Longitudinal Multiple Sclerosis Disease Activity (MSDA) Score Trajectories Following DMT Discontinuation: A Split-Cohort Analysis of Patients <55 vs. 55+ Years

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Introduction

As the mean age of the MS population increases, disease-modifying therapy (DMT) discontinuation (DC) may be considered for older (55+) patients[1]. Reasons for discontinuation may include age related immunosenescence, comorbidities, patient preference, and changing DMT risk:benefit profiles[2]. Currently there are no broadly accepted consensus guidelines on DMT DC and post-DC disease activity monitoring[2]. The analytically and clinically validated MS Disease Activity (MSDA) test integrates 18 biomarkers, age, and sex into a 1-10 score and is commercially available in the US[3,4].

Objectives

To evaluate if DMT DC vs. continuation is associated with differences in MSDA scores, separately for older and younger cohorts.

Methods

This was an exploratory retrospective study of MS patients with routine clinical use MSDA tests released before April 1, 2026 with inferred DMT status from clinician-reported test requisition forms. Permanent DC patients ("No Current DMT" over follow-up) were compared to continuers (on the same DMT). Inclusion required a ≥12-month observation horizon, a ≤12-month gap, and an index test followed by ≥1 test after a 3-month washout (**Figure 1**). Linear mixed-effects models (LMMs) of post-index MSDA scores — adjusted for index MSDA score, age, sex, and patient random intercept — were fitted on continuer status, time window (3–12 and ≥12 months), and their interaction. Differences in estimated marginal means (EMMs) between age groups for each time window were tested for superiority in patients <55 years and for equivalence (TOST; margin Δ=±1.24) in patients ≥55 years. CIs and p-values were adjusted with the multivariate t-distribution.



Figure 1: Retrospective Study Design and Temporal Inclusion Criteria. (MSDA = multiple sclerosis disease activity; Mos = months, T = time)

Baseline characteristics			Grouped by Cohort (Age Group, Years)			
Characteristic	Level	Overall	Continuer (Older [55+])	Continuer (Younger [<55])	Permanent Discontinuer (Older [55+])	Permanent Discontinuer (Younger [<55])
n		358	129	159	43	27
Sex, n (%)	Female	269 (75.1)	95 (73.6)	120 (75.5)	34 (79.1)	20 (74.1)
	Male	89 (24.9)	34 (26.4)	39 (24.5)	9 (20.9)	7 (25.9)
Index DMT Efficacy Category, n (%)	High	258 (72.1)	80 (62.0)	130 (81.8)	25 (58.1)	23 (85.2)
	Low	35 (9.8)	20 (15.5)	5 (3.1)	9 (20.9)	1 (3.7)
	Moderate	65 (18.2)	29 (22.5)	24 (15.1)	9 (20.9)	3 (11.1)
Number of MSDA Tests, n (%)	3	255 (71.2)	95 (73.6)	118 (74.2)	22 (51.2)	20 (74.1)
	4	77 (21.5)	23 (17.8)	33 (20.8)	16 (37.2)	5 (18.5)
	5	14 (3.9)	4 (3.1)	7 (4.4)	3 (7.0)	—
	6	9 (2.5)	6 (4.7)	—	1 (2.3)	2 (7.4)
	7	3 (0.8)	1 (0.8)	1 (0.6)	1 (2.3)	—
Index Age (Years), mean (SD)		53.2 (14.0)	65.0 (6.4)	41.8 (8.4)	66.7 (7.4)	42.5 (7.5)
Days between Index Date and Next Valid Test, mean (SD)		226.2 (71.4)	224.6 (69.7)	223.9 (72.4)	230.3 (70.9)	241.2 (76.5)
Index DA Score, mean (SD)		3.5 (2.0)	3.8 (2.1)	3.2 (2.0)	3.4 (1.8)	3.2 (1.6)

Table 1: Patient Demographics, DMT use, and MSDA testing history. (DMT = disease modifying therapy; MSDA = multiple sclerosis disease activity)

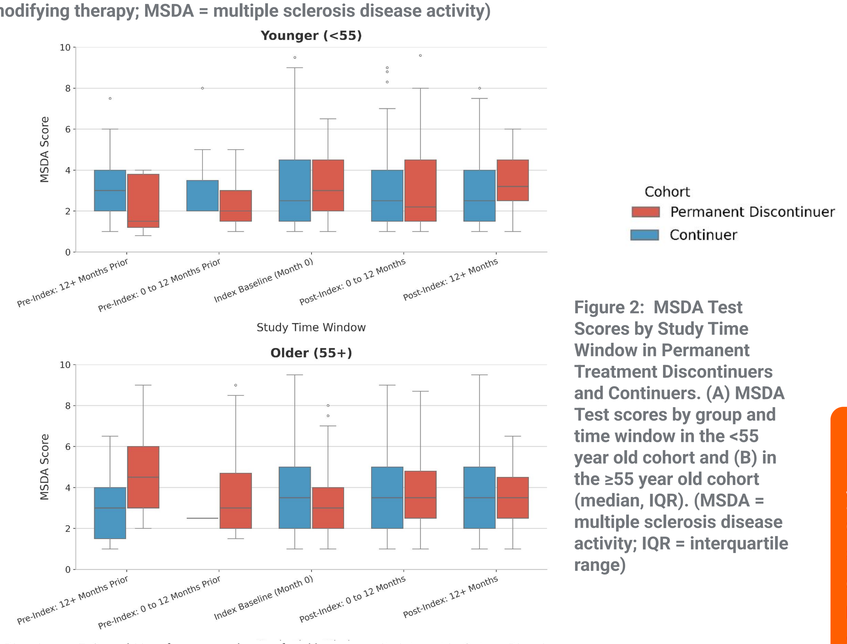


Figure 2: MSDA Test Scores by Study Time Window in Permanent Treatment Discontinuers and Continuers. (A) MSDA Test scores by group and time window in the <55 year old cohort and (B) in the ≥55 year old cohort (median, IQR). (MSDA = multiple sclerosis disease activity; IQR = interquartile range)

Results

This study included N=186 (<55 years) and N=172 (55+ years) patients, mean index age: 42 vs. 65 years, female: 75% vs. 75%; median records/patient: 3 vs. 3, respectively (**Table 1**). Median (IQR) MSDA scores for continuers and DC in <55 years and 55+ years are shown in **Figure 2**. In patients <55, post-DC MSDA trajectories did not differ from continuers at 3–12 months (ΔEMM=0.12, 95%CI[-0.39, 0.62], p=0.64) or 12+ months (ΔEMM=0.51, 95%CI[-0.11, 1.13], p=0.11) (**Figure 3**). In patients 55+, equivalence was established at 3-12 months (ΔEMM=0.20, 90%CI[-0.13, 0.54]; TOST p<0.0001) and 12+ months (ΔEMM=0.22, 90%CI[-0.16, 0.60]; TOST p<0.0001).

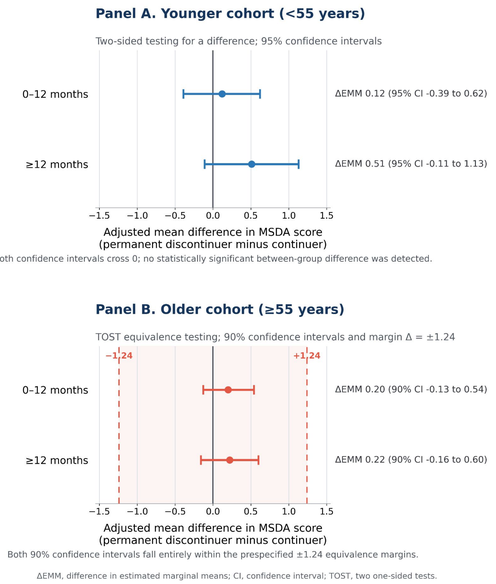


Figure 3: Post-Discontinuation MSDA Scores: Permanent Discontinuers vs. Continuers. Adjusted mean difference in MSDA score (permanent Discontinuer minus continuer) in the <55 year old cohort (A) and ≥55 year old cohort. (EMM = estimated marginal means; MSDA = multiple sclerosis disease activity; CI = confidence interval; TOST = two one sided t tests)

Conclusions

Post-DC MSDA scores showed no significant difference in patients <55 years of age and equivalence in patients ≥55 years of age compared to continuers. These findings are limited by retrospective selection bias and the risk of anti-conservative bias from applying a younger-derived equivalence margin to an older population. Given the limited representation of patients >65 years in the initial MSDA validation study, further evaluation is needed for this age group. Furthermore, because this analysis is exploratory, confirmatory evidence is required to verify whether score stability reflects clinical stability during DC.

Disclosure: S. McCurdy, E. Toy, G. Datta, J. Verrier, A. Osking, D. Brazel, and T. Livingston are employees of and have equity interests in Octave Bioscience. F. Qureshi is a former employee of and has an equity interest in Octave Bioscience.

References: [1] Corboy JR, Fox RJ, Kister I, et al. Risk of new disease activity in patients with multiple sclerosis who continue or discontinue disease-modifying therapies (DISCOMS): a multicentre, randomised, single-blind, phase 4, non-inferiority trial. Lancet Neurol. 2023;22(7):568-577. doi:10.1016/S1474-4422(23)00154-0 [2] Androdias G, Lünemann JD, Maillart E, et al. De-escalating and discontinuing disease-modifying therapies in multiple sclerosis. Brain. 2025;148(5):1459-1478. doi:10.1093/brain/awae409[3] Qureshi F, Hu W, Loh L, et al. Analytical validation of a multi-protein, serum-based assay for disease activity assessments in multiple sclerosis. Proteomics Clinical Applications. Feb 2023. https://doi.org/10.1002/prca.202200018 [4] Chitnis T, Foley J, Ionete C, et al. Clinical Validation of a Multi-protein, Serum-based Assay for Disease Activity Assessments in Multiple Sclerosis. Clinical Immunology. Aug 2023. https://doi.org/10.1016/j.clim.2023.109688

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