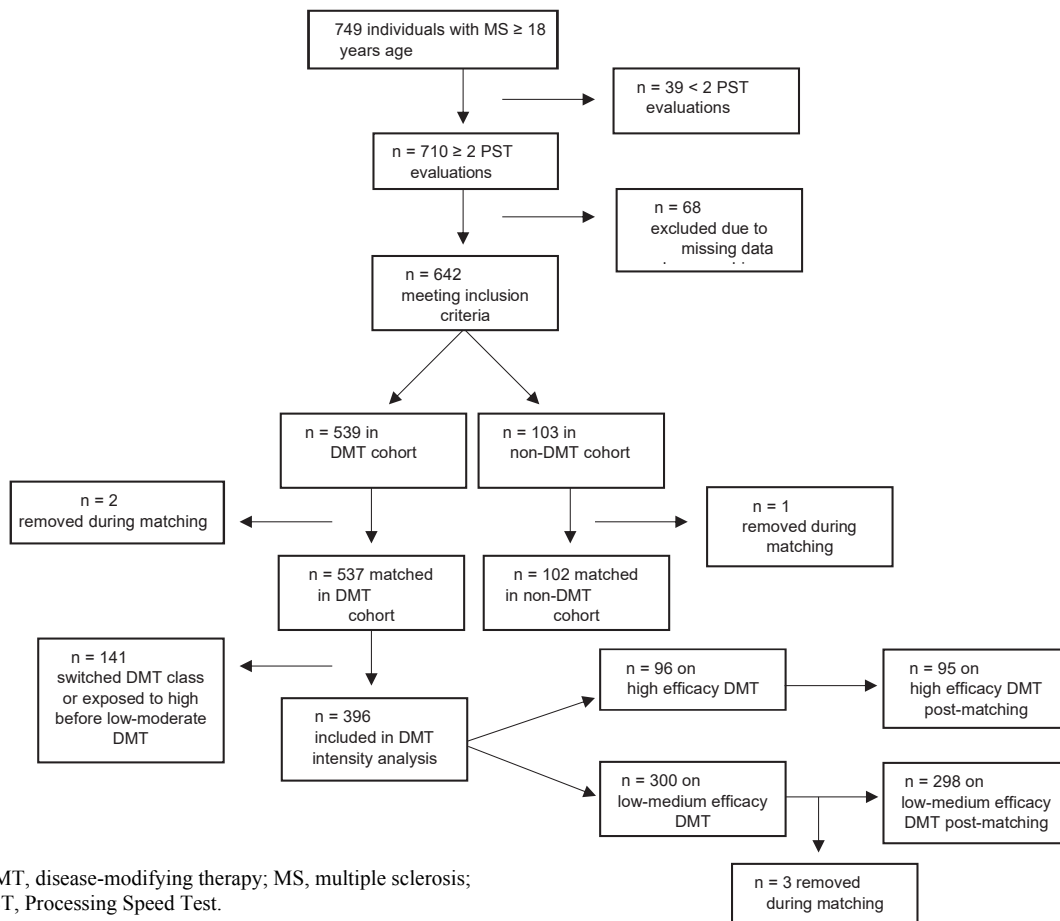


**Figure S1.** Patient Selection Flowchart



DMT, disease-modifying therapy; MS, multiple sclerosis; PST, Processing Speed Test.

**Table S2.** Clinical Characteristics of DMT Cohort at Time of First Test

	High-efficacy DMT: Median (IQR)	Low-/moderate- efficacy DMT: Median (IQR)	<i>P</i> value
<b>Age (y)</b>	<b>47.3 (40.0-56.8)</b>	<b>51.8 (44.4-58.7)</b>	<b>.004</b>
<b>Male, n (%)</b>	<b>35 (36.1)</b>	<b>75 (22.8)</b>	<b>.009</b>
Age of MS diagnosis (y)	32.7 (27.1-40.3)	36.3 (28.5-45.1)	.070
Disease duration (y)	15.2 (9.5-20.9)	17.4 (9.7-24.5)	.277
zPST	-0.82 (-1.70 to -0.20)	-0.65 (-1.53 to -0.21)	.138
<b>PDDS</b>	<b>3 (0-4)</b>	<b>1 (0-4)</b>	<b>.029</b>
<b>Education (y)</b>	<b>16 (13-18)</b>	<b>14 (12-16)</b>	<b>.035</b>
PHQ9 score	5 (2-10)	5 (2-8)	.500
Relapsing disease, n (%)	62 (63.9)	243 (73.9)	.056
Duration monitored (y)	1.7 (0.6-2.4)	1.9 (1.2-2.4)	.057
Number of PST assessments	3 (2-5)	3 (3-4)	.491
Cognitive slope, mean $\pm$ SD	0.139 $\pm$ 0.653	0.244 $\pm$ 1.104	.3732
MRI measures			
T2LV	14.3 (6.3-25.9)	11.0 (4.2-25.5)	.506
WBF	0.807 (0.786 to -0.824)	0.805 (0.781-0.825)	.995
GMF	0.459 (0.451-0.469)	0.461 (0.446-0.474)	.715
ThalF	0.0096 (0.0090-0.0102)	0.0096 (0.0089-0.0104)	.972

DMT, disease-modifying treatment; GMF, gray matter fraction; PDDS, Patient Determined Disease Steps; PHQ9, Patient Health Questionnaire-9; PST, Processing Speed Test; T2LV, T2

lesion volume; ThalF, thalamic fraction; WBF, whole brain fraction; zPST, Processing Speed Test z-score.

Note: Median values (IQR) represented unless stated otherwise. *P* values for Mann-Whitney *U* test or  $\chi^2$  are represented when applicable. Statistically significant results are highlighted in bold.

**Table S3.** MRI Metrics by Cohort

	DMT	Non-DMT	<i>P</i> value	High-efficacy DMT	Low-/moderate-efficacy DMT	<i>P</i> value
Patients with MRIs	n = 327	n = 47	N/A	n = 59	n = 171	N/A
Number of MRIs per patient	<b>1 (0-2)</b>	<b>0 (0-1)</b>	<b>.002</b>	1 (0-3)	1 (0-2)	<b>.009</b>
<b>T2LV</b>	<b>12.1 (5.6-25.8)</b>	<b>8.2 (3.5-15.6)</b>	<b>.015</b>	15.0 (9.1-27.4)	10.9 (4.9-19.8)	<b>.024</b>
WBF	0.806 (0.781-0.826)	0.805 (0.786-0.822)	.460	0.803 (0.781-0.820)	0.807 (0.781-0.832)	.093
<b>GMF</b>	<b>0.460 (0.447-0.473)</b>	<b>0.456 (0.444-0.456)</b>	<b>.035</b>	0.459 (0.451-0.471)	0.460 (0.445-0.473)	.421
<b>ThalF</b>	<b>0.0097 (0.0087-0.0104)</b>	<b>0.0099 (0.0091-0.0105)</b>	<b>.049</b>	<b>0.0095 (0.0089-0.0100)</b>	<b>0.0098 (0.0089-0.0105)</b>	<b>.027</b>

DMT, disease-modifying treatment; GMF, gray matter fraction; T2LV, T2 lesion volume; ThalF, thalamic fraction; WBF, whole brain fraction.

Note: Statistically significant differences using Mann-Whitney *U* test are highlighted in bold