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REVIEW

Sex ratio and age of onset in AQP4 antibody-associated NMOSD: a review and meta-analysis

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Abstract

Background Aquaporin-4 (AQP4) antibody-associated neuromyelitis optica spectrum disorder (NMOSD) is an antibody-mediated inflammatory disease of the central nervous system. We have undertaken a systematic review and meta-analysis to ascertain the sex ratio and mean age of onset for AQP4 antibody associated NMOSD. We have also explored factors that impact on these demographic data.

Methods A systematic search of databases was conducted according to the PRISMA guidelines. Articles reporting sex distribution and age of onset for AQP4 antibody-associated NMSOD were reviewed. An initially inclusive approach involving exploration with regression meta-analysis was followed by an analysis of just AQP4 antibody positive cases.

Results A total of 528 articles were screened to yield 89 articles covering 19,415 individuals from 88 population samples. The female:male sex ratio was significantly influenced by the proportion of AQP4 antibody positive cases in the samples studied ($p < 0.001$). For AQP4 antibody-positive cases the overall estimate of the sex ratio was 8.89 (95% CI 7.78–10.15). For paediatric populations the estimate was 5.68 (95% CI 4.01–8.03) and for late-onset cases, it was 5.48 (95% CI 4.10–7.33). The mean age of onset was significantly associated with the mean life expectancy of the population sampled ($p < 0.001$). The mean age of onset for AQP4 antibody-positive cases in long-lived populations was 41.7 years versus 33.3 years in the remainder.

Conclusions The female:male sex ratio and the mean age of onset of AQP4 antibody-associated NMOSD are significantly higher than MS. The sex ratio increases with the proportion of cases that are positive for AQP4 antibodies and the mean age of onset increases with population life expectancy.

Keywords Neuromyelitis optica · Risk factors · Environment · Aetiology · Epidemiology · Age of onset · Sex

Introduction

Aquaporin-4 (AQP4) antibody-associated neuromyelitis optica spectrum disorder (NMOSD) is an antibody-mediated autoimmune astrocytopathy that typically manifests as symptoms arising from inflammatory attacks of the optic nerves, diencephalon, periaqueductal grey matter, and spinal cord [1]. Involvement of the area postrema, periependymal brainstem, hypothalamus, and cerebral hemispheres also occurs [1]. Serum antibodies to AQP4, a water channel found in high density on the foot processes of astrocytes at the blood–brain barrier, appear to be pathogenic [2]. Without treatment, the condition is associated with significant morbidity and mortality [3].

Little is known about the aetiology of NMOSD, but studies suggest that genetic and environmental factors for MS are not shared by AQP4 antibody-associated NMOSD [4–6]. Epidemiological studies are an essential step in gaining clues to aetiology [7]. Recent systematic reviews of the worldwide distribution of NMOSD have indicated that the condition appears to occur in people of all ethnic backgrounds, but that prevalence is highest in Black Africans (ninefold), and

*A full list of members of the Guthy Jackson International Clinical Consortium is given in "Appendix 1".

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is higher in South-East Asians (threefold), when compared to populations with European Ancestry [8].

Prior studies have indicated that the sex ratio (female:male) is higher in NMOSD than for MS, but some variability of results has been noted [9]. This has been attributed to possible geographical variability or differing diagnostic criteria [10]. Several studies have also noted a different sex ratio in paediatric and late onset (typically defined as an onset age of 50 years or higher) [11, 12]. The age of onset in NMOSD has been noted to be higher than in MS [10]. The diagnostic criteria for NMOSD have changed over the past 25 years [1, 13–15] and the emergence of other antibody-mediated demyelinating diseases of the CNS, that have an overlapping clinical picture, such as myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) [16] which has a female:male sex ratio approaching 1.0 and mean age of onset similar to or possibly younger than MS [17], has complicated the task of defining seronegative NMOSD.

Here we have undertaken a systematic review and meta-analysis of studies reporting on the sex and age of onset distribution for NMOSD. The aim of the study was to define the sex and age of onset distribution around the world and explore potential associations with ethnicity and population structure. We have initially undertaken a more inclusive approach using various diagnostic criteria to provide a wider geographical range of surveys, before conducting a more focused analysis of studies looking at only AQP4 antibody positive cases. We would emphasise that all included studies were surveying what at the time was thought to be AQP4 antibody-associated NMOSD although it is now recognised that the earlier criteria are likely to have included a heterogeneous group of diagnoses including MOGAD and MS. We hypothesised that in AQP4 antibody associated NMOSD: (1) the proportion of females would be higher than is seen in multiple sclerosis (MS); (2) the proportion of females would be the same in different populations; and (3) the mean age of onset would be different in different parts of the world depending upon mean life expectancy and ethnicity.

Methods

Literature search

Two independent searches of Medline, Embase and PubMed databases using the following search strings: (1) ("neuromyelitis optica" OR "NMO" OR "NMOSD" OR "Devic's disease" AND "sex"); and (2) ("neuromyelitis optica" OR "NMO" OR "NMOSD" OR "Devic's disease" AND "age of onset" OR "age at onset") restricted to articles in English and published from 1 January 1999 to 17 July 2023 were undertaken. Articles were screened based on title and abstract looking for articles reporting on epidemiological studies of people with NMOSD assumed to be related to AQP4 antibodies. Full text articles were reviewed according to the following criteria. Inclusion criteria were: population-based or clinic-based surveys; incidence, prevalence, cross-sectional, cohort or case–control studies; diagnosis of AQP4 antibody related NMO or NMOSD as determined by the relevant diagnostic criteria of the time; and reporting data on sex or age of onset in any format. Exclusion criteria were: article not in English; selected population (e.g. on treatment); lack of raw or summary data; data subsequently updated; earlier more comprehensive study; review article; not NMOSD population; and case reports. Studies looking at whole population data and specific age groups (e.g. paediatric or late onset) were analysed separately for sex distribution. Age-specific groups were not included in the age-of-onset analysis.

Data extraction

The following data were extracted: first author; year of publication; prevalence year or last year of data collection; geographical location; study design (prevalence study or case series); setting; recruitment source (population-based or clinic-based); age cut-offs for paediatric and late-onset cohorts; ethnicity; diagnostic criteria used; AQP4 assay used; proportion of AQP4 antibody positive cases (of all cases not just those tested); size of study population; number of females and males (as assigned at birth); mean or median age of onset (years) with standard deviation, quartiles or range; and reason for exclusion (if excluded). Where age of onset distribution data was provided this was tabulated into decade age ranges. Mean life expectancy has been used as a simple measure of population age distribution, with a lower mean life expectancy indicating a downshifted, population age distribution profile (fewer people living to an older age) [18]. Thus, a lower mean life expectancy indicates that a smaller proportion of the population will have survived to acquire any given disease at an older age, thereby resulting in a lower mean age of onset for that disease. Mean life expectancy for females in the country of study in 2019 from the World Health Organisation website was used [19]. For multinational studies, life expectancy for the country with the largest proportion of cases was used.

Study quality was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for prevalence studies [20]. For the initial analysis, all studies were included, but studies assessed as "No" or "Unclear" for any item on the JBI prevalence checklist (except estimation of response rates) were removed as part of sensitivity analyses. Estimation of

response rates was deemed to be of less importance in the current context, as compared to a prevalence study. Review of studies and quality assessment were conducted by two researchers, any discrepancies were resolved by a third. This study used only previously published summary data and therefore institutional ethics review and participant consent was not required.

Statistical analysis

Where the age of onset data were presented as median and range or quartiles, appropriate methods were used to estimate the mean and standard deviation [21]. The sex ratio is reported as the female:male ratio. Meta-regression analysis was performed using the Comprehensive Meta-analysis v3 (Biostat® Inc., Englewood, NJ, US) statistical package [22]. The proportion of AQP4 antibody positive cases (> 90% or ≤ 90%), life expectancy (< 80 years or ≥ 80 years), mean age of onset (> 35 years or ≤ 35 years) and geographical location were included as covariates as appropriate. Zero counts for the sex distribution data were adjusted by the addition of 1 to both the number of males and females [23]. The natural log scale was used for sex ratio Forest plots. Fixed effects or random effects models were used as appropriate for the observed heterogeneity using I^2 and Tau^2 [24]. The risk of bias was assessed using Funnel Plots and Egger's test [25]. Sensitivity analyses restricted to studies using cell-based assays for AQP4 antibodies were undertaken and $p < 0.05$ was considered significant. Age standardisation [26] was applied to the age of onset distribution data using the population distribution for each country in the year of study from the Population Pyramid website [27].

Results

Literature search

From a total of 562 potential articles, 88 articles were included (64 whole population/adult studies [3, 28–90], 13 paediatric studies [11, 91–102] and 11 late onset studies [12, 103–112]) as shown in Fig. 1. Two of the whole population studies reported on two separate subpopulations which were analysed separately [50, 74]. Three studies had relevant updates or prior studies that provided additional relevant information regarding AQP4 antibody positive cases and were therefore included [113–115]. Thus, there were a total of 91 articles covering 89 separate populations. Study quality varied. Few studies included an estimate of the number of missed cases [28, 37, 86, 113]. Some studies lacked details about the sampling process, particularly in relation to the timing of the data collection and the type of AQP4 assay used. A summary of all included studies reviewed, together with a summary of the critical appraisal, is given in Supplementary Table S1. Excluded studies and reasons for exclusion are listed in Supplementary Table S2 [8, 9, 116–161]. There were nine studies that provided age of onset distribution data (Supplementary Table S3) [29, 36, 37, 39, 43, 47, 72, 82, 87] with one providing data for three separate years of onset data [87].

Sex distribution

Whole population studies

Meta-analysis for whole population studies ($N = 19{,}415$) grouped by geographical region (Supplementary Fig. S1) gave an overall sex ratio of 4.70 (95% CI 4.33–5.11). Superficially, this analysis suggests that the female:male sex ratio in Europe and East Asia may be higher, and may be lower in the Indian Subcontinent. However, there was considerable heterogeneity ($I^2 = 61\%$). Meta-regression analysis including the proportion of AQP4 antibody-positive cases and geographical location ($N = 6{,}917$) revealed a significant residual heterogeneity and that the sex ratio was significantly influenced by the proportion of AQP4 antibody-positive cases (Supplementary Table S4) but not by geographical location. The diagnostic criteria used had no effect once the proportion of AQP4 antibody cases was taken into account (data not shown). A higher proportion of AQP4 antibody positive cases was associated with a higher sex ratio ($p < 0.001$) and this is illustrated in a bubble chart (Fig. 2). Funnel plot (Supplementary Fig. S2A) and Egger's test ($p = 0.21$) indicated no publication bias. When analysis was restricted to studies with only AQP4 antibody-positive cases (Fig. 3), I^2 was reduced to 0% indicative of very low residual heterogeneity ($p = 0.53$) and gave a female:male ratio of 8.89 (95% CI 7.78–10.15) equivalent to 90% being female. Sensitivity analyses, restricted to studies using a cell-based assay (sex ratio = 8.87 [95% CI 7.14–11.03]) or restricting to the 13 studies meeting all JBI critical appraisal domains (except for response rate) in AQP4 antibody positive cases (sex ratio = 8.50 [95% CI 7.01–10.31]) did not significantly affect this finding.

Paediatric and late-onset studies

Data for all studies is given in Supplementary Fig. S3. Because of the above-noted effects of AQP4 antibody status on sex distribution, only data for seropositive cases

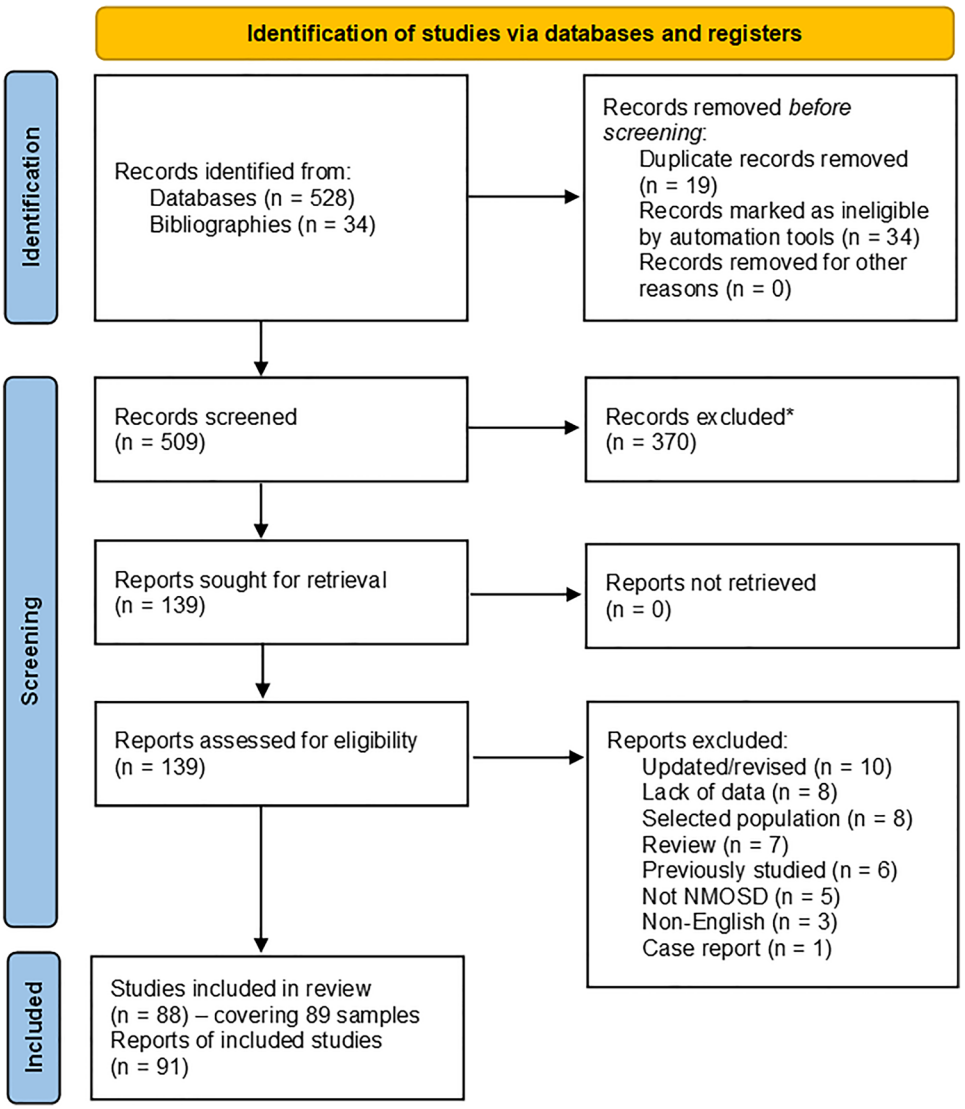

Fig. 1 PRISMA flow chart of outcomes from literature review. NMOSD = neuromyelitis optica spectrum disorder

were analysed (five paediatric and six late-onset studies). The overall estimate for the sex ratio in paediatric studies ($N = 203$) was 5.68 (95% CI 4.01–8.03). These confidence intervals overlap with those of the whole population studies (Fig. 4a). The sex ratio in late-onset cases ($N = 193$) was 5.48 (95% CI 4.10–7.33) as shown in Fig. 4b. Funnel plots (Supplementary Fig. S4) did not suggest any significant publication bias.

Age of onset

Mean age of onset and standard deviation data were either available or could be calculated for 54 populations covering a total of 6240 cases. The outcome of meta-regression analysis is given in Supplementary Table S5 and indicates that the mean age of onset was significantly influenced by population life expectancy ($p < 0.001$) and proportion of AQP4 antibody positive cases ($p = 0.019$), but not geographical region. These results are illustrated in Fig. 5 and Supplementary Fig. S5. Meta regression analysis restricted to only AQP4 antibody positive populations, stratified by mean female, life expectancy is illustrated in Fig. 6 and summarised in Supplementary Table S6. This analysis showed that the overall mean age of onset was 38.3 years (95% CI 35.9–40.8) and the age of onset ranged from 2 to 86 years. However, an I^2 of 93% and Tau^2 of 32.6 indicated a significant degree of heterogeneity ($p < 0.00001$). The mean age of onset for countries where the life expectancy of females

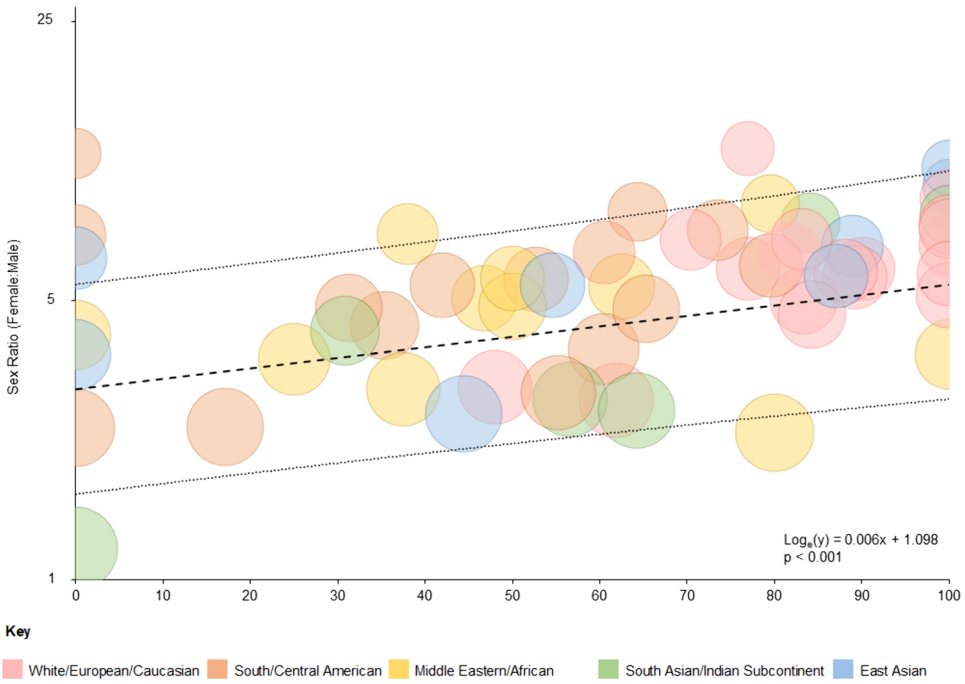

Fig. 2 Bubble plot of sex ratio for NMOSD studies plotted against the proportion of AQP4 antibody positive cases in the sample studied. The sex ratio is plotted on a log scale. Bubble size is proportional to the variance of the sex ratio. Meta-regression model included geographical regions. The dashed line indicates fitted regression from meta-regression analysis (indicated by formula) and dotted lines show a 95% confidence interval

was 80 or more years was 41.7 (95% CI 39.1–44.3) and for those where life expectancy was < 80 years was 33.5 (95% CI 30.1–36.8), a difference that was statistically significant ($p < 0.001$). Sensitivity analysis restricting studies meeting all JBI critical appraisal criteria in regions with live expectancy was 80 years or more gave the same result (42.0 years [95% CI 38.3–45.6]). The effect of life expectancy on the mean age of onset within AQP4 antibody positive populations is shown in Supplementary Fig. S6 ($p < 0.001$). Funnel plots (Supplementary Fig. S2B) and Egger's test ($p = 0.678$) did not suggest any publication bias.

There were nine studies that provided age of onset data per decade of life [29, 36, 37, 39, 43, 47, 72, 82, 87] with one study giving incidence data for three separate years of data collection [87] which were included as three separate cohorts (Supplementary Table S6). A summation of these data are provided in Fig. 7 ($N = 12{,}599$). The commonest age of onset was 40–49 years and the age of onset profile was flatter and broader than that seen in MS. Similar to MS, and contrary to MOGAD [16], AQP4 antibody associated NMOSD appears to be relatively uncommon below the age of 10 years. Unlike MS, small numbers of cases continue to occur into the eighth and ninth decades. The double peak of age of onset seen in MS [162] and MOGAD [163] was not evident for AQP4 antibody associated NMOSD. Adjustment of age of onset distribution to a flat age structure (Supplementary Fig. S7A) provides an indication of the relative risk of acquiring AQP4 antibody-associated NMOSD in each decade and suggests that the age range 50–59 may represent the period of greatest risk. Data restricted to AQP4 antibody positive cases only ($N = 106$) are again presented in Supplementary Fig. S7B and is similar to the larger dataset.

Discussion

This review and meta-analysis have shown that both the sex ratio and mean age of onset for AQP4 antibody-associated NMOSD are significantly influenced by the proportion of seropositive cases and population age profile. The effect of seropositive proportion on age of onset could be due to lower titres of antibody earlier in the disease course (i.e. at a younger age). There was a linear relationship between the sex ratio (plotted on the log scale) and the proportion of AQP4 antibody-positive cases ($p < 0.001$). Studies with lower proportions of AQP4 antibody-positive cases were associated with a lower sex ratio. It is harder to explain the effect of seropositive proportion on the sex ratio, where the sex ratio for false negative cases would be expected to be the same as seropositives. This finding suggests the accidental inclusion of cases with a diagnosis other than AQP4 antibody-associated NMOSD in these cohorts. This is likely to be a heterogenous group and might include MS, which has a lower female:male sex ratio (typically 2.73) [164], MOGAD (sex ratio typically 1.00) [17] or other yet-to-be-defined demyelinating disorders, as well as seronegative NMOSD. These findings are in line with prior studies of

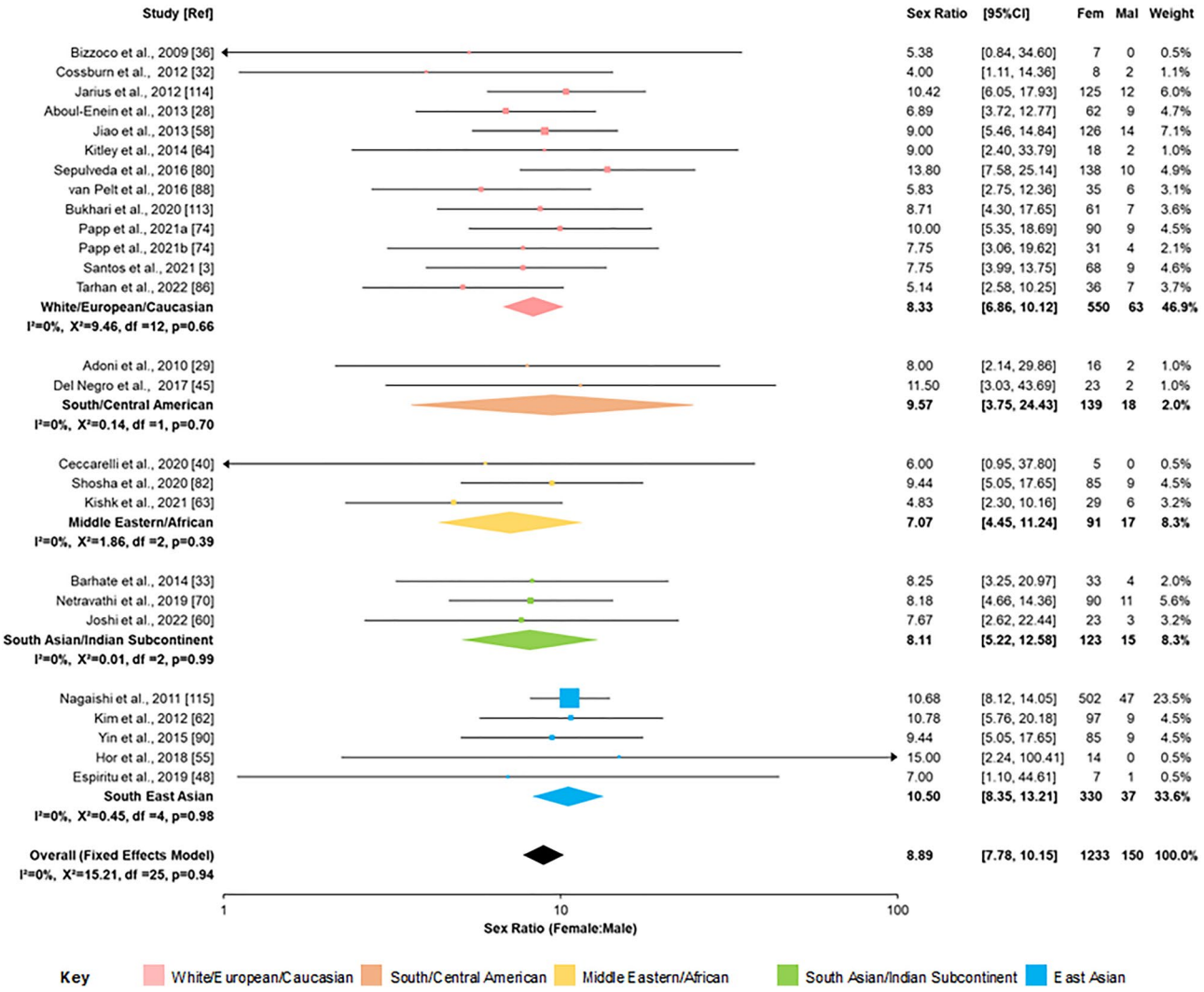

Fig. 3 Forest plot of sex ratio, sub-grouped by geographical region for studies only including AQP4 antibody positive cases. Fixed effects model. Plotted on log scale. Colour coding of geographical regions is indicated by the key. CI = confidence interval; Fem = female; Mal = male

AQP4 antibody-associated NMOSD that have shown a lower female:male sex ratio and younger age of onset in seronegative cases when compared to seropositive cases [63, 113, 114].

The effect of population profile on the mean age of onset is also interesting. Populations with age distributions skewed towards younger ages will inevitably have a younger age of onset for any condition where onset spans the full range of ages, such as NMOSD (2–86 years). Mean life expectancy is a simple measure of population distribution [165] and showed a persistent effect on mean age of onset even when restricted to AQP4 antibody-positive cases with a regression coefficient of 0.8 ($p < 0.001$).

Taking these factors into account the female:male sex ratio in NMOSD was 8.89 (95% CI 7.78–10.15) when restricted to AQP4 antibody positive cases. This is significantly higher than the 2.73 (95% CI 2.37–3.09) figure for contemporaneous cohorts of MS [164], as the confidence intervals do not overlap. The female:male predominance for NMOSD is similar to that seen for systemic lupus erythematosus (SLE) 7:1 [166] and Sjögren's syndrome 14:1 [167], two conditions that have been noted to co-exist in people with NMSOD [168]. This suggests a common pathophysiology or aetiology in which female sex is particularly important. It has been postulated that oestrogen may be of primary importance with a trial of an oestrogen receptor antagonist

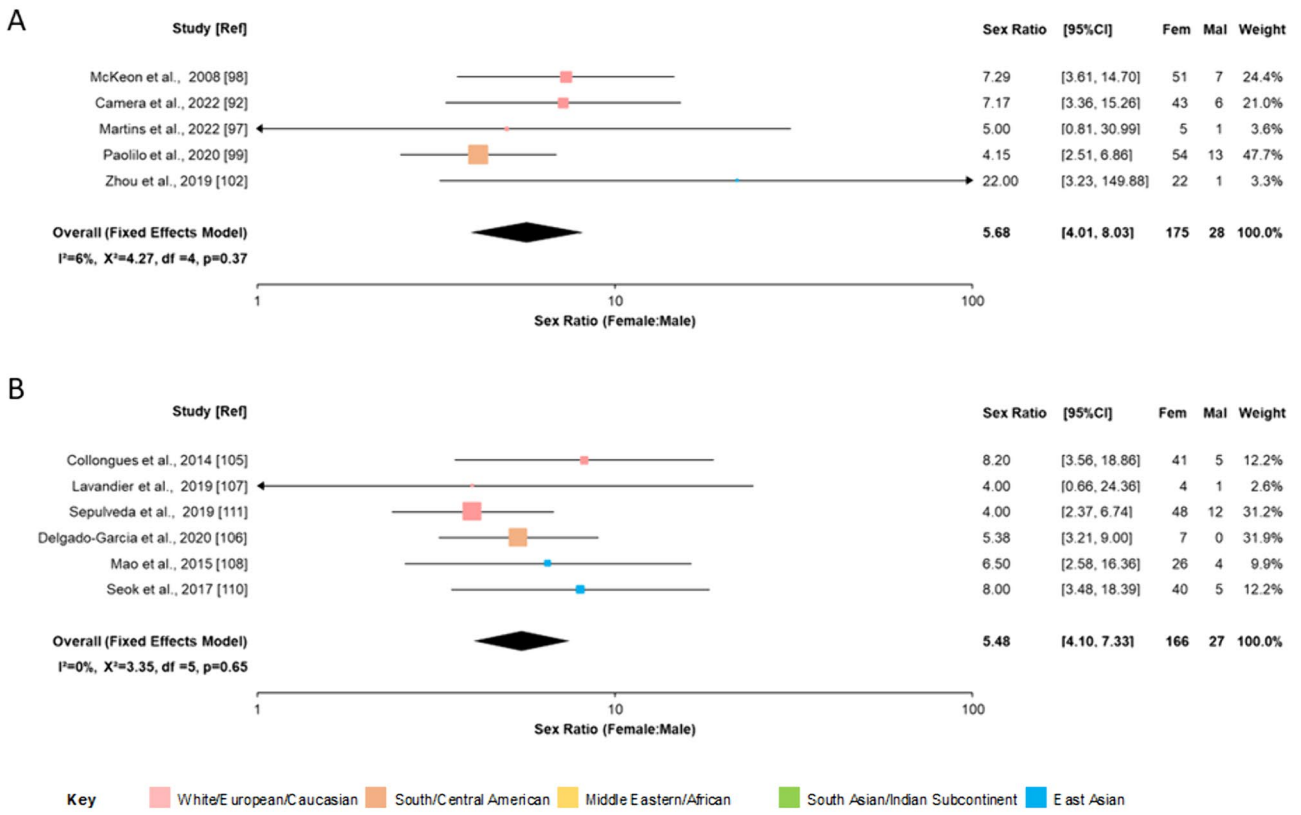

Fig. 4 Forest plots of sex ratio in paediatric (**A**) and late-onset (**B**) AQP4 antibody positive cases of NMOSD. Inverse variance method with fixed effects models. Colour coding of geographical regions is indicated by the key. CI = confidence interval

being of some benefit in SLE [166]. The sex ratio in AQP4 antibody-positive paediatric (5.69 [95% CI 3.45–9.38]) and late onset studies (5.48 [95% CI 4.10–7.33) were lower suggesting that the sex distribution of AQP4 antibody-associated NMOSD at the extremes of age may be different. One possible explanation for this may be an oestrogen effect during reproductive years increasing the risk of autoimmune disease in women [169].

The age of onset for AQP4 antibody-associated NMOSD ranged from 2 to 86 years and had a mean of 41.7 years (95% CI 38.5–43.8) when only AQP4 antibody-positive cases from longer-lived populations were considered. This is significantly higher (by almost 10 years) than the figure of 32 years for MS [164], although the latter may be increasing [170]. The distribution of age of onset across more than 12,000 cases shows a flatter profile than MS, with the commonest age of onset being 40–49 years, with a quarter of cases occurring in this decade. The decade of greatest risk per head of population was 50–59 years. The age profile for AQP4 antibody-associated NMOSD also includes approximately 20% of cases that occur in the seventh, eighth, and ninth decades. This contrasts with MS where age of onset greater than 60 years is rare (< 1%) [171, 172]. The flatter age of onset profile for AQP4 antibody-associated NMOSD is consistent with a triggering event that is relatively rare in the general population and shares similarities with Guillain–Barré syndrome [173]. The linear increase in incidence with age up to a peak around the fifth decade and then decrement in frequency at higher ages is consistent with either a latent period following exposure effect or genetic factors, where genetic load is associated with a younger age of onset [174].

This meta-analysis confirms that the female:male sex ratio for AQP4 antibody-associated NMOSD is significantly higher than that seen in MS (8.9:1 vs. 2.7:1). The mean age of onset in AQP4 antibody-associated NMOSD is approximately 10 years higher than is seen in MS or MOGAD. As with MS the number of cases of AQP4 antibody-associated

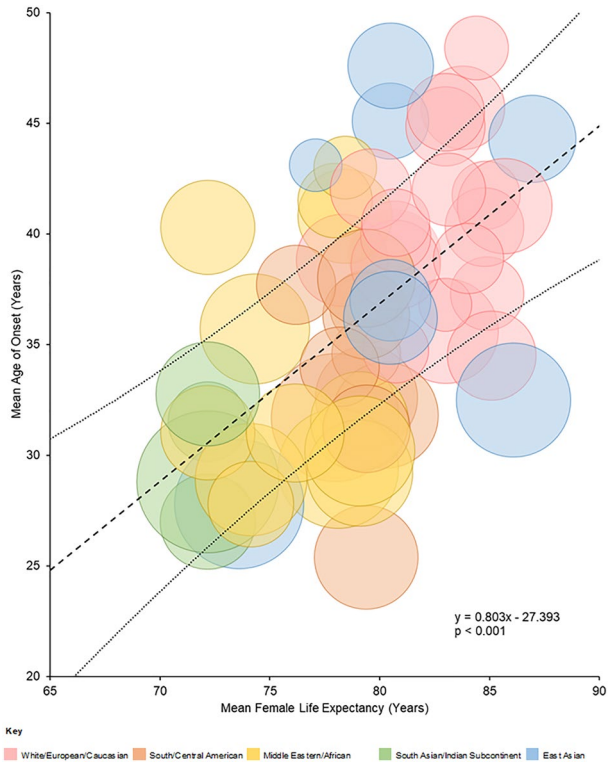

Fig. 5 Bubble plot of mean age of onset against mean female, life expectancy for the country of study. Bubble size is proportional to the variance of the mean age of onset. Meta-regression model included the proportion of AQP4 antibody positive cases. The dashed line indicates fitted regression from meta-regression analysis (indicated by formula) and dotted lines show a 95% confidence interval

NMOSD occurring before the age of 10 is relatively low [175], and contrasts with the distribution of MOGAD which has a distinct peak in childhood [176]. Finally, the peak age of risk per head of population may be 50–59 years for AQP4 antibody-associated NMOSD.

The strengths of this study were that a systematic approach, using published checklists, duplicate review, and standardised quality assessment tools, was used to undertake the literature search and record the data. The analysis was comprehensive and explored potential confounding factors with an initially inclusive approach, but ultimately more restrictive analysis focused on more homogeneous populations. The final results are robust with narrow confidence intervals and low heterogeneity when the analysis was restricted to seropositive cohorts in longer-lived populations. The potential weaknesses are that individual patient-level data were not generally available and some data (e.g. proportion of AQP4 antibody-positive cases) was not stated for every study. The collection of individual-level data should be considered in future analyses. Life expectancy is an unsophisticated measure of population distribution and unusual patterns of mortality age distributions could have an impact (e.g. high childhood mortality) [165]. Individual level data for the age of onset would permit a stratified analysis based on the population distribution for the region surveyed in each study, allowing calculation of age-specific, incidence rates [26].

This study provides a comprehensive update on the sex distribution and age of onset profile for AQP4 antibody-associated NMOSD that can be used as a benchmark for future comparative studies. The fact that studies using less stringent diagnostic criteria (seronegative cases) gave significantly different estimates of both sex ratio and mean age of onset points to phenotypic heterogeneity. We would recommend that future studies of AQP4 antibody-associated NMOSD report only on AQP4 antibody-positive cases or that data for seropositive cases be reported separately.

Appendix 1

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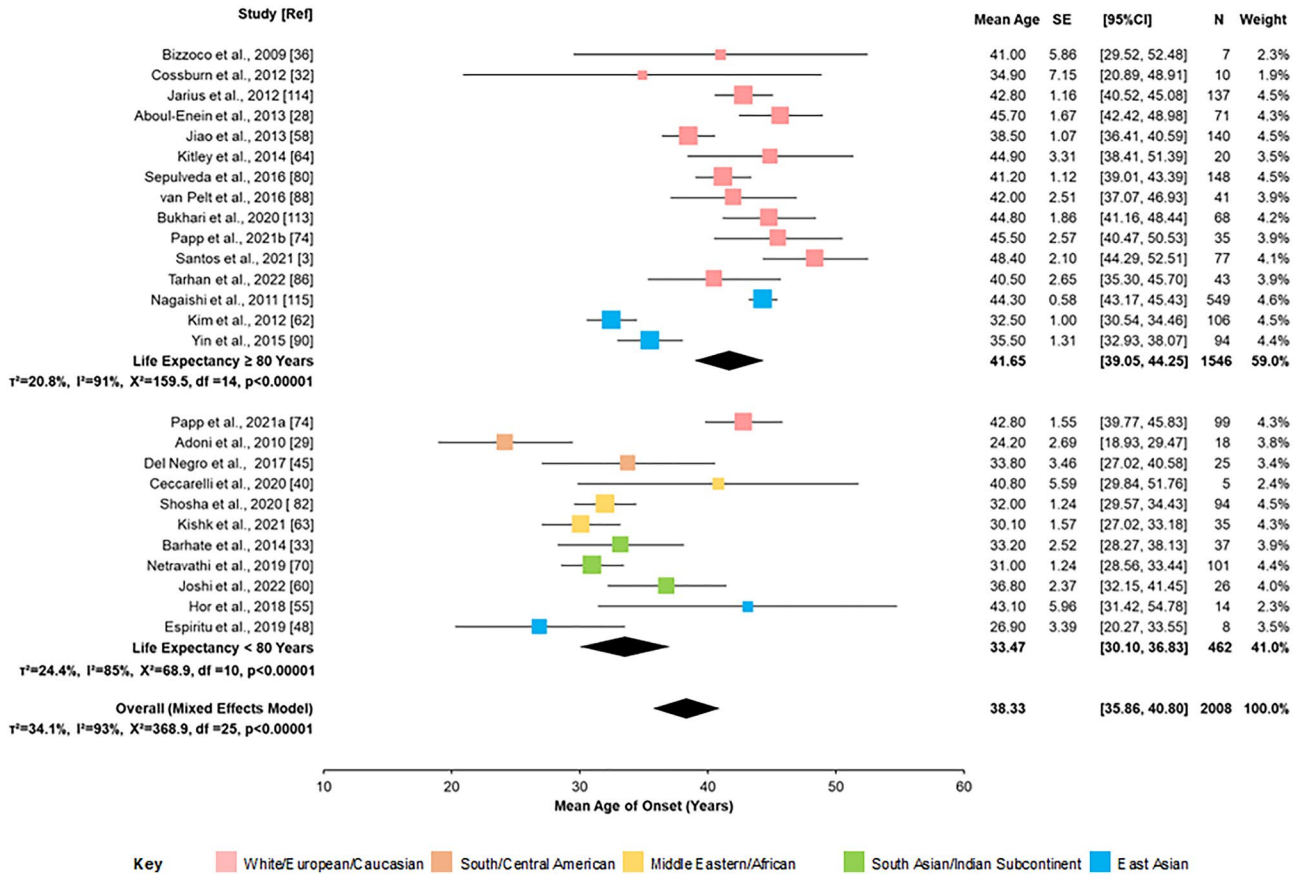

Fig. 6 Forest plot of mean age of onset, sub-grouped by mean life expectancy (≥ 80 year or < 80 years) for studies only including AQP4 antibody positive cases. Mixed effects model. Colour coding of geographical regions is indicated by the key. CI = confidence interval; *N* = number of cases

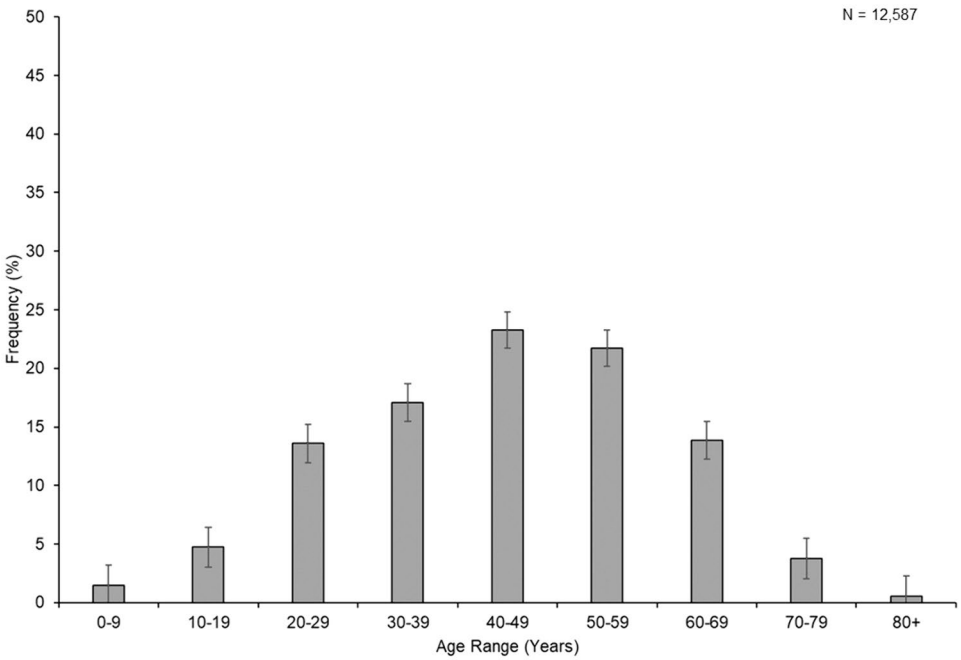

Fig. 7 Age of onset distribution by decade for NMOSD. Error bars indicate 95% confidence interval

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Protocol registration The protocol for this systematic review and meta-analysis has not been registered.

Statistical analysis This was performed by SA under the supervision of SAB and JS (Professor of Biostatistics at Griffith University and Distinguished Professor at Charles Sturt University).

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Author contributions SA, SHC, UL, JYH, MRY, BGW, KF, JS, NA, and SAB conceived the project and developed the design of this study. SA, SHC, and UL undertook the literature search and extracted the primary data. JYH, FP, ML, BGW, BLB, KF, IDB, GA, JP, NA and SAB contributed primary data (previously published) used in this analysis. SA, JS, and SAB conducted the statistical analyses. SA, SHC, and UL provide the first draft of the manuscript. FP, MRY, ML, BGW, BLB, KF, HA, IDB, GA, VEN, CQ, EM and JP provided expert review and regional context insights to the analysis. NA and SAB provided editorial oversight. All Authors approved the final version of the manuscript.

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Data availability Full data used in this analysis are available from the corresponding author upon request.

Declarations

Conflicts of interest SA, SHC, UL, JYH, GA, VEN, JQ, EM, JS and NA declare no conflicts of interest. FP has received research support from DFG, BMBF, KKNMS, and the Guthy-Jackson Charitable Foundation. He serves on steering committees of the OCTIMS study (Novartis) and the N-Momentum study (Viela Bio) and has received personal compensation and research support from Alexion, Bayer, Biogen, Roche, Merck, Teva, Shire, Celgene, Novartis, and Sanofi Genzyme. He is an associate editor of Neurology: Neuroimmunology and Neuroinflammation. MRY is the founder of NovaDigm Therapeutics, Inc, and Metacin, Inc. He is a member of the Genentech Scientific Advisory Committee and has received travel expenses or honoraria from Genentech and Alexion. ML has had roles as a pharmaceutical consultant for Alexion, Chugai, Horizon, Roche, Genzyme, UCB, and Quest Diagnostics, and has received grants from Alexion, Shire, Horizon, Genzyme, Sanofi, UCB. BGW has received royalties from RSR Ltd, Oxford University, Hospices Civil de Lyon, and MVZ Labor PD Dr. Volkmann und Kollegen GbR for a patent of NMO-IgG as a diagnostic test for NMO and related disorders, served on adjudication committee for clinical trials in NMO being conducted by MedImmune and Alexion, and consulted for Chugai, Mitsubishi-Tanabe regarding a clinical trial for NMO. BLB has received personal fees from Novartis. KF has received grants from Ministry of Education, Science and Technology of Japan and the Ministry of Health, Welfare, and Labor of Japan, and received honoraria, and/or travel expenses for speaking, and/or advisory boards from Mitsubishi Tanabe, Biogen, Bayer, Takeda, Novartis, Alexion, VielaBio, Asahi Kasei, Dainihon Sumitomo, Eisai, Teijin, Ono, Roche, and Chugai. H. Abboud has received consultancy and speaker fees from Biogen, Genentech-Roche, Bristol Myers Squibb, Alexion, and Horizon, and has received research support from Genentech-Roche, Novartis, Sanofi-Genzyme, and Bristol Myers Squibb to conduct clinical trials. IDB has been a site Principal Investigator in clinical trials and projects sponsored by Alexion Pharmaceuticals/Astra Zeneca and CorEvitas, has received travel reimbursement from The Guthy-Jackson Charitable Foundation, is a member of The Guthy-Jackson Charitable Foundation International Clinical Consortium; and received grant support from The Bodford Family Transverse Myelitis Center Research Fund. JP has received support for scientific meetings and honorariums for advisory work from Merck-Serono, Sandoz, Sanofi, Novartis, Chugai, Alexion, Clene, Roche, Medimmune, Amgen, Vitaccess, UCB, Mitsubishi, Amplo and Janssen. Grants from Alexion, Argenx, Roche, Medimmune, UCB and Amplo biotechnology. Patent ref P37347WO and license agreement Numares multimarker MS diagnostics. Has shares in AstraZenica. SAB has received honoraria for attendance at advisory boards and travel sponsorship from Biogen-Idec, Merck-Serono, Novartis and Sanofi-Genzyme; has received speakers honoraria from Biogen-Idec and Genzyme; is an investigator in clinical trials sponsored by Biogen Idec and Novartis.

References

1. Wingerchuk DM, Banwell B, Bennett JL, Cabre P, Carroll W, Chitnis T, de Seze J, Fujihara K, Greenberg B, Jacob A, Jarius S, Lana-Peixoto M, Levy M, Simon JH, Tenembaum S, Traboulsee AL, Waters P, Wellik KE, Weinshenker BG, International Panel for NMOD (2015) International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 85(2):177–189. https://doi.org/10.1212/WNL.0000000000001729
2. Hinson SR, Pittock SJ, Lucchinetti CF, Roemer SF, Fryer JP, Kryzer TJ, Lennon VA (2007) Pathogenic potential of IgG binding to water channel extracellular domain in neuromyelitis optica. Neurology 69(24):2221–2231. https://doi.org/10.1212/01.WNL.0000289761.64862.ce
3. Santos E, Rocha AL, Oliveira V, Ferro D, Samoes R, Sousa AP, Figueiroa S, Mendonca T, Abreu P, Guimaraes J, Sousa R, Melo C, Correia I, Duraes J, Sousa L, Ferreira J, de Sa J, Sousa F, Sequeira M, Correia AS, Andre AL, Basilio C, Arenga M, Mendes I, Marques IB, Perdigao S, Felgueiras H, Alves I, Correia F, Barroso C, Morganho A, Carmona C, Palavra F, Santos M, Salgado V, Palos A, Nzwalo H, Timoteo A, Guerreiro R, Isidoro L, Boleixa D, Carneiro P, Neves E, Silva AM, Goncalves G, Leite MI, Sa MJ (2021) Neuromyelitis optica spectrum disorders: a nationwide Portuguese clinical epidemiological study. Mult Scler Relat Disord 56:103258. https://doi.org/10.1016/j.msard.2021.103258
4. Watanabe M, Nakamura Y, Sato S, Niino M, Fukaura H, Tanaka M, Ochi H, Kanda T, Takeshita Y, Yokota T, Nishida Y, Matsui M, Nagayama S, Kusunoki S, Miyamoto K, Mizuno M, Kawachi I, Saji E, Ohashi T, Shimohama S, Hisahara S, Nishiyama K, Iizuka T, Nakatsuji Y, Okuno T, Ochi K, Suzumura A, Yamamoto K, Kawano Y, Tsuji S, Hirata M, Sakate R, Kimura T, Shimizu Y, Nagaishi A, Okada K, Hayashi F, Sakoda A, Masaki K, Shinoda K, Isobe N, Matsushita T, Kira JI (2021) HLA genotype-clinical phenotype correlations in multiple sclerosis and neuromyelitis optica spectrum disorders based on Japan MS/NMOSD Biobank data. Sci Rep 11(1):607. https://doi.org/10.1038/s41598-020-79833-7
5. Frau J, Coghe G, Lorefice L, Fenu G, Cocco E (2023) The role of microorganisms in the etiopathogenesis of demyelinating diseases. Life (Basel) 13(6):1309. https://doi.org/10.3390/life13061309
6. Liu S, Tan B, Zhou J, Xiao L, Li M, Yin J (2024) Vitamin D status and the risk of neuromyelitis optica spectrum disorders: a systematic review and meta-analysis. J Clin Neurosci 119:185–192. https://doi.org/10.1016/j.jocn.2023.12.010
7. Davey Smith G (2019) Post-modern epidemiology: when methods meet matter. Am J Epidemiol 188(8):1410–1419. https://doi.org/10.1093/aje/kwz064
8. Hor JY, Asgari N, Nakashima I, Broadley SA, Leite MI, Kissani N, Jacob A, Marignier R, Weinshenker BG, Paul F, Pittock SJ, Palace J, Wingerchuk DM, Behne JM, Yeaman MR, Fujihara K (2020) Epidemiology of neuromyelitis optica spectrum disorder and its prevalence and incidence worldwide. Front Neurol 11:501. https://doi.org/10.3389/fneur.2020.00501
9. Wingerchuk DM (2009) Neuromyelitis optica: effect of gender. J Neurol Sci 286(1–2):18–23. https://doi.org/10.1016/j.jns.2009.08.045
10. Pandit L, Asgari N, Apiwattanakul M, Palace J, Paul F, Leite MI, Kleiter I, Chitnis T, Consortium GIC, Biorepository for Neuromyelitis O (2015) Demographic and clinical features of neuromyelitis optica: a review. Mult Scler 21(7):845–853. https://doi.org/10.1177/1352458515572406
11. Chitnis T, Ness J, Krupp L, Waubant E, Hunt T, Olsen CS, Rodriguez M, Lotze T, Gorman M, Benson L, Belman A,

Weinstock-Guttman B, Aaen G, Graves J, Patterson M, Rose JW, Casper TC (2016) Clinical features of neuromyelitis optica in children: US Network of Pediatric MS centers report. Neurology 86(3):245–252. https://doi.org/10.1212/WNL.0000000000002283
12. Fragoso YD, Ruocco HH, Dias RM, Cabeca H, Goncalves R, de Carvalho Sousa NA, Spessotto CV, Tauil CB, Alves-Leon SV, Gomes S, Goncalves MVM, Machado SCN, Anacleto A, Correa EC, Pimentel MLV, Santos GAC (2019) Late onset of neuromyelitis optica spectrum disorders. Neurol Ther 8(2):477–482. https://doi.org/10.1007/s40120-019-0143-2
13. Wingerchuk DM, Hogancamp WF, O'Brien PC, Weinshenker BG (1999) The clinical course of neuromyelitis optica (Devic's syndrome). Neurology 53(5):1107–1114. https://doi.org/10.1212/wnl.53.5.1107
14. Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG (2006) Revised diagnostic criteria for neuromyelitis optica. Neurology 66(10):1485–1489. https://doi.org/10.1212/01.wnl.0000216139.44259.74
15. Wingerchuk DM, Lennon VA, Lucchinetti CF, Pittock SJ, Weinshenker BG (2007) The spectrum of neuromyelitis optica. Lancet Neurol 6(9):805–815. https://doi.org/10.1016/S1474-4422(07)70216-8
16. Banwell B, Bennett JL, Marignier R, Kim HJ, Brilot F, Flanagan EP, Ramanathan S, Waters P, Tenembaum S, Graves JS, Chitnis T, Brandt AU, Hemingway C, Neuteboom R, Pandit L, Reindl M, Saiz A, Sato DK, Rostasy K, Paul F, Pittock SJ, Fujihara K, Palace J (2023) Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: international MOGAD panel proposed criteria. Lancet Neurol 22(3):268–282. https://doi.org/10.1016/S1474-4422(22)00431-8
17. Boudjani H, Fadda G, Dufort G, Antel J, Giacomini P, Levesque-Roy M, Oskoui M, Duquette P, Prat A, Girard M, Rebillard RM, Meijer I, Pinchefsky E, Nguyen CE, Rossignol E, Rouleau J, Blanchard O, Khairallah N, Beauchemin P, Trudelle AM, Lapointe E, Saveriano A, Larochelle C (2023) Clinical course, imaging, and pathological features of 45 adult and pediatric cases of myelin oligodendrocyte glycoprotein antibody-associated disease. Mult Scler Relat Disord 76:104787. https://doi.org/10.1016/j.msard.2023.104787
18. Modig K, Rau R, Ahlbom A (2020) Life expectancy: What does it measure? BMJ Open 10(7):e035932. https://doi.org/10.1136/bmjopen-2019-035932
19. World Health Organization (2020) Life expectancy and health life expectancy data by country. Accessed 24 Oct 2023. World Health Organization, Geneva, Switzerland. https://www.who.int/data/gho/data/indicators/indicator-details/GHO/life-expectancy-at-birth-(years)
20. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C (2015) Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. Int J Evid Based Healthc 13(3):147–153. https://doi.org/10.1097/XEB.0000000000000054
21. Wan X, Wang W, Liu J, Tong T (2014) Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 14:135. https://doi.org/10.1186/1471-2288-14-135
22. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2008) Comprehensive meta-analysis (version 2.2.027). Organ Res Methods 11(1):188–191. https://doi.org/10.1177/1094428106296641
23. Möller S, Ahrenfeldt LJ (2021) Estimating relative risk when observing zero events-frequentist inference and Bayesian credibility intervals. Int J Env Res Pub Health 18(11):5527. https://doi.org/10.3390/ijerph18115527
24. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327(7414):557–560. https://doi.org/10.1136/bmj.327.7414.557
25. Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 315(7109):629–634. https://doi.org/10.1136/bmj.315.7109.629
26. Naing NN (2000) Easy way to learn standardization: direct and indirect methods. Malays J Med Sci 7(1):10–15
27. United Nations (2022) World population prospects: the 2022 revision. Accessed 24 Oct 2023. United Nations, Department of Economic and Social Affairs, Population Division, New York, NY, USA. https://www.populationpyramid.net/
28. Aboul-Enein F, Seifert-Held T, Mader S, Kuenz B, Lutterotti A, Rauschka H, Rommer P, Leutmezer F, Vass K, Flamm-Horak A, Stepansky R, Lang W, Fertl E, Schlager T, Heller T, Eggers C, Safoschnik G, Fuchs S, Kraus J, Assar H, Guggenberger S, Reisz M, Schnabl P, Komposch M, Simschitz P, Skrobal A, Moser A, Jeschow M, Stadlbauer D, Freimuller M, Guger M, Schmidegg S, Franta C, Weiser V, Koppi S, Niederkorn-Duft M, Raber B, Schmeissner I, Jecel J, Tinchon A, Storch MK, Reindl M, Berger T, Kristoferitsch W (2013) Neuromyelitis optica in Austria in 2011: to bridge the gap between neuroepidemiological research and practice in a study population of 8.4 million people. PLoS ONE 8(11):e79649. https://doi.org/10.1371/journal.pone.0079649
29. Adoni T, Lino AM, da Gama PD, Apostolos-Pereira SL, Marchiori PE, Kok F, Callegaro D (2010) Recurrent neuromyelitis optica in Brazilian patients: clinical, immunological, and neuroimaging characteristics. Mult Scler 16(1):81–86. https://doi.org/10.1177/1352458509353651
30. Altintas A, Karabudak R, Balci BP, Terzi M, Soysal A, Saip S, Tuncer Kurne A, Uygunoglu U, Nalbantoglu M, Gozubatik Celik G, Isik N, Celik Y, Gokcay F, Duman T, Boz C, Yucesan C, Mangan MS, Celebisoy N, Diker S, Colpak Isikay I, Kansu T, Siva A (2015) Neuromyelitis optica and neuromyelitis optica spectrum disorder patients in Turkish cohort: demographic, clinical, and laboratory features. Neurologist 20(4):61–66. https://doi.org/10.1097/NRL.0000000000000057
31. Alves CS, Santos FBC, Diniz DS (2022) Correlation between Amerindian ancestry and neuromyelitis optica spectrum disorders (NMSOD) among patients in Midwestern Brazil. Arq Neuropsiquiatr 80(5):497–504. https://doi.org/10.1590/0004-282X-ANP-2020-0527
32. Asgari N, Lillevang ST, Skejoe HP, Falah M, Stenager E, Kyvik KO (2011) A population-based study of neuromyelitis optica in Caucasians. Neurology 76(18):1589–1595. https://doi.org/10.1212/WNL.0b013e3182190f74
33. Barhate KS, Ganeshan M, Singhal BS (2014) A clinical and radiological profile of neuromyelitis optica and spectrum disorders in an Indian cohort. Ann Indian Acad Neurol 17(1):77–81. https://doi.org/10.4103/0972-2327.128559
34. Bennis A, El Otmani H, Benkirane N, Harrizi I, El Moutawakil B, Rafai MA, Slassi I (2019) Clinical course of neuromyelitis optica spectrum disorder in a moroccan cohort. Mult Scler Relat Disord 30:141–148. https://doi.org/10.1016/j.msard.2019.02.012
35. Bichuetti DB, Oliveira EM, Souza NA, Rivero RL, Gabbai AA (2009) Neuromyelitis optica in Brazil: a study on clinical and prognostic factors. Mult Scler 15(5):613–619. https://doi.org/10.1177/1352458508101935
36. Bizzoco E, Lolli F, Repice AM, Hakiki B, Falcini M, Barilaro A, Taiuti R, Siracusa G, Amato MP, Biagioli T, Lori S, Moretti M, Vinattieri A, Nencini P, Massacesi L, Mata S (2009) Prevalence of neuromyelitis optica spectrum disorder and phenotype distribution. J Neurol 256(11):1891–1898. https://doi.org/10.1007/s00415-009-5171-x

37. Bukhari W, Prain KM, Waters P, Woodhall M, O'Gorman CM, Clarke L, Silvestrini RA, Bundell CS, Abernethy D, Bhuta S, Blum S, Boggild M, Boundy K, Brew BJ, Brown M, Brownlee WJ, Butzkueven H, Carroll WM, Chen C, Coulthard A, Dale RC, Das C, Dear K, Fabis-Pedrini MJ, Fulcher D, Gillis D, Hawke S, Heard R, Henderson APD, Heshmat S, Hodgkinson S, Jimenez-Sanchez S, Killpatrick T, King J, Kneebone C, Kornberg AJ, Lechner-Scott J, Lin MW, Lynch C, Macdonell R, Mason DF, McCombe PA, Pender MP, Pereira JA, Pollard JD, Reddel SW, Shaw C, Spies J, Stankovich J, Sutton I, Vucic S, Walsh M, Wong RC, Yiu EM, Barnett MH, Kermode AG, Marriott MP, Parratt JDE, Slee M, Taylor BV, Willoughby E, Wilson RJ, Vincent A, Broadley SA (2017) Incidence and prevalence of NMOSD in Australia and New Zealand. J Neurol Neurosurg Psychiatry 88(8):632–638. https://doi.org/10.1136/jnnp-2016-314839
38. Cabre P, Heinzlef O, Merle H, Buisson GG, Bera O, Bellance R, Vernant JC, Smadja D (2001) MS and neuromyelitis optica in Martinique (French West Indies). Neurology 56(4):507–514. https://doi.org/10.1212/wnl.56.4.507
39. Cabrera-Gomez JA, Kurtzke JF, Gonzalez-Quevedo A, Lara-Rodriguez R (2009) An epidemiological study of neuromyelitis optica in Cuba. J Neurol 256(1):35–44. https://doi.org/10.1007/s00415-009-0009-0
40. Ceccarelli A, Mifsud VA, Dogar A, Hussain SI (2020) Seropositive neuromyelitis optica spectrum disorder in Emirati patients: a case series. J Clin Neurosci 72:185–190. https://doi.org/10.1016/j.jocn.2019.11.045
41. Chan KH, Lee R, Lee JC, Tse AC, Pang SY, Lau GK, Teo KC, Ho PW (2013) Central nervous system inflammatory demyelinating disorders among Hong Kong Chinese. J Neuroimmunol 262(1–2):100–105. https://doi.org/10.1016/j.jneuroim.2013.06.004
42. Collongues N, Marignier R, Zephir H, Papeix C, Blanc F, Ritleng C, Tchikviladze M, Outteryck O, Vukusic S, Fleury M, Fontaine B, Brassat D, Clanet M, Milh M, Pelletier J, Audoin B, Ruet A, Lebrun-Frenay C, Thouvenot E, Camu W, Debouverie M, Creange A, Moreau T, Labauge P, Castelnovo G, Edan G, Le Page E, Defer G, Barroso B, Heinzlef O, Gout O, Rodriguez D, Wiertlewski S, Laplaud D, Borgel F, Tourniaire P, Grimaud J, Brochet B, Vermersch P, Confavreux C, de Seze J (2010) Neuromyelitis optica in France: a multicenter study of 125 patients. Neurology 74(9):736–742. https://doi.org/10.1212/WNL.0b013e3181d31e35
43. Cossburn M, Tackley G, Baker K, Ingram G, Burtonwood M, Malik G, Pickersgill T, te Water Naude J, Robertson N (2012) The prevalence of neuromyelitis optica in South East Wales. Eur J Neurol 19(4):655–659. https://doi.org/10.1111/j.1468-1331.2011.03529.x
44. Daoudi S, Bouzar M (2016) Neuromyelitis optica spectrum disorders in Algeria: a preliminary study in the region of Tizi Ouzou. Mult Scler Relat Disord 6:37–40. https://doi.org/10.1016/j.msard.2015.12.005
45. Del Negro MC, Marinho PB, Papais-Alvarenga RM (2017) Neuromyelitis optica: phenotypic characteristics in a Brazilian case series. Arq Neuropsiquiatr 75(2):81–86. https://doi.org/10.1590/0004-282X20160193
46. Drulovic J, Martinovic V, Basuroski ID, Mesaros S, Mader S, Weinshenker B, Pekmezovic T (2019) Long-term outcome and prognosis in patients with neuromyelitis optica spectrum disorder from Serbia. Mult Scler Relat Disord 36:101413. https://doi.org/10.1016/j.msard.2019.101413
47. Eskandarieh S, Nedjat S, Azimi AR, Moghadasi AN, Sahraian MA (2017) Neuromyelitis optica spectrum disorders in Iran. Mult Scler Relat Disord 18:209–212. https://doi.org/10.1016/j.msard.2017.10.007
48. Espiritu AI, Mesina BVQ, Puerto AAD, Reyes NGD, Damian LF, Pascual VJ (2019) Neuromyelitis optica spectrum disorder in a tertiary hospital in the Philippines: a case series. Mult Scler Relat Disord 31:124–130. https://doi.org/10.1016/j.msard.2019.04.006
49. Etemadifar M, Sabeti F, Ebrahimian S, Momeni F (2020) Dorsal midbrain involvement in MRI as a core clinical manifestation for NMOSD diagnosis. Mult Scler Relat Disord 43:102150. https://doi.org/10.1016/j.msard.2020.102150
50. Flanagan EP, Cabre P, Weinshenker BG, St Sauver J, Jacobson DJ, Majed M, Lennon VA, Lucchinetti CF, McKeon A, Matiello M, Kale N, Wingerchuk DM, Mandrekar J, Sagen JA, Fryer JP, Borders Robinson A, Pittock SJ (2016) Epidemiology of aquaporin-4 autoimmunity and neuromyelitis optica spectrum. Ann Neurol 79(5):775–783. https://doi.org/10.1002/ana.24617
51. Fukuda TG, Silva ITF, Dos Santos TSS, Filho MBP, de Abreu FF, Oliveira-Filho J (2022) Clinical and prognostic aspects of patients with the Neuromyelitis Optica Spectrum Disorder (NMOSD) from a cohort in Northeast Brazil. BMC Neurol 22(1):95. https://doi.org/10.1186/s12883-022-02621-5
52. Gao M, Yao X, Ding J, Hong R, Wu Y, Huang H, Zhuang L, Li Z, Wang Y, Zhang Y, Guan Y (2019) Low levels of vitamin D and the relationship between vitamin D and Th2 axis-related cytokines in neuromyelitis optica spectrum disorders. J Clin Neurosci 61:22–27. https://doi.org/10.1016/j.jocn.2018.11.024
53. Gracia F, Ramirez D, Parajeles-Vindas A, Diaz A, Diaz de la Fe A, Sanchez NER, Escobar RC, Valle LAG, Weiser R, Santos B, Candelario A, Benzadon A, Araujo P, Valderrama C, Larreategui M, Carrillo G, Gracia K, Vazquez-Cespedes J, Monterrey-Alvarez P, Carazo-Cespedes K, Sanabria-Castro A, Miranda-Loria G, Balmaceda-Meza A, Rivera LIP, Leal IO, Salinas LCR, Thompson A, Torres EL, Pereira DE, Zepeda C, Lopez CA, Valse EAC, Urbina KZC, Urrutia MA, Van Sijtveld I, Armien B, Rivera VM (2022) Neuromyelitis optica spectrum disorder in central America and the caribbean: a multinational clinical characterization study. Neurol Int 14(1):284–293. https://doi.org/10.3390/neurolint14010023
54. Holroyd KB, Aziz F, Szolics M, Alsaadi T, Levy M, Schiess N (2018) Prevalence and characteristics of transverse myelitis and neuromyelitis optica spectrum disorders in the United Arab Emirates: a multicenter, retrospective study. Clin Exp Neuroimmunol 9(3):155–161. https://doi.org/10.1111/cen3.12458
55. Hor JY, Lim TT, Chia YK, Ching YM, Cheah CF, Tan K, Chow HB, Arip M, Eow GB, Easaw PES, Leite MI (2018) Prevalence of neuromyelitis optica spectrum disorder in the multi-ethnic Penang Island, Malaysia, and a review of worldwide prevalence. Mult Scler Relat Disord 19:20–24. https://doi.org/10.1016/j.msard.2017.10.015
56. Ibis SC, Omaira M, Arnoldo S, Elizabeth A, Sandra M, Carlota CM, Elizabeth C, Laura V, Rosalba L, Oscar V, Luisa DM, Nahir A, Hernandez F (2021) Epidemiological findings of neuromyelitis optica spectrum disorders in a Venezuelan study. Mult Scler Relat Disord 47:102652. https://doi.org/10.1016/j.msard.2020.102652
57. Jagtap SA, Mandliya A, Sarada C, Nair MD (2015) Neuromyelitis optica and neuromyelitis optica spectrum disorder: natural history and long-term outcome, an Indian experience. J Neurosci Rural Pract 6(3):331–335. https://doi.org/10.4103/0976-3147.158755
58. Jiao Y, Fryer JP, Lennon VA, Jenkins SM, Quek AM, Smith CY, McKeon A, Costanzi C, Iorio R, Weinshenker BG, Wingerchuk DM, Shuster EA, Lucchinetti CF, Pittock SJ (2013) Updated estimate of AQP4-IgG serostatus and disability outcome in neuromyelitis optica. Neurology 81(14):1197–1204. https://doi.org/10.1212/WNL.0b013e3182a6cb5c

59. Jonsson DI, Sveinsson O, Hakim R, Brundin L (2019) Epidemiology of NMOSD in Sweden from 1987 to 2013: a nationwide population-based study. Neurology 93(2):e181–e189. https://doi.org/10.1212/WNL.0000000000007746
60. Joshi PB, Shah SD, Patel MA, Shah SV, Darji SH, Mirche KC (2022) A study of neuromyelitis optica spectrum disorders (NMOSD): disease pattern based on antibody status. Neurol India 70(3):1131–1136. https://doi.org/10.4103/0028-3886.349679
61. Kashipazha D, Mohammadianinejad SE, Majdinasab N, Azizi M, Jafari M (2015) A descriptive study of prevalence, clinical features and other findings of neuromyelitis optica and neuromyelitis optica spectrum disorder in Khuzestan Province, Iran. Iran J Neurol 14(4):204–210
62. Kim SH, Kim W, Li XF, Jung IJ, Kim HJ (2012) Clinical spectrum of CNS aquaporin-4 autoimmunity. Neurology 78(15):1179–1185. https://doi.org/10.1212/WNL.0b013e31824f8069
63. Kishk NA, Abdelfattah W, Shalaby NM, Shehata HS, Hassan A, Hegazy MI, Abokrysha NT, Abdellatif D, Shawky SM, Abdo SS, Taha N, Fouad AM, Elmazny A, Ragab AH (2021) The aquaporin4-IgG status and how it affects the clinical features and treatment response in NMOSD patients in Egypt. BMC Neurol 21(1):53. https://doi.org/10.1186/s12883-021-02083-1
64. Kitley J, Waters P, Woodhall M, Leite MI, Murchison A, George J, Kuker W, Chandratre S, Vincent A, Palace J (2014) Neuromyelitis optica spectrum disorders with aquaporin-4 and myelin-oligodendrocyte glycoprotein antibodies: a comparative study. JAMA Neurol 71(3):276–283. https://doi.org/10.1001/jamaneurol.2013.5857
65. Kleiter I, Gahlen A, Borisow N, Fischer K, Wernecke KD, Wegner B, Hellwig K, Pache F, Ruprecht K, Havla J, Krumbholz M, Kumpfel T, Aktas O, Hartung HP, Ringelstein M, Geis C, Kleinschnitz C, Berthele A, Hemmer B, Angstwurm K, Stellmann JP, Schuster S, Stangel M, Lauda F, Tumani H, Mayer C, Zeltner L, Ziemann U, Linker R, Schwab M, Marziniak M, Then Bergh F, Hofstadt-van Oy U, Neuhaus O, Winkelmann A, Marouf W, Faiss J, Wildemann B, Paul F, Jarius S, Trebst C, Neuromyelitis Optica Study G (2016) Neuromyelitis optica: evaluation of 871 attacks and 1153 treatment courses. Ann Neurol 79(2):206–216. https://doi.org/10.1002/ana.24554
66. Mealy MA, Kessler RA, Rimler Z, Reid A, Totonis L, Cutter G, Kister I, Levy M (2018) Mortality in neuromyelitis optica is strongly associated with African ancestry. Neurol Neuroimmunol Neuroinflamm 5(4):e468. https://doi.org/10.1212/NXI.0000000000000468
67. Mireles-Ramirez MA, Pacheco-Moises FP, Gonzalez-Usigli HA, Sanchez-Rosales NA, Hernandez-Preciado MR, Delgado-Lara DLC, Hernandez-Cruz JJ, Ortiz GG (2022) Neuromyelitis optica spectrum disorder: pathophysiological approach. Int J Neurosci. https://doi.org/10.1080/00207454.2022.2153046
68. Mirmosayyeb O, Barzegar M, Afshari-Safavi A, Nehzat N, Heidari A, Emami P, Shaygannejad V (2021) Evaluation of month of birth in neuromyelitis optica spectrum disorders (NMSOD) and multiple sclerosis (MS). Mult Scler Int 2021:8874999. https://doi.org/10.1155/2021/8874999
69. Miyamoto K, Fujihara K, Kira JI, Kuriyama N, Matsui M, Tamakoshi A, Kusunoki S (2018) Nationwide epidemiological study of neuromyelitis optica in Japan. J Neurol Neurosurg Psychiatry 89(6):667–668. https://doi.org/10.1136/jnnp-2017-317321
70. Netravathi M, Bollampalli HK, Bhat MD, Ganaraja VH, Prasad S, Mahadevan A, Kamble N, Nalini A, Yadav R, Pal PK, Satishchandra P (2019) Clinical, neuroimaging and therapeutic response in AQP4-positive NMO patients from India. Mult Scler Relat Disord 30:85–93. https://doi.org/10.1016/j.msard.2019.01.032
71. Pandit L, Kundapur R (2014) Prevalence and patterns of demyelinating central nervous system disorders in urban Mangalore, South India. Mult Scler 20(12):1651–1653. https://doi.org/10.1177/1352458514521503
72. Papais-Alvarenga RM, Vasconcelos CC, Carra A, de Castillo IS, Florentin S, Diaz de Bedoya FH, Mandler R, de Siervi LC, Pimentel ML, Alvarenga MP, Alvarenga MP, Grzesiuk AK, Gama Pereira AB, Gomes Neto AP, Velasquez C, Soublette C, Fleitas CV, Diniz DS, Armas E, Batista E, Hernandez F, Pereira FF, Siqueira HH, Cabeca H, Sanchez J, Brooks JB, Goncalves MV, Barroso MC, Ravelo ME, Castillo MC, Ferreira ML, Rocha MS, Parolin MK, Molina O, Marinho PB, Christo PP, Brant de Souza R, Pessanha Neto S, Camargo SM, Machado SC, Neri VC, Fragoso YD, Alvarenga H, Thuler LC (2015) Central nervous system idiopathic inflammatory demyelinating disorders in south americans: a descriptive, multicenter, cross-sectional study. PLoS ONE 10(7):e0127757. https://doi.org/10.1371/journal.pone.0127757
73. Papp V, Iljicsov A, Rajda C, Magyari M, Koch-Henriksen N, Petersen T, Jakab G, Deme I, Nagy F, Imre P, Lohner Z, Kovacs K, Birkas AJ, Koves A, Rum G, Nagy Z, Kerenyi L, Vecsei L, Bencsik K, Jobbagy Z, Dioszeghy P, Horvath L, Galantai G, Kasza J, Molnar G, Simo M, Satori M, Rozsa C, Acs P, Berki T, Lovas G, Komoly S, Illes Z (2020) A population-based epidemiological study of neuromyelitis optica spectrum disorder in Hungary. Eur J Neurol 27(2):308–317. https://doi.org/10.1111/ene.14079
74. Papp V, Trones KDP, Magyari M, Koch-Henriksen N, Iljicsov A, Rajda C, Nielsen HH, Lovas G, Rozsa C, Kristiansen BH, Stenager E, Frederiksen JL, Komoly S, Sellebjerg F, Petersen T, Illes Z (2021) Population-based head-to-head comparison of the clinical characteristics and epidemiology of AQP4 antibody-positive NMOSD between two European countries. Mult Scler Relat Disord 51:102879. https://doi.org/10.1016/j.msard.2021.102879
75. Paz ES, Maciel P, D'Almeida JAC, Silva B, Sampaio HAC, Pinheiro ADV, Carioca AAF, de Melo MLP (2021) Excess weight, central adiposity and pro-inflammatory diet consumption in patients with neuromyelitis optica spectrum disorder. Mult Scler Relat Disord 54:103110. https://doi.org/10.1016/j.msard.2021.103110
76. Rafiee F, Tarjoman T, Moghadasi AN, Sahraian MA, Azimi A, Rezaeimanesh N, Eskandarieh S (2020) Stressful life events, socioeconomic status, and the risk of neuromyelitis optica spectrum disorder: a population-based case–control study. Mult Scler Relat Disord 46:102544. https://doi.org/10.1016/j.msard.2020.102544
77. Rivera JF, Kurtzke JF, Booth VJ, Corona VT (2008) Characteristics of Devic's disease (neuromyelitis optica) in Mexico. J Neurol 255(5):710–715. https://doi.org/10.1007/s00415-008-0781-2
78. Rojas JI, Alonso Serena M, Garcea O, Patrucco L, Carra A, Correale J, Vrech C, Pappolla A, Miguez J, Doldan ML, Silveira F, Alonso R, Cohen L, Pita C, Silva BA, Fiol M, Gaitan MI, Marrodan M, Negrotto L, Ysrraelit MC, Deri N, Luetic G, Caride A, Carnero Contentti E, Lopez PA, Pettinicchi JP, Curbelo C, Martinez AD, Steinberg JD, Balbuena ME, Tkachuk V, Burgos M, Knorre E, Leguizamon F, Piedrabuena R, Liwacki SDV, Barboza AG, Nofal P, Volman G, Alvez Pinheiro A, Hryb J, Tavolini D, Blaya PA, Silva E, Blanche J, Tizio S, Caceres F, Saladino ML, Zanga G, Fracaro ME, Sgrilli G, Pagani Cassara F, Vazquez G, Sinay V, Menichini ML, Lazaro L, Cabrera LM, Bestoso S, Divi P, Jacobo M, Kohler E, Kohler M, Giunta D, Mainella C, Manzi R, Parada Marcilla M, Viglione JP, Martos I, Reich E, Jose G, Cristiano E, Fernandez Liguori N, on behalf Relevar EMi (2020) Multiple sclerosis and neuromyelitis optica spectrum disorders in Argentina: comparing baseline data from the Argentinean MS

Registry (RelevarEM). Neurol Sci 41(6):1513–1519. https://doi.org/10.1007/s10072-019-04230-6
79. Salama S, Marouf H, Ihab Reda M, Mansour AR, ELKholy O, Levy M (2018) Clinical and radiological characteristics of neuromyelitis optica spectrum disorder in the North Egyptian Nile Delta. J Neuroimmunol 324:22–25. https://doi.org/10.1016/j.jneuroim.2018.08.014
80. Sepulveda M, Armangue T, Sola-Valls N, Arrambide G, Meca-Lallana JE, Oreja-Guevara C, Mendibe M, Alvarez de Arcaya A, Aladro Y, Casanova B, Olascoaga J, Jimenez-Huete A, Fernandez-Fournier M, Ramio-Torrenta L, Cobo-Calvo A, Vinals M, de Andres C, Meca-Lallana V, Cervello A, Calles C, Rubio MB, Ramo-Tello C, Caminero A, Munteis E, Antiguedad AR, Blanco Y, Villoslada P, Montalban X, Graus F, Saiz A (2016) Neuromyelitis optica spectrum disorders: comparison according to the phenotype and serostatus. Neurol Neuroimmunol Neuroinflamm 3(3):e225. https://doi.org/10.1212/NXI.0000000000000225
81. Shaygannejad V, Maljaei MB, Bank SS, Mirmosayyeb O, Maracy MR, Askari G (2018) Association between sun exposure, vitamin D intake, serum vitamin D level, and immunoglobulin G level in patients with neuromyelitis optica spectrum disorder. Int J Prev Med 9:68. https://doi.org/10.4103/ijpvm.IJPVM_45_16
82. Shosha E, Al Asmi A, Nasim E, Inshasi J, Abdulla F, Al Malik Y, Althobaiti A, Alzawahmah M, Alnajashi HA, Binfalah M, AlHarbi A, Thubaiti IA, Ahmed SF, Al-Hashel J, Elyas M, Nandhagopal R, Gujjar A, Harbi TA, Towaijri GA, Alsharooqi IA, AlMaawi A, Al Khathaami AM, Alotaibi N, Nahrir S, Al Rasheed AA, Al Qahtani M, Alawi S, Hundallah K, Jumah M, Alroughani R, with the Guthy-Jackson Charitable Foundation International Clinical C (2020) Neuromyelitis optica spectrum disorders in Arabian Gulf (NMOAG); establishment and initial characterization of a patient registry. Mult Scler Relat Disord 38:101448. https://doi.org/10.1016/j.msard.2019.101448
83. Singh N, Bhatia R, Bali P, Sreenivas V, Padma MV, Goyal V, Saxena R, Dash D, Garg A, Joseph SL (2021) Clinical features, gender differences, disease course, and outcome in neuromyelitis optica spectrum disorder. Ann Indian Acad Neurol 24(2):186–191. https://doi.org/10.4103/aian.AIAN_334_20
84. Stratos K, Lee L, Dai D, Pavenski K, Zuo F, Rotstein D (2020) Evaluation of ethnicity as a predictor of diagnostic phenotype and prognosis in neuromyelitis optica spectrum disorder in Toronto. Canada Mult Scler Relat Disord 40:101950. https://doi.org/10.1016/j.msard.2020.101950
85. Sun H, Sun X, Li J, Huo Y, Wu L, Huang D, Yu S, Wu W (2017) Gender differences among Chinese patients with neuromyelitis optica spectrum disorders. Mult Scler Relat Disord 17:5–8. https://doi.org/10.1016/j.msard.2017.06.008
86. Tarhan B, Rempe T, Rahman S, Rodriguez E, Sladky J, Tuna IS, Rees J (2022) A comparison of pediatric- and adult-onset aquaporin-4 immunoglobulin G-positive neuromyelitis optica spectrum disorder: a review of clinical and radiographic characteristics. J Child Neurol 37(8–9):727–737. https://doi.org/10.1177/08830738221103085
87. Tian DC, Li Z, Yuan M, Zhang C, Gu H, Wang Y, Shi FD (2020) Incidence of neuromyelitis optica spectrum disorder (NMOSD) in China: a national population-based study. Lancet Reg Health West Pac 2:100021. https://doi.org/10.1016/j.lanwpc.2020.100021
88. van Pelt ED, Wong YY, Ketelslegers IA, Hamann D, Hintzen RQ (2016) Neuromyelitis optica spectrum disorders: comparison of clinical and magnetic resonance imaging characteristics of AQP4-IgG versus MOG-IgG seropositive cases in the Netherlands. Eur J Neurol 23(3):580–587. https://doi.org/10.1111/ene.12898
89. Wu Y, Yang M, Gao P, Wang Z, Wu J, Wang J, Xu Q, Zhou H, Wu T, Wu W, Wei S, Hu YH (2022) Incidence of neuromyelitis optica spectrum disorders in China: a large cohort study using claim data. BMJ Open 12(1):e048942. https://doi.org/10.1136/bmjopen-2021-048942
90. Yin J, Long Y, Shan F, Fan Y, Wu L, Zhong R, Gao C, Chen X, Gao Q, Yang N (2015) Clinical manifestations of neuromyelitis optica in male and female patients. Neurol Res 37(11):967–973. https://doi.org/10.1179/1743132815Y.0000000081
91. Banwell B, Tenembaum S, Lennon VA, Ursell E, Kennedy J, Bar-Or A, Weinshenker BG, Lucchinetti CF, Pittock SJ (2008) Neuromyelitis optica-IgG in childhood inflammatory demyelinating CNS disorders. Neurology 70(5):344–352. https://doi.org/10.1212/01.wnl.0000284600.80782.d5
92. Camera V, Messina S, Elhadd KT, Sanpera-Iglesias J, Mariano R, Hacohen Y, Dobson R, Meletti S, Wassmer E, Lim MJ, Huda S, Hemingway C, Leite MI, Ramdas S, Palace J (2022) Early predictors of disability of paediatric-onset AQP4-IgG-seropositive neuromyelitis optica spectrum disorders. J Neurol Neurosurg Psychiatry 93(1):101–111. https://doi.org/10.1136/jnnp-2021-327206
93. Collongues N, Marignier R, Zephir H, Papeix C, Fontaine B, Blanc F, Rodriguez D, Fleury M, Vukusic S, Pelletier J, Audoin B, Thouvenot E, Camu W, Barroso B, Ruet A, Brochet B, Vermersch P, Confavreux C, de Seze J (2010) Long-term follow-up of neuromyelitis optica with a pediatric onset. Neurology 75(12):1084–1088. https://doi.org/10.1212/WNL.0b013e3181f39a66
94. Huppke P, Bluthner M, Bauer O, Stark W, Reinhardt K, Huppke B, Gartner J (2010) Neuromyelitis optica and NMO-IgG in European pediatric patients. Neurology 75(19):1740–1744. https://doi.org/10.1212/WNL.0b013e3181fc2823
95. Lin WS, Wang HP, Chen HM, Lin JW, Lee WT (2020) Epidemiology of pediatric multiple sclerosis, neuromyelitis optica, and optic neuritis in Taiwan. J Neurol 267(4):925–932. https://doi.org/10.1007/s00415-019-09647-9
96. Lotze TE, Northrop JL, Hutton GJ, Ross B, Schiffman JS, Hunter JV (2008) Spectrum of pediatric neuromyelitis optica. Pediatrics 122(5):e1039–e1047. https://doi.org/10.1542/peds.2007-2758
97. Martins C, Moura J, Figueiroa S, Garrido C, Martins J, Samoes R, Guimaraes J, Melo C, Sousa R, Palavra F, Ferreira J, da Silva AM, Sa MJ, Santos E (2022) Pediatric neuromyelitis optica spectrum disorders in Portugal: a multicentre retrospective study. Mult Scler Relat Disord 59:103531. https://doi.org/10.1016/j.msard.2022.103531
98. McKeon A, Lennon VA, Lotze T, Tenenbaum S, Ness JM, Rensel M, Kuntz NL, Fryer JP, Homburger H, Hunter J, Weinshenker BG, Krecke K, Lucchinetti CF, Pittock SJ (2008) CNS aquaporin-4 autoimmunity in children. Neurology 71(2):93–100. https://doi.org/10.1212/01.wnl.0000314832.24682.c6
99. Paolilo RB, Hacohen Y, Yazbeck E, Armangue T, Bruijstens A, Lechner C, Apostolos-Pereira SL, Martynenko Y, Breu M, de Medeiros RC, Wassmer E, Baumann M, Papetti L, Capobianco M, Kornek B, Rostasy K, da Paz JA, Ciccarelli O, Lim M, Saiz A, Neuteboom R, Marignier R, Hemingway C, Sato DK, Deiva K (2020) Treatment and outcome of aquaporin-4 antibody-positive NMOSD: a multinational pediatric study. Neurol Neuroimmunol Neuroinflamm 7(5):e837. https://doi.org/10.1212/NXI.0000000000000837
100. Yamaguchi Y, Torisu H, Kira R, Ishizaki Y, Sakai Y, Sanefuji M, Ichiyama T, Oka A, Kishi T, Kimura S, Kubota M, Takanashi J, Takahashi Y, Tamai H, Natsume J, Hamano S, Hirabayashi S, Maegaki Y, Mizuguchi M, Minagawa K, Yoshikawa H, Kira J, Kusunoki S, Hara T (2016) A nationwide survey of pediatric acquired demyelinating syndromes in Japan. Neurology

87(19):2006–2015. https://doi.org/10.1212/WNL.0000000000003318
101. Yoon HH, Park JY, Kim SY, Lee NM, Yi DY, Yun SW, Lim IS, Chae SA (2021) Epidemiology of demyelinating diseases in korean pediatric patients. J Child Neurol 36(2):141–147. https://doi.org/10.1177/0883073820959543
102. Zhou Y, Zhong X, Shu Y, Cui C, Wang J, Wang Y, Li X, Chen Z, Peng L, Kermode A, Qiu W (2019) Clinical course, treatment responses and outcomes in Chinese paediatric neuromyelitis optica spectrum disorder. Mult Scler Relat Disord 28:213–220. https://doi.org/10.1016/j.msard.2018.12.038
103. Cai LJ, Zhang Q, Zhang Y, Chen HX, Shi ZY, Du Q, Zhou HY (2020) Clinical characteristics of very late-onset neuromyelitis optica spectrum disorder. Mult Scler Relat Disord 46:102515. https://doi.org/10.1016/j.msard.2020.102515
104. Carnero Contentti E, Daccach Marques V, Soto de Castillo I, Tkachuk V, Ariel B, Castillo MC, Cristiano E, Diegues Serva GB, Dos Santos AC, Finkelsteyn AM, Lopez PA, Patrucco L, Molina O, Pettinicchi JP, Toneguzzo V, Caride A, Rojas JI (2020) Clinical features and prognosis of late-onset neuromyelitis optica spectrum disorders in a Latin American cohort. J Neurol 267(5):1260–1268. https://doi.org/10.1007/s00415-020-09699-2
105. Collongues N, Marignier R, Jacob A, Leite MI, Siva A, Paul F, Zephir H, Akman-Demir G, Elsone L, Jarius S, Papeix C, Mutch K, Saip S, Wildemann B, Kitley J, Karabudak R, Aktas O, Kuscu D, Altintas A, Palace J, Confavreux C, De Seze J (2014) Characterization of neuromyelitis optica and neuromyelitis optica spectrum disorder patients with a late onset. Mult Scler 20(8):1086–1094. https://doi.org/10.1177/1352458513515085
106. Delgado-Garcia G, Antonio-Luna E, Lopez-Mena D, Rivas-Alonso V, Flores-Rivera J, Corona-Vazquez T (2020) AQP4-IgG-positive neuromyelitis optica spectrum disorder with late onset in Mexico. Mult Scler Relat Disord 43:102221. https://doi.org/10.1016/j.msard.2020.102221
107. Lavandier N, Bonnan M, Carra-Dalliere C, Charif M, Labauge P, Camdessanche JP, Edan G, Naudin A, Brassat D, Ciron J, Clavelou P, Dulau C, Moroso A, Brochet B, Ouallet JC, on behalf Societe Francophone de la Sclerose en P (2019) First clinical inflammatory demyelinating events of the central nervous system in a population aged over 70 years: a multicentre study. Mult Scler Relat Disord 28:309–312. https://doi.org/10.1016/j.msard.2018.12.016
108. Mao Z, Yin J, Zhong X, Zhao Z, Qiu W, Lu Z, Hu X (2015) Late-onset neuromyelitis optica spectrum disorder in AQP4-seropositivepatients in a Chinese population. BMC Neurol 15:160. https://doi.org/10.1186/s12883-015-0417-y
109. Nakahara K, Nakane S, Nagaishi A, Narita T, Matsuo H, Ando Y (2021) Very late onset neuromyelitis optica spectrum disorders. Eur J Neurol 28(8):2574–2581. https://doi.org/10.1111/ene.14901
110. Seok JM, Cho HJ, Ahn SW, Cho EB, Park MS, Joo IS, Shin HY, Kim SY, Kim BJ, Kim JK, Cho JY, Huh SY, Kwon O, Lee KH, Kim BJ, Min JH (2017) Clinical characteristics of late-onset neuromyelitis optica spectrum disorder: a multicenter retrospective study in Korea. Mult Scler 23(13):1748–1756. https://doi.org/10.1177/1352458516685416
111. Sepulveda M, Delgado-Garcia G, Blanco Y, Sola-Valls N, Martinez-Lapiscina EH, Armangue T, Montejo C, Pulido-Valdeolivas I, Martinez-Hernandez E, Arino H, Escudero D, Ruiz-Garcia R, Llufriu S, Dalmau J, Graus F, Saiz A (2019) Late-onset neuromyelitis optica spectrum disorder: the importance of autoantibody serostatus. Neurol Neuroimmunol Neuroinflamm 6(6):e607. https://doi.org/10.1212/NXI.0000000000000607
112. Zhang LJ, Yang LN, Li T, Wang J, Qi Y, Zhang DQ, Yang CS, Yang L (2017) Distinctive characteristics of early-onset and late-onset neuromyelitis optica spectrum disorders. Int J Neurosci 127(4):334–338. https://doi.org/10.1080/00207454.2016.1254630
113. Bukhari W, Clarke L, O'Gorman C, Khalilidehkordi E, Arnett S, Prain KM, Woodhall M, Silvestrini R, Bundell CS, Ramanathan S, Abernethy D, Bhuta S, Blum S, Boggild M, Boundy K, Brew BJ, Brownlee W, Butzkueven H, Carroll WM, Chen C, Coulthard A, Dale RC, Das C, Dear K, Fabis-Pedrini MJ, Fulcher D, Gillis D, Hawke S, Heard R, Henderson APD, Heshmat S, Hodgkinson S, Jimenez-Sanchez S, Kilpatrick TJ, King J, Kneebone C, Kornberg AJ, Lechner-Scott J, Lin MW, Lynch C, Macdonnell RAL, Mason DF, McCombe PA, Pereira J, Pollard JD, Reddel SW, Shaw C, Spies J, Stankovich J, Sutton I, Vucic S, Walsh M, Wong RC, Yiu EM, Barnett MH, Kermode AG, Marriott MP, Parratt J, Slee M, Taylor BV, Willoughby E, Wilson RJ, Brilot F, Vincent A, Waters P, Broadley SA (2020) The clinical profile of NMOSD in Australia and New Zealand. J Neurol 267(5):1431–1443. https://doi.org/10.1007/s00415-020-09716-4
114. Jarius S, Ruprecht K, Wildemann B, Kuempfel T, Ringelstein M, Geis C, Kleiter I, Kleinschnitz C, Berthele A, Brettschneider J, Hellwig K, Hemmer B, Linker RA, Lauda F, Mayer CA, Tumani H, Melms A, Trebst C, Stangel M, Marziniak M, Hoffmann F, Schippling S, Faiss JH, Neuhaus O, Ettrich B, Zentner C, Guthke K, Hofstadt-van Oy U, Reuss R, Pellkofer H, Ziemann U, Kern P, Wandinger KP, Bergh FT, Boettcher T, Langel S, Liebetrau M, Rommer PS, Niehaus S, Munch C, Winkelmann A, Zettl UU, Metz I, Veauthier C, Sieb JP, Wilke C, Hartung HP, Aktas O, Paul F (2012) Contrasting disease patterns in seropositive and seronegative neuromyelitis optica: a multicentre study of 175 patients. J Neuroinflammation 9:14. https://doi.org/10.1186/1742-2094-9-14
115. Nagaishi A, Takagi M, Umemura A, Tanaka M, Kitagawa Y, Matsui M, Nishizawa M, Sakimura K, Tanaka K (2011) Clinical features of neuromyelitis optica in a large Japanese cohort: comparison between phenotypes. J Neurol Neurosurg Psychiatry 82(12):1360–1364. https://doi.org/10.1136/jnnp-2011-300403
116. Alvarenga MP, Schimidt S, Alvarenga RP (2017) Epidemiology of neuromyelitis optica in Latin America. Mult Scler J Exp Transl Clin 3(3):2055217317730098. https://doi.org/10.1177/2055217317730098
117. Asgari N, Lillevang ST, Skejoe HPB, Kyvik KO (2019) Epidemiology of neuromyelitis optica spectrum disorder in Denmark (1998–2008, 2007–2014). Brain Behav 9(7):e01338. https://doi.org/10.1002/brb3.1338
118. Ashtari F, Safaei A, Shaygannejad V, Najafi MA, Vesal S (2017) Neuromyelitis optica spectrum disease characteristics in Isfahan, Iran: a cross-sectional study. J Res Med Sci 22:41. https://doi.org/10.4103/1735-1995.202142
119. Badihian S, Manouchehri N, Mirmosayyeb O, Ashtari F, Shaygannejad V (2018) Neuromyelitis optica spectrum disorder and menstruation. Rev Neurol (Paris) 174(10):716–721. https://doi.org/10.1016/j.neurol.2018.01.373
120. Bergamaschi R, Ghezzi A (2004) Devic's neuromyelitis optica: clinical features and prognostic factors. Neurol Sci 25(Suppl 4):S364–S367. https://doi.org/10.1007/s10072-004-0342-0
121. Bukhari W, Khalilidehkordi E, Mason DF, Barnett MH, Taylor BV, Fabis-Pedrini M, Kermode AG, Subramanian S, Waters P, Broadley SA, New Zealand NMOC (2022) NMOSD and MS prevalence in the Indigenous populations of Australia and New Zealand. J Neurol 269(2):836–845. https://doi.org/10.1007/s00415-021-10665-9
122. Cabre P, Gonzalez-Quevedo A, Lannuzel A, Bonnan M, Merle H, Olindo S, Chausson N, Lara-Rodriguez R, Smadja D, Cabrera-Gomez J (2009) Descriptive epidemiology of neuromyelitis optica in the Caribbean basin. Rev Neurol (Paris) 165(8–9):676–683. https://doi.org/10.1016/j.neurol.2009.02.012

123. Carnero Contentti E, Daccach Marques V, Soto de Castillo I, Tkachuk V, Lopez PA, Rojas JI (2020) Age at onset correlate with disability in Latin American aquaporin-4-IgG-positive NMOSD patients. Mult Scler Relat Disord 44:102258. https://doi.org/10.1016/j.msard.2020.102258
124. Cheng Q, Miao L, Zhang J, Guan YT, Liu ZG, Wang X, Sun XJ, Zhao ZX, Song YJ, Ding XY, Guo ZI, Cheng XJ, Chen SD, Jiang GX, Fredrikson S (2008) Clinical features of patients with multiple sclerosis from a survey in Shanghai. China Mult Scler 14(5):671–678. https://doi.org/10.1177/1352458507087844
125. Choy BNK, Ng ALK, Lai JSM (2018) Clinical characteristics of optic neuritis in Hong Kong population: 10-year review. Int Ophthalmol 38(2):557–564. https://doi.org/10.1007/s10792-017-0491-9
126. Collongues N, Marignier R, Zephir H, Blanc F, Vukusic S, Outteryck O, Fleury M, Ruet A, Borgel F, Thouvenot E, Moreau T, Defer G, Derache N, Pelletier J, Audoin B, Debouverie M, Labauge P, Gout O, Camu W, Brassat D, Brochet B, Vermersch P, Confavreux C, de Seze J (2011) High-risk syndrome for neuromyelitis optica: a descriptive and comparative study. Mult Scler 17(6):720–724. https://doi.org/10.1177/1352458510396923
127. Cristiano E, Patrucco L, Miguez J, Giunta D, Peroni J, Rojas JI (2016) Increasing incidence of multiple sclerosis among women in Buenos Aires: a 22 year health maintenance organization based study. Neurol Sci 37(10):1621–1626. https://doi.org/10.1007/s10072-016-2637-3
128. Dale GH, Svendsen KB, Gjelstrup MC, Christensen T, Houen G, Nielsen E, Bek T, Petersen T (2018) Incidence of neuromyelitis optica spectrum disorder in the Central Denmark Region. Acta Neurol Scand 137(6):582–588. https://doi.org/10.1111/ane.12903
129. Domingos J, Isidoro L, Figueiredo R, Brum M, Capela C, Barros P, Santos E, Macario Mdo C, Pinto Marques J, Pedrosa R, Vale J, Sa MJ (2015) Neuromyelitis optica in Portugal (NEMIPORT)—a multicentre study. Clin Neurol Neurosurg 134:79–84. https://doi.org/10.1016/j.clineuro.2015.04.001
130. Eskandarieh S, Nedjat S, Abdollahpour I, Moghadasi AN, Azimi AR, Sahraian MA (2017) Comparing epidemiology and baseline characteristic of multiple sclerosis and neuromyelitis optica: a case–control study. Mult Scler Relat Disord 12:39–43. https://doi.org/10.1016/j.msard.2017.01.004
131. Eskandarieh S, Nedjat S, Abdollahpour I, Azimi AR, Moghadasi AN, Asgari N, Sahraian MA (2018) Environmental risk factors in neuromyelitis optica spectrum disorder: a case–control study. Acta Neurol Belg 118(2):277–287. https://doi.org/10.1007/s13760-018-0900-5
132. Etemadifar M, Dashti M, Vosoughi R, Abtahi SH, Ramagopalan SV, Nasr Z (2014) An epidemiological study of neuromyelitis optica in Isfahan. Mult Scler 20(14):1920–1922. https://doi.org/10.1177/1352458514537699
133. Etemadifar M, Mehrbod N, Dehghani L, Golabbakhsh A, Fereidan-Esfahani M, Akbari M, Nasr Z (2014) Prevalence of Lhermitte's sign in multiple sclerosis versus neuromyelitis optica. Iran J Neurol 13(1):50–51
134. Fragoso YD, Sousa NAC, Saad T, Alves-Leon SV, Pimentel MLV, Goncalves MVM, Stella CV, Diniz DS, Santos GC, Gomes S, Adoni T, Anacleto A, Claudino R, Malfetano FR, Winckler TCD, Damasceno A, Eboni ACB, Farinhas JGD, Mota RSS (2019) Clinical characteristics of patients with neuromyelitis optica spectrum disorders with early onset. J Child Neurol 34(9):487–490. https://doi.org/10.1177/0883073819842421
135. Gold SM, Willing A, Leypoldt F, Paul F, Friese MA (2019) Sex differences in autoimmune disorders of the central nervous system. Semin Immunopathol 41(2):177–188. https://doi.org/10.1007/s00281-018-0723-8
136. Hoftberger R, Sepulveda M, Armangue T, Blanco Y, Rostasy K, Calvo AC, Olascoaga J, Ramio-Torrenta L, Reindl M, Benito-Leon J, Casanova B, Arrambide G, Sabater L, Graus F, Dalmau J, Saiz A (2015) Antibodies to MOG and AQP4 in adults with neuromyelitis optica and suspected limited forms of the disease. Mult Scler 21(7):866–874. https://doi.org/10.1177/1352458514555785
137. Houzen H, Niino M, Hirotani M, Fukazawa T, Kikuchi S, Tanaka K, Sasaki H (2012) Increased prevalence, incidence, and female predominance of multiple sclerosis in northern Japan. J Neurol Sci 323(1–2):117–122. https://doi.org/10.1016/j.jns.2012.08.032
138. Houzen H, Kondo K, Horiuchi K, Niino M (2018) Consistent increase in the prevalence and female ratio of multiple sclerosis over 15 years in northern Japan. Eur J Neurol 25(2):334–339. https://doi.org/10.1111/ene.13506
139. Jacob A, Panicker J, Lythgoe D, Elsone L, Mutch K, Wilson M, Das K, Boggild M (2013) The epidemiology of neuromyelitis optica amongst adults in the Merseyside county of United Kingdom. J Neurol 260(8):2134–2137. https://doi.org/10.1007/s00415-013-6926-y
140. Jarius S, Frederikson J, Waters P, Paul F, Akman-Demir G, Marignier R, Franciotta D, Ruprecht K, Kuenz B, Rommer P, Kristoferitsch W, Wildemann B, Vincent A (2010) Frequency and prognostic impact of antibodies to aquaporin-4 in patients with optic neuritis. J Neurol Sci 298(1–2):158–162. https://doi.org/10.1016/j.jns.2010.07.011
141. Jarius S, Ruprecht K, Kleiter I, Borisow N, Asgari N, Pitarokoili K, Pache F, Stich O, Beume LA, Hummert MW, Trebst C, Ringelstein M, Aktas O, Winkelmann A, Buttmann M, Schwarz A, Zimmermann H, Brandt AU, Franciotta D, Capobianco M, Kuchling J, Haas J, Korporal-Kuhnke M, Lillevang ST, Fechner K, Schanda K, Paul F, Wildemann B, Reindl M, in cooperation with the Neuromyelitis Optica Study G (2016) MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 1: Frequency, syndrome specificity, influence of disease activity, long-term course, association with AQP4-IgG, and origin. J Neuroinflammation 13(1):279. https://doi.org/10.1186/s12974-016-0717-1
142. Kim SH, Mealy MA, Levy M, Schmidt F, Ruprecht K, Paul F, Ringelstein M, Aktas O, Hartung HP, Asgari N, Tsz-Ching JL, Siritho S, Prayoonwiwat N, Shin HJ, Hyun JW, Han M, Leite MI, Palace J, Kim HJ (2018) Racial differences in neuromyelitis optica spectrum disorder. Neurology 91(22):e2089–e2099. https://doi.org/10.1212/WNL.0000000000006574
143. Kim JE, Park SH, Han K, Kim HJ, Shin DW, Kim SM (2020) Prevalence and incidence of neuromyelitis optica spectrum disorder and multiple sclerosis in Korea. Mult Scler 26(14):1837–1844. https://doi.org/10.1177/1352458519888609
144. Krumbholz M, Hofstadt-van Oy U, Angstwurm K, Kleiter I, Jarius S, Paul F, Aktas O, Buchholz G, Kern P, Straube A, Kumpfel T (2015) Very late-onset neuromyelitis optica spectrum disorder beyond the age of 75. J Neurol 262(5):1379–1384. https://doi.org/10.1007/s00415-015-7766-8
145. Lee JD, Guimond C, Yee IM, Vilarino-Guell C, Wu ZY, Traboulsee AL, Sadovnick AD (2015) Incidence of multiple sclerosis and related disorders in Asian Populations of British Columbia. Can J Neurol Sci 42(4):235–241. https://doi.org/10.1017/cjn.2015.36
146. Lee HL, Kim JY, Seok JM, Hong YH, Lim NG, Shin HY, Kim BJ, Hwang SY, Min JH, Kim BJ (2020) Prevalence and incidence of neuromyelitis optica spectrum disorder in Korea: population based study. J Korean Med Sci 35(17):e115. https://doi.org/10.3346/jkms.2020.35.e115
147. Li Y, Zhang J, Zhou Y, Xie H, Duan R, Jing L, Yao Y, Teng J, Jia Y (2021) Analysis of predictive risk factors in aquaporin-4-IgG

positive highly active neuromyelitis optica spectrum disorders. Front Neurol 12:731835. https://doi.org/10.3389/fneur.2021.731835
148. Marignier R, Cobo Calvo A, Vukusic S (2017) Neuromyelitis optica and neuromyelitis optica spectrum disorders. Curr Opin Neurol 30(3):208–215. https://doi.org/10.1097/WCO.0000000000000455
149. Mealy MA, Wingerchuk DM, Greenberg BM, Levy M (2012) Epidemiology of neuromyelitis optica in the United States: a multicenter analysis. Arch Neurol 69(9):1176–1180. https://doi.org/10.1001/archneurol.2012.314
150. O'Connell K, Hamilton-Shield A, Woodhall M, Messina S, Mariano R, Waters P, Ramdas S, Leite MI, Palace J (2020) Prevalence and incidence of neuromyelitis optica spectrum disorder, aquaporin-4 antibody-positive NMOSD and MOG antibody-positive disease in Oxfordshire. UK J Neurol Neurosurg Psychiatry 91(10):1126–1128. https://doi.org/10.1136/jnnp-2020-323158
151. Ortiz Salas PA, Gaviria Carrillo M, Cortes Bernal GA, Moreno Medina K, Roa LF, Rodriguez Quintana JH (2022) Neuromyelitis optica spectrum disorder: do patients positive and negative for anti-aquaporin-4 antibodies present distinct entities? A Colombian perspective. Neurologia (Engl Ed) 38(7):504–510. https://doi.org/10.1016/j.nrleng.2020.08.022
152. Papp V, Illes Z, Magyari M, Koch-Henriksen N, Kant M, Pfleger CC, Roemer SF, Jensen MB, Petersen AE, Nielsen HH, Rosendahl L, Mezei Z, Christensen T, Svendsen K, Hyldgaard Jensen PE, Lydolph MC, Heegaard N, Frederiksen JL, Sellebjerg F, Stenager E, Petersen T (2018) Nationwide prevalence and incidence study of neuromyelitis optica spectrum disorder in Denmark. Neurology 91(24):e2265–e2275. https://doi.org/10.1212/WNL.0000000000006645
153. Park TJ, Kim JH, Kim HJ, Bae JS, Cheong HS, Park BL, Shin HD (2014) Lack of association between AQP4 polymorphisms and risk of inflammatory demyelinating disease in a Korean population. Gene 536(2):302–307. https://doi.org/10.1016/j.gene.2013.12.007
154. Pittock SJ, Lennon VA, Bakshi N, Shen L, McKeon A, Quach H, Briggs FB, Bernstein AL, Schaefer CA, Barcellos LF (2014) Seroprevalence of aquaporin-4-IgG in a northern California population representative cohort of multiple sclerosis. JAMA Neurol 71(11):1433–1436. https://doi.org/10.1001/jamaneurol.2014.1581
155. Rezaeimanesh N, Sahraian MA, Moghadasi AN, Eskandarieh S (2020) Epidemiology of neuromyelitis optica spectrum disorder in Tehran, Iran: the prevalence, baseline characteristics, and clinical aspects. Neurol Sci 41(9):2647–2648. https://doi.org/10.1007/s10072-020-04393-7
156. Sahraian MA, Moinfar Z, Khorramnia S, Ebrahim MM (2010) Relapsing neuromyelitis optica: demographic and clinical features in Iranian patients. Eur J Neurol 17(6):794–799. https://doi.org/10.1111/j.1468-1331.2009.02928.x
157. Saiz A, Zuliani L, Blanco Y, Tavolato B, Giometto B, Graus F, Spanish-Italian NMOSG (2007) Revised diagnostic criteria for neuromyelitis optica (NMO). Application in a series of suspected patients. J Neurol 254(9):1233–1237. https://doi.org/10.1007/s00415-007-0509-8
158. Sepulveda M, Aldea M, Escudero D, Llufriu S, Arrambide G, Otero-Romero S, Sastre-Garriga J, Romero-Pinel L, Martinez-Yelamos S, Sola-Valls N, Armangue T, Sotoca J, Escartin A, Robles-Cedeno R, Ramio-Torrenta L, Presas-Rodriguez S, Ramo-Tello C, Munteis E, Pelayo R, Gubieras L, Brieva L, Ortiz N, Hervas M, Mane-Martinez MA, Cano A, Vela E, Tintore M, Blanco Y, Montalban X, Graus F, Saiz A (2018) Epidemiology of NMOSD in Catalonia: influence of the new 2015 criteria in incidence and prevalence estimates. Mult Scler 24(14):1843–1851. https://doi.org/10.1177/1352458517735191
159. Simaniv TO, Kochergin IA, Zakharova MN, Korobko DS, Zaslavskii LG, Zelenova OV, Abramov SI (2021) [Clinical and epidemiological aspects of neuromyelitis optic spectrum diseases in the russian population]. Zh Nevrol Psikhiatr Im S S Korsakova 121(7):96–103. https://doi.org/10.17116/jnevro202112107196
160. Vanikieti K, Poonyathalang A, Jindahra P, Bouzika P, Rizzo JF 3rd, Cestari DM (2017) Clinical characteristics and long-term visual outcome of optic neuritis in neuromyelitis optica spectrum disorder: a comparison between Thai and American-Caucasian cohorts. Mult Scler Relat Disord 17:87–91. https://doi.org/10.1016/j.msard.2017.07.013
161. Wang H, Dai Y, Qiu W, Zhong X, Wu A, Wang Y, Lu Z, Bao J, Hu X (2011) HLA-DPB1 0501 is associated with susceptibility to anti-aquaporin-4 antibodies positive neuromyelitis optica in southern Han Chinese. J Neuroimmunol 233(1–2):181–184. https://doi.org/10.1016/j.jneuroim.2010.11.004
162. Mumford CJ, Fraser MB, Wood NW, Compston DA (1992) Multiple sclerosis in the Cambridge health district of east Anglia. J Neurol Neurosurg Psychiatry 55(10):877–82. 1015180
163. Nakamura M, Ogawa R, Fujimori J, Uzawa A, Sato Y, Nagashima K, Kuriyama N, Kuwabara S, Nakashima I (2023) Epidemiological and clinical characteristics of myelin oligodendrocyte glycoprotein antibody-associated disease in a nationwide survey. Mult Scler 29(4–5):530–539. https://doi.org/10.1177/13524585231156736
164. Trojano M, Lucchese G, Graziano G, Taylor BV, Simpson S, Jr., Lepore V, Grand'maison F, Duquette P, Izquierdo G, Grammond P, Amato MP, Bergamaschi R, Giuliani G, Boz C, Hupperts R, Van Pesch V, Lechner-Scott J, Cristiano E, Fiol M, Oreja-Guevara C, Saladino ML, Verheul F, Slee M, Paolicelli D, Tortorella C, D'Onghia M, Iaffaldano P, Direnzo V, Butzkueven H, Group MSS, the New Zealand MSPSG (2012) Geographical variations in sex ratio trends over time in multiple sclerosis. PLoS ONE 7(10):e48078. https://doi.org/10.1371/journal.pone.0048078
165. Silcocks PB, Jenner DA, Reza R (2001) Life expectancy as a summary of mortality in a population: statistical considerations and suitability for use by health authorities. J Epidemiol Community Health 55(1):38–43. https://doi.org/10.1136/jech.55.1.38
166. Rider V, Abdou NI, Kimler BF, Lu N, Brown S, Fridley BL (2018) Gender bias in human systemic lupus erythematosus: A problem of steroid receptor action? Front Immunol 9:611. https://doi.org/10.3389/fimmu.2018.00611
167. Kvarnstrom M, Ottosson V, Nordmark B, Wahren-Herlenius M (2015) Incident cases of primary Sjogren's syndrome during a 5-year period in Stockholm County: a descriptive study of the patients and their characteristics. Scand J Rheumatol 44(2):135–142. https://doi.org/10.3109/03009742.2014.931457
168. Pittock SJ, Lennon VA, de Seze J, Vermersch P, Homburger HA, Wingerchuk DM, Lucchinetti CF, Zephir H, Moder K, Weinshenker BG (2008) Neuromyelitis optica and non-organ-specific autoimmunity. Arch Neurol 65(1):78–83. https://doi.org/10.1001/archneurol.2007.17
169. Desai MK, Brinton RD (2019) Autoimmune Disease in Women: Endocrine Transition and Risk Across the Lifespan. Front Endocrinol (Lausanne) 10:265. https://doi.org/10.3389/fendo.2019.00265

170. Romero-Pinel L, Bau L, Matas E, Leon I, Munoz-Vendrell A, Arroyo P, Masuet-Aumatell C, Martinez-Yelamos A, Martinez-Yelamos S (2022) The age at onset of relapsing-remitting multiple sclerosis has increased over the last five decades. Mult Scler Relat Disord 68:104103. https://doi.org/10.1016/j.msard.2022.104103
171. Hooge JP, Redekop WK (1992) Multiple sclerosis with very late onset. Neurology 42(10):1907–1910. https://doi.org/10.1212/wnl.42.10.1907
172. Bermel RA, Rae-Grant AD, Fox RJ (2010) Diagnosing multiple sclerosis at a later age: more than just progressive myelopathy. Mult Scler 16(11):1335–1340. https://doi.org/10.1177/1352458510377334
173. McGrogan A, Madle GC, Seaman HE, de Vries CS (2009) The epidemiology of Guillain-Barre syndrome worldwide. A systematic literature review. Neuroepidemiology 32(2):150–163. https://doi.org/10.1159/000184748
174. Childs B, Scriver CR (1986) Age at onset and causes of disease. Perspect Biol Med 29(3):437–460. https://doi.org/10.1353/pbm.1986.0056
175. Lee JY, Chitnis T (2016) Pediatric multiple sclerosis. Semin Neurol 36(2):148–153. https://doi.org/10.1055/s-0036-1579738
176. Li Y, Xie H, Zhang J, Zhou Y, Jing L, Yao Y, Duan R, Jia Y (2021) Clinical and radiological characteristics of children and adults with first-attack myelin oligodendrocyte glycoprotein antibody disease and analysis of risk factors for predicting the severity at disease onset in central China. Front Immunol 12:752557. https://doi.org/10.3389/fimmu.2021.752557

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