

Characterizing Double-Negative Neuromyelitis Optica Spectrum Disorder: A Systematic Review and Meta-Analysis

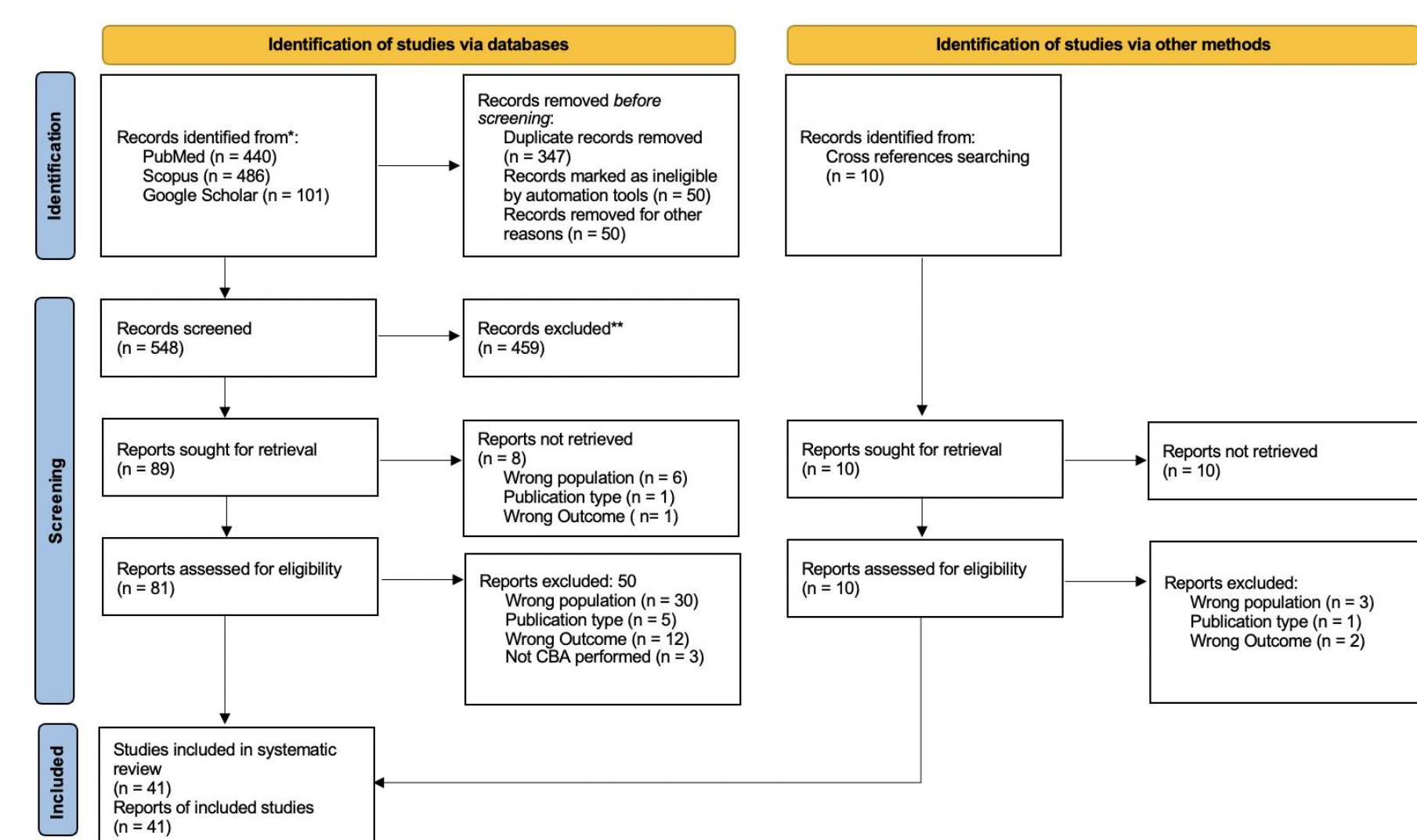
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Background

Neuromyelitis-optica spectrum disorders (NMOSD) usually associate with aquaporin-4 (AQP4) or myelin oligodendrocyte glycoprotein (MOG) antibodies. Seronegative-NMOSD (SN-NMOSD) has been described [1, 2], but the clinical-therapeutic profile is poorly defined [1,2].

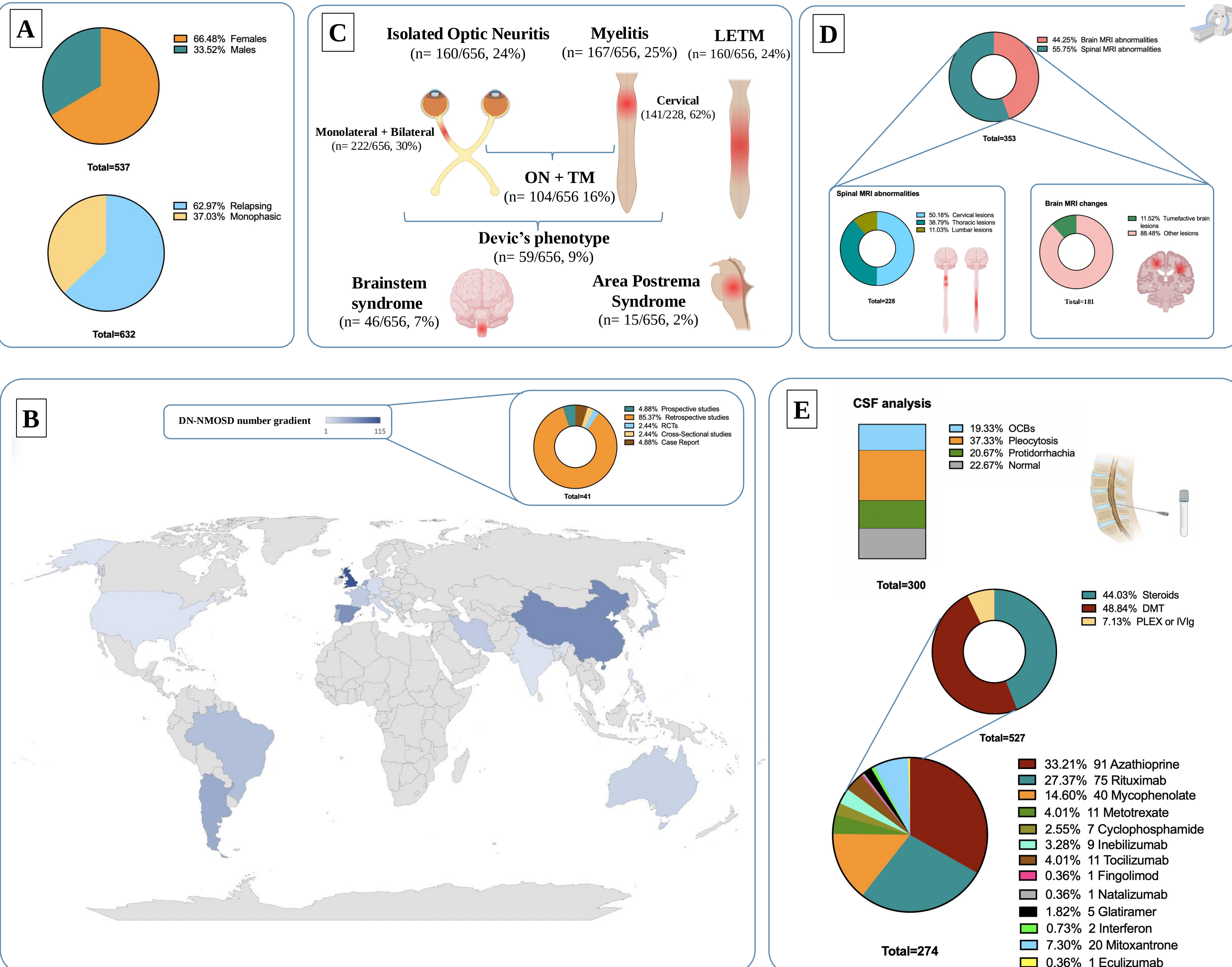
Materials and Methods



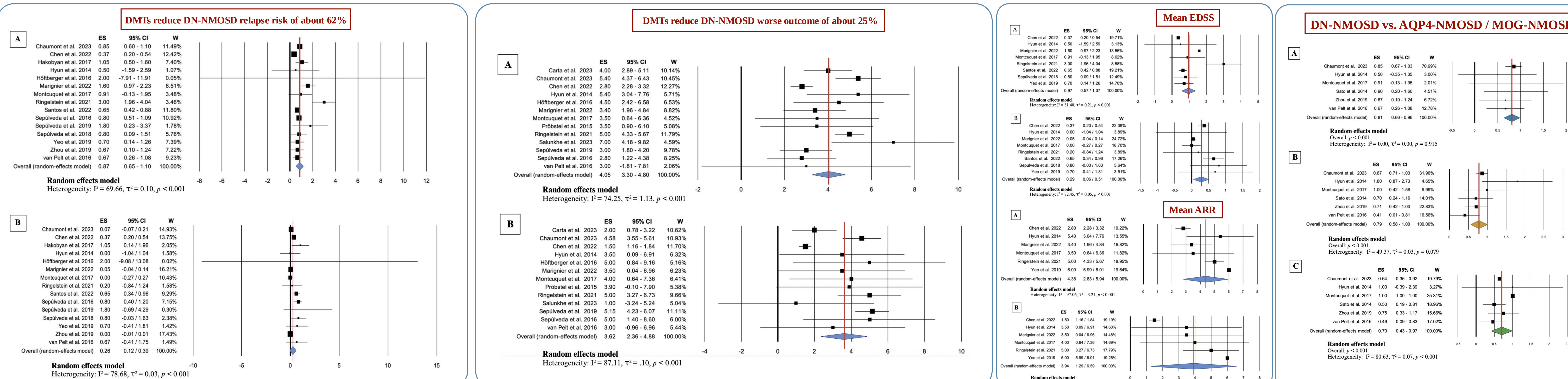
- ✓ Both anti-AQP4 and anti-MOG antibodies tested with L-CBA
- ✓ 2015 Wingerchuk's criteria satisfied
- ✓ Clinical and/or radiological and/or treatment and/or clinical outcome (Annualized Relapse Risk [ARR] and/or EDSS scale)

- ✓ PRISMA guidelines assessment [3]
- ✓ JBI tool for Risk of bias and Quality Assessment [4]
- ✓ PICO's assessment and ProMeta3 version software
- ✓ Random-effects models were used to pool results across studies
- ✓ Trimm and Fill analysis, Weighted regression analysis

Systematic Review– Qualitative analysis



Meta-Analysis – Quantitative analysis



Forest plots (I). Random effects model (n=168). **(A)** Pre-treatment mean annualized relapse ratio (ARR) was 0.87 (95%CI 0,65-1.1; I²=69.66; p<0.001). **(B)** Post-treatment mean annualized relapse ratio (ARR) was 0.26 (95%CI 0,12-0.39; I²=78.68; p<0.001). Standardized mean difference (SMD) analysis confirmed the results: **reduction of 0.62** (95%CI 0,25-0.98; I²=80.61; p<0.001).

Forest plots (II). Random effects model (n=142). **(A)** Pre-treatment Expanded Disability Status Scale (EDSS) was 4.05 (95%CI 3,30-4.8; I²=74.25; p<0.001). **(B)** Post-treatment Expanded Disability Status Scale (EDSS) was 3.62 (95%CI 2,36-4.88; I²=87.11; p<0.001). Standardized mean difference (SMD) analysis confirmed the results: **reduction of 1.16** (95%CI 0,64-1.67; I²=0.00; p<0.001).

Forest plots (III). Random effects model. **(A, B)** Relapsing cohort (n=90) pre/post-treatment mean ARR (0.97, 95%CI 0,57-1.37; I²=81.40; 0.29, 95%CI 0,06-0.51; I²=72.45; p<0.001). **(A,B)** Relapsing cohort pre/post-treatment mean EDSS (4.38, 95%CI 2,83-5.94; I²=97.06; 3.94, 95%CI 1,29-6.59; I²=99.25; p<0.001). **(A-C)** DN-NMOSD (n=168), AQP4-NMOSD (n=317) and MOG-NMOSD (n=44) mean ARR comparison (p<0.001), respectively.

Conclusions and future directions

DN-NMOSD is a heterogeneous condition with distinctive clinical, radiological and prognostic features compared to AQP4-NMOSD and MOG-NMOSD. The administration of DMTs seems to be effective, but randomized clinical trials are needed.

References

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Disclosures

The authors have no potential conflict of interest to disclose.

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