



# Patient demographic factors and disease characteristics, but not brain volumes, predict likelihood of clinical benefit on patient-reported outcome measures in multiple sclerosis

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## Background

- MS treatment has been shifting away from injectable drugs, toward oral and infusible therapies that show greater efficacy in reducing disease activity.<sup>1-3</sup>
- Objective measures provide some useful information about patient function, but self-report measures may better reflect a patient’s lived experience.
- Clinical benefit has been observed on these high-efficacy DMTs<sup>4-5</sup>, but factors that contribute to the likelihood of benefit are unknown.

## Objective

- To assess the impact of patient demographics, multiple sclerosis (MS) disease characteristics, and brain volumetrics on the likelihood of clinical benefit in patients treated with high-efficacy disease-modifying therapies (DMTs), as assessed by patient-reported outcome (PRO) measures.

## Methods

### Sample and Data Collection:

This retrospective chart review included adults with MS (>18 years) who had completed 2 unique Patient-Determined Disease Steps (PDDS) measures, and at least 2/10 Neurology Quality of Life (NeuroQOL) Short Form scales, at a minimum of 2 separate regularly scheduled standard-of-care clinic visits spaced at least 10 months apart (1/2014 – 6/2019), taking a high-efficacy DMT at their baseline visit. Qualifying DMTs included fingolimod (F), dimethyl fumarate (DMF), natalizumab (N), rituximab (R), and ocrelizumab (O).

### Patient Factors Under Investigation:

We investigated the influence of the following factors on likelihood of clinical benefit: age, sex, BMI, marital status, smoking history, type of MS, MS disease duration, prior number of DMTs before the baseline drug, assigned DMT at baseline, number of clinical relapses (within one year prior to baseline and within the study period), and normalized brain volumes including whole brain and thalamus. Brain volumetric data was derived from NeuroQuant volumetric reports, produced from brain MRIs using 1.5 or 3T magnets. Percentage of intracranial volume data was used for imaging analyses.

We also evaluated scores on 10 subscales of the NeuroQOL Short Form battery at baseline and over time as additional predictors of clinical benefit:

- Fatigue, Depression, Anxiety, Positive Affect and Well-Being, Cognitive Function, Emotional and Behavioral Dyscontrol, Sleep Disturbance, Upper Extremity Function, Lower Extremity Function, and Ability to Participate in Social Roles and Activities
- Raw scores converted to standardized T-scores for analyses

### Outcome Measures:

- Primary outcome: change in PDDS scores over time
- Patients were grouped as Clinical Benefit (improvement or no change) vs. Clinical Worsening (decline) over time, with +/- 1 point used as the benchmark for clinically significant change on the PDDS.

### Statistical Analyses

Initial Chi Square and Satterthwaite t-tests were used to detect differences between groups for each variable. Logistic regression was then used to determine relative contributions of each variable to likelihood of clinical benefit.

## Results

Table 1. Sample demographic characteristics

	Clinical Benefit (n=230)	Clinical Worsening (n=84)
Age (Years, SD)	46.5 (11.0)	48.4 (10.7)
Gender - Female	180 (78.0%)	58 (69.0%)
Race		
White	209 (90.9%)	72 (85.7%)
African-American	3 (1.3%)	3 (3.3%)
Asian	2 (0.9%)	--
Other/Unknown	9 (3.9%)	4 (4.8%)
Type of MS		
Relapsing-Remitting (RRMS)	193 (84.0%)	65 (77.0%)
Primary Progressive (PPMS)	12 (5.0%)	6 (7.0%)
Secondary Progressive (SPMS)	25 (11.0%)	13 (16.0%)
Number Prior DMTs (SD)	1.7 (1.5)	1.9 (1.4)
Mean Disease Duration (Years, SD)	9.6 (7.3)	11.0 (8.3)
Number Clinical Relapses (SD, Range)		
Prior Year	0.20 (0.5, 0-2)	0.1 (0.4, 0-2)
Study Period	0.20 (0.5, 0-3)	0.4 (0.6, 0-2)
Mean Time PRO1 to PRO2 (Years, SD)	2.3 (1.0)	2.7 (1.1)

Table 3. NeuroQOL subscale scores influencing likelihood of clinical benefit

NeuroQOL Subscale	OR Estimate	p	95% CI
Fatigue (baseline)	0.959	<b>0.004</b>	0.932, 0.986
Fatigue (change)	0.982	0.365	0.944, 1.022
Depression (baseline)	0.977	0.201	0.944, 1.012
Depression (change)	0.982	0.344	0.945, 1.020
Anxiety (baseline)	0.973	0.074	0.945, 1.003
Anxiety (change)	1.001	0.969	0.969, 1.034
Cognitive Function (baseline)	1.025	0.051	1.000, 1.051
Cognitive Function (change)	0.990	0.585	0.957, 1.025
Sleep Disturbance (baseline)	0.957	<b>0.004</b>	0.930, 0.986
Sleep Disturbance (change)	1.000	0.992	0.965, 1.036
Lower Extremity Function (baseline)	1.047	<b>0.0004</b>	1.021, 1.074
Lower Extremity Function (change)	1.066	<b>0.010</b>	1.015, 1.118
Upper Extremity Function (baseline)	0.979	0.517	0.917, 1.045
Upper Extremity Function (change)	1.155	<b>0.003</b>	1.052, 1.268
Positive Affect and Wellbeing (baseline)	1.034	<b>0.046</b>	1.001, 1.068
Positive Affect and Wellbeing (change)	0.994	0.698	0.964, 1.025
Emotional and Behavioral Dyscontrol (baseline)	0.971	<b>0.033</b>	0.945, 0.998
Emotional and Behavioral Dyscontrol (change)	1.009	0.513	0.982, 1.036
Social Participation (baseline)	1.014	0.381	0.983, 1.046
Social Participation (change)	1.089	<b>0.0003</b>	1.039, 1.141

OR = odds ratio; CI = confidence interval; Social Participation = Ability to Participate in Social Roles and Activities

Table 4. Influence of brain volumes on clinical benefit (n=247)

Region of Interest	OR Estimate	p	95% CI
Whole Brain	1.003	0.949	0.915, 1.100
Thalamus	4.082	0.272	0.332, 50.000

<sup>a</sup>CB n=184, CW n=63; OR = odds ratio; CI = confidence interval

Table 2. Baseline DMT

Assigned DMT (PRO1)	Total N (%)
Fingolimod	62 (19.7)
Dimethyl fumarate	71 (22.6)
Rituximab	67 (21.3)
Natalizumab	114 (36.3)
Drug Switch	Total N
Yes	149
No	165

Of those who switched:

- 89 (59%) ended up on ocrelizumab within the study period
- Most common reasons for switching rituximab to ocrelizumab was out of pocket costs for the patient and insurance denial
- Note: no patients were on ocrelizumab at baseline

Table 5. Demographic and disease factors influencing clinical benefit

	OR Estimate	p	95% CI
Baseline DMT		0.886	
- Fingolimod v. Rituximab	0.830	0.646	0.376, 1.833
- Fingolimod v. DMF	0.899	0.787	0.415, 1.947
- Fingolimod v. Natalizumab	1.078	0.830	0.541, 2.149
- Rituximab v. DMF	1.083	0.841	0.499, 2.351
- Rituximab v. Natalizumab	1.299	0.459	0.650, 2.595
- DMF v. Natalizumab	1.200	0.595	0.613, 2.346
Sex (F v. M)	1.614	0.093	0.923, 2.822
Age	0.984	0.182	0.962, 1.007
Disease Duration (Years)	0.976	0.126	0.945, 1.007
Type of MS		0.411	
- PPMS v. RRMS	0.674	0.447	0.243, 1.867
- PPMS v. SPMS	1.040	0.948	0.317, 3.409
- RRMS v. SPMS	1.544	0.241	0.747, 3.194
Race (Other v. White)	0.603	0.191	0.282, 1.286
Marital Status (No v. Yes)	0.983	0.678	0.524, 1.522
Smoking History		<b>0.029</b>	
- Current v. Former	0.799	0.617	0.332, 1.922
- Current v. Never	0.429	<b>0.046</b>	0.187, 0.983
- Former v. Never	0.536	<b>0.028</b>	0.308, 0.935
BMI	0.954	<b>0.015</b>	0.918, 0.991
Number Clinical Relapses – Prior Year	1.455	0.219	0.800, 2.645
Number Clinical Relapses – Study Period	0.611	<b>0.023</b>	0.399, 0.934
Prior Number DMTs	0.946	0.524	0.799, 1.121

DMF = dimethyl fumarate; OR = odds ratio; CI = confidence interval

## Conclusions

- In a real-world sample of MS patients, we found actionable demographic and disease factors including lower BMI, lack of prior smoking history, and fewer clinical relapses that were associated with clinical benefit
- Regional brain volumes did not influence likelihood of better outcomes
- As better baseline and follow-up functioning in numerous NeuroQOL domains was associated with clinical benefit, clinicians who actively treat symptoms including fatigue, sleep disturbances, and psychological issues may see enhanced patient outcomes

## References

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