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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. *Lancet Neurol* 2023; published online Jan 24. https://doi.org/10.1016/S1474-4422(22)00431-8.

Supplementary material

Supplementary Table 1: Frequency of bilateral and unilateral optic neuritis in patients with MOG-IgG

Reference	ON as presenting phenotype vs any ON event	Age demographic	Bilateral	Unilateral
Ramanathan S, Reddel SW, Henderson A, et al. Antibodies to myelin oligodendrocyte glycoprotein in bilateral and recurrent optic neuritis. *Neurology neuroimmunology & neuroinflammation* 2014; **1**(4): e40.	Presenting phenotype as ON	All adults	8/9 (89%)	
Ramanathan S, Prelog K, Barnes EH, et al. Radiological differentiation of optic neuritis with myelin oligodendrocyte glycoprotein antibodies, aquaporin-4 antibodies, and multiple sclerosis. *Mult Scler* 2016; **22**(4): 470-82.	Presenting phenotype as ON in 18/19 (95%)	Adults and children	16/19 (84%)	
Ramanathan S, Mohammad S, Tantsis E, et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. *J Neurol Neurosurg Psychiatry* 2018; **89**(2): 127-37.	Presenting phenotype as ON	26 adults, 33 children	8/33 children (24%) 11/26 adults (42%) 19/50 total (32%)	5/33 children (15%) 8/26 adults (31%) 13/59 total (22%)
Chen JJ, Flanagan EP, Jitprapaikulsan J, et al. Myelin Oligodendrocyte Glycoprotein Antibody-Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues, and Outcome. *Am J Ophthalmol* 2018; **195**: 8-15	Any ON event	Both adults and children but breakdown not clear with respect to clinical phenotype - median age at neurologic symptom onset was 31 years (range 2–79 years), with 66% older than 18 years.	32/86 (37%)	
Giacomini et al. Pediatric optic neuritis and anti MOG antibodies: a cohort of Italian patientsMult Scler Relat Disord. 2019 Dec 24;39:101917	Presenting phenotype as ON	22 children	4/10 (40%)	
Ducloyer et al. MOG-Ab prevalence in optic neuritis and clinical predictive factors for diagnosis.Br J Ophthalmol. 2020 Jun;104(6):842-845.	Any ON event	9 adults	4/9 (44%)	
Padungkiatsagul et al. Differences in Clinical Features of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Optic Neuritis in White and Asian Race Am J Ophthalmol . 2020 Nov;219:332-340.	Any ON event	Adults	61/146 (42%)	

Yang et al. Clinical predictive factors for diagnosis of MOG-IgG and AQP4-IgG related paediatric optic neuritis: a Chinese cohort study Br J Ophthalmol. 2020 Nov 16;bjophthalmol-2020-317524.	Presenting phenotype as ON	33 children	19/33 (58%)	
Shor N, Aboab J, Maillart E, et al. Clinical, imaging and follow-up study of optic neuritis associated with myelin oligodendrocyte glycoprotein antibody: a multicentre study of 62 adult patients. *European Journal of Neurology* 2020; **27**(2): 384-91.	Any ON event	62 adults	26/62 (42%)	
Zhao Y, Tan S, Chan TCY, et al. Clinical features of demyelinating optic neuritis with seropositive myelin oligodendrocyte glycoprotein antibody in Chinese patients. *Br J Ophthalmol* 2018; **102**(10): 1372-7.	Presenting phenotype as ON	Adults vs paeds cut off not clear	Clinically bilateral 9/20 (45%); radiologically bilateral 14/20 (70%)	
Biotti D, Bonneville F, Tournaire E, et al. Optic neuritis in patients with anti-MOG antibodies spectrum disorder: MRI and clinical features from a large multicentric cohort in France. *Journal of Neurology* 2017; **264**(10): 2173-5.	All ON events	Do not specify – mean age 37, unclear if any had paediatric onset	19/47 (40%)	
Eyre M, Hameed A, Wright S, et al. Retinal nerve fibre layer thinning is associated with worse visual outcome after optic neuritis in children with a relapsing demyelinating syndrome. *Dev Med Child Neurol* 2018; **60**(12): 1244-50.	All ON events	16 children	9/16 (56%)	
Stiebel-Kalish H, Lotan I, Brody J, et al. Retinal Nerve Fiber Layer May Be Better Preserved in MOG-IgG versus AQP4-IgG Optic Neuritis: A Cohort Study. *PLoS One* 2017; **12**(1): e0170847.	All ON events	6 adults	3/6 (50%)	

Supplementary Table 2: Comparison of the relative frequency of key clinical and MRI features of optic nerve involvement in MOGAD, AQP4-IgG seropositive NMOSD and MS

ON Features		MOGAD	AQP4-IgG NMOSD	MS
Simultaneous bilateral involvement[1-13]		Frequent*	May be present	Infrequent
Optic disc swelling on fundoscopy[1,2,4,5,9-12,14-17]		Extremely frequent	May be present	May be present
Severe optic disc swelling +/- haemorrhages		Frequent	Infrequent***	Extremely rare
Severe visual acuity deficit at onset: <20/200 (Snellen) or <6/60 (metric equivalent)[16,18]		Frequent	Frequent	Infrequent
Radiologically visible optic nerve head swelling[2]		May be present	Infrequent	Extremely rare
Longitudinally extensive optic nerve involvement[$2,4,9,14,17,19]		Frequent-Extremely frequent	Frequent	Extremely rare
Optic nerve lesion location[2,4,6,9,14,17,20,21]	Orbital	Longitudinally extensive Frequent-Extremely frequent	Frequent	Focal involvement Frequent
	Canalicular	Frequent	Frequent	Focal involvement Infrequent
	Intracranial	Frequent	Frequent	Focal involvement May be present
Optic nerve T2 hyperintensity[2,4,17,19,22,23]		Extremely frequent	Extremely frequent	Extremely frequent
Optic nerve gadolinium enhancement[2,4,17,19,22]		Extremely frequent	Extremely frequent	Extremely frequent
Optic nerve oedematous appearance		Extremely frequent	Extremely frequent	May be present
Optic sheath involvement[4,8,9,12,18,19,22-24]		May be present	Extremely rare	Not reported
Chiasmal involvement[2,4,14,17,19]		Infrequent and when present, is often a result of extension of a longitudinally extensive optic nerve lesion	May be present; can be present in isolation	Extremely rare
Optic tract involvement[2,14,17,19]		Extremely rare	Infrequent	Extremely rare

Legend: Not reported; Extremely rare: <5%; Infrequent: 5-20%; May be present: 21-50%; Frequent: 50-80%; Extremely frequent: >80%. Frequency of features for optic nerve and spinal cord involvement refers to patients presenting with ON or myelitis, respectively. [$] >50% of optic nerve length. *** Expert opinion

Supplementary Table 3: Comparative features of spinal cord involvement in MOGAD, AQP4-IgG seropositive NMOSD and MS

Features	MOGAD	AQP4+NMOSD	MS
Clinical features			
Simultaneous clinical/MRI brain or optic nerve involvement during myelitis [18,25-28]	May be present/Frequent	Infrequent	Extremely frequent
Typical severity at nadir[26,27,29]	Moderate to severe	Severe	Mild to moderate
Acute attack-related severe bladder dysfunction [27]	Frequent	Frequent	Infrequent
Typical motor recovery[26,27,29,30]	Very good	Moderate to poor	Very good
Residual severe bladder dysfunction despite good motor function[26,27,29,31]	May be present	Infrequent	Infrequent
Painful tonic spasms***[32,33]	Extremely rare	May be present	Infrequent
Progressive myelopathy[34-36]	Not reported	Not reported	May be present/frequent; occurs during progressive phase
MRI findings			
Sagittal Extension of T2-lesion during acute phase (LETM, ≥3 vertebral segments; short, <3 vertebral segments)[6,25-27,29,37-41]	LETM: Frequent/ extremely frequent; Short lesions: may be present	LETM: Extremely frequent; Short lesions: Infrequent	Short lesions: Extremely frequent; LETM: extremely rare in adults, and children and may reflect coalescence of lesions
Multiple lesions[26,27,29]	May be present	Infrequent	Frequent
Spinal location[26,27,29]	Cervical-thoracic-lumbar	Cervical-thoracic	Cervical > thoracic region
Conus involvement [26,27,29,39,40,42]	Frequent	Infrequent	Infrequent
T2 signal features and degree of swelling[26,27,29,43]	Hyperintense signal, often ill-defined borders; Cord swelling may be present	Hyperintense signal; Longitudinal cord swelling frequent/may be present	Focal well-defined hyperintense signal; Focal cord swelling may be present
Axial Distribution of T2 lesion[6,26,27,29,38,41,44-46]	Frequent central (Grey & white matter) involvement; Lesion restricted to grey matter forming a H-sign may be present	Frequent central cord involvement (grey matter and white matter); Lesion restricted to grey matter forming a H-sign occurs infrequently	Frequent peripherally located (wedge-shaped, dorsal/lateral columns often involved)
Axial brighter spotty lesions[47]	Extremely rare	May be present	Extremely rare
Enhancement[26,48]	Lesion enhancement may be present/frequent; No clear pattern; leptomeningeal enhancement may be present	Lesion enhancement frequent; Irregular, patchy pattern frequent; ring or lens-shaped pattern may be present	Lesion enhancement frequent; Variable pattern; ring pattern may be present
T2 lesion resolution after treatment[27,45,49,50]	Frequent	Infrequent	Infrequent

Legend: Not reported; Extremely rare: <5%; Infrequent: 5-20%; May be present: 21-50%; Frequent: 50-80%; Extremely frequent: >80%. Frequency of features for optic nerve and spinal cord involvement refers to patients presenting with ON or myelitis, respectively. *** Expert opinion for MOGAD

Supplementary Table 4: Comparative features of brain involvement in MOGAD, AQP4-IgG seropositive NMOSD and MS

COMPARATIVE FEATURES OF BRAIN INVOLVEMENT			
Clinical features	**MOGAD**	**AQP4+ NMOSD**	**MS**
ADEM[1,2]	Frequent in children Extremely rare in adults	Extremely rare	Infrequent in children Extremely rare in adults
Diencephalic syndrome/ narcolepsy[3,4]	Not reported	May be present	Not reported
Cerebral cortex encephalitis with seizures/status epilepticus[5,6]	Infrequent	Not reported	Not reported
Brainstem/cerebellar syndrome			
Area postrema syndrome[7]	Extremely rare/infrequent	May be present/frequent	Not reported
Oculomotor, facial palsy, facial numbness, ataxia[8,9]	May be present	May be present	Frequent/extremely frequent
MRI findings			
General findings	Multifocal large T2 hyperintense WM lesions Brain MRI may be normal associated with ON or myelitis	Brain MRI may be normal associated with ON or myelitis	Multifocal T2 hyperintense WM lesions
Lesion appearance	Fluffy/poorly demarcated [10] Only well-defined lesions are infrequent Leukodystrophy-like pattern[5,11]	Large tumefactive[12,13] Linear shape in medulla Linear along corticospinal tracts	Ovoid/round, well-demarcated[13,14] Dawson´s fingers S-shaped U-fibre lesions Central venule sign Smouldering/slowly evolving lesions
Lesion location	Deep/subcortical brain WM[10,15] Deep GM (thalami, basal ganglia)[16] Cortical GM in encephalitis[5,6] Brainstem and cerebellum/ middle cerebellar peduncles[17]	Periependymal lining surrounding the ventricular system[12,13] Area Postrema Diencephalic lesions surrounding third ventricle[12,13]	Periventricular WM[13,14] Juxtacortical Corpus callosum Brainstem and middle cerebellar peduncles[13,14] Inferior temporal lobe WM
Enhancement	Nonspecific, leptomeningeal around brainstem[16,17] Uni- or bilateral cortical (linear) leptomeningeal enhancement (with cerebral cortical encephalitis)[5,6]	Patchy, “cloud-like” lesion enhancement pattern Pencil-thin pattern of the ependymal surface of lateral ventricles[12,13,]	Ovoid, ring/open-ring lesion enhancement pattern[14]
Evolution of brain lesions over time	Partial or complete resolution of T2 lesions Residual T1 hypointense lesions extremely rare[18]	Resolution of T2 lesions may be present Residual T1 hypointense lesions may be present[18]	Accrual of clinically silent T2 lesions Residual T1 hypointense lesions[14,18]
COMPARATIVE FEATURES OF BRAIN INVOLVEMENT			
Clinical features	**MOGAD**	**AQP4+ NMOSD**	**MS**
ADEM[51,52]	Frequent in children Extremely rare in adults	Extremely rare	Infrequent in children and rare in teenagers Extremely rare in adults
Diencephalic syndrome/ narcolepsy[53,54]	Not reported	May be present	Not reported
Cerebral cortex encephalitis with seizures/status epilepticus[37,55]	Infrequent	Not reported	Not reported
Brainstem/cerebellar syndrome			
Area postrema syndrome[56]	Extremely rare/infrequent	May be present/frequent	Not reported
Oculomotor, facial palsy, facial numbness, ataxia[57,58]	May be present	May be present	Frequent/extremely frequent
MRI findings			
General findings	Multifocal large T2 hyperintense WM lesions Brain MRI may be normal associated with ON or myelitis	Brain MRI may be normal associated with ON or myelitis	Multifocal T2 hyperintense WM lesions

Lesion appearance	Fluffy/poorly demarcated [59] Only well-defined lesions are infrequent Leukodystrophy-like pattern[37,60]	Large tumefactive[61,62] Linear shape in medulla Linear along corticospinal tracts	Ovoid/round, well-demarcated[62,63] Dawson´s fingers S-shaped U-fibre lesions Central venule sign Smouldering/slowly evolving lesions
Lesion location	Deep/subcortical brain WM[59,64] Deep GM (thalami, basal ganglia)[65] Cortical GM in encephalitis[37,55] Brainstem and cerebellum/ middle cerebellar peduncles[66]	Periependymal lining surrounding the ventricular system[61,62] Area Postrema Diencephalic lesions surrounding third ventricle[61,62]	Periventricular WM[62,63] Juxtacortical Corpus callosum Brainstem and middle cerebellar peduncles[62,63] Inferior temporal lobe WM
Enhancement	Nonspecific, leptomeningeal around brainstem[65,66] Uni- or bilateral cortical (linear) leptomeningeal enhancement (with cerebral cortical encephalitis)[37,55]	Patchy, “cloud-like” lesion enhancement pattern Pencil-thin pattern of the ependymal surface of lateral ventricles[61,62]	Ovoid, ring/open-ring lesion enhancement pattern[63]
Evolution of brain lesions over time	Partial or complete resolution of T2 lesions[25] Residual T1 hypointense lesions extremely rare[49]	Resolution of T2 lesions may be present Residual T1 hypointense lesions may be present[49]	Accrual of clinically silent T2 lesions[63] Residual T1 hypointense lesions[49,63]

Abbreviations: ADEM, acute disseminated encephalomyelitis; AQP4+NMOSD, aquaporin-4 IgG antibody positive neuromyelitis optica spectrum disorder; GM, grey matter; LV, lateral ventricle; MOGAD, myelin oligodendrocyte glycoprotein antibody-associated disease; MRI, magnetic resonance imaging; MS, multiple sclerosis; PRES, posterior reversible encephalopathy; WM, white matter;
Definition of Frequencies: Not reported; Extremely rare: <5%; Infrequent: 5-20%; May be present: 21-50%; Frequent: 50-80%; Extremely frequent: >80%.

* The limited available data indicates that smoldering lesions are absent in MOGAD and AQP4-IgG seropositive NMOSD[67,68]

Supplementary Table 5: Comparison between serum MOG-IgG cell-based assays

Live or fixed CBA[a]	Instrumentation	Secondary Ab	Serum dilution	Machine quantification or visual scoring	Positivity cut-off	Low Positive range	Provision of diagnostic results: yes/no	Provision of titres yes/no/ upon request	MOG-IgG results included in diagnostic report	Need of core/supporting criteria for MOGAD diagnostic[b]	Provider[c]	Ref.
Europe												
Live	Microscopy[d]	IgG-(H+L), IgG-Fcγ, IgG1	Single dilution (1:20)	Visual scoring	≥1	1-1.5 (score)	yes	upon request	Negative, low positive, and positive[e]	Low positive (score 1-1.5): core and supporting Positive (score ≥2): core only	University of Oxford (UK)	69
Live	Microscopy	IgG-(H+L), IgG-Fcγ	end-point dilution	Visual scoring	1:160	1:160-1:320 (dilution)	yes	yes	Negative, Positive with end titre	1:160 - <1:320: core and supporting ≥1:640: core only	Medical University of Innsbruck (Austria), University of Verona (Italy), University of Kiel (Germany, Medical University Vienna (Austria)	50,70-72
Live	Microscopy	IgG-Fcγ	Multiple dilution (1:160-1:320)	Visual scoring	≥1:160	1:160-<1:320 (dilution)	yes	upon request	Negative, low positive, positive	Low positive (1:160-<1:320): core and supportive Positive (≥1:320): core only	Hospital Clinic of the University of Barcelona (Spain)	50,73,74
Live	Microscopy	IgG-Fcγ	end-point dilution	Visual scoring	>1:160	1:160-1:320 (dilution)	yes	yes	Negative, Positive with end titre	1:160 - <1:320: core and supporting ≥1:320: core only	Mondino National Institute of Neurology Foundation (Italy)	75
Live	Flow cytometry	IgG (H+L)	Single dilution (1:200)	Flow fluorescence intensity	>Mean controls + 10SD	ND	yes	no	Negative, Low positive and high positive	Low positive: core and supporting High positive: core only	Sanquin Diagnostics (Netherlands)	76
Fixed[f, g]	Microscopy	IgG-Fcγ	Single dilution (1:10)	Visual scoring or imaging systems	≥1	≥1 (score)	yes	upon request	Negative, Positive[g]	Positive (1:10 and score ≥1): core and supporting Result at ≥1:100 would need to be requested and if positive: core only	University Hospital of Lyon (France)	77,78

Live[g]	Flow cytometry	IgG-Fcγ	Single dilution (1:640)	Flow fluorescence intensity	>1:640	ND	yes	upon request	Negative, Positive[g]	Positive (≥1:640): core only	University Hospital of Lyon (France)	[77,78]
Live	Flow cytometry	IgG (H+L)	Single dilution (1:50)	Flow fluorescence intensity	ND	ND	no	NA	NA	NA	Ludwig-Maximilians Univerisity (Germany)	[79]
Live	Flow cytometry	IgG (H+L)	Single dilution (1:50)	Flow fluorescence intensity	FACS ratio >1.45	ND	no	NA	NA	NA	University of Basel (Switzerland)	[80]
Fixed[f]	Microscopy	IgG-Fcγ	Single dilution (1:10)	Visual scoring or imaging systems	≥1	≥1 (score)	yes	yes	Negative, Positive with end titre	Positive (from 1:10 to <1:100 and score ≥1): core and supporting Result at ≥1:100 and score ≥ 1: core only	Euroimmu(Germany), University of Heidelberg (Germany)	[71,81,82]
Asia Pacific												
Live[h]	Microscopy	IgG (H+L), IgG-Fcγ	Single dilution (1:20)	Visual scoring	≥1	1 (score)	yes[h]	upon request	Negative, Borderline[i], Positive with visual scoring	Low positive (score 1): core and supporting Positive (score ≥2): core only	National Cancer Center (South Korea)	[83]
Live[h]	Flow cytometry	IgG (H+L), IgG-Fcγ	Single dilution (1:40)	Flow fluorescence intensity	FACS ratio >3.4	3.4-6.8 (FACS ratio)	no[h]	upon request	Negative, Borderline[i], Positive with FACS ratio	Low positive (ratio 3.4 - <6.8): core and supporting Positive (ratio ≥6.8): core only	National Cancer Center (South Korea)	[83]
Live	Flow cytometry	IgG1	ND	Flow fluorescence intensity	FACS ratio >3.65	ND	yes	NA	Negative, Borderline[i], Positive	Positive (ratio >3.65): core and supporting	Eone Laboratories (South Korea)	[83]
Live	Flow cytometry	IgG (H+L)	Single dilution (1:50)	Flow fluorescence intensity	>Mean controls +4SD	1-1.5 (FACS ratio)	yes	yes	Negative, Low positive, Clear positive and interpretative comment	Low positive (ratio 1-1.5): core and supporting Clear positive (ratio >1.5): core only	University of Sydney (Australia), the Children's Hospital at Westmead (Australia), New South Wales Health Pathology-Westmead (Australia)	[84-86]
Live	Microscopy	IgG-Fcγ IgG1	Single dilutions (1:128, IgG-Fcγ) and (1:16, IgG1)	Visual scoring	1:128 (IgG-Fcγ) 1:16 (IgG1)	ND	yes	upon request	Negative, Positive	IgG-Fcγ Positive (≥ 1:128): core and supporting	Tohoku University (Japan)	[40]

										IgG1 Positive (≥1:16): core and supportive		
Live	Microscopy	IgG1	Single dilution (1:16)	Visual scoring	1:16	ND	yes	no	Negative, Positive	Positive (≥ 1:16): core and supportive	Cosmic Corporation Co., Ltd. (Japan)	[40]
Fixed[f]	Microscopy	IgG-Fcγ	Single dilution (1:10)	Visual scoring or imaging systems	≥1	ND	yes	ND	Negative, Positive	Positive (1:10 score ≥1): core and supporting Result at ≥1:100 would need to be requested and if positive: core only	Douglas Hanly Moir (Australia), Pathology Queensland (Australia), Sullivan Nicolaides Pathology (Australia), EuroImmun (Japan)[h], EuroImmun (Korea)[h]	NA
Americas												
Live	Flow cytometry	IgG1	end-point dilution	Flow fluorescence intensity	≥1:20 and FACS ratio ≥2.5	1:20-1:40 (dilution)	yes	yes	Negative, Positive with end titre and interpretative comment	Low positive (from 1:20 to 1:40): core and supporting Clear positive (≥1:100): core only	Mayo Clinic (USA)	[87-89]
Live	Flow cytometry	IgG (H+L)	Single dilution (1:50)	Flow fluorescence intensity	FACS ratio >5	ND	no	NA	NA	NA	Harvard University (USA)	[90]
Live	Flow cytometry	IgG-Fcγ	Single dilution (1:100)	Flow fluorescence intensity	FACS ratio >2.07	ND	yes	yes	Negative, Positive	Positive ratio (>2.07): core only	Pontifícia Universidade Católica do Rio Grande do Sul (Brazil)	[91]
Live	Microscopy	IgG1 and IgG-Fcγ	Single dilution (1:20 for IgG1 and 1:200 for IgG-Fcγ)	Visual scoring	≥1	1 (score)	yes	upon request[k]	Negative, borderline[i], low positive, and positive	Low positive (score 1): core and supporting Positive (score ≥1): core only	BCNeuroimmunology (Canada)	NA[l]
Fixed[f]	Microscopy	IgG-Fcγ	Single dilution (1:10)	Visual scoring or imaging systems	≥1	ND	yes	upon request[k]	Negative, Positive	Positive (1:10 score ≥ 1): core and supporting Result at ≥1:100 would need to be requested and if positive: core only	ARUP (USA), Athena (USA), Labcorp, Quest (USA), MitogenDX (Canada)	NA

CBA = cell-based assay. Ab=antibody. IgG (H+L) = Immunoglobulin G (heavy + Light). IgG-Fcγ = Immunoglobulin G Fragment crystallizable γ. IgG1=Immunoglobulin G1. NA= not applicable. ND = not determined. SD = standard deviation.

[a] While some providers are required to clearly state the exact type of CBA used to provide MOG-IgG diagnostic results, detailed information may be difficult to find for some others. See Panel 1 for recommendations. [b] Core and supporting criteria are described in Figure 2. [c] Test accreditations vary according to regions. See Panel 1 for recommendations. [d] Microscopy CBA may be referred to immunofluorescence (IF) by some providers. [e] A composite result of IgG1 and IgG-Fcγ testing is reported. [f] Based on Euroimmun commercial biochips. [g] Testing algorithm: samples are routinely tested by fixed CBA. All positive samples tested by fixed CBA are validated by live CBA. Samples tested negative by fixed CBA but with known clinical picture suggestive of MOGAD are further tested by live CBA. Reports include results from fixed and live CBA. [h] Flow cytometry CBA is used to confirmed microscopy assay with equivocal result. [i] The term "borderline" refers to the need of a repeated testing if MOGAD is clinically suspicious. [j] Commercial biochips are distributed and sold by Euroimmun without provision of a diagnostic testing service. [k] Additional charges may apply to obtain end titre. [l] Validation data may be obtained upon request.

Supplementary Table 6: Differential diagnoses of MOGAD

OPTIC NERVE INVOLVEMENT		
A-CLINICAL SIGNS	**ADDITIONAL FEATURES**	**ALTERNATIVE DIAGNOSES**
Bilateral disc oedema with normal visual acuity	Headaches, transient visual obscurations, pulsatile intracranial noises	Papilloedema due to idiopathic intracranial hypertension, venous sinus thrombosis, or CNS inflammation[92]
Bilateral disc oedema with mild visual acuity loss	Mild vitritis, encephalitis, meningoencephalitis, seizure, perivascular radial enhancement on brain MRI	GFAP-IgG associated disorder[92,93]
Unilateral or bilateral disc oedema with moderate vision loss	Vitritis, retinitis, iritis, macular exudates	CRMP5 paraneoplastic optic neuropathy[92,94]
Subacute painless vision loss	Macular star, viral prodrome, cat scratch disease	Neuroretinitis due to *Bartonella Henselae* or other infection[92]
Acute, subacute, or chronic vision loss with or without pain	Disc oedema, retinitis, episcleritis, uveitis, meningitis, cranial nerve palsies, encephalitis	Syphilis[92]
Subacute vision loss with disc edema	Periphlebitis, uveitis, vitritis, episcleritis	Neurosarcoidosis[92,95,96]
Subacute vision loss with orbital disease	Proptosis, ocular dysmotility, orbital inflammation, hypertrophic pachymeningitis on MRI	IgG4-related disease[92,97]
Subacute vision loss with sinus disease	Scleritis, conjunctivitis, vasculitis, orbital inflammation	Granulomatosis with polyangiitis[92]
Acute or subacute vision loss with dry eye syndrome	Xerostomia, pancreatitis, dental disease	Sjögren syndrome[92]
Acute or subacute vision loss with skin rash	Myalgia, arthralgia, erythema migrans, disc oedema, neuroretinitis	Lyme Disease[92]
Acute or subacute vision loss with facial rash	Chorioretinitis, retinal necrosis, fever, lymphadenopathy	Zoster ophthalmicus[92]
Acute or subacute vision loss with ocular dysmotility	Uveitis, orbital apex syndrome, meningitis, sinus or pulmonary disease	Tuberculosis, aspergillosis, mucormycosis[92]
Acute or subacute vision loss with oral or genital ulcers	Uveitis, papulopustular lesions, erythema nodosum, articular and gastrointestinal involvement	Behçet Disease[92,98]
B- MRI FINDINGS	**ADDITIONAL FEATURES**	**ALTERNATIVE DIAGNOSES**
Linear radial perivascular enhancement	meningitis, leptomeningeal or ependymal enhancement	GFAP-IgG associated disorder [92,93]
Leptomeningeal enhancement	Assorted white matter lesions: brainstem, cerebral white matter, basal ganglia, internal capsule, thalamus and spinal cord	Behçet Disease[92,98]
	Inflammation and enlargement of pituitary gland (hypophysitis), visual field defect, decreased visual acuity	IgG4-related disease[92,97]
Optic nerve and optic sheath enhancement	Orbital apex inflammation, leptomeningeal lesion, pituitary and hypothalamic lesions	Neurosarcoidosis[92,95,96]
	Orbital cellulitis, orbital mass, orbital inflammation, pachymeningitis	Granulomatosis with polyangiitis[92]
	Orbital inflammation and myositis	Idiopathic orbital inflammatory syndrome[92]
	Orbital fat enhancement, leptomeningeal enhancement, myelitis	Syphilis[92]
	Orbital tuberculoma, dacryoadenitis, ependymitis, leptomeningeal enhancement	Tuberculosis[92]
Bilateral optic nerve enhancement	Cerebellar atrophy, myelitis (LETM), temporal lobe lesions	CRMP-5 optic neuropathy[92,94]
BRAIN INVOLVEMENT		

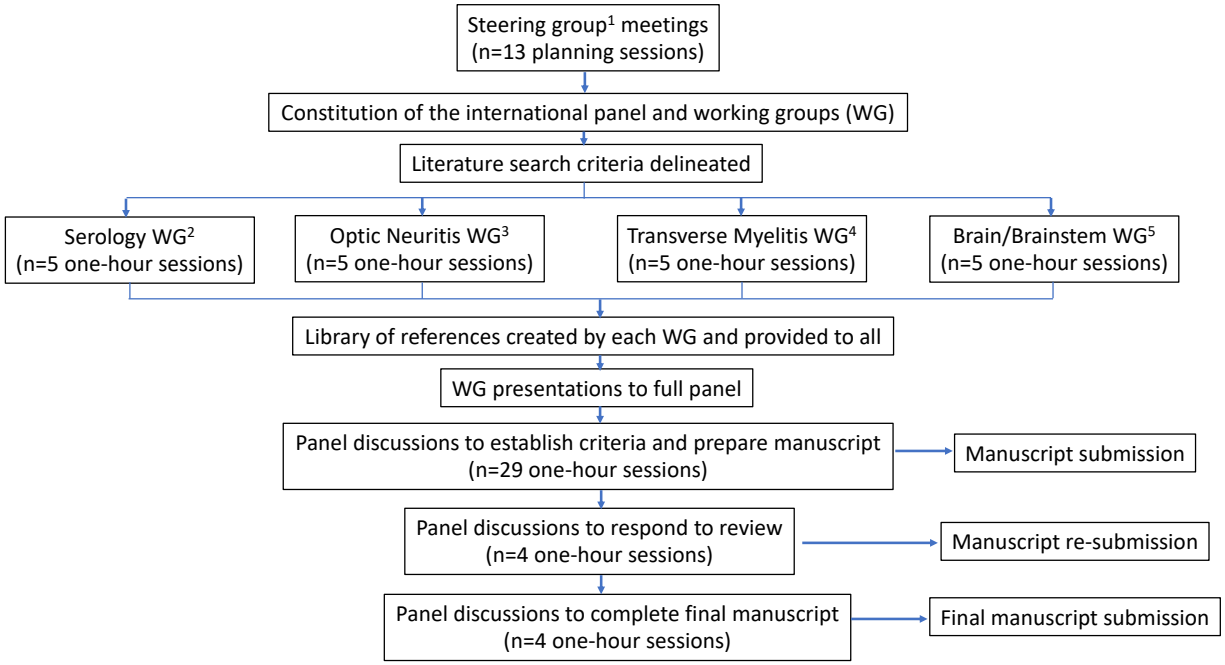
A- CLINICAL SIGNS	ADDITIONAL FEATURES	ALTERNATIVE DIAGNOSES
Acute onset encephalopathy with persistent fever	Constitutional symptoms, meningeal signs, seizures, and focal neurological deficits	CNS Infection[99]
Acute/subacute encephalopathy with orofacial dyskinesias	Other movement disorders, seizures	NMDAR antibody associated encephalitis[100]
Acute or subacute encephalopathy with cranial neuropathies	VII or VIII cranial nerve involvement	Neurosarcoidosis[95] CNS infection[99]
Acute/subacute encephalopathy with seizures and movement disorders	EEG with epileptiform discharges, cortical GM + subcortical WM signal changes on MRI	$GABA_A$ receptor antibody-associated encephalitis[101] CNS infection[99]
Acute confusional state, psychosis, mood disorder, seizures, chorea	Associated systemic features (malar rash, cytopenia). Brain WM lesions (variable sizes)	Systemic Lupus Erythematosus (SLE)[102]
Acute or subacute encephalopathy, fever, hepato-splenomegaly		Primary or secondary Haemophagocytic Lymphohistiocytosis (HLH)[103]
Severe headaches preceding altered mental status	With focal neurological deficits	CNS vasculitis/ Cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)[102]
	With hearing loss	Susac Syndrome[102,104]
	With papilledema	Intracranial hypertension[102]
	With arterial hypertension	Posterior reversible encephalopathy syndrome (PRES)[102,105,106]
Progressive encephalopathy	Despite anti-inflammatory therapies	Leukodystrophies[102] Mitochondrial diseases[102] CNS malignancy[102]
Acute neurological deficits without encephalopathy		
Acute hemiparesis	Antecedent varicella infection	Focal inflammatory arteriopathy[102]
	Headaches and livedo reticularis	Non-inflammatory thrombotic vasculopathy (Sneddon Syndrome) Other forms of stroke[102]
Acute ataxia	Normal MRI, or cerebellar focal or diffuse signal changes	Acute cerebellar ataxia / Cerebellitis[107]
Transient, recurrent events of focal deficits	Antecedent of cranial radiotherapy	Stroke-like migraine attacks after radiation therapy (SMART Syndrome)[108]
Subacute ataxia, oculomotor abnormalities, pseudobulbar affect	Punctate and curvilinear enhancement "peppering" the pons and adjacent rhombencephalic structures	Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS)[109]
B- BRAIN MRI FINDINGS	**ADDITIONAL FEATURES**	**ALTERNATIVE DIAGNOSES**
Normal brain MRI		Autoimmune or infectious viral encephalitis[100,101]
Well-defined T2/FLAIR hyperintense periventricular WM lesions	"Dawson fingers" pattern	Multiple sclerosis[102,110,111]
Well-defined hypointense T1 brain lesions	Supratentorial and/or infratentorial	Chronic disorder (vascular or MS)[102]
Diffuse, symmetric brain WM involvement	Different MRI patterns Progressive clinical course	Genetic disorder/ Leukodystrophies[102]
Microbleeds on Gradient-echo T2 or SWI images, lacunar infarcts, signs of cerebral atrophy		CNS Vasculitis[102] SLE[102] IgG4-related disease[97]
Progressive brain atrophy with persistent signs of inflammation	Signs of hemophagocytosis and cytokine storm Decrease NK cell activity	Primary or secondary HLH[103]
Splenium of corpus callosum involvement on DWI images	Decrease values on ADC images Lesion resolution on follow-up MRI	Mild encephalopathy with reversible splenial lesion (MERS) not associated to ADEM[106]

Cortical GM changes	Cortical leptomeningeal enhancement, cortical DWI restriction Absence of optic nerve or spinal cord involvement	Infectious encephalitis[99] IgG4-related disease[97,112,113]
Subcortical punctate WM lesions	Recurrent headaches	Migraine[102]
Unilateral/ bilateral thalamic necrotizing lesions	Edematous swelling with hemorrhagic changes	Acute necrotizing encephalopathy (ANE)[114] Deep cerebral venous thrombosis[102]
Unilateral brain WM changes		Vascular disorders[102]
Mass-like brain lesions	With calcifications	Brain tumor (astrocytoma, oligodendroglioma)[102]
	Granulomatous non-neoplastic mass lesions, basal infiltration, leptomeningeal enhancement (linear or nodular)	Tuberculous granulomas[102] Neurosarcoidosis[95,102]
	Brainstem, deep GM involvement Oral and genital ulcerations	Behçet disease[102]
	With hypointense component, and homogeneous enhancement	Primary CNS lymphoma[115-117]
Multiple hyperintense callosal lesions (snowballs) on sagittal T2/FLAIR sequences	Hypointense lesions on sagittal T1 (microinfarcts), DWI restriction in the brain WM, internal capsule, corpus callosum	Susac Syndrome[102,118]
Recurrent hyperintense brain lesions with progressive atrophy	Elevated lactate on MRS, bilateral and symmetric basal ganglia/ thalamic involvement	Mitochondrial disorder: Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), *POLG* gene mutation[102,106,111]
Leptomeningeal enhancement	Persistent enhancement despite anti-inflammatory therapy	CNS infection, HLH[103] IgG4-related disease[97,112,113] Neurosarcoidosis/granulomatous disease[95,102]
	Linear or nodular enhancement in brain, cerebellar folia, cranial nerves	Neurosarcoidosis[95,102]
	Cortical gyriform or nodular enhancement Antecedent of cranial radiotherapy	SMART Syndrome[108]
Ring enhancement	Multiple brain lesions (“starry-sky” appearance)	Neurocysticercosis Miliary CNS tuberculosis[102]
	Isolated ring-enhancing lesion with perilesional edema	Histoplasmosis, neurocysticercosis[102,119] Brain abscess
Radial perivascular enhancement		GFAP-IgG associated disorder [92,93,102] Neurosarcoidosis[95,102] Primary CNS lymphoma[115-117] CNS vasculitis[102]
SPINAL CORD INVOLVEMENT		
A- CLINICAL SIGNS	**ADDITIONAL FEATURES**	**ALTERNATIVE DIAGNOSES**
Hyperacute symptom evolution	Less than 4 hours to attack nadir	Spinal cord ischemia / infarction[102,111]
Antecedent of aortic surgery	With an hyperacute evolution	Spinal cord infarction[102,111]
Symptom trigger	Exercise, erect posture Valsalva maneuver, trivial fall	Low-flow spinal AV fistula[120] Fibrocartilaginous embolism[121]
Acute flaccid myelopathy (AFM)	Associated with a cluster of AFM in the region/area Predominant asymmetric upper limb weakness; additional respiratory failure	Infectious myelopathy[122]
Atrophy of hand musculature	Long-lasting spinal cord injury	Compression of cervical spinal cord[122] Hirayama disease[123]
Established diagnosis of cancer		Paraneoplastic myelopathy[122,124]
Progressive myelopathy	Despite anti-inflammatory therapies	Neoplastic or non-neoplastic spinal cord compression[124]

Progressive spastic gait and urinary dysfunction	With severe spinal cord atrophy (medulla and cervical cord)	Juvenile and adult forms of Alexander disease[125]
Associated systemic symptoms	Malar rash, discoid rash, photosensitivity, arthritis, renal disorder, cytopenia	Lupus myelopathy[126]
Associated orogenital ulcerations, uveitis		Behçet's disease[102,111]
B- SPINAL CORD MRI FINDINGS		
Isolated or multiple short and peripheral lesions	Sagittal and axial T2/STIR/PD images	Multiple sclerosis[102,110,111]
Intramedullary oedema with signs of bleeding		Traumatic spinal cord damage[122]
Intramedullary "cystic cavities"	Long-lasting spinal cord injury	Post-traumatic or post-inflammatory changes
Hemorrhagic longitudinal extensive myelitis	Non-traumatic event in an immunocompromised individual	VZV or HSV-2 associated myelitis
"Butterfly-shaped"	Predominant involvement of anterior GM, high signal on T2 and STIR	Infectious myelitis[122]
Pencil-shaped signal involving the anterior spinal cord	Linear restricted diffusion on sagittal DWI images	Spinal cord infarct[111,127]
Hyperintense lesions with owl- or snake-eye pattern on axial T2 (hypointense on axial T1)	Chronic lesions on follow-up images	Infectious myelitis[122] Vascular myelopathy[111,127] Hirayama disease[123] Hopkins syndrome
Spinal cord involvement with dorsal flow voids		Dural AV fistula[120]
"Popcorn"- like lesion	Well-defined, lobulated lesion with central T2 hyperintensity and a T2 hypointense rim, with longitudinally extensive signal extending above and below the lesion	Cavernous malformation
Progressively enlarging lesion	Marked cord expansion with persistent gadolinium enhancement	Spinal cord tumor
No lesion improvement despite anti-inflammatory therapy		Spinal cord tumor, biotinidase or vitamin deficiency[106,128,129]
Cervical cord atrophy and tadpole atrophy of brainstem	Sagittal images: severe atrophy of medulla oblongata with well-preserved pontine base	Juvenile and adult forms of Alexander disease[125]
"Inverted V" sign	T2 high signal abnormality involving spinal dorsal columns (inverted V), less frequent lateral columns	Vitamin B12 or cooper deficiency[106,129]
"Pancake-like Gd enhancement", or "transverse band"	Focal enhancement at the center of a spindle-shaped T2 hyperintensity; width is greater than or equal to its height; axial circumferential enhancement spares GM	Compressive (spondylotic) myelopathy
Linear dorsal subpial enhancement	Extending over multiple segments (≥2 vertebral segments) Persisting enhancement >2 months	Neurosarcoidosis[130]
"Trident sign"	Subpial dorsal + central canal enhancement	Neurosarcoidosis[130]
Nerve root enhancement	With leptomeningeal enhancement With anterior horn GM involvement	Neurosarcoidosis or Infectious myelopathy[122,130]
Bright homogeneous central enhancement		Primary intramedullary lymphoma[115,130]
Patchy enhancement of dorsal veins		Dural AV fistula[120]
Persistent lesion enhancement	Despite anti-inflammatory therapy	Spinal cord tumor Neurosarcoidosis/granulomatous disease

Abbreviations: ADC, apparent diffusion coefficient; AV, arteriovenous; CRMP5, collapsin response mediator protein 5; DWI, diffusion weighted imaging; FLAIR, fluid-attenuated inversion recovery; $GABA_A$, gamma aminobutyric acid-A; GFAP: glial fibrillary acidic protein; GM, grey matter; PD, proton density; STIR, short tau inversion recovery; VZV, varicella zoster virus; WM, white matter

Supplemental Figure 1: International Panel Composition and Work Process

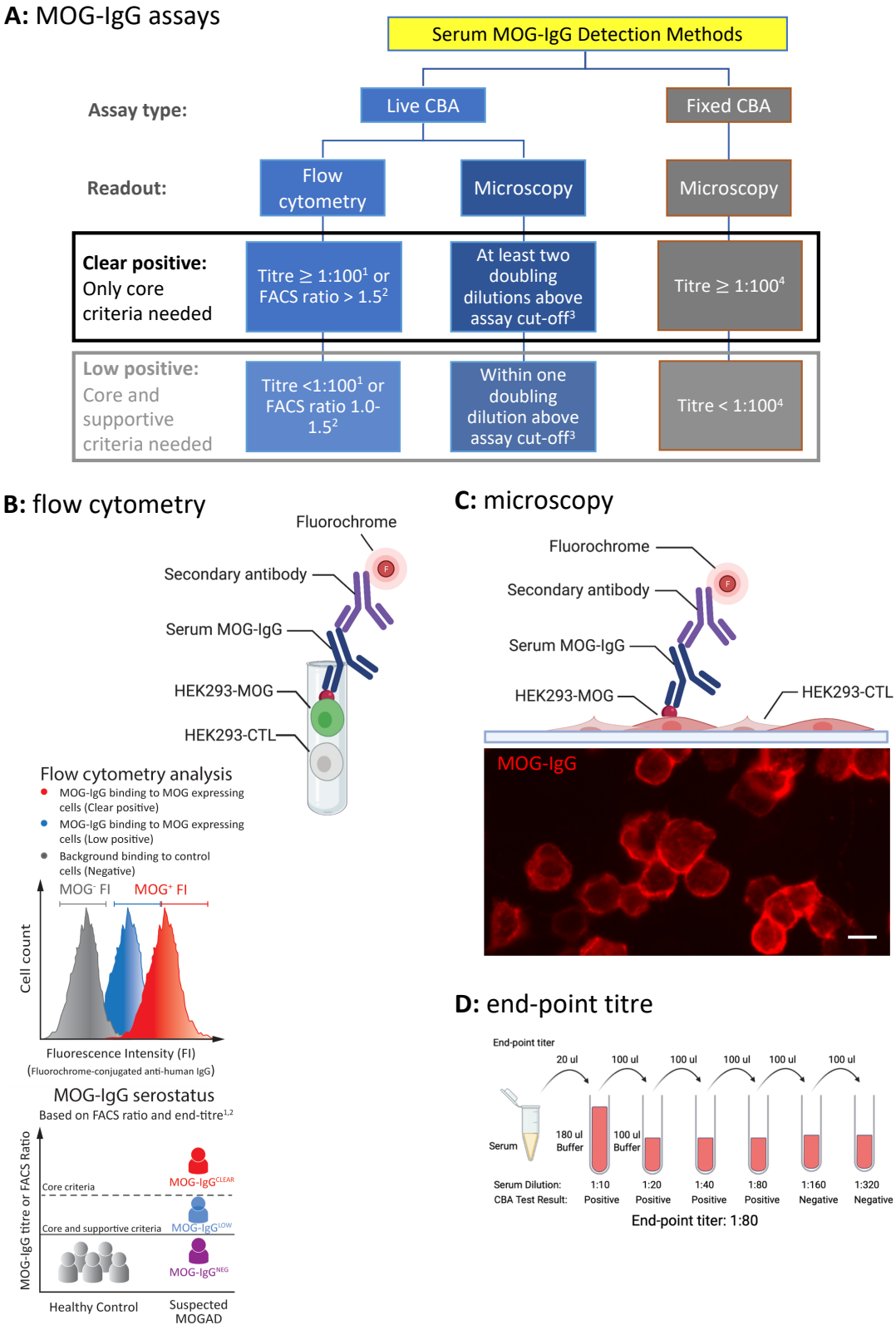


As illustrated, the composition of the international panel was constituted by invitation by the steering group[1] with the intent to create working groups (WGs) focused on key facets of the clinical features, neuroimaging and laboratory testing. Invited panel members were identified by their expertise in paediatric and adult CNS acquired demyelinating disorders and by their leadership roles in organizations or committees dedicated to the field. Panel members were selected to ensure equal gender, representation of both paediatric and adult clinicians and scientists and diverse geographic distribution. Panel members are currently or in the past have served as leaders and board members of ECTRIMS, ACTRIMS, BCTRIMS, PACTRIMS, LACTRIMS, MSIF, IPMSSG and EAN. Panel members were also selected based on their expertise in the creation of diagnostic criteria including the current international diagnostic criteria for multiple sclerosis and NMOSD.[110,131] A number of panel members are lead investigators of national study groups evaluating MOGAD, are principle investigators of funded grants to study MOGAD, and have been invited to lead educational sessions on MOGAD and CNS demyelination nationally and internationally. Panel member also serve as active volunteer representatives or are on the medical advisory boards of patient/carer led organisations including the Guthy Jackson Foundation, The Sumaira Foundation, MOG project, and their local or national patient societies, and sought informal input from these organisations.

A total of 70 meetings occurred between March 19, 2020 and June 30, 2022 (inclusive of 13 meetings of the steering group, an average of five meetings for each of the four working groups to make a total of 20 working group (WG) meetings, and 37 whole group meetings). Initial planning meetings within each WG defined literature search criteria, and a shared reference library was created with key references added by the respective working groups. Each WG presented their data to the full panel for discussion. Weekly meetings of the full panel then occurred over a span of eight months, with each meeting dedicated to creation of the proposed criteria, manuscript text, and to the creation of the Figures, Tables and Supplemental materials. All panel members actively participated in these meetings and provided detailed commentary and edits to the work in progress. Our process included discussions from the full panel on the data presented by each WG, with votes on discussion points and all features of the diagnostic criteria. Any time we achieved less than 80% consensus, we held iterative discussions which led to the final product which was endorsed by 100% of the panel. The Guthy Jackson Foundation provided some funding for this work.

[1]Steering group members (JP, KF, BB, HJK, JB, FP, KR, JB, SJP)
[2]Serology WG (SJP, PW, MR, TC, FB)
[3]Optic neuritis WG (JG, JB, SR, FP, KR, AB)
[4]Transverse myelitis WG (JP, HJK, EF, DS, RN, ST)
[5]Brain/brainstem WG (KF, BB, ST, AS, LP, RM, CH)

Supplementary Figure 2: An overview on MOG-IgG assays



(A) MOG-IgG assay results and their significance according to the proposed MOGAD criteria (Figure 2). **(B)** Detection of MOG-IgG by immunofluorescence with readout quantified by flow cytometry. **(C)** Detection of MOG-IgG by immunofluorescence with readout by fluorescence microscopy which is semi-quantified by end-point titres or visual scoring. **(D)** An example of a semi-quantitative result (titre) determined by end-point titration, the resulting end-point titre in this example is 1:80. Different MOG-IgG assays are available with different cut-offs so the end-point titre result is only informative within the context of a specific test (Supplementary Table 4).

[1] Different methods are used to score MOG-IgG levels by flow cytometry using live cells. For an example at the Mayo Clinic (MN, USA) serum sample are screened at 1:20 and end-point titrated. Samples positive at a dilution of 1:100 or greater are considered clear positive, while those scoring 1:20 to <1:100 are considered low positive.

[2] Binding or FACS ratios (MOG IF+/MOG IF-) such as at the University of Sydney (Australia) or ΔMFI (MOG IF+ - MOG IF-) can also be used to score MOG-IgG by flow cytometry. More details on these quantifications are listed and referenced in Supplementary Table 4.

[3] Live CBAs scored by microscopy are titrated using 2-fold dilutions. Any sample with an end-point titre within one dilution above the assay cut-off is considered low positive, whereas an end-point titre two or more dilutions above are considered clear positive e.g. if a live CBA cut-off is 1:160, such as at the Medical University of Innsbruck (Austria), samples with an end-point titre of 1:160 to 1:320 are considered low positive. Samples scoring 1:640 or higher are considered clear positive. If an assay has a cut-off of 1:20 such as at the University of Oxford (UK), then 1:20-1:40 are low positive and 1:80 or greater are clear positive.

[4] Commercial fixed CBA IF performed in centres providing end-point titres (sample tested at 1:10; titration at 3-fold dilutions, 1:10, 1:32, 1:100, 1:320, 1:1000 or 10-fold dilutions 1:10, 1:100, 1:1000). Other methodologies are listed in Supplementary Table 4.

CBA = cell-based assay, FACS = fluorescent activated cell sorting, FI = fluorescence intensity, IF = immunofluorescence, MFI = median fluorescence intensity. Scale bar: 10 μM.

Figure created with Biorender.com

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