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Review article

NMOSD and MOGAD in Latin America: A consensus-informed regional perspective

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ABSTRACT

Background: Neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are rare autoimmune disorders of the central nervous system whose diagnosis increasingly relies on highly sensitive antibody assays and timely access to targeted therapies. Despite major advances in the diagnosis and management of these disorders worldwide, substantial challenges continue to compromise patient care across Latin America (LATAM).

Methods: This consensus-informed regional perspective was developed as an initiative of the European Charcot Foundation (ECF) Young Investigators/Fellows, following discussions held during the "2025 Update on NMOSD & MOGAD" ECF Meeting in São Paulo/Brazil, and in collaboration with international and Latin American experts. This manuscript synthesizes current evidence on the epidemiology, clinical characteristics, diagnosis, treatment, and healthcare challenges of NMOSD and MOGAD in LATAM, together with a consensus-informed assessment of regional priorities and unmet needs.

Key findings: Recent epidemiological studies have improved understanding of the burden of NMOSD and MOGAD across LATAM. Nevertheless, delayed diagnosis, disease misclassification, unequal access to specialized neuroimmunology services, and considerable variability in antibody testing methodologies remain major barriers to optimal patient management. Although commercial fixed cell-based assays (fixed-CBAs) have become increasingly available throughout the region, access to gold-standard live cell-based assays (live-CBAs) remains

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restricted to a limited number of specialized centers, potentially compromising diagnostic accuracy in some settings. Likewise, despite growing evidence supporting early initiation of highly effective therapies, particularly for AQP4-IgG-positive NMOSD, access to these treatments is limited in many locations, resulting in continued reliance on conventional immunosuppressive agents.

Conclusions: Based on the available evidence and expert consensus, this regional perspective identifies two strategic priorities for advancing the diagnosis and management of NMOSD and MOGAD in LATAM: (I) expanding access to locally performed live-CBA and (II) ensuring equitable access to highly effective emerging therapies. Together, these priorities have the potential to harmonize clinical practice and reduce healthcare disparities across countries. They may also foster regional neuroimmunology collaborations, facilitating the generation of reliable region-specific real-world evidence, ultimately benefiting patients with NMOSD and MOGAD throughout LATAM.

Latin America (LATAM) is characterized by marked ethnic and genetic admixture, reflecting varying contributions from Indigenous American, European, African, and, in some regions, Asian ancestry, alongside important linguistic, cultural, and historical commonalities (Ruiz-Linares et al., 2014). The region spans a vast latitudinal range, extending from the northern border of Mexico with the United States to the southernmost areas of Chilean and Argentinean Patagonia, and includes countries where Spanish and Portuguese are the predominant languages. Recent estimates indicate that LATAM has a population of more than 650 million people, with substantial variation in population size, urbanization, and demographic structure across countries. In this context, populations across the region, and even within the same country, may experience substantial disparities in socioeconomic development, healthcare organization, and access to healthcare services (Costa et al., 2022; Oliveira and Pereira, 2024). These disparities may compromise timely diagnosis and optimal disease management while also limiting the generation of reliable epidemiological evidence.

1. NMOSD and MOGAD within the spectrum of immune-mediated CNS disorders

Immune-mediated disorders of the central nervous system (CNS), including multiple sclerosis (MS), aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4-IgG-positive NMOSD), myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD), and double-seronegative NMOSD, span a clinical spectrum from common to rare conditions. AQP4-IgG-positive NMOSD is an autoimmune astrocytopathy in which antibodies target the AQP4 water channel on astrocytes, triggering complement-mediated injury and inflammation (Lennon et al., 2005). As no curative treatment exists, therapy focuses on relapse prevention through long-term immunosuppression, and several targeted therapies have been developed to reduce disease activity (Levy et al., 2021).

Alongside AQP4-IgG-positive NMOSD, MOGAD is now recognized as a distinct antibody-mediated inflammatory disorder of the CNS. Although MOG was identified as a target antigen in experimental autoimmune encephalomyelitis (EAE) models in the 1980s, it was not until the introduction of reliable cell-based assays (CBAs) that MOG-IgG antibodies could be accurately detected in patients, ultimately leading to the recognition of MOGAD as a clinical entity (O'Connor et al., 2007; Reindl and Waters, 2019; Sato et al., 2014).

The clinical phenotype of MOGAD may include optic neuritis (ON), myelitis, or acute disseminated encephalomyelitis (ADEM), and the disease may follow a monophasic or relapsing course (Banwell et al., 2023; Carnero Contentti et al., 2025; Sechi et al., 2026; Tunç et al., 2025).

Of note, despite recent advances in autoantibody detection, a subset of patients remains seronegative. Double-seronegative NMOSD refers to patients who fulfil the diagnostic criteria for NMOSD but test negative for both AQP4-IgG and MOG-IgG antibodies.

This group remains less well characterized, and it is likely heterogeneous, possibly comprising a mix of as-yet-unidentified antibody-mediated diseases and antibody-negative variants of known disorders. Understanding the pathophysiology and disease trajectories of this subgroup remains an important unmet need (Banwell et al., 2023; Sechi et al., 2026; Tunç et al., 2025).

2. NMOSD in LATAM

2.1. Epidemiology of NMOSD in LATAM

A systematic review by Papp et al. provided a comprehensive global analysis of the epidemiology of AQP4-IgG-positive NMOSD, synthesizing data from 41 studies across 20 countries, despite heterogeneity in antibody testing methods. The study found marked geographic and ethnic variability in both prevalence and incidence. For instance, in Asian populations, a higher prevalence was reported (1.57–4.9/100,000) compared with the lower prevalence rates (0.7–1.09/100,000) observed in Catalonia, Denmark, Sweden, and Australia/New Zealand (Papp et al., 2021). Among populations of African ancestry, such as those in Martinique, prevalence rates have been reported to reach up to 10.0/100,000, among the highest described to date (Flanagan et al., 2016). In LATAM, widely varying estimates of NMOSD prevalence have been reported (Alvarenga et al., 2017, 2026; Alves et al., 2022; Balduino Nogueira et al., 2026; Gracia et al., 2022; Henríquez et al., 2022; Ibis et al., 2021; Lana-Peixoto et al., 2021; Mireles-Ramírez et al., 2022; Monsalve Muñoz et al., 2022; Rivera et al., 2008; Silva et al., 2023; Torres-Camacho et al., 2023), as summarized in Table 1.

Methodological differences across studies, including variability in diagnostic criteria, AQP4-IgG testing methods, study design, population sampling, case validation, and statistical approaches, likely contribute to the wide variation in reported incidence and prevalence estimates and limit cross-study comparability, underscoring the need for standardized epidemiological methods in NMOSD research (Papp et al., 2021).

Building on these regional estimates, several LATAM cohorts provide additional detail on demographics, serostatus, and clinical presentation.

2.2. Demographic characteristics of NMOSD in LATAM

Recent data from 13 LATAM centers across Argentina, Chile, Colombia, Mexico, Brazil and Ecuador, comprising 613 patients with AQP4-IgG-positive and 178 patients with AQP4-IgG-negative NMOSD, showed that Mestizos (AQP4-IgG-positive: 90.5% and AQP4-IgG-negative: 84.8%) are the predominant ethnic group among overall patients with NMOSD (89.0%) in LATAM (Alonso et al., 2025a), which is consistent with previous observations in the region (Rivera et al., 2021). Regarding age at disease onset, a recent meta-analysis including data from 33 studies and 5,105 patients with NMOSD from LATAM and the Caribbean reported a pooled mean age at onset of 36.0 years [95% confidence interval (CI), 34.7–37.3] (Petersen et al., 2025). Similarly, another meta-analysis which included 54 populations comprising 6,240 patients with AQP4-IgG-positive NMOSD estimated an overall mean age at onset of 38.3 years (95% CI, 35.9–40.8). Importantly, the authors found a significantly younger age at onset in populations from regions with lower life expectancy (33.3 years) than in those from regions with higher life expectancy (41.7 years) (Arnett et al., 2024). Pediatric-onset

Table 1
Epidemiology of NMOSD in LATAM.

	LATAM country	Prevalence	References
1	**Brazil** (Volta Redonda City)	0.37/100,000	(Alvarenga et al., 2017)
2	**Mexico** (Jalisco State)	0.71/100,000	(Mireles-Ramírez et al., 2022)
3	**Dominican Republic** (National)	0.73/100,000	(Gracia et al., 2022)
4	**Brazil** (Goias State)	0.79/100,000	(Alves et al., 2022)
5	**Chile** (National)	0.95/100,000	(Henríquez et al., 2022)
6	**Mexico** (Mexico City)	1.00/100,000 (among Mestizos)	(Rivera et al., 2008)
7	**Panama** (National)	1.62/100,000	(Gracia et al., 2022)
8	**Brazil** (Federal District)	1.84/100,000	(Balduino Nogueira et al., 2026)
9	**Brazil** (São Paulo City)	2.10/100,000	(Silva et al., 2023)
10	**Venezuela** (West and Central regions)	2.11/100,000	(Ibis et al., 2021)
11	**Brazil** (Volta Redonda-Barra Mansa region)	3.84–3.87/100,000	(Alvarenga et al., 2026)
12	**Colombia** (Antioquia State)	4.03/100,000	(Monsalve Muñoz et al., 2022)
13	**Brazil** (Belo Horizonte City)	4.52/100,000	(Lana-Peixoto et al., 2021)
14	**Colombia** (Coquimbo region)	5.30/100,000	(Torres-Camacho et al., 2023)

NMOSD is generally uncommon, accounting for approximately 3.0–5.0% of cases in most published series (Tenembaum & Yeh, 2020). So far, a higher proportion (19.6%) of pediatric cases has been reported in a single Argentinean study (Villa et al., 2023). Yet, late-onset NMOSD (≥50 years) appears to be less frequent in LATAM (8.7–17.1%) (Carnero Contentti et al., 2020a; Villa et al., 2023) than in cohorts from Spain (29.0%) (Sepulveda et al., 2019), Germany (34.3%) (Kretschmer et al., 2025), and China (41.5–44.9%) (Zhang et al., 2016; Hu et al., 2022).

Moreover, from a serological perspective, Brazilian patients with AQP4-IgG-negative (seronegative) NMOSD apparently exhibit a lower frequency of MOG-IgG seropositivity (10.7%) (Pedrosa et al., 2025). This contrasts with pooled MOG-IgG seropositivity rates of 31.0% (95% CI, 22.1–39.9%) in Asian and 34.3% (95% CI, 21.9–46.7%) in European seronegative NMOSD cohorts, respectively (Li et al., 2021). Altogether, these findings suggest that ethnicity and regional factors may contribute to the observed heterogeneity in the age distribution and serological profile of NMOSD across populations.

2.3. Clinical course and diagnosis of NMOSD in LATAM

The LATAM region is primarily composed of countries with resource-constrained healthcare and research settings. From a clinical perspective, its diverse and multiethnic population presents both unique challenges and opportunities for studying NMOSD. Clinical research in the region faces significant structural and logistical challenges (Rivera et al., 2021). Nevertheless, NMOSD research in LATAM has expanded in recent years. In 2021, 62 investigators from 21 LATAM countries reported clinical and epidemiological data on 2,154 patients with NMOSD, with the 2015 IPND diagnostic criteria applied in 93.3% of cases. The combination of ON and transverse myelitis (TM) was the most common clinical presentation, and AQP4-IgG seropositivity was detected in 65.0% of patients. Intravenous corticosteroids were the most frequently used treatment for acute relapses, while rituximab (RTX) and azathioprine (AZA) were the most commonly prescribed long-term therapies (Rivera et al., 2021).

Validation of the 2015 NMOSD diagnostic criteria was also assessed in 2018 (Carnero Contentti et al., 2018a), demonstrating a 63.0% increase in diagnostic rates. The median time to fulfillment of the 2015 NMOSD criteria was 1 month, compared with 18 months for the 2006 NMO criteria (log-rank test: $p < 0.0001$). A similar validation was also reported by an independent group from Ecuador (Edgar Patricio et al., 2020).

In line with previous reports, a subsequent study including a cohort of 496 patients from specialized MS/NMOSD referral centers in LATAM identified an NMOSD misdiagnosis rate of 12.0% (56 cases) (Carnero Contentti et al., 2023a). Notably, 33.9% of the initial misdiagnoses had been made by MS/NMOSD specialists. The most common misdiagnosis was MS or clinically isolated syndrome (CIS) (84.0%), with MS disease-modifying therapies (including glatiramer acetate, interferons, fingolimod, and natalizumab) prescribed in 71.5% of cases for a mean duration of 3 ± 4.7 years. More than half of the patients (57.0%) consulted two or more neurologists before receiving the correct NMOSD diagnosis. Isolated or combined atypical ON (42.5%), myelitis (52.5%), and brainstem syndromes, including area postrema syndrome with intractable vomiting (10.0%), were frequently observed. The median delay in establishing the correct NMOSD diagnosis was approximately 5.5 years. AQP4-IgG testing was not performed in 40.0% of patients at the time of misdiagnosis; once the correct diagnosis was established, testing was requested in 82.0% of cases, of whom 74.0% were seropositive. Following diagnostic correction, NMOSD-directed therapies [RTX, satralizumab, eculizumab, AZA, or mycophenolate mofetil (MMF)] were initiated in 87.0% of patients (Carnero Contentti et al., 2023a).

In the context of diagnostic accuracy, a web- and case-based cross-sectional survey involving 106 neurologists identified through LAC-TRIMS revealed that most neurologists accurately recognized typical NMOSD MRI lesions. However, periventricular juxtacortical, fluffy infratentorial, corticospinal tract, and hypothalamic lesions were frequently misidentified (Carnero Contentti et al., 2024b). Between 10.4% and 49.1% of neurologists inaccurately assessed clinical or paraclinical criteria for dissemination in space, while only 32.1% correctly identified the three non-cardinal syndromes (brainstem, diencephalic, and cerebral) relevant to seronegative NMOSD. Regarding AQP4-IgG testing, 35.8–64.1% correctly identified the optimal testing timing for testing, and 56.6% recognized live-CBA as the diagnostic gold-standard. These findings highlight areas where the 2015 NMOSD criteria may be misinterpreted or misapplied, underscoring the importance of targeted educational initiatives to improve diagnostic accuracy and patient care in LATAM (Carnero Contentti et al., 2024b).

Importantly, in recognition of the differences in diagnostic performance between fixed- and live-CBAs, the 2025 IPND consensus diagnostic criteria, presented at ECTRIMS 2025 (Barcelona, Spain), established live-CBA as the reference standard for AQP4-IgG detection ("ECTRIMS 2025 Late Breaking Poster," 2025). However, the limited availability of information regarding local testing availability and the methodologies used in published studies represents a significant barrier to comprehensively understanding the current diagnostic landscape in the region. For instance, a study published in June 2025, including 1,264 patients with NMOSD from multiple LATAM cohorts, reported AQP4-IgG seropositivity in 780 cases (61.7%). CBA was the most frequently used method, performed in 685 patients (58.5%), followed by indirect immunofluorescence on tissue and/or enzyme-linked immunosorbent assay (IIF/ELISA) in 455 (38.9%). Testing methods were not reported in 29 cases (2.5%) (Rojas et al., 2025). However, despite the large number of individuals included, the lack of detailed information from participating centers regarding the type of CBA employed (whether commercial fixed, *in-house* fixed, or live) together with missing data on where testing was performed (locally or at external reference laboratories outside LATAM), limit a comprehensive assessment of local diagnostic practices and access.

Further highlighting this issue, a comprehensive review of 85 studies reporting local use of CBA showed that only 21.1% employed live-CBA

as the exclusive method for AQP4-IgG detection, increasing modestly to 27.1% when live-CBA was used in combination with fixed-CBA. Notably, 43.5% of studies relied solely on fixed-CBA, while nearly one-third (29.4%) combined fixed assays with non–gold-standard techniques (such as IIF or ELISA), raising concerns about the diagnostic accuracy of NMOSD testing in the region (Boldrini and Carnero Contentti, 2026a).

In Brazil, for instance, the commercial fixed-CBA for AQP4-IgG testing was incorporated into the Unified Health System (Sistema Único de Saúde, SUS) in June 2025 (Boldrini and Damasceno, 2025). Despite delays between its incorporation and effective implementation, as well as ongoing uncertainties regarding the subsequent stages of its rollout, this measure represents an important advance in the diagnosis of NMOSD in the country (Boldrini and Damasceno, 2025). Of note, approximately 75.0% of the Brazilian population relies exclusively on the SUS (Pimentel et al., 2023). Yet, in LATAM, the challenge extends beyond the limited availability of testing. The scarcity of trained personnel, coupled with the lack of head-to-head validation studies comparing local platforms, may undermine confidence in locally generated results. Therefore, expanding the implementation of gold-standard testing methods in the region, alongside improving the validation and reliability of locally generated results, is critical for improving diagnostic precision, generating more robust epidemiological data, and ensuring timely access to effective therapies for patients with NMOSD in LATAM (Fig. 1).

Regarding clinical outcomes and prognostic factors, a recent study investigated 260 attacks in 137 patients with NMOSD and reported higher remission rates following ON than following myelitis (Carnero Contentti et al., 2021). Another study analyzing 195 patients with ON (159 NMOSD-ON and 36 MOGAD-ON) identified older age at disease onset as a predictor of severe visual disability; additionally, older age at onset, a higher number of relapses, and RTX treatment predicted permanent motor disability, while ON combined with myelitis at onset predicted wheelchair dependence (Carnero Contentti et al., 2023b). A retrospective study including 140 patients with NMOSD from Brazil, Argentina, and Venezuela showed that patients with late-onset NMOSD reached the Expanded Disability Status Scale (EDSS) score of 4 more rapidly than those with early-onset disease (Carnero Contentti et al., 2020a). Mortality data, based on 158 patients with NMOSD followed for 11 years, revealed a 7.0% mortality rate and an incidence density of 2.06×10^{-4} deaths per patient-day; extensive cervical myelitis with respiratory failure accounted for 45.0% of deaths (Carnero Contentti et al., 2023c).

Moreover, MRI findings in LATAM cohorts further illustrate disease heterogeneity. In a multicenter cohort of 79 patients with NMOSD from Brazil, Argentina, and Venezuela, 53.1% exhibited typical NMOSD lesions at presentation (Carnero Contentti et al., 2018c), while rates in other LATAM cohorts ranged from 25.7% to 65.5% (Fragoso et al., 2019; Ibis et al., 2021; Uribe-San Martin et al., 2017). Short-segment transverse myelitis (STM) was observed in 8.0% of 76 patients with NMOSD across 340 relapses, often preceded by ON (Carnero Contentti et al., 2018b). Other studies reported STM frequencies ranging from 7.3% to 19.8%, with STM occurring as the sole initial presentation in up to 26.0% of patients (Fang* et al., 2020). Analysis of CNS lesion topography and morphology in a cohort of 68 patients (25 AQP4-IgG-positive

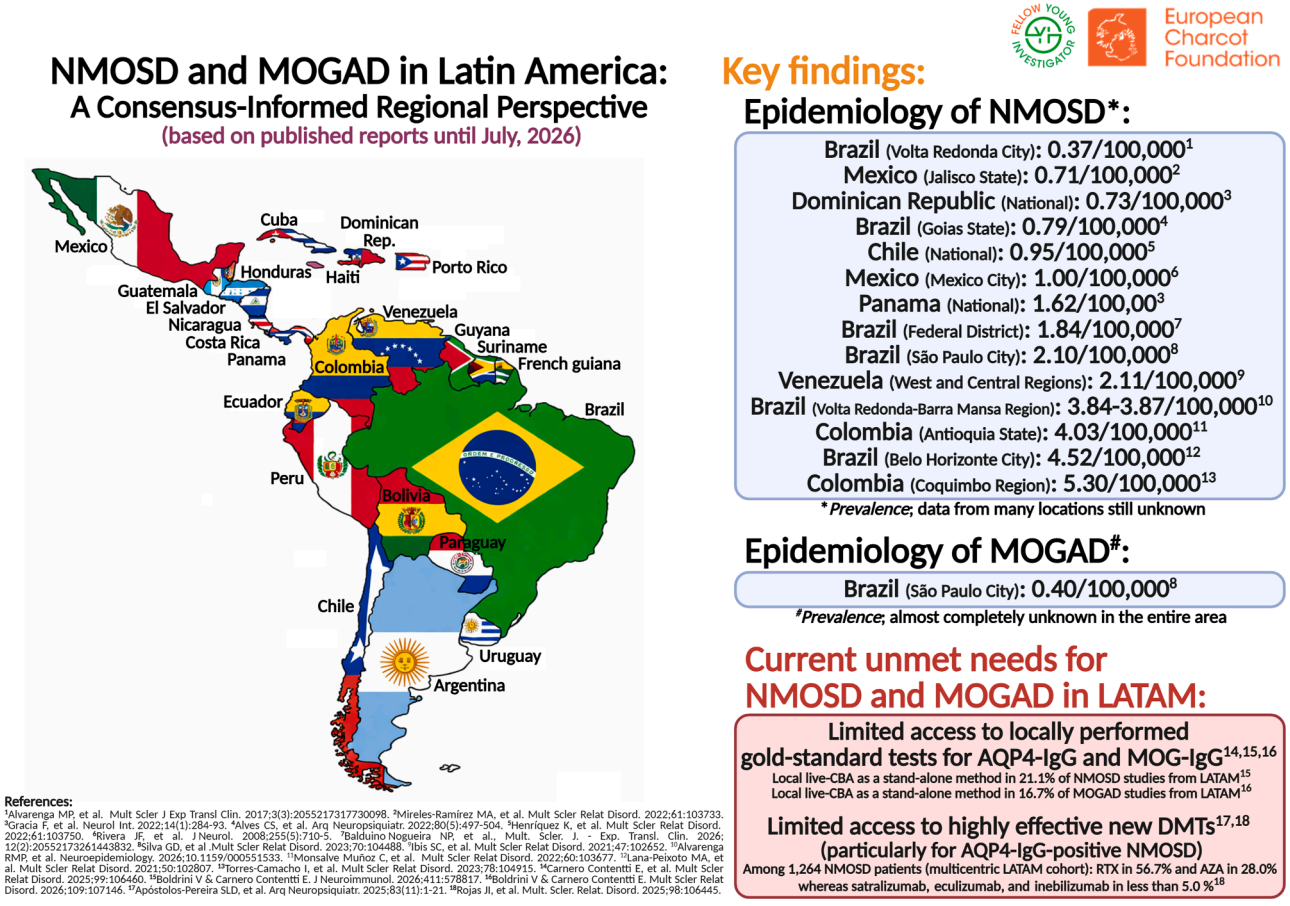

Fig. 1. Current unmet needs in the access to diagnosis and care for NMOSD and MOGAD in Latin America (LATAM).
To date, only a limited number of countries in LATAM have published epidemiological data on NMOSD and MOGAD. Furthermore, most of the available data are derived from local or regional estimates rather than national multicenter studies. Low availability of locally performed gold-standard diagnostic tests and limited access to high-efficacy emerging therapies have been identified as major challenges to the prompt diagnosis and management of NMOSD and MOGAD in LATAM. Created with Biorender.com.

NMOSD, 28 MOGAD, and 16 double-seronegative NMOSD) showed the potential utility of imaging patterns for differential diagnosis (Fragoso et al., 2023). Finally, an evaluation of 675 MRIs (in which 255 were performed during attacks and 450 during relapse-free periods) found that asymptomatic lesions, most commonly involving the optic nerves and the spinal cord in the form of STM, were frequent but were not associated with a shorter time to relapse (Carnero Contentti et al., 2023d).

2.4. Access to therapies and prognostic consequences for NMOSD in LATAM

Another crucial aspect of NMOSD management is access to rapid acute treatments, as disability accrual is largely relapse-dependent. In this context, plasma exchange (PLEX) has demonstrated favorable outcomes, particularly with respect to visual acuity, in several studies from the region (De Almeida et al., 2024; Gómez-Figueroa et al., 2021; Gonzalez et al., 2022; Restrepo-Aristizábal et al., 2021).

However, significant challenges persist regarding long-term treatment in LATAM, as many of the newly approved, highly effective therapies for NMOSD are not widely available in the region. In some settings, such as Brazil, even the well-established off-label use of anti-CD20 therapies, including RTX, is not covered by the public healthcare system for patients with NMOSD. This situation stands in marked contrast to accumulating evidence demonstrating that early initiation of RTX reduces disease-related costs and improves quality of life over a five-year period. A Brazilian study showed that a median delay of three years before switching to RTX resulted in an additional cost of €15,363 and a reduction in quality of life, primarily driven by disability accrual in patients with NMOSD (Silva et al., 2024). Similarly, RTX has been shown to produce sustained reductions in annualized relapse rates (ARR) in NMOSD cohorts from Mexico (Gómez-Figueroa et al., 2021), Ecuador (Correa-Díaz et al., 2021), and multicenter cohorts across LATAM (Rojas et al., 2023).

More recently, a study investigated 298 patients with NMOSD from the RelevarEM registry who received AZA, MMF, or RTX as first-line therapy, with a mean follow-up duration of 41.3 ± 11.4 months and a median EDSS of 3 at treatment initiation. The authors reported ARR reductions from pre- to post-treatment of 56.0% for AZA, 48.0% for MMF, and 79.0% for RTX. Treatment failure was observed in 42.8%, 40.0%, and 10.3% of patients, respectively (Carnero Contentti et al., 2024a). In addition, one of the largest studies conducted in the region, which included data from three nationwide registries from Argentina and seven observational cohorts across LATAM, showed that RTX (56.7%) was the most commonly used therapy, followed by AZA (28.0%) (Rojas et al., 2025). Within this scenario, LATAM consensus recommendations were established to facilitate diagnosis and improve long-term outcomes in the NMOSD population in the region (Carnero Contentti et al., 2020b; Alonso et al., 2025b).

In conclusion, NMOSD is a rare and heterogeneous disease that requires collaborative studies to better understand its clinical course, particularly in regions where healthcare inequities create substantial obstacles to the availability of gold-standard diagnostic methods (e.g., live-CBA) and limit access to highly effective emerging therapies.

2.5. Treatment guidelines for NMOSD in LATAM

Important regional challenges in the context of NMOSD include the pressing need for context-adapted clinical recommendations.

Data from multicenter LATAM cohorts have revealed high rates of permanent disability following relapses and frequent suboptimal responses to conventional immunosuppressants, such as AZA and MMF (Carnero Contentti et al., 2024a, 2023b, 2020b; Carnero Contentti et al., 2021; San Martin et al., 2024). Despite strong evidence supporting the early initiation of RTX to reduce disability accumulation and healthcare costs, its use remains limited in several countries across the region, largely due to disparities in access to treatment (Rojas et al., 2023; Tkachuk et al., 2023).

Detailed findings are summarized as follows:

- **Clinical outcomes**: Long-term disability remains a major concern, with high rates of severe permanent visual impairment (55.0%), motor disability (22.0%), and wheelchair dependence (11.0%) reported after a median follow-up of 3.5 years (Carnero Contentti et al., 2023b). Partial recovery following relapses is often limited, particularly in ON (12.0–18.0%). These findings underscore the urgent need for early and effective treatment strategies (Carnero Contentti et al., 2021).
- **Suboptimal therapeutic response:** Conventional immunosuppressants such as AZA and MMF continue to be widely used in countries including Brazil and Argentina, with treatment failure rates ranging from approximately 40.0% to 55.0%. Although RTX demonstrates superior efficacy (10.3% of failure rate), its utilization remains low in some settings (Carnero Contentti et al., 2024a).
- **Access and cost-effectiveness:** A Brazilian cost-effectiveness analysis demonstrated that early initiation of RTX leads to lower disease-related costs and improved quality of life over a five-year period compared with an escalation strategy beginning with AZA (Silva et al., 2024). Although these findings support RTX as a cost-effective preventive approach, disparities in treatment pricing and reimbursement continue to limit its widespread adoption.

Differential diagnoses must be carefully considered in the LATAM region, particularly endemic infectious conditions such as tuberculosis, schistosomiasis, neurocysticercosis, and HTLV-1 infection, as well as nutritional deficiencies including vitamin B12, copper, and folate deficiency, all of which may complicate diagnostic assessment.

Healthcare infrastructure disparities represent a major barrier to equitable NMOSD care across LATAM. Data from the OECD and World Bank (2023) reveal substantial variation in access to diagnostic resources, including MRI availability per capita and hospital bed capacity, both of which are critical for acute management and long-term follow-up (*Health at a Glance 2023*, 2023). In addition, approval timelines for newer therapies, including inebilizumab, satralizumab, eculizumab, and ravulizumab, vary considerably between countries, highlighting the need for coordinated regulatory strategies and harmonized treatment recommendations across the region. In this regard, as of June 2025, less than 5.0% of patients with AQP4-IgG–positive NMOSD from one of the largest multicenter cohorts in LATAM were receiving inebilizumab, satralizumab or eculizumab (Rojas et al., 2025).

In response to these challenges, the 2025 Latin American consensus recommendations on NMOSD treatment were developed using the RAND/UCLA Appropriateness Method. This process involved 19 neurologists representing diverse healthcare settings across LATAM and resulted in consensus on 31 clinical statements addressing general management principles, treatment of patients with AQP4-IgG-positive and AQP4-IgG-negative NMOSD, switching strategies, and safety considerations (Alonso et al., 2025b). The panel advocated for early initiation of disease-modifying therapy in AQP4-IgG-positive NMOSD, prioritizing on-label monoclonal antibodies such as eculizumab, satralizumab, inebilizumab, and ravulizumab when available. In settings with limited access, RTX and tocilizumab were considered acceptable alternatives. For patients with AQP4-IgG-negative NMOSD, despite limited evidence, immunosuppressive therapies including RTX, MMF, and AZA were recommended as first-line options. The consensus also addressed region-specific considerations, including the importance of infection screening prior to immunosuppression, particularly for pathogens endemic to LATAM. Additional statements emphasized the need to tailor therapeutic strategies to local healthcare system capacities, ensuring continuity of treatment access and long-term adherence.

Complementing this regional initiative, the Brazilian NMOSD guideline employed a Delphi-based methodology and the GRADE

framework to assess evidence and formulate clinical recommendations (Apóstolos-Pereira et al., 2025). The guideline development process involved a core steering committee and advisory board and included multiple voting rounds by 44 national experts. Recommendations included the use of high-dose intravenous methylprednisolone (1 g/day for ≥5 days) and early initiation of plasma exchange (≥5 cycles) for acute attacks, irrespective of AQP4-IgG serostatus. Intravenous immunoglobulin was not recommended, except in patients with suspected MOGAD. For preventive therapy, the Brazilian panel proposed a serology-based algorithm favoring monoclonal antibodies in patients with AQP4-IgG-positive NMOSD, while recommending RTX, tocilizumab, or conventional immunosuppressants for patients with AQP4-IgG-negative NMOSD when appropriate.

Thus, although meaningful progress has been achieved in establishing expert-based treatment frameworks, significant challenges remain in their implementation. Ongoing disparities in regulatory approval processes, medication costs, and healthcare infrastructure continue to restrict access to optimal care. While these consensus initiatives provide a robust foundation, future efforts must prioritize real-world data collection, longitudinal outcome assessment, and cross-country collaboration to advance equitable NMOSD care throughout the region.

3. MOGAD in LATAM

3.1. Epidemiology of MOGAD in LATAM

Several important questions emerge regarding of clinical presentation and care for patients with MOGAD in LATAM. The first consideration concerns disease prevalence. Globally, the prevalence of MOGAD is estimated at 1.8–2.5 per 100,000 individuals, with an annual incidence of approximately 3.0 per million, and these figures are approximately threefold higher in children (Hor and Fujihara, 2023). In contrast to MS, no clear racial differences in prevalence have been identified, nor has a strong association with human leukocyte antigen (HLA) been demonstrated in MOGAD (Grant-Peters et al., 2021), although Hispanic and non-White adults appear to experience a higher frequency of relapses (Martin et al., 2024).

MOGAD also demonstrates geographic and demographic variation in its clinical presentation. In southern China, pediatric cases frequently present with ADEM or encephalitic phenotypes, with a median age at onset of 6 years (IQR, 4–8 years) (Li et al., 2023). Similarly, Japanese cohorts report a higher frequency of encephalitic variants (Nakamura et al., 2023). Despite these regional differences in clinical phenotype, multinational studies suggest no major racial variation in the overall prevalence of MOGAD (Hor and Fujihara, 2023).

Strikingly, so far, a single population-based study from São Paulo/Brazil, estimated the prevalence of MOGAD in the LATAM area (Silva et al., 2023) (Table 2). Compared with the prevalence of NMOSD (2.1 per 100,000) reported in the same study, the prevalence of MOGAD was lower (0.4 per 100,000). This discrepancy may be explained by the inclusion of adult patients only.

It is also important to evaluate whether the clinical profile and prognosis of MOGAD in LATAM differ from those observed globally. Compared with the largest epidemiological study to date (Trewin et al., 2025), which included 4,699 patients, LATAM cohorts show a higher proportion of female patients (59.0–79.0%) (Guzmán et al., 2023; Carnero Contentti et al., 2024c). Beyond this difference in sex distribution, no other major differences in clinical characteristics or prognosis have been identified between LATAM cohorts and global MOGAD populations.

Table 2
Epidemiology of MOGAD in LATAM.

	LATAM country	Prevalence	References
1	**Brazil** (São Paulo City)	2.10/100,000	(Silva et al., 2023)

3.2. Clinical course and diagnosis of MOGAD in LATAM

Another major issue in MOGAD care is diagnostic accuracy. Of note, a recent study assessed the 2023 diagnostic criteria for MOGAD (Banwell et al., 2023), in cohorts from various LATAM countries (Carnero Contentti et al., 2024c). Overall, the criteria demonstrated good diagnostic performance, with a sensitivity of 86.0% (95% CI: 0.80–0.91) and a specificity of 100% when compared with the 2018 criteria.

Consistent with these findings, first demyelinating events in adults most commonly present as ON, followed by myelitis. In pediatric patients, encephalomyelitis was the most frequent initial manifestation, followed by ON (Carnero Contentti et al., 2024c).

Importantly, a critical challenge remains regarding the accessibility and quality of antibody testing for MOGAD in LATAM. A recent comprehensive review of 24 studies conducted in the region highlights that only 16.7% of studies employed live-CBA as a standalone method, whereas more than half relied exclusively on commercial fixed-CBA assays (Boldrini and Carnero Contentti, 2026b). This imbalance raises significant concerns regarding the potential underdiagnosis and misclassification of MOGAD across the region, particularly in light of growing evidence demonstrating the substantially lower sensitivity of commercial fixed-CBA compared with live-CBA for MOG-IgG detection (Said et al., 2025).

Moreover, since the diagnostic pathways in LATAM are further complicated by limited access to resources and gold-standard tests, as a result, many countries tend to prioritize AQP4-IgG testing in suspected NMOSD before considering MOG-IgG testing. This diagnostic gap warrants attention, particularly given the growing recognition of MOGAD as a distinct clinical entity.

In terms of neuroimaging, a LATAM study (Guzmán et al., 2023) reported that MRI commonly demonstrated multiple T2 lesions, optic nerve involvement, longitudinally extensive myelitis, and the characteristic “H-sign,” consistent with classical MOGAD imaging patterns (Banwell et al., 2023). The differential diagnosis of MOGAD remains challenging, and region-specific differential diagnoses and disease prevalence should be considered in the diagnostic assessment of patients in LATAM.

3.3. Access to therapies and prognostic consequences for MOGAD in LATAM

Treatment of MOGAD remains challenging, as many therapeutic interventions, particularly for long-term disease management, are used off-label. Several studies have examined treatment approaches for MOGAD in LATAM, generally following international expert consensus recommendations (Bruijstens et al., 2020; Messias et al., 2023).

A Brazilian study (Messias et al., 2023) described clinical characteristics and treatment patterns in 41 patients with MOGAD, of whom 83.0% received immunosuppressive therapy, most commonly AZA (59.0%). In a multicenter study (Rojas et al., 2023) involving several LATAM countries, 217 patients were included (20 with MOGAD and 197 with NMOSD). RTX was the most frequently used therapy in both groups (65.0% in MOGAD and 48.2% in NMOSD). The most common RTX regimen consisted of two 1000-mg infusions administered 15 days apart, followed by 1000-mg every six months.

In another study from Argentina (Carnero Contentti et al., 2021), acute and long-term treatment strategies in NMOSD and MOGAD were evaluated, with results often reported jointly. Intravenous corticosteroids were the most common therapy for acute relapses (81.4%), followed by PLEX (15.5%). Following the first demyelinating event, 67.7% of patients with MOGAD received preventive treatment. Although AZA was frequently used initially, at last follow-up RTX was the most commonly prescribed long-term therapy in both NMOSD and MOGAD

(50.6% and 54.5%, respectively).

3.4. Treatment guidelines for MOGAD in LATAM

Currently, there are no region-specific, formally approved treatment guidelines for MOGAD in LATAM, and management largely follows international consensus recommendations (Bruijstens et al., 2020). Most patients receive acute immunotherapy and off-label chronic immunosuppression in line with these expert recommendations.

4. Conclusion

In conclusion, NMOSD and MOGAD in LATAM reflect a complex interplay of biological, demographic, and structural factors that shape disease burden, diagnosis, and management across the region. AQP4-IgG-positive NMOSD is characterized by a relatively high prevalence, younger age at onset, and substantial relapse-related disability, while MOGAD shows prevalence broadly comparable to global estimates but with regional variation in age distribution, sex ratio, and clinical phenotype. Across both disorders, delayed diagnosis, misclassification as MS or seronegative NMOSD, and limited access to high-quality antibody testing remain major challenges. Although important progress has been made through improved epidemiological characterization, growing regional research collaboration, and the development of consensus recommendations and national guidelines, inequities in access to gold-standard diagnostic assays and highly effective therapies continue to adversely affect patient outcomes.

This consensus-informed regional perspective identifies the following as two strategic priorities for advancing the diagnosis and care of NMOSD and MOGAD in LATAM: (I) expanding access to locally performed gold-standard antibody tests (local live-CBA), and (II) improving equitable access to highly effective emerging therapies. Addressing these priorities will be essential to harmonize clinical practice, strengthen collaborative neuroimmunology research networks across the region, and thus generate reliable local real-world evidence. Collectively, these measures have the potential to reduce healthcare disparities and ultimately improve outcomes for patients with NMOSD and MOGAD throughout LATAM.

CRediT authorship contribution statement

Vinícius Boldrini: Conceptualization, Data curation, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Sara Samadzadeh:** Conceptualization, Data curation, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Edgar Carnero Contentti:** Writing – original draft, Writing – review & editing. **Vitória Pimentel:** Writing – original draft, Writing – review & editing. **Natalia Szejko:** Writing – original draft, Writing – review & editing. **Ethel Ciampi:** Writing – original draft, Writing – review & editing. **Jacqueline Palace:** Writing – original draft, Writing – review & editing. **Friedemann Paul:** Writing – original draft, Writing – review & editing. **Jefferson Becker:** Supervision, Writing – original draft, Writing – review & editing. **Alfredo Damasceno:** Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare no conflicts of interest.

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