**Supplementary Table 1. Summary of included studies, quoted and estimated statistics and Johanna Briggs critical appraisal assessment**

| No. | Seq | Study [Ref] | Year of study | | Region | | Female Life-expectancy (Yrs) | | Study design | | Setting | Recruitment | Diagnostic criteria | AQP4 assay | AQP4 antibody postive (%) | Estimated response rate | N | | Fem | | Mal | Age of onset (Yrs)  Mean ± SD  Median (range) | | Sample frame | | | Sampling | | | Sample size | | | Subjects & setting | | | Coverage | | | Identifi-cation | | Measure | Statistics | Response  rate |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***Whole Population Studies*** | | | |  | |  | |  | |  | |  |  |  |  |  |  |  | | |  |  | | |  | | |  | | |  | | |  | | |  | | |  |  |  |  |
| 1 | 1 | Aboul-Enein et al., 2013 [28] | 2011 | | Austria | | 83.78 | | Prevalence study | | National testing laboratory, supported by national collaboration of neurologists | Positive AQP4 antibody result in clinically suspected cases of NMO or NMOSD | AQP4 antibody positive | M23 AQP4 immunofluorescence live cell-based assay | 100 | >28% of expected | 71 | | 62 | | 9 | 45.7 ± 14.1#  (12 - 79) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | Yes |
| 2 | 1 | Adoni et al., 2010 [29]\* | 2010 | | São Paulo, Brazil | | 79.39 | | Case series | | Single centre | Neurology clinic | Wingerchuk 1999 | Mayo Clinic live cell-based assay | 64.3 | Not estimated | 28 | | 25 | | 3 | 25.4 ± 11.4  26 (7 - 55) | | Yes | | | Yes | | | No | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 | Not estimated | 18 | | 16 | | 2 | 24.2 ± 12.9  25 (7 -55) | | Yes | | | Yes | | | No | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
| 3 | 1 | Altintas et al., 2015 [30] | 2015 | | Turkey | | 80.67 | | Case series | | Academic hospitals | Neurology clinics | Wingerchuk 2006 | Euroimmun transfected fixed cell-based assay | 62.5 | Not estimated | 77 | | 65 | | 12 | 39.0 ± 12.7 | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
| 4 | 1 | Alves et al., 2022 [31] | 2020 | | Goiás, Brazil | | 79.39 | | Case series | | Single centre | Population-based cross-sectional study from a CNS demyelinating disease centre | IPND 2015 | Not stated | 35.4 | Not estimated | 48 | | 39 | | 9 | 36.7 ± 16.0  (9 - 66) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 5 | 1 | Asgari et al., 2011 [32] | 2008 | | Southern Denmark | | 83.02 | | Prevalence study | | Neurology and ophthalmology clinics | Clinics and national registry diagnostic codes for hospital visits | Wingerchuk 2006 | AQP4 transfected HEK293 live cell-based assay | 61.9 | Not estimated | 42 | | 31 | | 11 | 35.6 ± 11.2#  (15 - 64) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 6 | 1 | Barhate et al., 2014 [33] | 2013 | | Mumbai, India | | 72.17 | | Case series | | Single centre | Hospital (in-patient and out-patient) | Wingerchuk 2006 & Wingerchuk 2007 | M1 or M23 AQP4 transfected HEK293 live cell-based assay | 84.1 | Not estimated | 44 | | 39 | | 5 | 31.5 ± 14.8†  (8 - 72) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 37 | | 33 | | 4 | 33.2 ± 15.3†  (8 - 72) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 7 | 1 | Bennis et al., 2019[34] | 2015 | | Casablanca, Morocco | | 74.31 | | Case series | | Single centre | Hospital (in-patient and out-patient) | IPND 2015 | Biomnis transfected fixed cell-based assay | 25.0 | Not estimated | 64 | | 50 | | 14 | 35.7 ± 10.7  36 (16 - 63) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 8 | 1 | Bichuetti et al., 2009 [35] | 2007 | | São Paulo, Brazil | | 79.39 | | Case series | | Single centre | Neuroimmunology clinic | Wingerchuk 2006 | Commercial assay (not further specified) | 17.1 | Not estimated | 41 | | 29 | | 12 | 32.6 ± 11.5  (20 - 60) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 9 | 1 | Bizzoco et al., 2009 [36]\* | 2006 | | Firenze & Prato, Italy | | 84.9 | | Prevalence study | | Adult and paediatric centres | Neurology clinics | Wingerchuk 2007 | Tissue (rat) immunofluorescence | 76.9 | Not estimated | 13 | | 12 | | 1 | 37.3 ± -16.0†  40 (9 - 69) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 7 | | 7 | | 0 | 41.0 ± 15.5  40 (25 - 69) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 10 | 1 | Bukhari et al., 2017 [37]\* | 2013 | | Australia & New Zealand | | 84.84 | | Prevalence study | | National networks of neuroimmunology clinics | Suspected NMOSD from 36 adult and paediatric clinics | IPND 2015 | Oxford live cell-based assay, Euroimmun AQP transfected fixed cell-based assay or tissue (mouse) indirect immunofluoresence | 90.1 | 76% (capture-recapture method) | 147 | | 126 | | 21 | 41.7 ± 17.4  40 (13 - 85) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | Yes |
|  | 2 | Bukhari et al., 2020 [113] |  | |  | |  | |  | |  |  |  |  | 100 |  | 68 | | 61 | | 7 | 44.8 ± 15.3‡  40.5 (13 - 85) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | Yes |
| 11 | 1 | Cabre et al., 2001 [38] | 1999 | | Martinique, Caribbean | | 77.96 | | Prevalence study | | Single centre | Review of local case files (including private neurologists) | Wingerchuk 1999 | N/A | 0 | Not estimated | 17 | | 17 | | 0 | 31.7 ± 9.2 | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | No | Yes | No |
| 12 | 1 | Cabrera-Gomez et al., 2009 [39]\* | 2004 | | Cuba | | 80.25 | | Prevalence study | | Hospitals and clinics | Nationwide survey involving neurologists, ophthalmologists and general physicians | Wingerchuk 1999 | N/A | 0 | Not estimated | 58 | | 51 | | 7 | 31.8 ± 11.1  (11 - 62) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | No | Yes | No |
| 13 | 1 | Ceccarelli et al., 2020 [40] | 2017 | | United Arab Emirates | | 78.42 | | Case series | | Single centre | Chart review of neurological institute | IPND 2015 | Not stated or referenced (testing performed by BN Labcorp, Burlington - possibly ELISA) | 100 | Not estimated | 5 | | 5 | | 0 | 40.8 ± 12.5†  46 (19 - 50) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 14 | 1 | Chan et al., 2013 [41] | 2010 | | Hong Kong, China | | 80.49 | | Case series | | Single centre | Consecutive CNS IDD cases | Wingerchuk 2006 & AQP4 antibody positive | AQP4 transfected HEK293 live cell-based assay | 88.9 | Not estimated | 47 | | 41 | | 6 | 45.1 ± 15.4  (16 - 76) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 15 | 1 | Collongues et al., 2010 [42] | 2008 | | France | | 85.09 | | Case series | | 25 centres across France | Suspected NMO from MS centres using a questionnaire | Wingerchuk 2006 | Tissue (rat) immunofluorescence | 48.0 | Not estimated | 125 | | 94 | | 31 | 34.5 ± 13.2  34.7 (4 - 66) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 16 | 1 | Cossburn et al., 2012 [43]\* | 2006 | | South East Wales, UK | | 82.99 | | Prevalence study | | Single centre with outreach satellite clinics | Regional neuro-inflammatory database, neurologist referral, hospital databases and laboratory data | Wingerchuk 2007 | Not stated or referenced | 76.9 | Not estimated | 14 | | 12 | | 2 | 36.8 ± 22.2  40 (4 - 70) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | No | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 10 | | 8 | | 2 | 34.9 ± 22.6  42.5 (4 - 62) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | No | Yes | No |
| 17 | 1 | Daoudi & Bouzar, 2016 [44] | 2014 | | Tizi-Ouzou, Algeria | | 78.12 | | Case series | | Single centre | Chart review of MS clinic attendees | IPND 2015 | Not clearly defined - state cell-based assay preferred | 37.5 | Not estimated | 8 | | 6 | | 2 | 29.4 ± 9.8#  (16 - 44) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | No | Yes | No |
| 18 | 1 | Del Negro et al., 2017 [45] | 2012 | | Brasilia, Brazil | | 79.39 | | Case series | | Single centre | Subjects for whom AQP4 antibody testing requested | Wingerchuk 2006 | M1 AQP4 ELISA-R kit | 73.5 | Not estimated | 34 | | 30 | | 4 | 34.6 ± 17.2  (4 - 68) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 25 | | 23 | | 2 | 33.8 ± 17.3 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 19 | 1 | Drulovic et al., 2019 [46] | 2017 | | Belgrade, Serbia | | 78.28 | | Case series | | Single centre | Retrospective casenote review | IPND 2015 | Euroimmun AQP4 transfected fixed cell-based assay | 89.2 | Not estimated | 74 | | 63 | | 11 | 38.8 ± 12.8‡  40 (7 – 68) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 20 | 1 | Eskandarieh et al., 2017 [47]\* | 2016 | | Tehran, Iran | | 79.09 | | Prevalence study | | Single centre | Hospital diagnosed cases and register of cases | IPND 2015 | ELISA | 46.8 | Not estimated | 103 | | 86 | | 17 | 31.5 ± 12.0#  (8 - 68) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 21 | 1 | Espiritu et al., 2019 [48] | 2019 | | Manila, Phillippines | | 73.6 | | Prevalence study | | Single centre | Consecutive cases at tertiary hospital | Not stated | AQP4 transfected EU90 cells (Eurofins Biomnis) | 44.4 | Not estimated | 18 | | 13 | | 5 | 27.8 ± 9.1  26 (12 - 47) | | Yes | | | Yes | | | No | | | Unclear | | | Unclear | | | Unclear | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 8 | | 7 | | 1 | 26.9 ± 9.6  24 (17 - 47) | | Yes | | | Yes | | | No | | | Unclear | | | Unclear | | | Unclear | | Yes | Yes | No |
| 22 | 1 | Etemadifar et al., 2020 [49] | 2019 | | Isfahan, Iran | | 79.09 | | Case series for MRI analysis | | Single centre | Retrospective casenote review | IPND 2015 | Euroimmun AQP4 transfected fixed cell-based assay | 48.1 | Not estimated | 108 | | 89 | | 19 | Not stated | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 23 | 1 | Flanagan et al., 2016a [50] | 2012 | | Olmstead County, Minnesota, US | | 80.73 | | Prevalence study | | Population-based survey | Retrospective casenote review of subjects with CNS demyelinating disease | Wingerchuk 2006 | Mayo Clinic live M1 AQP4 transfected cell-based assay | 83.3 | Not estimated | 6 | | 5 | | 1 | 34.8 ± 17.8‡  37 (10 - 55) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 24 | 1 | Flanagan et al., 2016b [50] | 2012 | | Martinque, Carribean | | 77.96 | | Prevalence study | | Population-based survey | Retrospective casenote review of subjects with CNS demyelinating disease | Wingerchuk 2006 | Mayo Clinic live M1 AQP4 transfected live cell-based assay | 79.5 | Not estimated | 39 | | 35 | | 4 | 41.5 ± 15.8‡  35 (14 - 82) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 25 | 1 | Fukuda et al., 2022 [51] | 2019 | | Bahai, Brazil | | 79.39 | | Case series | | Single centre | Consecutive clinic attendees at tertiary clinic | IPND 2015 | Not stated | 60.4 | Not estimated | 91 | | 72 | | 19 | 36.3 ± 13.6 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 26 | 1 | Gao et al., 2019[52] | 2018 | | Shanghai, China | | 80.49 | | Case series | | Single centre | Retrospective review of demyelinating disease registry | IPND 2015 | Euroimmun transfected fixed cell-based assay | 70.2 | Not estimated | 84 | | 74 | | 10 | Not stated | | Yes | | | Yes | | | Yes | | | No | | | Yes | | | Yes | | Yes | Yes | No |
| 27 | 1 | Gracia et al., 2022 [53] | 2020 | | Central America and Caribbean | | 76.19 | | Case series | | Multicentre, multinational | Retrospective study of cases across centres | IPND 2015 and Wingerchuk 2006 | Cell-based assay (not further specified) | 52.7 | Not estimated | 186 | | 158 | | 28 | 37.5 ± 3.7‡  37 (28 - 48) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 28 | 1 | Holroyd et al., 2018 [54] | 2016 | | Abu Dhabi, United Arab Emirates | | 78.42 | | Prevalence study | | Four hospital sites | Retrospective chart review of patients with CNS demyelinating disease identified by ICD codes | IPND 2015 | Not stated | 80.0 | Not estimated | 10 | | 7 | | 3 | 43.0 ± 18.7  43 (8 - 74) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 29 | 1 | Hor et al., 2018 [55] | 2017 | | Penang, Malaysia | | 77.08 | | Prevalence study | | Single centre | Retrospective chart review of hospital clinic attendees and referrals from neurologists in private practice | IPND 2015 | Euroimmun transfected fixed cell-based assay | 100 | Not estimated | 14 | | 14 | | 0 | 43.1 ± 22.3#  (18 - 94) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 30 | 1 | Ibis et al., 2021 [56] | 2018 | | Venezuela | | 78.17 | | Prevalence study | | Multicentre | National database | IPND 2015 | Mayo Clinic live cell-based assay | 31.3 | Not estimated | 249 | | 206 | | 43 | 34.0 ± 14.8  39 (5 - 71) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 31 | 1 | Jagtap et al., 2015 [57] | 2012 | | Kerala, India | | 72.17 | | Case series | | Single centre | Local database | Miller 2008 | Not stated | 30.8 | Not estimated | 26 | | 21 | | 5 | 27.0 ± 12.4#  (9 - 58) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 32 | 1 | Jiao et al., 2013 [58] | 2011 | | US | | 80.73 | | Case series | | Central referral laboratory | Cases referred for AQP4 antibody testing | Wingerchuk 2006 plus AQP4 antibody positivity | Mayo Clinic tissue (mouse) immunofluorescence, ELISA, Euroimmun fixed cell-based and FACS live cell-based assays | 88.1 | Not estimated | 159 | | 136 | | 23 | 38.6 ± 13.2‡  (5 -71) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 140 | | 126 | | 14 | 38.5 ± 12.6‡  39 (5 -71) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 33 | 1 | Jonsson et al., 2019 [59] | 2013 | | Sweden | | 83.97 | | Prevalence study | | Population-based survey | National registry of hospitalisations | Wingerchuk 2006 | Immunoblot or cell-based assay | Not stated | Not estimated | 92 | | 68 | | 24 | Not stated | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 34 | 1 | Joshi et al., 2022 [60] | 2016 | | Gujarat, India | | 72.17 | | Case series | | Single centre | CNS inflammatory diseases clinic survey | Wingerchuk 2006 | AQP4 transfected cell-based FACS assay | 56.6 | Not estimated | 46 | | 34 | | 12 | 28.8 ± 8.3#  (13 - 50) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 26 | | 23 | | 3 | 36.8 ± 12.1#  (17 - 65) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 35 | 1 | Kashipazha et al., 2015 [61] | 2015 | | Khuzestan, Iran | | 79.09 | | Prevalence study | | Population-based survey | MS registry, neurology clinic referrals and private neurologist clinics with ON, TM or NMO | Wingerchuk 2006 | Not stated | 38.0 | Not estimated | 50 | | 44 | | 6 | 29.2 ± 11.1# | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Unclear | Yes | No |
| 36 | 1 | Kim et al., 2012 [62] | 2010 | | Goyang, Korea | | 86.09 | | Case series | | Single centre | Consecutive attendees at national referral centre | AQP4 antibody positive | ELISA and Euroimmun fixed cell-based assay | 100 | Not estimated | 106 | | 97 | | 9 | 32.5 ± 10.3‡  32 (7 - 59) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 37 | 1 | Kishk et al., 2021 [63] | 2018 | | Cairo, Egypt | | 74.14 | | Case series | | Single centre | Retrospective casenote review of cases with NMO/NMOSD | IPND 2015 | ELISA or cell-based assay (specific assay not stated) | 50.0 | Not estimated | 70 | | 58 | | 12 | 28.9 ± 10.5 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 35 | | 29 | | 6 | 30.1 ± 9.3 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 38 | 1 | Kitley et al., 2014 [64] | 2013 | | Oxford, UK | | 82.99 | | Case series | | Single centre | Prospective clinical NMO database | AQP4 antibody positive | Oxford, M23 AQP4 transfected HEK live cell-based assay | 100 | Not estimated | 20 | | 18 | | 2 | 44.9 ± 14.8 | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 39 | 1 | Kleiter et al., 2016[65] | 2013 | | Germany | | 84.77 | | Case series | | National survey | NEMOS registry | Wingerchuk 2006 or AQP4 antibody positive | Not stated | 84.3 | Not estimated | 185 | | 152 | | 33 | 40.3 ± 14.9 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
|  | 2 | Jarius et al., 2012 [114] | 2011 | |  | |  | |  | |  |  |  |  | 100 |  | 137 | | 125 | | 12 | 42.8 ± 13.6‡  40 (10 - 81) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 40 | 1 | Mealy et al., 2018 [66] | 2018 | | Baltimore and New York, US | | 80.73 | | Case series for mortality study | | Two centres | Retrospective, clinic-based survey | IPND 2015 | Not stated | 79.6 | Not estimated | 427 | | 367 | | 60 | 39.9 ± 16.7 | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Unclear | Yes | No |
| 41 | 1 | Mireles-Ramirez et al., 2022 [67] | 2019 | | Western Mexico | | 78.86 | | Prevalence study | | Single regional referral centre | Consecutive cases at tertiary hospital | IPND 2015 | Not stated | 55.2 | Not estimated | 67 | | 50 | | 17 | 36.0 ±  ( - 65) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 42 | 1 | Mirmosayyeb et al., 2021 [68] | 2021 | | Isfahan, Iran | | 79.09 | | Case series | | Single centre | CND demyelinating disease clinic survey | IPND 2015 | Not stated | Not stated | Not estimated | 220 | | 167 | | 53 | Not stated | | Yes | | | Yes | | | Yes | | | No | | | Yes | | | Yes | | Unclear | Yes | No |
| 43 | 1 | Miyamoto et al., 2018 [69] | 2011 | | Japan | | 86.94 | | Prevalence study | | Nationwide survey | Clinic-based random sampling | Wingerchuk 2006 | Not stated | Not stated | Not estimated | 1042 | | 901 | | 141 | 42.2 ± | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
|  | 2 | Nagaishi et al., 2011 [115] | 2011 | |  | |  | |  | |  |  |  |  | 100 |  | 549 | | 502 | | 47 | 44.3 ± 13.5‡  44 (3 - 86) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 44 | 1 | Netravathi et al., 2019 [70] | 2018 | | Bangalore, India | | 72.17 | | Case series | | Single centre | Retrospective study at tertiary hospital | IPND 2015 + AQP4 antibody positive | Not stated | 100 | Not estimated | 101 | | 90 | | 11 | 31.0 ± 12.5  (9 - 65) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 45 | 1 | Pandit & Kundapur., 2014 [71] | 2013 | | Mangalore, India | | 72.17 | | Prevalence study | | Clinic-based survey | Prospectively maintained CNS demyelinating disease registry | Wingerchuk 2006/2007 | Not stated | Not stated | Not estimated | 11 | | 6 | | 5 | 40.3 ± 12.5‡ | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 46 | 1 | Papais-Alvarenga et al., 2015 [72]\* | 2011 | | South America | | 79.39 | | Case series | | Multicentre | Cross-sectional survey across MS centres | Wingerchuk 2006/2007 | Not stated | 42.0 | Not estimated | 226 | | 191 | | 35 | 31.2 ± 13.5  (2 - 68) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 47 | 1 | Papp et al., 2020 [73] | 2016 | | Budapest, Hungary | | 79.59 | | Prevalence study | | Multicentre population-based survey | Positive AQP4 antibody result from participating laboratories. | IPND 2015 | Euroimmun transfected fixed cell-based assay | 83.1 | Not estimated | 154 | | 135 | | 19 | 42.0 ± 14.5‡  39.5 (6 - 83) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 | Papp et al., 2021a [74]§ | 2015 | | Budapest, Hungary | |  | | Prevalence study | | Multicentre population-based survey | Local registry and laboratory results | IPND 2015 plus AQP4 antibody positive | Euroimmun transfected fixed cell-based assay or Oxford live cell-based assay | 100 | Not estimated | 99 | | 90 | | 9 | 42.8 ± 15.4‡  41 (6 - 83) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 48 | 1 | Papp et al., 2021b [74]§ | 2015 | | Denmark | | 83.02 | | Prevalence study | | Nationwide survey | National registry | IPND 2015 plus AQP4 antibody positive | Euroimmun transfected fixed cell-based assay or Oxford live cell-based assay | 100 | Not estimated | 35 | | 31 | | 4 | 45.5 ± 15.2‡  47 (12 - 76) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 49 | 1 | Paz et al., 2021 [75] | 2017 | | Fortaleza, Brazil | | 79.39 | | Case series | | Single centre | Cross-sectional survey in a neurology clinic | IPND 2015 | Not stated | 60.5 | Not estimated | 38 | | 33 | | 5 | 38.0 ± 12.0 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 50 | 1 | Rafiee et al., 2020 [76] | 2019 | | Tehran, Iran | | 79.09 | | Case-control study | | Single centre | Neurology clinic | IPND 2015 | Not stated | Not stated | Not estimated | 153 | | 123 | | 30 | 30.2 ± 10.7 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 51 | 1 | Rivera et al., 2008 [77] | 2005 | | Mexico City, Mexico | | 78.86 | | Case series | | Single centre | Retrospective casenote review | Wingerchuk 1999 | Not tested | Not tested | Not estimated | 34 | | 24 | | 10 | 34.0 ± | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | No | Yes | No |
| 52 | 1 | Rojas et al., 2020 [78] | 2020 | | Argentina | | 79.5 | | Case series | | Multicentre | Prospective database maintained by MS specialists | IPND 2015 | Tissue indirect immunofluorescence or ELISA | 54.7 | Not estimated | 75 | | 59 | | 16 | Not stated | | Yes | | | Yes | | | Yes | | | No | | | Yes | | | Yes | | Yes | Yes | No |
| 53 | 1 | Salama et al., 2018 [79] | 2018 | | Alexandria, Egypt | | 74.14 | | Case series | | Single centre | Casenote review of neuroimmunology clinic | IPND 2015 | ELISA | 50.0 | Not estimated | 20 | | 17 | | 3 | 27.8 ± 13.7  25.5 ( - ) | | Yes | | | Yes | | | No | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
| 54 | 1 | Santos et al., 2021[3] | 2019 | | Portugal | | 84.4 | | Case series | | Multicentre | Nationwide network of MS Centres | IPND 2021 | Euroimmun transfected fixed cell-based assay, Oxford live cell-based assay and Mayo FACS assay | 100.0 | Not estimated | 77 | | 68 | | 9 | 48.4 ± 18.4  (10-87) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 55 | 1 | Sepulveda et al., 2016 [80] | 2015 | | Spain | | 85.68 | | Case series | | Multicentre | National network of MS study centres | Wingerchuk 2006 or AQP4 antibody positive | Tissue indirect immunofluorescence and AQP4 transfected HEK293 live cell-based assay | 81.8 | Not estimated | 181 | | 157 | | 24 | 41.3 ± 12.4‡  39 (10 - 77) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 148 | | 138 | | 10 | 41.2 ± 13.6‡  (10-77) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 56 | 1 | Shaygannejad et al., 2018 [81] | 2015 | | Isfahan, Iran | | 79.09 | | Case series | | Single centre | Newly diagnosed NMOSD from an MS clinic | Not stated | Euroimmun transfected fixed cell-based assay | 31.0 | Not estimated | 29 | | 22 | | 7 | Not stated | | Yes | | | Yes | | | No | | | No | | | Yes | | | No | | Yes | Yes | No |
| 57 | 1 | Shosha et al., 2020 [82]\* | 2020 | | Arabian Gulf | | 76.15 | | Case series | | 15 neurology/MS centres across 5 countries | NMOSD registry | IPND 2015 | Cell-based assay, indirect immunofluorescence or ELISA | 65.3 | Not estimated | 144 | | 119 | | 25 | 31.0 ± 12.0 | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 94 | | 85 | | 9 | 32.0 ± 12.0 | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
| 58 | 1 | Singh et al., 2021 [83] | 2018 | | New Delhi, India | | 72.17 | | Case series | | Single centre | Retrospective casenote review | IPND 2015 | Not stated | 64.2 | Not estimated | 106 | | 77 | | 29 | 32.8 ± 11.4 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 59 | 1 | Stratos et al., 2020 [84] | 2020 | | Toronto, Canada | | 84.05 | | Case series | | Two centres | Retrospective review of casenotes with suspected NMOSD | IPND 2015 | Not stated | 70.4 | Not estimated | 81 | | 71 | | 10 | 38.9 ± 16.8 | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Unclear | Yes | No |
| 60 | 1 | Sun et al., 2017 [85] | 2015 | | Beijing, China | | 80.49 | | Case series | | Single centre | Consecutive cases at tertiary hospital | IPND 2015 | Indirect immunofluorescence cell-based assay (not further specified or referenced) | 54.6 | Not estimated | 97 | | 82 | | 15 | 37.0 ± 14.5‡  (14 - 66) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 61 | 1 | Tarhan et al., 2022 [86] | 2020 | | Gainesville, FL, US | | 80.73 | | Case series | | Single centre | Retrospective, clinic-based survey | IPND 2015 plus AQP4 antibody positive | ELISA or Mayo Clinic cell-based assay (8/43) | 100 | 11/54 (20%) excluded due to inadequate documentation | 43 | | 36 | | 7 | 40.5 ± 17.4‡  37 (6 - 82) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | Yes |
| 62 | 1 | Tian et al., 2020 [87]\* | 2018 | | China | | 80.49 | | National survey | | National database | National administrative healthcare database | ICD-10 G36.0 (IPND 2015) | Cell-based assay (not further specified) or ELISA | Not stated | 98.5% of specialist neurology referral centres | 11,973 | | 9,825 | | 2148 | Not stated | | Yes | | | Yes | | | Yes | | | No | | | Yes | | | Yes | | Unclear | Yes | No |
| 63 | 1 | van Pelt et al., 2016 [88] | 2015 | | Amsterdam, Netherlands | | 83.15 | | Case series | | Single centre | Retrospective survey | AQP4 antibody positive | AQP4 transfected HEK293 live cell-based assay | 100 | Not estimated | 41 | | 35 | | 6 | 42.0 ± 16.1 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 64 | 1 | Wu et al., 2022 [89] | 2017 | | China | | 80.49 | | Incidence study | | National survey | Nationwide medical insurance claim database | IPND 2015 | Not stated | Not stated | Not estimated | 1313 | | 1031 | | 282 | 47.6 ± 13.7  (19 - 89) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 65 | 1 | Yin et al., 2015 [90] | 2015 | | Guangzhou, China | | 80.49 | | Case series | | Single centre | Retrospective analysis of consecutive attendees to a neurology clinic | Wingerchuk 2006 | Euroimmun AQP4 transfected fixed cell-based assay | 87.0 | Not estimated | 108 | | 92 | | 16 | 36.2 ± 12.6  37 (15 - 70) | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 94 | | 85 | | 9 | 35.5 ± 12.7 | | Yes | | | Yes | | | Yes | | | Unclear | | | Yes | | | Yes | | Yes | Yes | No |
| ***Paediatric Studies*** | | |  | |  | |  | |  | |  |  |  |  |  |  |  | | |  |  |  |  | | |  | | |  | | |  | | |  | | |  | | |  |  |  |
| 66 | 1 | Banwell et al., 2008 [91] | 2008 | | Toronto, Canada and Buenos Aires, Argentina | |  | | Case series | | Two paediatric CNS inflammatory disease clinics | Retrospective survey (onset <18 years) | Wingerchuk 1999 | Tissue immunofluorescence | 47.1 | Not estimated | 17 | | 14 | | 3 | 10.0 ± 3.1‡  10.4 (4 - 15) | | Yes | | | Unclear | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 67 | 1 | Camera et al., 2022 [92] | 2022 | | UK | |  | | Case series | | Six tertiary referral centres for NMO | Retrospective survey (onset <18 years) | IPND 2015 plus AQP4 antibody positive | Oxford live cell-based assay | 100 | Not estimated | 49 | | 43 | | 6 | 12 ± 4.1 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 68 | 1 | Chitnis et al., 2016 [11] | 2013 | | US | |  | | Case series | | US Network of Paediatric MS Centres | Retrospective survey (children and adolescents) | Wingerchuk 2006 | Not stated | 63.2 | Not estimated | 38 | | 26 | | 12 | 10.2 ± 4.7 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 69 | 1 | Collongues et al., 2010 [93] | 2008 | | France | |  | | Case series | | Network of 25 French MS centres | Retrospective survey (onset <18 years) | Wingerchuk 2006 | NMO IgG (not otherwise stated) | 66.7 | Not estimated | 12 | | 9 | | 3 | 12.9 ± 4.4  14 (4 - 17) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 70 | 1 | Huppke et al., 2010 [94] | 2009 | | Göttingen, Germany | |  | | Case series | | National referral centre | Retrospective survey (age <18 years) | Wingerchuk 2006 | Radioimmunoprecipitation assay | 28.6 | Not estimated | 7 | | 5 | | 2 | 10.3 ± 3.7†  11 (5 - 14) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 71 | 1 | Lin et al., 2020 [95] | 2015 | | Taiwan | |  | | Case series | | National Health Insurance database | Retrospective survey (onset <20 years) | ICD-9-CM 341.0 code | Not stated | Not stated | Not estimated | 42 | | 30 | | 12 | Not stated | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 72 | 1 | Lotze et al., 2008 [96] | 2007 | | Houston, TX, US | |  | | Case series | | Single centre | Retrospective casenote review (age <18 years) | Krupp 2007 | Not stated | 66.7 | Not estimated | 9 | | 9 | | 0 | 12.1 ± 4.7  14 (2 - 16) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 73 | 1 | Martins et al., 2022 [97] | 2019 | | Portugal | |  | | Multicentre | | Nationwide survey | Retrospective survey (onset <18 years) | IPND 2015 | Euroimmun AQP4 transfected fixed cell-based assay, Oxford live cell-based assay or Mayo Clinic live cell FACS assay | 100 | Not estimated | 6 | | 5 | | 1 | 12.2 ± 4.6  13.5 (4 - 17) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 74 | 1 | McKeon et al., 2008 [98] | 2007 | | Rochester, MN, US | |  | | Case series | | Single centre | Retrospective casenote review following laboratory result survey (age <19 years) | Wingerchuk 2006 | Tissue immunofluorescence or Mayo Clinic AQP4 transfectied HEK293 live cell-based assay | 100 | Not estimated | 58 | | 51 | | 7 | 11.5 ± 3.0‡  12 (4 - 18) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 75 | 1 | Paolilo et al., 2020 [99] | 2020 | | Brazil and Europe | |  | | Case series | | Multicentre, multinational study | Retrospective survey (onset <18 years) | IPND 2015 plus AQP4 antibody positive | Live cell-based assay | 100 | Not estimated | 67 | | 54 | | 13 | 10.2 ± 3.6 | | Yes | | | Unclear | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 76 | 1 | Yamaguchi et al., 2016 [100] | 2009 | | Japan | |  | | National survey | | Nationwide survey | Retrospective survey (onset <16 years) | Wingerchuk 2006 | Not stated | 50.0 | Not estimated | 10 | | 8 | | 2 | 10.3 ± 1.2  9.5 (3 - 15) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 77 | 1 | Yoon et al., 2021 [101] | 2017 | | Korea | |  | | Case series | | National survey | National Health Insurance database (age <18 years) | ICD-10 G360 | Not stated | Not stated | Not estimated | 68 | | 42 | | 26 | 11.6 ± | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 78 | 1 | Zhou et al., 2019 [102] | 2017 | | Guangzhou, China | |  | | Case series | | Two centres | Retrospective survey (onset <18 years) | Wingerchuk 2006 plus AQP4 antibody positive | In-house live cell-based assay (precise details could not be located even after following quoted reference and supplementary data) | 100 | Not estimated | 23 | | 22 | | 1 | 13.8 ± 1.8‡  14 (10 - 17) | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| ***Late Onset Studies*** | | |  | |  | |  | |  | |  |  |  |  |  |  |  | | |  |  |  |  | | |  | | |  | | |  | | |  | | |  | | |  |  |  |
| 79 | 1 | Cai et al., 2020 [103] | 2020 | | Chengdu, China | |  | | Case series | | Single centre | Retrospective casenote review (onset >50 years) | IPND 2015 | Euroimmun AQP4 transfected fixed cell-based assay | 85.3 | Not estimated | 116 | | 100 | | 16 | 58.2 ± 8.5‡  (52 - 76) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 80 | 1 | Carnero Contentti et al., 2020 [104] | 2020 | | Argentina, Brazil and Venezuela | |  | | Case series | | Multinational, multicentre | Retrospective casenote review (onset >49 years) | IPND 2015 | Cell-based assay (not further defined) or tissue indirect immunofluoresence | 66.7 | Not estimated | 24 | | 20 | | 4 | 59.8 ± 6.8 | | Yes | | | Unclear | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 81 | 1 | Collongues et al., 2014 [105] | 2012 | | Europe | |  | | Case series | | Multinational, multicentre | Retrospective casenote review (onset >50 years) | Wingerchuk 2007 | M23 AQP4 transfected HEK293 live cell-based assay, radioimmunoprecipitation assay or indirect immunofluorescence assay | 85.0 | Not estimated | 108 | | 88 | | 20 | 56.6 (50 - 82) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 46 | | 41 | | 5 | 61.0 ± 7.2‡  56 (50 - 82) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 82 | 1 | Delgado-Garcia et al., 2020 [106] | 2019 | | Mexico | |  | | Case series | | Multinational, multicentre | Retrospective casenote review (onset >49 years) | AQP4 antibody positive | Not stated | 100 | Not estimated | 7 | | 7 | | 0 | 54.5 ± 4.7 | | Yes | | | Yes | | | No | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 83 | 1 | Fragoso et al., 2019 [12] | 2019 | | Brazil | |  | | Case series | | Multicentre | Retrospective casenote review (onset >50 years) | IPND 2015 | Immunofluorescence technique (not otherwise stated) | 64.9 | Not estimated | 37 | | 30 | | 7 | 56.4 ± 5.6 | | Yes | | | Unclear | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 84 | 1 | Lavandier et al., 2019 [107] | 2019 | | France | |  | | Case series | | Multicentre | Retrospective casenote review (onset >70 years) | IPND 2015 | Not stated | 83.3 | Not estimated | 6 | | 5 | | 1 | 74.3 ± 4.3  73.5 (71 - 81) | | Yes | | | Unclear | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
|  | 2 |  |  | |  | |  | |  | |  |  |  |  | 100 |  | 5 | | 4 | | 1 | 74.2 ± 4.3  72 (71 - 81) | | Yes | | | Unclear | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 85 | 1 | Mao et al., 2015[108] | 2014 | | Guangdong, China | |  | | Case series | | Single centre | Retrospective chart review of consecutive cases (onset >49 years) | Wingerchuk 2006 plus AQP4 antibody positive | Euroimmun AQP4 transfected fixed cell-based assay | 100 | Not estimated | 30 | | 26 | | 4 | 58.8 ± 4.9‡  57.5 (50 - 70) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 86 | 1 | Nakahara et al., 2021 [109] | 2020 | | Kunamoto, Japan | |  | | Case series | | Single centre | Retrospective casenote review (onset >49 years) | IPND 2015 | Cell-based assay (not further defined) or ELISA | 90.0 | Not estimated | 30 | | 24 | | 6 | 60.7 ± 8.6‡  (51 - 72) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Unclear | Yes | No |
| 87 | 1 | Seok et al., 2017 [110] | 2014 | | Korea | |  | | Case series | | Multicentre | Retrospective casenote review (onset >49 years) | IPND 2015 plus AQP4 antibody positive | Euroimmun AQP4 transfected fixed cell-based assay | 100 | Not estimated | 45 | | 40 | | 5 | 58.1 ± 6.2 | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 88 | 1 | Sepulveda et al., 2019 [111] | 2018 | | Spain | |  | | Case series | | Multicentre | Retrospective casenote review (onset >49 years) | IPND 2015 | M23 AQP4 transfected HEK293 live cell-based assay | 100 | Not estimated | 60 | | 48 | | 12 | 63.0 ± 8.3‡  59 (50 - 84) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |
| 89 | 1 | Zhang et al., 2017 [112] | 2014 | | Tianjin, China | |  | | Case series | | Single centre | Retrospective casenote review (onset >50 years) | IPND 2015 | AQP4 transfected HEK293 cell-based assay or fluorescence immunoprecipitation assay | 88.1 | Not estimated | 59 | | 47 | | 12 | 59.4 ±  (51 - 80) | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | | Yes | | Yes | Yes | No |

No. = study number; Seq = sequence for serial studies within one article; AQP4 = aquaporin-4; IPND = International Panel for Neuromyelitis Optica Diagnosis; ICD = International Classification of Diseases: HEK = human embryonic kidney;

\* = study also provided age of onset distribution data

§ = please note that this study is listed in PubMed by the authors first name “Viktoria et al., 2021” and the original article is also incorrect

† = calculated from raw data provided in manuscript or supplementary data

‡ = estimated from summary data provided as detailed in methods

# = standard deviation estimated from range

**Supplementary Table 2. List of excluded studies and reason for exclusion.**

| Study [Ref] | Reason for exclusion (prior/subsequent reference) [ref] |
| --- | --- |
| Alvarenga et al., 2017 [116] | Review of prior studies |
| Asgari et al., 2019 [117] | Review of prior studies |
| Ashtari et al., 2017 [118] | Subsequently updated (Shaygannejad et al., 2018) [81] |
| Badihian et al., 2018 [119] | No relevant data |
| Bergamaschi & Ghezzi, 2004 [120] | Review article |
| Bukhari et al., 2022 [121] | Previously described population (Bukhari et al., 2017) [37] |
| Cabre et al., 2009 [122] | Non-English |
| Carnero Contentti et al., 2020 [123] | No relevant data |
| Cheng et al., 2008 [124] | Not NMOSD population (MS) |
| Choy et al., 2018 [125] | Selected population (ON) |
| Collongues et al., 2011 [126] | Not NMOSD population ("high risk for NMO") |
| Cristiano et al., 2016 [127] | Not NMOSD population (MS) |
| Dale et al., 2018 [128] | No relevant data |
| Domingos et al., 2015 [129] | Subsequently updated (Santos et al., 2021) [3] |
| Eskandarieh et al., 2017 [130] | Previously described population (Eskandarieh et al., 2017) [47] |
| Eskandarieh et al., 2018 [131] | Previously described population (Eskandarieh et al., 2017) [47] |
| Etemadifar et al., 2014 [132] | Subsequently updated (Etemadifar et al., 2020) [49] |
| Etemadifar et al., 2014 [133] | Subsequently updated (Etemadifar et al., 2020) [49] |
| Fragoso et al., 2019 [134] | Selected population (early onset) |
| Gold et al., 2019 [135] | Review article |
| Höftberger et al., 2015 [136] | Subsequently updated (Sepulveda et al., 2016) [80] |
| Hor et al., 2020 [8] | Review article |
| Houzen et al., 2012 [137] | Subsequently updated (Miyamoto et al., 2018) [69] |
| Houzen et al., 2018 [138] | Not NMOSD population (MS) |
| Jacob et al., 2013 [139] | No relevant data |
| Jarius et al., 2010 [140] | Selected population (AQP4 Ab +ve ON) |
| Jarius et al., 2016 [141] | Not AQP4 Ab related NMOSD population (MOG Ab +ve) |
| Kim et al., 2018 [142] | Previously described population (Kim et al., 2012) [62] and data presented based on ethnic ancestry |
| Kim et al., 2020 [143] | No relevant data |
| Krumbholz et al., 2015 [144] | Case report |
| Lee et al., 2015 [145] | Selected population (Asian ancestry) |
| Lee et al., 2020 [146] | No relevant data |
| Li et al., 2021 [147] | Selected population (highly active NMSOD) |
| Marignier et al., 2017 [148] | Review article |
| Mealy et al., 2012 [149] | Subsequently updated (Mealy et al., 2018) [66] |
| O'Connell et al., 2020 [150] | No relevant data |
| Ortiz Salas et al., 2022 [151] | Non-English |
| Papp et al., 2018 [152] | Subsequently updated (Papp et al., 2021b) [74] |
| Park et al., 2014 [153] | Previously described population (Kim et al., 2012) [62] |
| Pittock et al., 2014 [154] | Selected population (previously diagnosed as MS) |
| Rezaeimanesh et al., 2020 [155] | No relevant data |
| Sahraian et al., 2010 [156] | Subsequently update (Eskandarieh et al., 2017) [47] |
| Saiz et al., 2007 [157] | Subsequently updated (Sepulveda et al., 2016) [80] |
| Sepulveda et al., 2018 [158] | Previously described population (Sepulveda et al., 2016) [80] |
| Simaniv et al., 2021 [159] | Non-English |
| Vanikieti et al., 2017 [160] | Selected population (NMOSD with ON) |
| Wang et al., 2011 [161] | Selected population (genetic analysis of NMOSD) |
| Wingerchuk et al., 2009 [9] | Review article |

**Supplementary Table 3. Age of onset distribution data for NMOSD**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Age Range (Years)** | | | | | | | | |  |
| **Study [Ref]** | **Year** | **Region** | **0-9** | **10-19** | **20-29** | **30-39** | **40-49** | **50-59** | **60-69** | **70-79** | **80+** | **Total** |
| Cabrera-Gomez et al., 2009 [39] | 2004 | Cuba | 0 | 2 | 5 | 17 | 18 | 13 | 3 | 0 | 0 | 58 |
| Bizzoco et al 2009 [36] | 2006 | Italy | 1 | 0 | 5 | 1 | 3 | 2 | 1 | 0 | 0 | 13 |
| Cossburn et al., 2012 [43] | 2010 | UK | 2 | 3 | 0 | 1 | 4 | 1 | 2 | 1 | 0 | 14 |
| Adoni et al., 2010 [29] | 2010 | Brazil | 3 | 4 | 13 | 5 | 1 | 1 | 0 | 0 | 0 | 27 |
| Papais-Alvarenga et al., 2015 [72] | 2017 | Latin America | 10 | 36 | 69 | 48 | 38 | 22 | 3 | 0 | 0 | 226 |
| Bukhari et al., 2017 [37] | 2013 | Australia/New Zealand | 0 | 10 | 12 | 17 | 15 | 11 | 10 | 3 | 1 | 79 |
| Eskandarieh et al., 2017 [47] | 2016 | Iran | 4 | 15 | 37 | 26 | 18 | 2 | 1 | 0 | 0 | 103 |
| Tian et al., 2020a [87] | 2016 | China | 42 | 150 | 526 | 626 | 960 | 843 | 500 | 136 | 13 | 3796 |
| Tian et al., 2020b [87] | 2017 | China | 65 | 171 | 519 | 664 | 901 | 840 | 589 | 160 | 24 | 3933 |
| Tian et al., 2020c [87] | 2018 | China | 75 | 185 | 498 | 711 | 965 | 984 | 636 | 173 | 29 | 4256 |
| Shosha et al., 2020 [82] | 2020 | Arabian Gulf | 4 | 12 | 25 | 32 | 7 | 9 | 4 | 1 | 0 | 94 |
| **Combined** |  |  | **206** | **588** | **1709** | **2148** | **2930** | **2728** | **1749** | **474** | **67** | **12599** |

**Supplementary Table 4. Outcomes from meta-regression analysis of sex ratio for all studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Coefficient** | **(95% CI)** | **z** | **p** |
| Intercept | 1.025 | (0.752 – 1.298) | 7.360 | <0.001 |
| Proportion AQP4 Antibody Positive | 0.008 | (0.005 – 0.011) | 5.411 | <0.001 |
| South/Central American\* | 0.220 | (-0.001 – 0.440) | 1.951 | 0.051 |
| Middle Eastern/African\* | 0.180 | (-0.072 – 0.432) | 1.397 | 0.162 |
| South Asian/Indian Subcontinent\* | -0.283 | (-0.569 – 0.003) | -1.939 | 0.052 |
| South East Asian\* | 0.225 | (-0.041 – 0.491) | 1.659 | 0.097 |

CI = confidence interval

\* = Compared to White/European/Caucasian

**Supplementary Table 5. Outcomes from meta-regression analysis for age of onset**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Coefficient** | **(95% CI)** | **z** | **p** |
| Intercept | -19.088 | (-44.557 – 6.381) | -1.469 | 0.142 |
| Mean Female Life-expectancy | 0.657 | (0.326 – 0.988) | 3.887 | <0.001 |
| Proportion AQP4 Antibody Positive | 0.053 | (0.009 – 0.096) | 2.343 | 0.019 |

CI = confidence interval

**Supplementary Table 6. Outcomes from meta-regression analysis of age of onset for AQP4 antibody positive cases only.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Coefficient** | **(95% CI)** | **z** | **p** |
| Intercept | -30.349 | (-64.257 – 3.559) | -1.754 | 0.079 |
| Mean Female Life-expectancy | 0.854 | (0.433 – 1.275) | 3.979 | <0.001 |

CI = confidence interval

**References**

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