Why is an early diagnosis of generalised myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD) important?

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Online activity details

This resource has been downloaded from a touchEXPERT BRIEFING, hosted on touchOPHTHALMOLOGY. The full activity, which includes video resources, can be accessed at:

https://www.touchophthalmologytmc.com/neuro-ophthalmology/learning-zone/why-is-an-early-diagnosis-of-gmg-and-nmosd-important/

This content is for healthcare professionals outside of the USA only.

Learning objectives

After watching the touchEXPERT BRIEFING activity, you should understand that:

- ✓ Describe the disease presentation of gMG and NMOSD, and the typical patient journey from initial ocular signs and symptoms to diagnosis.
- ✓ Outline the importance of early diagnosis of gMG and NMOSD including current criteria, and challenges to establishing an accurate diagnosis.
- ✓ Discuss the implications of early diagnosis for burden of disease and treatment outcomes.

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Early diagnosis of myasthenia gravis (MG)

Early symptoms of MG

In 85% of patients the initial symptoms of MG are ocular[1]

Ptosis (drooping eyelids)

Diplopia (double vision)

MG, myasthenia gravis.

1. Grob D, et al. *Muscle Nerve.* 2008;37(2):141-9.

Challenges to an early MG diagnosis

An MG diagnosis may require multiple tests to diagnose[1]

Potential misdiagnosis
As mimics with ophthalmoparesis and ptosis[2]

Symptom fluctuation
Lack of characteristic daily fluctuation can confound diagnosis[4]

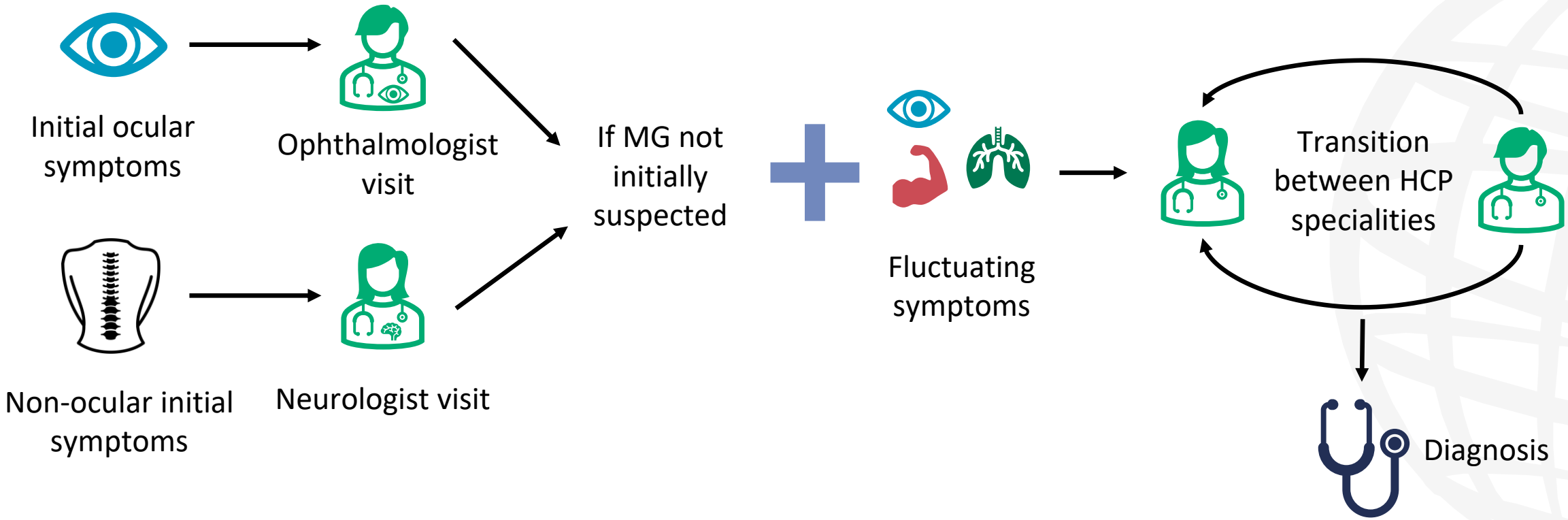
Symptom severity
If the most characteristic symptoms are mild or restricted to only a few muscles, diagnosis may be harder[3]

Absence of autoantibodies
~55–75% of ocular MG cases are AchR Ab positive[5,6]

Ab, antibody; AchrR, acetylcholine receptor; MG, myasthenia gravis.

1. Sussman J, et al. *Pract Neurol.* 2015;15(3):199-206; 2. Harrison P, et al. *Neuromuscul Disord.* 2023; 33(3):250-6; 3. National Institutes of Health. Available at: https://www.ninds.nih.gov/health-information/disorders/myasthenia-gravis (accessed April 2024); 4. Dragusin A, et al. *Neurol Ther.* 2022;11(1):481-7; 5. Hendricks TM, et al. *Am J Ophthalmol.* 2019;205:99-105; 6. Monte G, et al. *J Neurol.* 2021; 268(5):1803-7.

A possible patient journey from diagnosis



Ocular symptoms have been reported to increase time to referral and initial ophthalmologist consultation time to second opinion from a neurologist[1]

HCP, healthcare practitioner; MG, myasthenia gravis.

1. Nguyen M, et al. *Neurol Clin Pract.* 2024;14(1):e200244.

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Impact of a delayed diagnosis

Psychosocial impact
Impacts including difficulty explaining symptoms and justifying absences are greater with vs without delayed diagnosis[1]

Disease progression
~65–85% of patients with ocular symptoms progress to gMG,[4,5] usually within the year of onset[5]

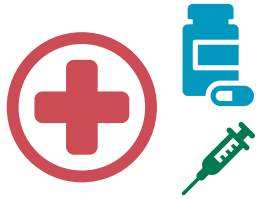
Targeting symptom remission
A time of diagnosis >1 year predicts decreased likelihood of achieving the MG treatment goals of symptom remission[2,3]

Diminished QoL and ADL
QoL and ADL are diminished, particularly in patients with greater disease severity[6,7]

ADL, activities of daily living; gMG, generalised myasthenia gravis; MG, myasthenia gravis; QoL, quality of life.

1. Benito-Lozano J, et al. *PLoS One*. 2023;18(7):e0288875; 2. Mao ZF, et al. *Eur J Neurol*. 2010; 17(7):913-21; 3. Sanders DB, et al. *Neurology*. 2016;87(4):419-25; 4. Evoli A, et al. *Acta Neurol Scand.* 1988;77(1):31-5; 5. Grob D, et al. *Ann N Y Acad Sci.* 1987;505:472-99; 6. Gelinas D, et al. *J Neurol Sci.* 2022;437:120268; 7. Dewilde S, et al. *BMJ Open.* 2023;13(1):e066445.

Implications of a MG diagnosis



Early intervention
Consensus guidelines recommend initial early treatment with an AchE inhibitor and corticosteroids (± non-steroidal immunosuppressant[a]) in most patients[1,2]

Risk of generalisation
Early treatment can reduce the risk of generalisation in patients with ocular MG[3]

Improved QoL
Improved symptom control is associated with better QoL[4,5]

[a]In patients with corticosteroid side effects are significant, response to corticosteroids is inadequate and corticosteroid dose cannot be reduced.
AChE, acetylcholinesterase; MG, myasthenia gravis; Qol, quality of life.
1. Sanders DB, et al. *Neurology*. 2016;87(4):419-25; 2. Sussman J, et al. *Pract Neurol.* 2015;15(3):199-206; 3. Li M, et al. *Ther Adv Neurol Disord*. 2019;12:1756286419876521; 4. Gelinas D, et al. *J Neurol Sci.* 2022;437:120268; 5. Diez Porras L, et al. *J Clin Med.* 2022;11(8):2189.

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Early diagnosis of neuromyelitis optica spectrum disorder (NMOSD)

Most common initial presenting symptoms

Pain
49–81% of patients[1,2]

Difficulty walking
54% of patients[1]

Spasticity/stiffness
23–63% of patients[1,2]

Impacted vision
53–62% of patients[1,2]

Fatigue
34–81% of patients[1,2]

Bladder dysfunction
20–26% of patients[1,2]

Patients with visual impact[2]

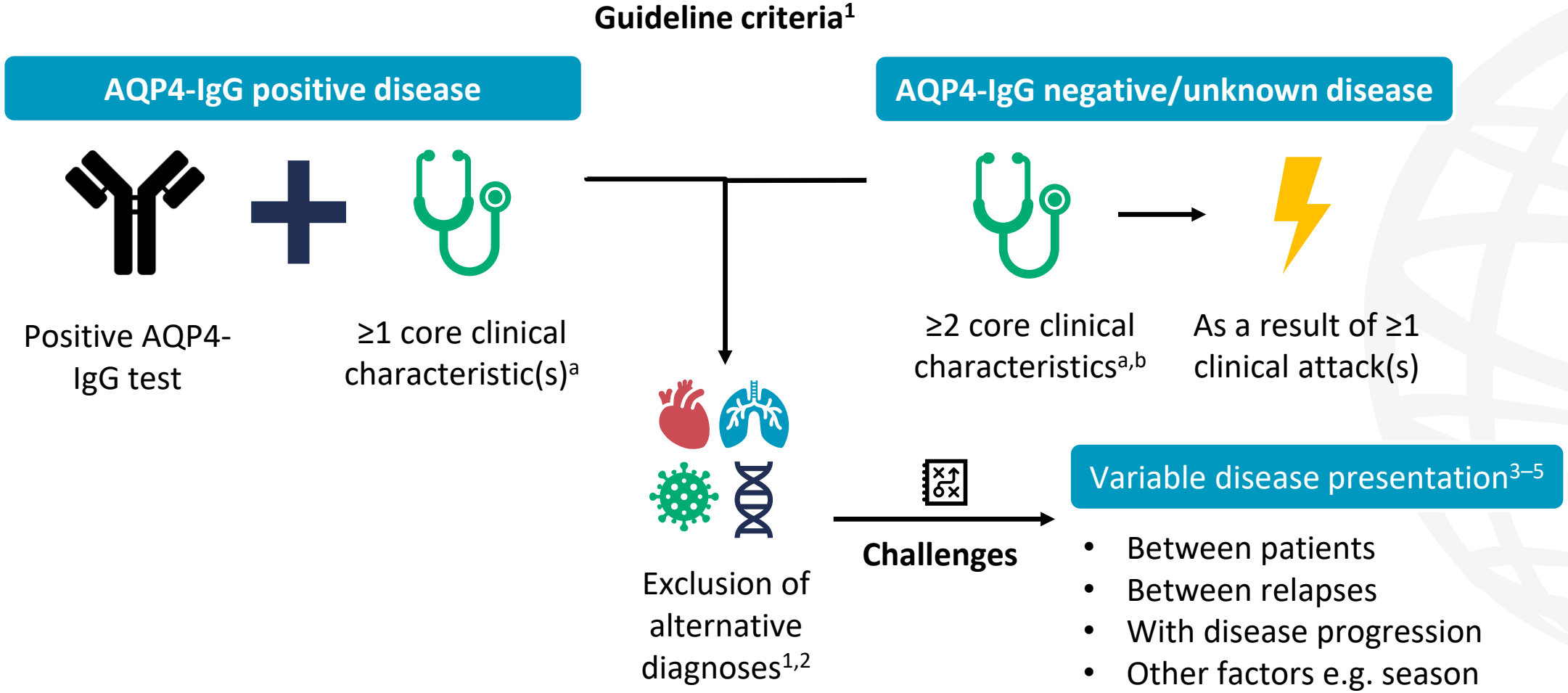
Double vision
39% of patients

Loss of peripheral vision
71% of patients

Loss of central vision
61% of patients

1. Beekman J, et al. *Neurol Neuroimmunol Neuroinflamm*. 2019; 6(4):e580; 2. Delgado-Garcia G, et al. *Front Neurol*. 2022;13:966428.

Avoiding NMOSD misdiagnosis

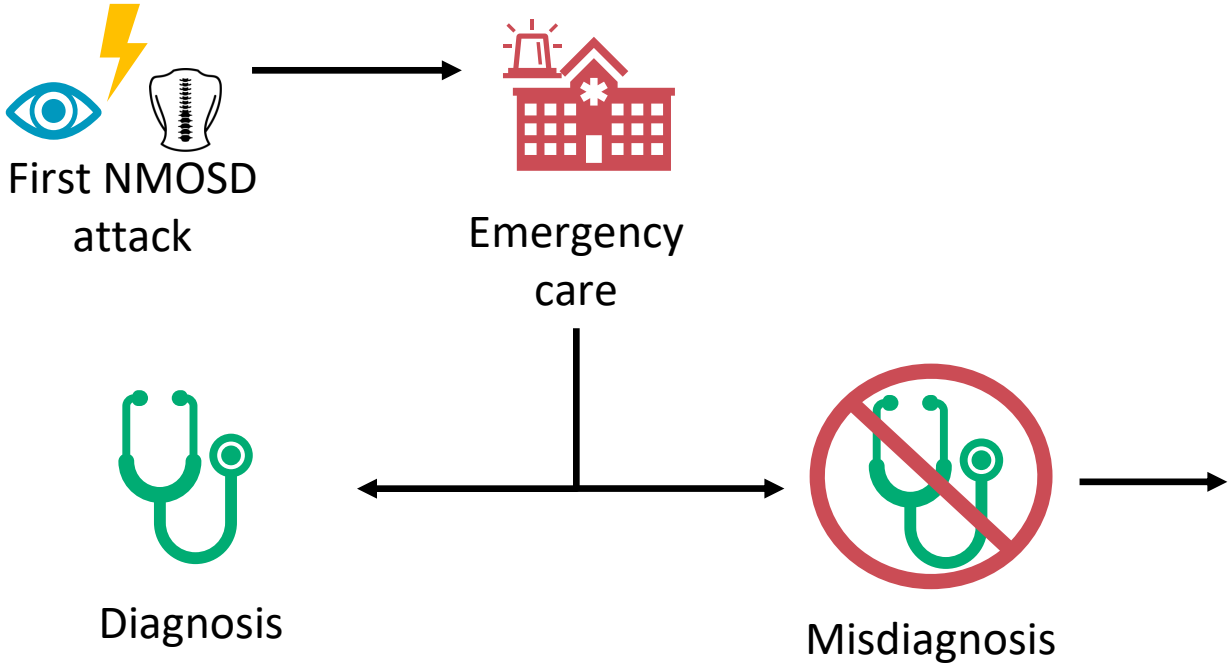


AQP4; aquaporin-4; IgG. Immunoglobulin-G; MRI, magnetic resonance imaging; NMOSD, neuromyelitis optica spectrum disorder.

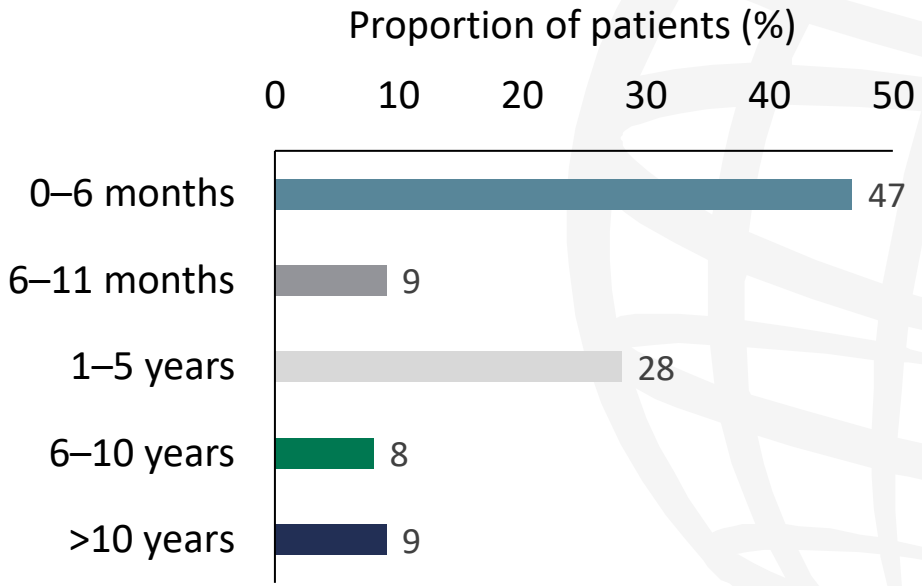
[a]Includes optic neuritis, acute myelitis, postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions and symptomatic cerebral syndrome with NMOSD-typical brain lesions; [b]≥1 characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome; additional MRI requirements should also be fulfilled.

1. Wingerchuk DM, et al. *Neurology.* 2015;85(2):177-89; 2. Jarius S, et al. *J Neurol.* 2023;270(7):3341-68; 3. Delgado-Garcia G, et al. *Front Neurol.* 2022;13:966428; 4. Carnero Contentti E, et al. *Mult Scler Relat Disord.* 2022;58:103466; 5. Khalilidehkordi E, et al. *Front Neurol.* 2020;11:537.

The patient journey from diagnosis



Diagnostic delay:
Time from first symptom onset to diagnosis[1]

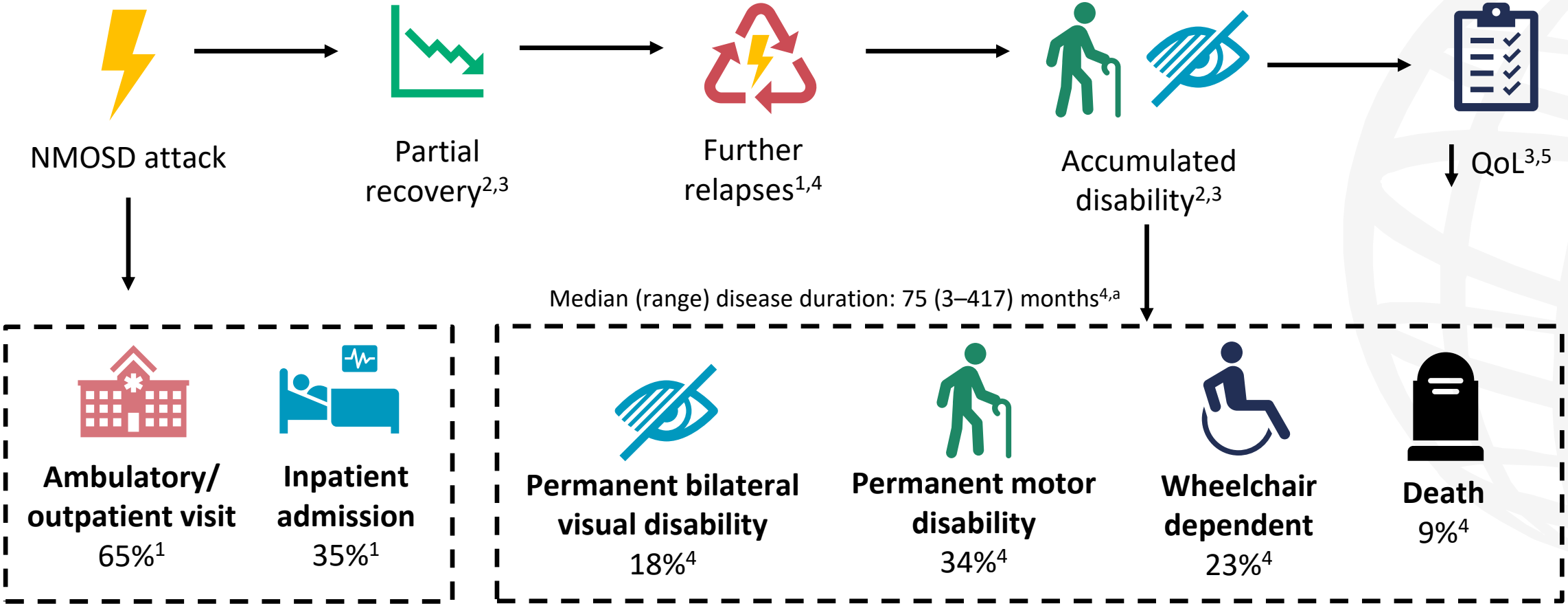


Misdiagnosis, particularly due to lack of MRI is an important factor in diagnostic delays[2]

MRI, magnetic resonance imaging; NMOSD, neuromyelitis optica spectrum disorder.

1. Delgado-Garcia G, et al. *Front Neurol.* 2022;13:966428; 2. Smith AD, et al. *Mult Scler Relat Disord.* 2023;70:104498.

Impact of a delayed diagnosis

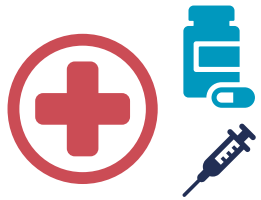


aAll patients were AQP4 seropositive.

AQP4; aquaporin-4; NMOSD, neuromyelitis optica spectrum disorder; QoL, quality of life.

1. Royston M, et al. *Neurol Ther.* 2021;10(2):767-783; 2. Wingerchuk DM, et al. *Neurology*. 1999;53(5):1107-14; 3. Berthele A, et al. *Front Neurol*. 2023;14:1099376; 4. Kitley J, et al. *Brain*. 2012;135(Pt 6):1834-49; 5. Qian P, et al. *Arch Neurol*. 2012; 69(11):1482-7.

Implications of a NMOSD diagnosis



An early correct diagnosis allows for appropriate treatment selection[1]

Appropriate treatment may reduce potential for relapse (80–90% of patients relapse in 1–3 years of an initial episode)[2]

As recovery from NMOSD attacks if often only partial,[2,3] NMOSD requires early intervention to avoid further relapses

NMOSD, neuromyelitis optica spectrum disorder.

1. Smith AD, et al. *Mult Scler Relat Disord.* 2023;70:104498; 2. Wingerchuk DM, et al. *Neurology*. 1999;53(5):1107-14; 3. Berthele A, et al. *Front Neurol*. 2023;14:1099376.

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