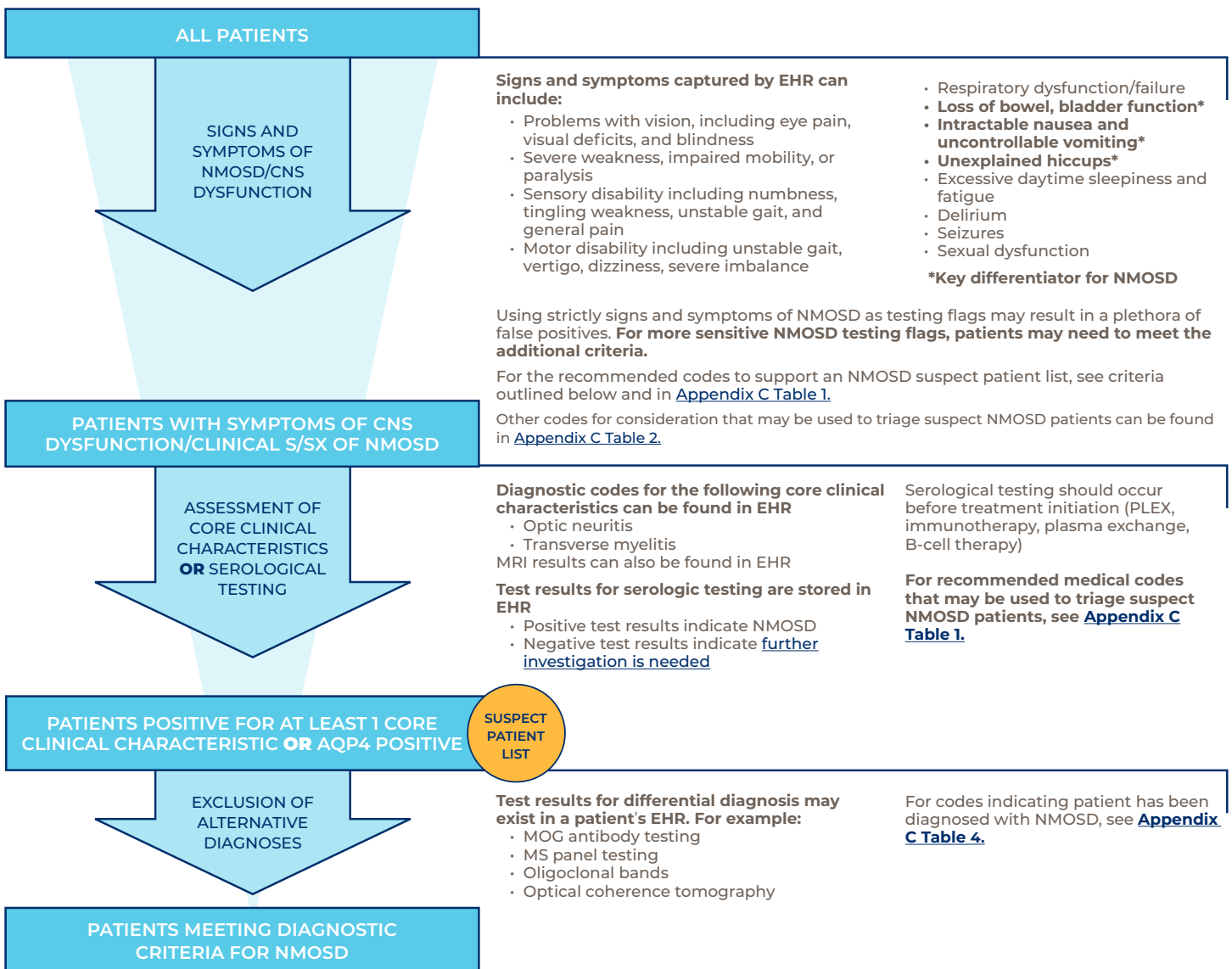# A Guide to Generating Suspect NMOSD Patient Lists

2

In NMOSD, patients are often either undiagnosed or misdiagnosed.[46] This can be particularly apparent in underrepresented populations as NMOSD has a higher prevalence and disproportionately impacts patients of Asian and African descent.[8-11] This toolkit may help reduce the incidence of undiagnosed and misdiagnosed patients by utilizing the EHR and evidence-based diagnostic criteria to generate suspect patient lists, which may help increase awareness of suspect NMOSD patients for further evaluation by HCPs.[47]
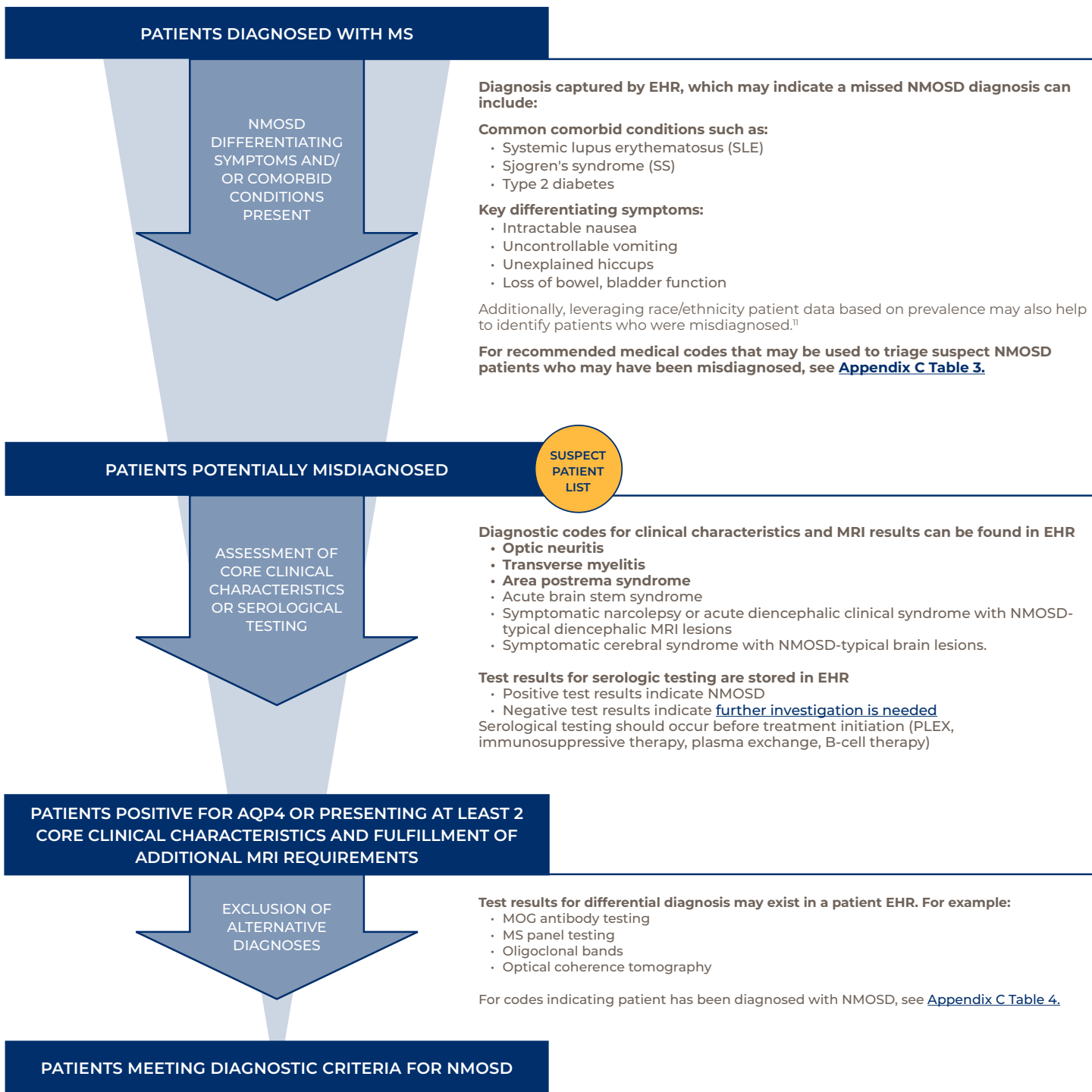
Suggested Clinical Criteria for Suspect NMOSD Patient Lists

In an EHR system, a suspect patient list, also referred to as a patient list report, is a list of patients meeting certain clinical criteria. Generating a suspect patient list requires the same clinical criteria used to make an NMOSD diagnosis. In addition to creating a list of suspect NMOSD patients for further clinical evaluation, a suspect patient list can also be used to flag patient charts with a best practice alert to recommend NMOSD testing using order sets or clinical referral.

Please see the chart below for guidance.

Patient presents with new neurological symptoms (has never been diagnosed with another neurological condition)[7,19,36,43]

ALL PATIENTS

SIGNS AND SYMPTOMS OF NMOSD/CNS DYSFUNCTION

Signs and symptoms captured by EHR can include:
- Problems with vision, including eye pain, visual deficits, and blindness
- Severe weakness, impaired mobility, or paralysis
- Sensory disability including numbness, tingling weakness, unstable gait, and general pain
- Motor disability including unstable gait, vertigo, dizziness, severe imbalance

- Respiratory dysfunction/failure
- **Loss of bowel, bladder function***
- **Intractable nausea and uncontrollable vomiting***
- **Unexplained hiccups***
- Excessive daytime sleepiness and fatigue
- Delirium
- Seizures
- Sexual dysfunction

*Key differentiator for NMOSD

Using strictly signs and symptoms of NMOSD as testing flags may result in a plethora of false positives. **For more sensitive NMOSD testing flags, patients may need to meet the additional criteria.**

For the recommended codes to support an NMOSD suspect patient list, see criteria outlined below and in Appendix C Table 1.

Other codes for consideration that may be used to triage suspect NMOSD patients can be found in Appendix C Table 2.

PATIENTS WITH SYMPTOMS OF CNS DYSFUNCTION/CLINICAL S/SX OF NMOSD

ASSESSMENT OF CORE CLINICAL CHARACTERISTICS OR SEROLOGICAL TESTING

Diagnostic codes for the following core clinical characteristics can be found in EHR
- Optic neuritis
- Transverse myelitis

MRI results can also be found in EHR

Test results for serologic testing are stored in EHR
- Positive test results indicate NMOSD
- Negative test results indicate further investigation is needed

Serological testing should occur before treatment initiation (PLEX, immunotherapy, plasma exchange, B-cell therapy)

For recommended medical codes that may be used to triage suspect NMOSD patients, see Appendix C Table 1.

PATIENTS POSITIVE FOR AT LEAST 1 CORE CLINICAL CHARACTERISTIC OR AQP4 POSITIVE

SUSPECT PATIENT LIST

EXCLUSION OF ALTERNATIVE DIAGNOSES

Test results for differential diagnosis may exist in a patient's EHR. For example:
- MOG antibody testing
- MS panel testing
- Oligoclonal bands
- Optical coherence tomography

For codes indicating patient has been diagnosed with NMOSD, see **Appendix C Table 4.**

PATIENTS MEETING DIAGNOSTIC CRITERIA FOR NMOSD

Patients potentially misdiagnosed with multiple sclerosis (MS)[7,19,48]

PATIENTS DIAGNOSED WITH MS

NMOSD DIFFERENTIATING SYMPTOMS AND/OR COMORBID CONDITIONS PRESENT

Diagnosis captured by EHR, which may indicate a missed NMOSD diagnosis can include:

Common comorbid conditions such as:
- Systemic lupus erythematosus (SLE)
- Sjogren's syndrome (SS)
- Type 2 diabetes

Key differentiating symptoms:
- Intractable nausea
- Uncontrollable vomiting
- Unexplained hiccups
- Loss of bowel, bladder function

Additionally, leveraging race/ethnicity patient data based on prevalence may also help to identify patients who were misdiagnosed.[11]

For recommended medical codes that may be used to triage suspect NMOSD patients who may have been misdiagnosed, see Appendix C Table 3.

PATIENTS POTENTIALLY MISDIAGNOSED

SUSPECT PATIENT LIST

ASSESSMENT OF CORE CLINICAL CHARACTERISTICS OR SEROLOGICAL TESTING

Diagnostic codes for clinical characteristics and MRI results can be found in EHR
- **Optic neuritis**
- **Transverse myelitis**
- **Area postrema syndrome**
- Acute brain stem syndrome
- Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
- Symptomatic cerebral syndrome with NMOSD-typical brain lesions.

Test results for serologic testing are stored in EHR
- Positive test results indicate NMOSD
- Negative test results indicate further investigation is needed

Serological testing should occur before treatment initiation (PLEX, immunosuppressive therapy, plasma exchange, B-cell therapy)

PATIENTS POSITIVE FOR AQP4 OR PRESENTING AT LEAST 2 CORE CLINICAL CHARACTERISTICS AND FULFILLMENT OF ADDITIONAL MRI REQUIREMENTS

EXCLUSION OF ALTERNATIVE DIAGNOSES

Test results for differential diagnosis may exist in a patient EHR. For example:
- MOG antibody testing
- MS panel testing
- Oligoclonal bands
- Optical coherence tomography

For codes indicating patient has been diagnosed with NMOSD, see Appendix C Table 4.

PATIENTS MEETING DIAGNOSTIC CRITERIA FOR NMOSD

IMPORTANT NOTE: While EHR systems may assist providers in generating suspect patient lists, it is the sole responsibility of the HCP to make a diagnosis based on in-person patient evaluation. It is important to indicate that the final suspect list of patients will be sent to the HCP(s) for review. Including criteria for a suspect patient list helps explain to the HCP why the patient is on the report.

For IT Department: High-Level Technical Considerations for Generating Suspect Patient Lists

To leverage EHR codes effectively to build a suspect patient list, you should engage with your healthcare organization's IT department to manage and configure suspect patient lists. See below for an example process and considerations for establishing a suspect patient list in Epic EHR.

In Epic EHR, a suspect patient list is referred to as a **patient list report** (a report that identifies all patients meeting certain clinical criteria).

When configuring a suspect patient list, consider addressing the following questions:

- What will the suspect patient list be named?

- Who will own the suspect patient list? (eg, HCP super user or practice)

- What criteria will be used to determine which patients appear on the suspect patient list?

- What information will be included on the patient list report? (see clinical criteria above, eg, MRI findings, AQP4 findings)

Additional considerations for creating an effective suspect patient list:

- The suspect patient list should exclude patients who are deceased or have been ruled out as NMOSD patients

- Suspect patient lists will be impacted by the data stored in your EHR; for example, any testing that has been conducted and recorded by an outside facility may not be recorded in the EHR, which may lead to a patient being erroneously excluded from the suspect patient list

- Identify and engage with users who have the security privileges and/or technical expertise to configure and monitor suspect patient lists in your EHR

- Consider consulting with epidemiologists to optimize suspect patient list criteria, if available to your institution[49]

Note: The above considerations may not be applicable to all EHR systems. Please consult with your IT department for specific processes and considerations. An example of creating patient lists in other EHR software can be found here:

- https://support.drchrono.com/hc/en-us/articles/202376054

Alternatively, your IT department can create patient lists by creating SQL queries allowing near real-time information extraction that can more rapidly account for any changes to suspect patient list criteria.[49,50] This method may be more efficient and can allow for machine learning and rapid patient list requirement updates, but will only be applicable if all EHR data is mapped to an existing data warehouse.

SQL=structured query language

Order Sets for NMOSD

Order sets are a clinical decision support tool in EHR systems consisting of groups of related, evidence-based orders for a particular disease state that physicians can order instantly within their EHR system.[51,52]

Order sets are available for use and customization in most EHR systems. Order sets allow for efficient and simultaneous ordering of the necessary components associated with effective clinical care such as lab tests, X-rays, and treatment, etc.[51,53] Listed below are examples of order sets for NMOSD. **These lists are not exhaustive and should be modified to meet the clinical needs of your healthcare organization and providers. They can include differential diagnosis for other neurological conditions with similar presentation (eg, MS, MOGAD). For example:**

Lab Investigations for Differential Diagnosis

Orders suggested may include:

Differential	Lab Test(s)
NMOSD	• **Key orders:** » MRI of brain and spine[19,54] » AQP4 serological testing using cell-based assay[19] • **Other orders:** » Optical coherence tomography (OCT)[55] » Visual evoked potentials (VEPs)[19]
MS	• **Key orders:** » MRI of brain and spine (same as NMOSD)[54] » Serum and cerebrospinal fluid (CSF) collected at the same time for MS profile test (IgG and albumin quantitation in both serum and spinal fluid samples; CSF, IgG:CSF albumin ratio; CSF IgG index; CSF IgG synthesis rate; oligoclonal banding)[19,33] • **Other orders:** » Visual evoked potentials (VEPs) (same as NMOSD)[19]
MOGAD	• **Key order:** » Myelin oligodendrocyte glycoprotein (MOG) antibody serological testing[43]

When bringing an order set build request to your IT department or EHR support person, consider including the following information[51,56-58]**:**

- The name of the order set, for example MS/NMOSD Diagnostics and Labs
- A list of common and medically appropriate labs, diagnostic orders, and clinical tests to include in the order set
- Any subheadings of the order set and more specific tests
- Clinicians who will have access to the order set, for example Neurology only
- Who will be responsible for adding or removing tests based on clinical need

The use of order sets has been found to promote adherence to evidence-based guidelines, enhance workflow with intuitive instructions, reduce potential for medical errors, and ultimately, improve patient outcomes. However, if standard order sets are not carefully designed, reviewed, and maintained to reflect best practices and ensure clear communication, they may actually contribute to errors.[52,56]

For full Institute for Safe Medication Practices (ISMP) guidelines, see here.

4

Best Practice Alerts to Help Triage a Suspect NMOSD Patient

Use Suspect Patient Criteria and Diagnostic Best Practices to Create Alerts

Using the data in the EHR to surface information in a patient's health record can be the first step in recognizing a suspect NMOSD patient. BPAs can be created using clinical criteria and the data in the EHR to help alert and guide an HCP in further assessing for NMOSD. An example BPA can be found below.

(!) PATIENT IS AT RISK FOR NMOSD   RECOMMEND FURTHER EVALUATION

Concern for NMOSD, if the clinical scenario is supportive, please consider: Placing neurologist referral and utilizing order set to triage patient.

Please utilize the order set below to place orders for further workup:

| Order | Do Not Order | Referral to Neurology |
| Order | Do Not Order | NMOSD/MS order set |

Acknowledgment reason:

| Test already ordered | Known NMOSD diagnosis | Not clinically indicated |

To learn more about NMOSD see *insert link here**

These boxes will allow orders to be placed directly from the alert screen

Allow institutions to understand why alert may not be used

Illustrative example. BPA should meet institutional guidelines and be specific based on criteria that led to BPA. Consult with clinical and IT teams for effective implementation.

*Further disease state education may be linked to an NMOSD page in your institution's EHR system or to an outside resource such as:

- https://nmosd.com/hcp
- https://rarediseases.org/rare-diseases/neuromyelitis-optica/
- https://www.uptodate.com/contents/neuromyelitis-optica-spectrum-disorders-nmosd-clinical-features-and-diagnosis

High-Level Technical Considerations for Generating BPAs

Automated BPAs can promote quality care by assisting HCPs in providing timely access to diagnostic best practices (eg, gold-standard techniques to test for NMOSD), reducing false negatives driven by less accurate testing. BPAs can also reduce inefficiency by decreasing the manual effort for HCPs in the diagnostic process.[59] Each EHR system is unique in how to establish automated BPAs, so you should engage with your healthcare organization's IT department. For example, in Epic EHR, a system is in place called "Best Practice Advisories" that allows organizations to deliver HCPs with messages through storyboard alerts, interruptive/active alerts, or passive alerts.[59,60]* These customized, practice-specific alerts can be programmed by the institution's IT team with assistance from clinical leadership to fire according to predetermined triggers, either individual or in combination, using inclusionary or exclusionary logic.[60] IT staff can be provided the suggested BPAs listed above triggered for patients meeting the suggested clinical criteria.

When making IT request, clinical leaders should be involved in establishing the clinical criteria for BPAs. Consider including the following information to ensure that the suspect patient list is appropriately configured:

- The name for the alert
- The frequency of the alert based on established clinical guidelines
- Indicate where the alert should be placed
- Identify which providers should see the alert

Additional consideration for creating a BPA:

- Privileges on who can configure BPAs may be selective to specific users with security privileges or technical expertise (eg, data scientists in the IT department); therefore, these stakeholders should be identified and engaged with as early as possible.

Optimizing BPAs

Improving the visual design of clinical BPAs may help providers recognize medical conditions faster.[60,61] Five presentation elements that have been suggested for EHR alerts include[61]:

1. Physically organize different information by placing it into bordered blocks
2. Be consistent with visual cues (eg, typeface fonts and colors)
3. Use typeface font size and "weight" to help organize and emphasize information
4. Apply color to the boxes used to organize the information
5. Consider the use of three-dimensional effects (to accommodate users who are color blind)

*It has been found that there is a **7.7x greater likelihood a BPA will be followed** by an HCP if the alert is active rather than passive.[62]

Note: BPAs may require governance oversight, consult with your CMIO/CIO.[62]

For a comprehensive list of suggestions, please see *Informatics and interaction: Applying human factors principles to optimize the design of clinical decision support for sepsis*.[61]

Additional Considerations

There are subtle differences between the various EHR systems. Each has similar functionality, but there may be differences such as the naming conventions of EHR system features. Additionally, organizations may have established protocols or patient portals for communicating sensitive health information identified by a BPA. The following section highlights some of these considerations.

The toolkit is provided for informational purposes only and does not substitute the internal review of your institution. Please coordinate with your institution's approval process before implementing an EHR build.

Naming Conventions

- Generating and maintaining suspect patient lists empower organizations to surface patients who meet certain clinical and demographic criteria. These may also be named "worklists" depending on the system[59,63]

- BPAs allow organizations to notify providers when certain clinical activities should be prioritized for a particular patient. This functionality can account for a variety of clinical variables throughout the patient journey and may also be named "discern alerts"[60,64-66]

- Standardized order sets allow providers to easily understand and order the most relevant tests and treatment options for patients who meet certain disease criteria or are being seen in a particular department. These may also be known as "power plans" depending on the system[67,68]

Each organization may also have its own vocabulary/terms allowed in drop-down lists, formulary, and lab codes. Engage with IT stakeholders at your organization to align on institution-specific variations.

Patient Communication Considerations

HCPs should follow established communication protocols, especially those related to communicating sensitive information to patients. HCPs may also be provided with resources they can give their patient as they begin to understand their diagnosis.

Note: EHR systems have patient portals that allow patients to stay in touch with their care teams, review their schedules, access personalized patient educational materials, and be more involved in managing their health. These portals may be one way to communicate the need for a follow-up appointment. Some examples of patient portals include:

- » Epic MyChart
- » Cerner® HealtheLife℠
- » Meditech Health Portal
- » Allscripts® FollowMyHealth®

6

Implementing, Monitoring, and Maintaining a Program

The following section provides further guidance on how to implement the deciphEHR™ program in your healthcare organization as well as how to monitor and maintain the program. To assess the program, including surfaced suspect patients, you will need to monitor it on an ongoing basis. Remember, it will be essential to be clear about what you want to achieve and how you will measure it.

Step 1:

Establish a Clinical Program Lead

- It is important to establish a Clinical Program Lead for the project (a medical specialist with EHR experience and expertise in NMOSD, most likely a neurologist) who can answer questions and help direct and oversee successful program implementation.

- The Clinical Program Lead can communicate the value of the program to stakeholders throughout the healthcare organization by sharing the deciphEHR™ NMOSD Disease Overview and the Rare Disease Overview.

- The Clinical Program Lead may provide ongoing support, including monitoring the program and continuing to champion the use of EHR across multiple specialties for rapid triage of suspect NMOSD patients.

- Clinical Program Leads provide support to establish a diagnostic plan based on the clinical criteria for NMOSD, suggestions for developing suspect patient lists, order sets, and BPAs to help HCPs triage suspected NMOSD patients.

Step 2:

Identify, engage, and communicate with organizational stakeholders*

- Identify and collaborate with relevant stakeholders within your healthcare organizations who are important in implementing the deciphEHR™ program and encouraging sustainable success.

- Stakeholders may vary depending on the organization but may include:

Clinical Leadership	Administrative Leadership
» Pathology and Specialty Medical Staff*	» IT/EHR Resource(s)
» Laboratory	» Data Scientist (if available)
» Pharmacy	» Quality Director

*You may consider inviting input from representative medical staff during the initiation, implementation, and maintenance of this program.

- For stakeholder involvement see here.

Step 3:

Establish an implementation and support team

- Consider including the following members on your implementation team*:

  - » Clinical Program Lead[†]
  - » Specialty/Physician Representative(s)[‡]
  - » Implementation/Project Manager

  - » Super User
  - » EHR Analyst (EHR Builder, Suspect Patient List, BPA Builder)

  - » Workflow Redesign/ Process Engineer
  - » Report Writer/ Measurement and Tracking Lead

*Depending on the size and type of your organization, your organization may assign employees to more than one role.
[†]You may consider an additional stakeholder who has experience leading the implementation of BPAs.
[‡]For most applicable physicians see here.

Step 4:

Develop and execute the implementation plan

- Engage relevant stakeholders and implementation team to establish the adoption, scope, implementation, and rollout of the program

- Leverage the clinical criteria for NMOSD (see Section 1) to create suspect patient list for future clinical evaluation by (see Section 2 for technical considerations):

  - » Including recommended medical codes in the Appendix C

  - » Engaging clinical leadership and Super User with IT departments for most effective implementation

- Establish BPAs for HCPs based on clinical criteria (see Section 3 for technical considerations)

  - » Provide NMOSD education within the clinical alert using web links such as: https://rarediseases. info.nih.gov/diseases/6267/neuromyelitis-optica-spectrum-disorder or https://rarediseases.org/rare-diseases/neuromyelitis-optica/

  - » Provide NMOSD resources for HCPs with suspect or confirmed NMOSD patients such as: https:// nmosd.com/hcp

  - » Engage clinical leadership and Super User with IT departments for most effective implementation

Step 5:

Develop a monitoring and evaluation framework[69-71]

- The Measurement and Tracking Lead may be in charge of continuing to monitor and evaluate suspect NMOSD patient lists on a routine (eg, monthly, bimonthly) basis to assess the effectiveness of the program (the Super User may be engaged in this process)

- Effectiveness of the program should be measured based on defined metrics for success (for examples see Step 6)

- The Clinical Program Lead and Super User can monitor and evaluate the BPA program to assess its usefulness and effectiveness in assisting HCPs (eg, through HCP interview)

Step 6:

Measure success[69]

Metrics for success should be determined at the start of implementation and should be continually measured to assess the success of the program. Metrics for success may include:

- Amount of time from suspect patient alert or on a report to the HCP for evaluation to rule in or rule out NMOSD

- Number of times an HCP acts on a BPA

- Number of patients for which an alert helps the HCP to confirm an NMOSD diagnosis

Step 7:

Ongoing improvement[69]

- Engage with Clinical Program Lead to assess NMOSD diagnostic criteria to ensure they are current

  » Determine the appropriate timeframe for reassessment based on institutional standards (eg, annually)

  » Check deciphEHRrare.com for updates

- Evaluate the effectiveness of NMOSD suspect patient lists and BPAs to triage suspect patients to confirm or rule out NMOSD

- In case of clinical concerns, reference your implementation and support team

- For EHR implementation troubleshooting and support, consider contacting your EHR provider

Appendix A:
Medical Staff Considerations

Identify and collaborate with relevant stakeholders within your healthcare organizations (including specialists) who may see undiagnosed NMOSD patients. See the list of possible specialists below. Learn, understand, and comply with your institution's requirements for implementing.

Patients Presenting NMOSD Symptoms Are Most Likely to Visit the Following HCPs[5]:

- 5%
- 12%
- 25%
- 37%
- 21%

Legend:
- Neurologist
- ER MD
- PCP
- Ophthalmologist
- Other*
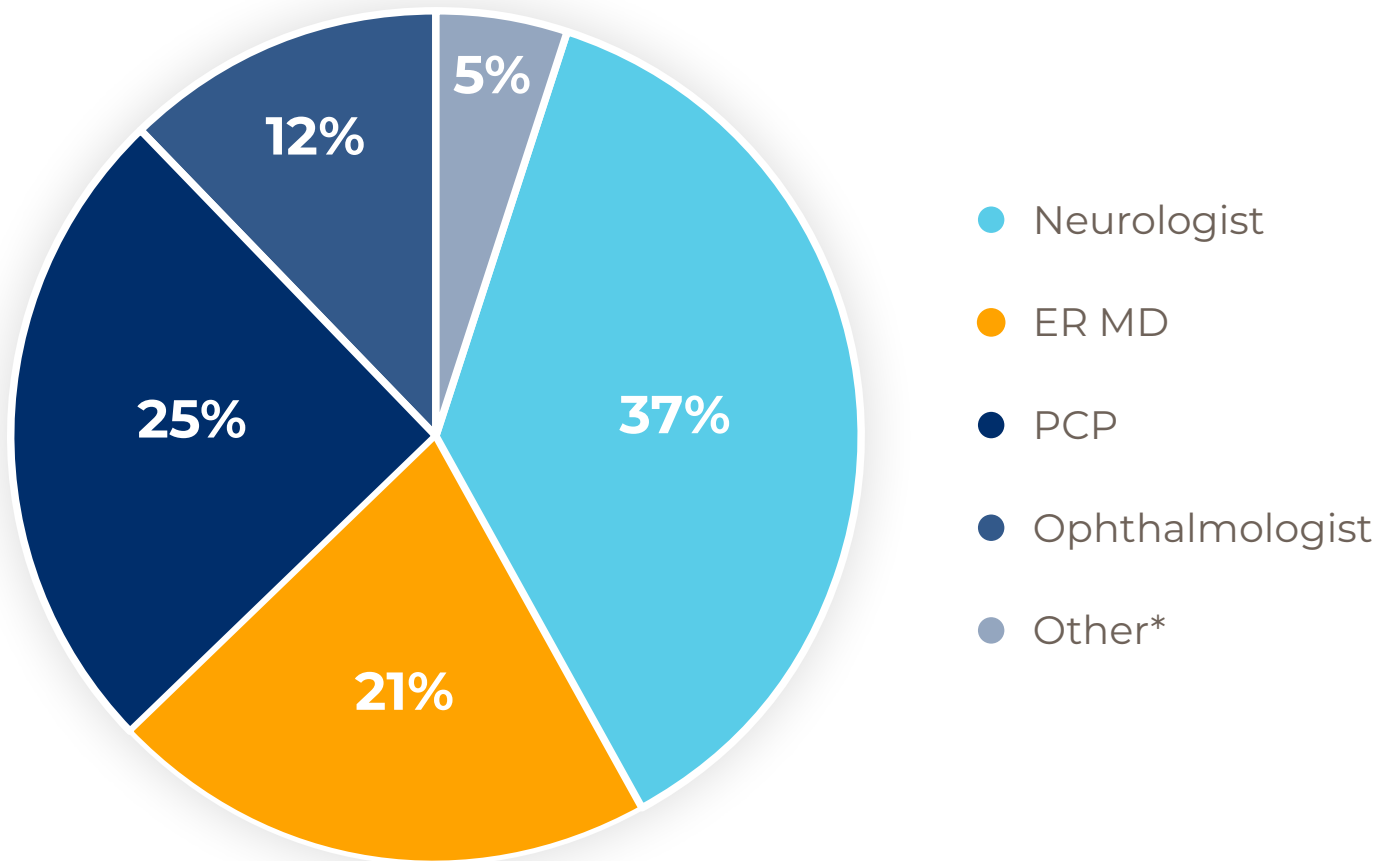
*Additional HCPs seeing NMOSD patients include[5]:

- MS specialists
- Rheumatologists
- Gastroenterologists
- Orthopedists
- Hematologists
- Physiatrists
- Hospitalists/Neuro Intensivists

ER MD=emergency room physician, PCP=primary care physician.

Appendix B: Additional Clinical Considerations

7

Additional, Less Common, Core Clinical Characteristics[19]:

Acute brain stem syndrome

Presenting Symptoms

Vomiting, hiccups, oculomotor dysfunction, pruritus, hearing loss, facial palsy, vertigo or vestibular ataxia, trigeminal neuralgia.[72]

Considerations for Differential Diagnosis

- Diffuse medulla, pons, or midbrain MRI lesions occasionally occurred in AQP4-IgG-NMOSD but rarely in MS.[72,73]

Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions

Presenting Symptoms

Excessive daytime sleepiness, hypotension, secondary amenorrhea, inappropriate antidiuretic hormone secretion, hypothermia, bradycardia. [43,74]

Considerations for Differential Diagnosis

- Although rarely manifested through symptoms suggestive of diencephalic involvement, NMOSD should be considered when encountering patients with diencephalic syndrome to triage the primary cause of these manifestations.[43]

Symptomatic cerebral syndrome with NMOSD-typical brain lesions

Presenting Symptoms

Acute seizures, confusion, decreased mental status, or hypersomnolence.[75]

Considerations for Differential Diagnosis

- Ovoid lesions perpendicular to a lateral ventricle (Dawson's fingers) may be more common in MS patients relative to NMOSD.[76]

Common Comorbidities With NMOSD

Diseases with immune-based pathogenesis are the most frequently reported comorbidities associated with NMOSD, most commonly Sjögren's syndrome (SS) and systemic lupus erythematosus (SLE).[15] Other autoimmune diseases associated with NMOSD include rheumatoid arthritis and autoimmune encephalitis.[21,77] Common nonimmune comorbidities include type 2 diabetes, cardiovascular disease, hyperglycemia, and liver disease.[77]

7

Appendix C: Medical Codes to Support Suspect Patient Lists, Order Sets, and BPAs

The medical codes that represent the clinical criteria for NMOSD that are required for a patient to appear on the suspect patient list are found here in the appendix.

EHR Code Types

The EHR system contains multiple code types, each containing unique information. These codes can be used in combination to triage suspect NMOSD patients. Below are examples of code types that can be found in the EHR:

- **ICD-10:** International Classification of Diseases, tenth revision, a globally used diagnostic code for epidemiology, health management, and clinical purposes

- **SNOMED:** Systematized Nomenclature of Medicine Clinical Terms, a common language for systems to adopt for indexing, storing, retrieving, and aggregating clinical data

- **LOINC:** Logical Observation Identifiers Names and Codes, a database and universal standard for identifying medical laboratory observations

- **CPT:** Current Procedural Terminology, a uniform language for coding medical services and procedures such as surgeries, diagnostic tests, evaluation, and management services

- **HCPCS:** Healthcare Common Procedure Coding System, a collection of standardized codes that represent basic medical procedures, supplies, products, and services

Suggestions for Leveraging EHR Codes

All codes are listed at the parent level. Determining level of specificity (eg, specific codes within parent trees) is at the discretion of the institution. The institution is responsible for selection of codes based on the specific situation and patient needs.

- No one code has been found to have high specificity and sensitivity for NMOSD; therefore, it is suggested codes be used in combination to develop suspect patient lists

- Codes may change over time; please visit the respective code sites for up-to-date codes

  » An Excel spreadsheet version is also available on the web page for your convenience

- The codes used to triage patients to the suspect patient list may also be used to develop BPAs and suggest order sets

Suggested Codes for the Suspect Patient List Indicated in <u>Section 2</u>

Table 1: Recommended codes for patients at risk for NMOSD who are presenting with new neurological symptoms (ie, patients who have never been diagnosed with another neurological condition)

It is suggested that any code that indicates optic neuritis, transverse myelitis, or an order for AQP4 testing should immediately flag patients to the suspect patient list for further clinical evaluation for NMOSD. Since AQP4 testing does have substantial risk for false negative based on when the test is ordered and which test is ordered (eg, ELISA vs cell-based), it is suggested a negative AQP4 test should not exclude patients from being flagged to the suspect patient list for NMOSD. In clinics that have high plasma exchange (PLEX) populations, it may be considered to include codes that indicate PLEX as a flag for NMOSD evaluation.

Code Type	Code	Code Description	Suggestions for Implementation
Optic Neuritis Diagnostic Codes			
SNOMED	66760008	Optic neuritis	High-priority code
ICD-10	H46.9	Unspecific optic neuritis	High-priority code
Transverse Myelitis Diagnostic Codes			
SNOMED	47000000	Acute transverse myelitis	High-priority code
ICD-10	G37.3	Acute transverse myelitis in demyelinating disease of central nervous system	High-priority code
Ordered AQP4 Codes			
LOINC	68548-7	Aquaporin 4 water channel IgG Ab [Units/volume] in Serum or Plasma by Immunoassay	An order of an AQP4 testing is a high-priority code
LOINC	61430-5	Aquaporin 4 water channel Ab:ACnc:Pt:Ser/Plas:Qn:IA	An order of an AQP4 testing is a high-priority code
LOINC	63439-4	Aquaporin 4 water channel Ab.IgG:PrThr:Pt:Ser/Plas:Ord:IF	An order of an AQP4 testing is a high-priority code
LOINC	43752-5	Aquaporin 4 water channel IgG Ab [Units/volume] in Serum or Plasma by Immunofluorescence	An order of an AQP4 testing is a high-priority code
LOINC	44794-6	Aquaporin 4 water channel Ab.IgG:Titr:Pt:Ser/Plas:Qn:IF	An order of an AQP4 testing is a high-priority code
LOINC	43638-6	Aquaporin 4 water channel IgG Ab [Presence] in Serum or Plasma	An order of an AQP4 testing is a high-priority code
LOINC	46718-3	Aquaporin 4 water channel IgG Ab [Presence] in Cerebral spinal fluid	An order of an AQP4 testing is a high-priority code
LOINC	86241-7	Aquaporin 4 water channel Ab.IgG:Titr:Pt:Ser/Plas:Qn:Flow cytometry	An order of an AQP4 testing is a high-priority code
PLEX Codes			
CPT	36514	Under Venous Catheterization, Therapeutic Apheresis and Photopheresis Procedures	May be used as a high-priority code in clinics with high PLEX populations
CPT	36516	Under Venous Catheterization, Therapeutic Apheresis and Photopheresis Procedures	May be used as a high-priority code in clinics with high PLEX populations
HCPCS	S2120	Low density lipoprotein (LDL) apheresis using heparin-induced extracorporeal LDL precipitation S2120	May be used as a high-priority code in clinics with high PLEX populations
CPT	0342T	Under Imaging, Testing, Implantation, and Other Services	May be used as a high-priority code in clinics with high PLEX populations
CPT	36511	Under Venous Catheterization, Therapeutic Apheresis, and Photopheresis Procedures	May be used as a high-priority code in clinics with high PLEX populations
CPT	36512	Under Venous Catheterization, Therapeutic Apheresis, and Photopheresis Procedures	May be used as a high-priority code in clinics with high PLEX populations
CPT	36513	Under Venous Catheterization, Therapeutic Apheresis, and Photopheresis Procedures	May be used as a high-priority code in clinics with high PLEX populations

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Code Type	Code	Code Description	Suggestions for Implementation
PLEX Codes (continued)			
ICD-10	6A550Z0	Pheresis of Erythrocytes, Single	May be used as a high-priority code in clinics with high PLEX populations
ICD-10	6A550Z1	Pheresis of Leukocytes, Single	May be used as a high-priority code in clinics with high PLEX populations
ICD-10	6A550Z2	Pheresis of Platelets, Single	May be used as a high-priority code in clinics with high PLEX populations
ICD-10	6A550Z3	Pheresis of Plasma, Single	May be used as a high-priority code in clinics with high PLEX populations
ICD-10	6A551Z0	Pheresis of Erythrocytes, Multiple	May be used as a high-priority code in clinics with high PLEX populations
ICD-10	6A551Z1	Pheresis of Leukocytes, Multiple	May be used as a high-priority code in clinics with high PLEX populations
ICD-10	6A551Z2	Pheresis of Platelets, Multiple	May be used as a high-priority code in clinics with high PLEX populations
ICD-10	6A551Z3	Pheresis of Plasma, Multiple	May be used as a high-priority code in clinics with high PLEX populations

Table 2: Other codes for patients at risk for NMOSD who are presenting with new neurological symptoms

Additional codes that may be useful in identifying NMOSD patients are listed below. These codes may not have high specificity for NMOSD, but may still indicate a suspect NMOSD patient. The decision on if/how to implement these codes should be aligned with your institution's Clinical Leadership.

Code Type	Code	Code Description	Suggestions for Implementation
Signs and Symptoms of NMOSD Codes			
SNOMED	41370002	Myelitis (disorder)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	G04.91	Myelitis, unspecified	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	41652007	Pain in eye	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	H57.10	Ocular pain (unspecified eye)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	8510008	Reduced mobility	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	Z74.09	Other reduced mobility	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	44695005	Paralysis (finding)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	J96.90	Respiratory failure, unspecified, unspecified whether with hypoxia or hypercapnia	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	271825005	Respiratory distress	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	R06.03	Acute respiratory distress	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	101000119102	Numbness and tingling sensation of the skin	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	R20.2	Paresthesia of skin	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	44077006	Numbness	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Code Type	Code	Code Description	Suggestions for Implementation
Signs and Symptoms of NMOSD Codes (continued)			
ICD-10	R20.0	Anesthesia of skin	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	R53.1	Weakness	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	399153001	Vertigo	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	R42	Dizziness and giddiness	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	387603000	Impairment of balance	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	84229001	Fatigue	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	R53.83	Fatigue	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	91175000	Seizure	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	G40.909	Epilepsy, unspecified, not intractable, without status epilepticus	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	H53.2	Double vision	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	24982008	Diplopia (disorder)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	95677002	Disorder of vision (disorder)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	H54.2	Moderate visual impairment, binocular	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	H54.3	Mild or no visual impairment, binocular	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	H54.7	Unspecified visual loss	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	267727004	Blindness and/or vision impairment level (disorder)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	86260003	Pain around eye (finding)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	R52	Pain, not elsewhere, classified	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	G36.8	Other specified acute disseminated demyelination	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	G95.9	Disease of spinal cord, unspecified	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	83942000	Acute disseminated encephalomyelitis (disorder)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	G04.00	Acute disseminated encephalitis and encephalomyelitis, unspecified	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
SNOMED	31541009	Sarcoidosis (disorder)	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	D86.9	Sarcoidosis, unspecified	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1
ICD-10	G37.9	Demyelinating disease of central nervous system, unspecified	Sign/symptom of NMOSD, may consider implementing this code in addition to other more specific codes from Table 1

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Code Type	Code	Code Description	Suggestions for Implementation
Lab Tests and Procedures Codes			
LOINC	55121-8	Multiple sclerosis panel:-:Pt:Ser+CSF	May indicate suspicion of MS and potential NMOSD
LOINC	48668-8	Protein fractions.oligoclonal bands. IT:PrThr:Pt:Ser+CSF:Ord	May indicate suspicion of MS and potential NMOSD
SNOMED	113073005	Cerebrospinal fluid oligoclonal bands	May indicate suspicion of MS and potential NMOSD
LOINC	35569-3	Protein fractions.oligoclonal bands:Num:Pt:Ser/Plas:Qn	May indicate suspicion of MS and potential NMOSD
SNOMED	413017004	Cerebrospinal fluid oligoclonal band screening test (procedure)	May indicate suspicion of MS and potential NMOSD
SNOMED	113073005	Cerebrospinal fluid oligoclonal bands (procedure)	May indicate suspicion of MS and potential NMOSD
SNOMED	41489001	Oligoclonal protein measurement (procedure)	May indicate suspicion of MS and potential NMOSD
SNOMED	72221006	Magnetic resonance imaging of neck (procedure)	May indicate suspicion of neurologic condition
SNOMED	241601008	Magnetic resonance imaging of head (procedure)	May indicate suspicion of neurologic condition
SNOMED	241645008	Magnetic resonance imaging of spine (procedure)	May indicate suspicion of neurologic condition
CPT/HCPCS	83916	The lab analyst measures the oligoclonal immune bands, generally on spinal fluid and a serum specimen. These bands are not usually present in normal spinal fluid, but are usually present in patients with multiple sclerosis	May indicate suspicion of MS and potential NMOSD
CPT/HCPCS	70549	The provider performs magnetic resonance angiography of the vessels of the neck and surrounding areas without contrast and then takes images again using contrast	May indicate suspicion of neurologic condition
CPT/HCPCS	70551	The provider uses magnetic resonance imaging, or MRI, to examine the brain and brain stem. The provider does not administer contrast for this exam	May indicate suspicion of neurologic condition
CPT/HCPCS	70552	The provider uses magnetic resonance imaging, or MRI, to examine the brain and brain stem using contrast	May indicate suspicion of neurologic condition
CPT/HCPCS	70553	In this procedure, the provider performs a magnetic resonance imaging, or MRI, study of the brain including the brain stem. He performs this procedure without using contrast material. He then follows with contrast material and takes more images	May indicate suspicion of neurologic condition
CPT/HCPCS	70554	The provider performs a functional magnetic resonance imaging (fMRI) of the brain, which tracks brain activity by assessing the metabolic changes that occur in response to neural activity	May indicate suspicion of neurologic condition
CPT/HCPCS	72141	In this diagnostic procedure, the provider performs a magnetic resonance imaging (MRI) study of the cervical spinal canal and contents without using contrast material	May indicate suspicion of neurologic condition
CPT/HCPCS	72146	In this diagnostic procedure, the provider performs magnetic resonance imaging (MRI) of the thoracic spinal canal and contents without using contrast	May indicate suspicion of neurologic condition

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Code Type	Code	Code Description	Suggestions for Implementation
Lab Tests and Procedures Codes (continued)			
CPT/HCPCS	72148	In this diagnostic procedure, the provider performs magnetic resonance imaging (MRI) of the lumbar spinal canal and contents without using contrast	May indicate suspicion of neurologic condition
CPT/HCPCS	72142	In this diagnostic procedure, the provider performs a magnetic resonance imaging (MRI) study of the cervical spinal canal and contents using contrast material	May indicate suspicion of neurologic condition
CPT/HCPCS	72147	In this diagnostic procedure, the provider performs a magnetic resonance imaging (MRI) of the thoracic spinal canal and contents using contrast	May indicate suspicion of neurologic condition
CPT/HCPCS	72149	In this diagnostic procedure, the provider performs magnetic resonance imaging (MRI) of the lumbar spinal canal and contents using contrast	May indicate suspicion of neurologic condition
CPT/HCPCS	72156	In this diagnostic procedure, the provider performs magnetic resonance imaging (MRI) of the cervical spinal canal and contents first without using contrast and again after injecting contrast material	May indicate suspicion of neurologic condition
CPT/HCPCS	72157	In this diagnostic procedure, the provider performs magnetic resonance imaging (MRI) of the thoracic spinal canal and contents first without using contrast and again after injecting contrast material	May indicate suspicion of neurologic condition
CPT/HCPCS	72158	In this diagnostic procedure, the provider performs magnetic resonance imaging (MRI) of the lumbar spinal canal and contents first without using contrast and again after injecting contrast material	May indicate suspicion of neurologic condition

Table 3: Recommended codes for patients who may have been misdiagnosed with MS at risk for NMOSD

It has been proposed that a substantial number of NMOSD patients are initially misdiagnosed with MS. The following codes may be suggested for identifying patients at risk for NMOSD who have been previously diagnosed with MS based on differentiating symptoms (eg, hiccups, nausea, vomiting, bladder dysfunction) and common comorbidities more frequently associated with NMOSD (SS, SLE, type 2 diabetes). Additionally, it may be considered to flag patients of African and Asian descent previously diagnosed with MS to the NMOSD suspect patient list based on the prevalence of NMOSD vs MS in minority populations. When implementing these codes, it would be suggested that all codes are combined with the MS diagnostic code to limit the population to only patients potentially misdiagnosed. The codes used to triage patients to this suspect patient list may also be used to develop BPAs and suggest order sets.

Code Type	Code	Code Description	Suggestions for Implementation
MS Diagnostic Codes			
ICD-10	G35	Multiple sclerosis	High-priority code, may be used in combination with codes for hiccups, vomiting, bladder dysfunction, nausea, SLE, SS, or type 2 diabetes to triage suspect misdiagnosed NMOSD patients
SNOMED	24700007	Multiple sclerosis (disorder)	High-priority code, may be used in combination with codes for hiccups, vomiting, bladder dysfunction, nausea, SLE, SS, or type 2 diabetes to triage suspect misdiagnosed NMOSD patients
Differentiating Symptoms Diagnostic Codes			
SNOMED	65958008	Hiccoughs	May be used in combination with codes for MS to improve specificity
ICD-10	R06.6	Hiccoughs	May be used in combination with codes for MS to improve specificity
SNOMED	16932000	Nausea and vomiting	May be used in combination with codes for MS to improve specificity
ICD-10	R11.2	Nausea with vomiting, unspecified	May be used in combination with codes for MS to improve specificity
ICD-10	R11.11	Vomiting without nausea	May be used in combination with codes for MS to improve specificity
SNOMED	422587007	Nausea	May be used in combination with codes for MS to improve specificity

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Code Type	Code	Code Description	Suggestions for Implementation
Differentiating Symptoms Diagnostic Codes (continued)			
SNOMED	40492006	Bladder dysfunction (finding)	May be used in combination with codes for MS to improve specificity
ICD-10	N31.9	Neuromuscular dysfunction of bladder, unspecified	May be used in combination with codes for MS to improve specificity
ICD-10	N31.8	Other neuromuscular dysfunction of bladder	May be used in combination with codes for MS to improve specificity
ICD-10	N32.9	Bladder disorder, unspecified	May be used in combination with codes for MS to improve specificity
ICD-10	N32.89	Other specified disorders of bladder	May be used in combination with codes for MS to improve specificity
ICD-9	596	Other disorders of bladder	May be used in combination with codes for MS to improve specificity
ICD-9	596.5	Other functional disorders of bladder	May be used in combination with codes for MS to improve specificity
ICD-9	596.54	Neurogenic bladder NOS	May be used in combination with codes for MS to improve specificity
ICD-9	596.59	Other functional disorder of bladder	May be used in combination with codes for MS to improve specificity
ICD-9	596.8	Other specified disorders of bladder	May be used in combination with codes for MS to improve specificity
ICD-9	596.89	Other specified disorders of bladder	May be used in combination with codes for MS to improve specificity
ICD-9	596.9	Unspecified disorder of bladder	May be used in combination with codes for MS to improve specificity
Common Comorbidities Diagnostic Codes			
SNOMED	83901003	Sjögren's syndrome (disorder)	May be used in combination with codes for MS to improve specificity
SNOMED	55464009	Systemic lupus erythematosus (disorder)	May be used in combination with codes for MS to improve specificity
SNOMED	45170000	Encephalitis (disorder)	May be used in combination with codes for MS to improve specificity
SNOMED	200938002	Discoid lupus erythematosus (disorder)	May be used in combination with codes for MS to improve specificity
ICD-10	M35.0	Sjögren's syndrome (disorder)	May be used in combination with codes for MS to improve specificity
ICD-10	M32.10	Systemic lupus erythematosus, organ or system involvement unspecified	May be used in combination with codes for MS to improve specificity
ICD-10	L93.0	Discoid lupus erythematosus	May be used in combination with codes for MS to improve specificity
ICD-10	G04.90	Encephalitis and encephalomyelitis, unspecified	May be used in combination with codes for MS to improve specificity
SNOMED	44054006	Diabetes mellitus type 2 (disorder)	May be used in combination with codes for MS to improve specificity
ICD-10	E11.9	Type 2 diabetes mellitus	May be used in combination with codes for MS to improve specificity

Table 4: Codes indicating an NMOSD diagnosis

These codes may indicate NMOSD diagnosis and may be considered as exclusionary criteria for the suspect patient list to decrease continued flagging of patients who have already been triaged and assessed.

Code Type	Code	Code Description	Suggestions for Implementation
NMOSD Diagnosis Codes for Exclusion			
ICD-10	G36.0	Neuromyelitis optica - Devic	Indicates NMOSD diagnosis, may consider removing from suspect patient list to decrease continued flagging
SNOMED	25044007	Neuromyelitis optica	Indicates NMOSD diagnosis, may consider removing from suspect patient list to decrease continued flagging

The above codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

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ALEXION
AstraZeneca Rare Disease