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## Implementing Shared Decision-Making for Multiple Sclerosis: The MS-SUPPORT Tool

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## Original article

## Implementing Shared Decision-Making for Multiple Sclerosis: The MS-SUPPORT Tool

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## ABSTRACT

**Background:** Disease modifying therapies (DMTs) offer opportunities to improve the course of multiple sclerosis (MS), but decisions about treatment are difficult. People with multiple sclerosis (pwMS) want more involvement in decisions about DMTs, but new approaches are needed to support shared decision-making (SDM) because of the number of treatment options and the range of outcomes affected by treatment. We designed a patient-centered tool, MS-SUPPORT, to facilitate SDM for pwMS. We sought to evaluate the feasibility and impact of MS-SUPPORT on decisions about disease modifying treatments (DMTs), SDM processes, and quality-of-life.

**Methods:** This multisite randomized controlled trial compared the SDM intervention (MS-SUPPORT) to control (usual care) over a 12-month period. English-speaking adults with relapsing MS were eligible if they had an upcoming MS appointment and an email address. To evaluate clinician perspectives, participants' MS clinicians were invited to participate. Patients were referred between November 11, 2019 and October 23, 2020 by their MS clinician or a patient advocacy organization (the Multiple Sclerosis Association of America). MS-SUPPORT is an online, interactive, evidence-based decision aid that was co-created with pwMS. It clarifies patient treatment goals and values and provides tailored information about MS, DMTs, and adherence. Viewed by patients before their clinic appointment, MS-SUPPORT generates a personalized summary of the patient's treatment goals and preferences, adherence, DMT use, and clinical situation to share with their MS clinician. Outcomes (DMT utilization, adherence, quality-of-life, and SDM) were assessed at enrollment, post-MS-SUPPORT, post-appointment, and quarterly for 1 year.

**Results:** Participants included 501 adults with MS from across the USA (84.6% female, 83% white) and 34 of their MS clinicians (47% neurologists, 41% Nurse Practitioners, 12% Physician Assistants). Among the 203 patients who completed MS-SUPPORT, most (88.2%) reported they would recommend it to others and that it helped them talk to their doctor (85.2%), understand their options (82.3%) and the importance of taking DMTs as prescribed (82.3%). Among non-users of DMTs at baseline, the probability ratio of current DMT use consistently trended higher over one-year follow-up in the MS-SUPPORT group (1.30 [0.86-1.96]), as did the cumulative probability of starting a DMT within 6-months, with shorter time-to-start (46 vs 90 days,  $p=0.24$ ). Among the 222 responses from 34 participating clinicians, more clinicians in the MS-SUPPORT group (vs control) trended towards recommending their patient start a DMT (9 of 108 (8%) vs 5 of 109 (5%), respectively,  $p=0.26$ ). Adherence (no missed doses) to daily-dosed DMTs was higher in the MS-SUPPORT group (81.25% vs 56.41%,  $p=.026$ ). Fewer

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patients forgot their doses ( $p=.046$ ). The MS-SUPPORT group (vs control) reported 1.7 fewer days/month of poor mental health ( $p=0.02$ ).

**Conclusions:** MS-SUPPORT was strongly endorsed by patients and is feasible to use in clinical settings. MS-SUPPORT increased the short-term probability of taking and adhering to a DMT, and improved long-term mental health. Study limitations include selection bias, response bias, social desirability bias, and recall bias. Exploring approaches to reinforcement and monitoring its implementation in real-world settings should provide further insights into the value and utility of this new SDM tool.

## 1.1. Introduction

Disease modifying therapies (DMTs) offer opportunities to improve the course of multiple sclerosis (MS), especially when started early in the disease and when taken as directed. (Rae-Grant et al., 2018, Burks et al., 2017) However, nearly a third of people with MS (pwMS) under 40 years of age are not treated with DMTs (Zhang et al., 2021) and non-adherence is common. (Burks et al., 2017) Clinical guidelines (Rae-Grant et al., 2018) recommend incorporating patient preferences for treatment safety, route of administration, lifestyle, cost, efficacy, adverse effects, and tolerability into DMT decisions. However, implementing shared decision-making (SDM), where clinicians share their knowledge and patients share their values and preferences in order to select a treatment plan consistent with the patient's values, can be challenging; evidence of widespread implementation of SDM is lacking. (Colligan et al., 2017)

Decision aids are often used to facilitate SDM and have been shown to consistently improve patient knowledge, risk perceptions, and decisional conflict. (Stacey et al., 2017) Their impact on SDM processes (Shay and Lafata, 2015), adherence, or quality of life has been inconsistent.

Decision Aids typically address decisions involving few options, describing and comparing all options. The attributes that are used to compare options are typically selected by the investigators with limited or no input by patients themselves. With over 27 DMTs approved for use in the US and limited head-to-head comparisons, each with numerous distinguishing features, the attributes chosen to compare treatments can lead to bias or confusion. When faced with numerous options, people typically simplify decision-making by removing options that appear incongruent with their values. This process, which focuses on negative attributes, can prematurely eliminate viable options and lead to poor decisions. (Nelson, 2004) Focusing people on their goals and values before presenting options can improve decision-making.

To address the complexities and nuances of MS and DMT decisions, we collaborated with MS patients to systematically develop a patient-centered decision aid, called MS-SUPPORT (Sharing and Understanding Personal Preferences and Objectives Regarding Treatment). Because the benefit-risk profile of DMTs critically depends on the timing of initiation and the patient's adherence to treatment, MS-SUPPORT, unlike typical decision aids, also addresses timing and adherence, generating a summary report populated by patient-reported preferences to prompt and guide a goals-driven SDM conversation.

This trial aims to assess the feasibility and impact of MS-SUPPORT on DMT decisions (utilization and adherence), SDM processes, and quality of life.

## 2.1. Materials and Methods

### 2.1.1. Study design and participants

This multisite randomized controlled trial compared the SDM intervention (MS-SUPPORT) to control (usual care) over a 12-month period. Eligible people with MS (pwMS) were at least 18 years old, had relapsing MS (including relapsing-remitting disease, active secondary progressive MS, and clinically isolated syndrome), an upcoming MS appointment, an email address, and were English-speaking. To evaluate clinician perspectives, participants' MS clinicians were eligible

to participate.

### 2.1.2. Procedures

Patients were referred to the study between November 11, 2019 and October 23, 2020 by their MS clinician or a patient advocacy organization (the Multiple Sclerosis Association of America). 34 MS clinicians from 19 practices across the US referred potential participants to the study website. Eligible patient participants were randomized (1:1) at the clinician level to intervention (MS-SUPPORT) or control (usual care), using Qualtrics randomization software. Patients were assessed at enrollment (T0), after viewing MS-SUPPORT (T1, MS-SUPPORT group only), immediately post-appointment (T2), and quarterly for 1 year after their appointment. Clinicians were assessed at T2. The intervention and all assessments were conducted online using Qualtrics software.

Analyses were powered to detect a 15% point change in DMT utilization ( $n=497$ ) and a 15% improvement in adherence, from a base rate of 70% ( $SD=.30$ ), (Halpern et al., 2011) at 3 month follow-up ( $n=300$  participants using DMT) assuming a type-I error ( $\alpha$ ) of 0.05, power of 0.80, 2-tailed test and 11% attrition.

All participants (patients and clinicians) gave online consent; the study was approved and overseen by WIRB-Copernicus Group® (WCG) IRB. The trial was registered at ClinicalTrials.gov NCT04122989.

### 2.1.3. The intervention

MS-SUPPORT is an online, interactive, evidence-based decision aid. Informed by International Patient Decision Aid Standards (IPDAS) criteria, (Elwyn et al., 2009, Wittman et al., 2021) relevant theory, (Nelson, 2004, de Vries et al., 2013) extensive formative work (Col et al., 2022) and pilot testing, (Col et al., 2019) it includes previously validated values clarification modules. (Col et al., 2018) Other modules, co-created with pwMS, explain MS, symptom management, DMTs, health behaviors, and adherence behaviors. MS-SUPPORT generates a personalized summary of the patient's preferences, adherence behaviors, DMT use, and clinical situation to share with clinicians (a sample summary report is shown in Supplement, Figure 1). The summary report does not make treatment recommendations but rather is designed to help guide the patient-clinician discussion and facilitate SDM. Details about the tool and its development process have been previously published. (Col et al., 2019)

### 2.1.4. Outcomes

Study outcomes are key SDM processes and their potential impact on DMT decisions, behaviors, and quality of life (see conceptual model in Fig. 1). Our prespecified primary outcomes were DMT utilization and adherence. Participants were asked about their plans to start, switch, or stop a DMT (at T0, T2, and quarterly for 1 year). Adherence was assessed by asking patients if they took their last scheduled DMT dose, the number of doses missed during the previous month or relevant dosing interval, reasons for missing any doses, and anticipated barriers to future adherence, drawing from previous studies on adherence. (Remington et al., 2013, Patti, 2010, Katsarava et al., 2015, Mohr et al., 1996) We calculated the proportion who were non-adherent ( $< 80\%$  adherent) and 100% adherent, and the proportion of missed doses.

Prespecified secondary outcomes were risk communication (using COMRADE: Combined Outcome Measure for Risk communication and treatment Decision-making effectiveness), (Edwards et al., 2004) preferred involvement in decision-making (Control Preferences Scale), (Degner et al., 1997) stage of decision-making, (O'Connor, 2000) uncertainty about the decision (4-item decisional conflict scale), (Légaré et al., 2010) congruence of the treatment plan with patient values (Decision Quality), (Sepucha and Ozanne, 2010) illness representations (The Brief Illness Perception Questionnaire), (Broadbent et al., 2006) quality of care (Consumer Assessment of Healthcare Providers & Systems Health Plan Survey (CAHPS® Health Plan Survey and Instructions)), and physical and mental health quality of life (the 4-item Healthy Days Core Module of the HR-QOL-14). (Moriarty et al., 2003) Health literacy was assessed using a validated single-item screener. (Chew et al., 2008)

2.1.5. Statistical analyses

Generalized estimating equations (GEE) with log link and binomial error distribution estimated the probability ratio of current DMT use overall and at each of the time points via linear contrasts. We report probability ratio estimates and corresponding 95% confidence intervals. We used Kaplan-Meier product limit analysis to compute time to start and cumulative probability of starting a DMT. We calculated the difference in the proportion of participants who were adherent to their DMT between the two treatment groups and used GEE to estimate the probability ratio of the adherence metric (MS-SUPPORT to control) at each time point.

Chi-square tests assessed differences in proportions between groups, using two-tailed p values of 0.05 as the threshold for statistical significance. For measures assessed at 2 different timepoints, we calculated the difference in scores for each group between time points, and the difference in the changes between groups. Analyses were done with SAS V9.4 statistical software (SAS Institute Inc, Cary, NC, US).

3.1. Results

A total of 501 adults with relapsing forms of MS and 34 MS clinicians were included in the trial (Fig. 2). Mean patient age was 48.4 years (range 19-78), 84.6% were women, 83% were white, and 52.1% had a college degree (Table 1). Mean duration of MS was 11.86 years. Participants encompassed 42 states and Puerto Rico. Most (82%) of the 34 participating clinicians were female, 16 (47%) were neurologists, 13 of

whom specialized in MS; 14 (41%) were Nurse Practitioners, and 4 (12%) were Physician Assistants. Most (68%) were affiliated with an MS Center. Mean years since completion of training was 14.52 (range 3-35).

3.1.2. Tool completion

Among the 262 patients assigned to MS-SUPPORT, 203 (77.5%) completed the intervention and 94 (46.3%) shared their summary report with their clinician. The median time to complete both the MS-SUPPORT and its evaluation was 46.1 minutes (mode 21.4, minimum 10.7).

25 of the 262 people assigned to MS-SUPPORT partially completed it; 34 did not start it. Non-completers tended to be younger, less educated, with lower health literacy (Supplementary Table 1).

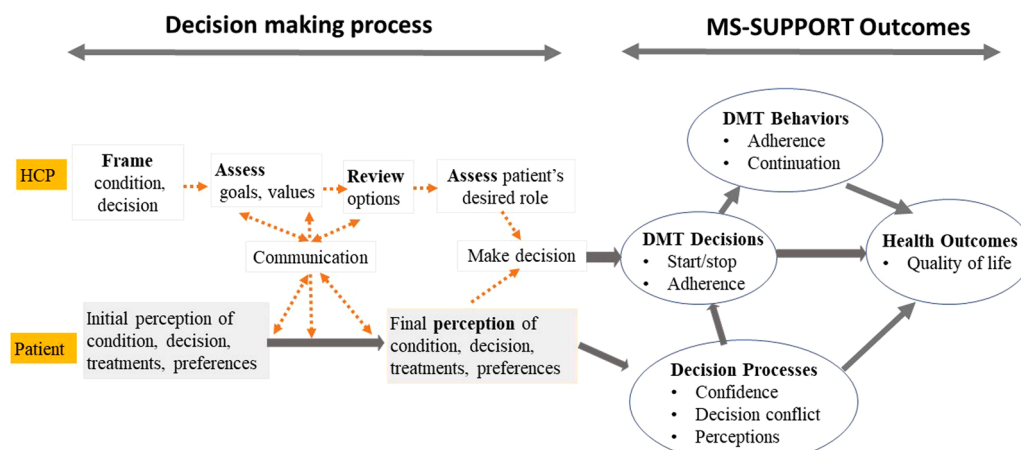
3.1.3. Acceptability to patients

Among the 203 patients who completed MS-SUPPORT, most (88.2%) agreed or strongly agreed that they would recommend it to others and that it helped them talk to their doctor (85.2%), understand their options (82.3%) and the importance of taking DMTs as prescribed (82.3%) (Table 2).

3.1.4. Clinician responses

Among the 222 responses from 34 participating clinicians (71.84% response rate), more clinicians in the MS-SUPPORT group (vs control) trended towards recommending their patient start a DMT (9 of 108 (8%) vs 5 of 109 (5%), respectively, p=0.26) or change DMTs (14 (13%) vs 9 (8%), p=0.26). The most frequently reported reason for changing DMTs was to escalate to a more effective DMT (29%), followed by patient preference (18%), change in patient risk profile (16%), inability to tolerate side effects (16%), and progression to non-relapsing MS (11%).

More clinicians in the MS-SUPPORT group (vs control) rated as excellent: communication with patients (84.3% vs 79.3%), ability to engage patients in decision-making (86.1% vs 82.0%) and tailor discussion about DMTs to what's important to patients (85.2% vs 81.1%), though differences were not significant. There were no differences in the reported efficiency of the visit, which 76.9% and 78.0%, respectively, reported as excellent (Table 3).



**Fig. 1. Conceptual Model.** This figure depicts the framework underlying the shared decision making intervention and the selection of outcomes for the clinical study. The figure models the respective shared decision making roles (processes) of healthcare providers (left top row) and patients (left bottom row) and the outcomes that are potentially affected by these processes. DMT: disease modifying therapy; HCP: health care provider.

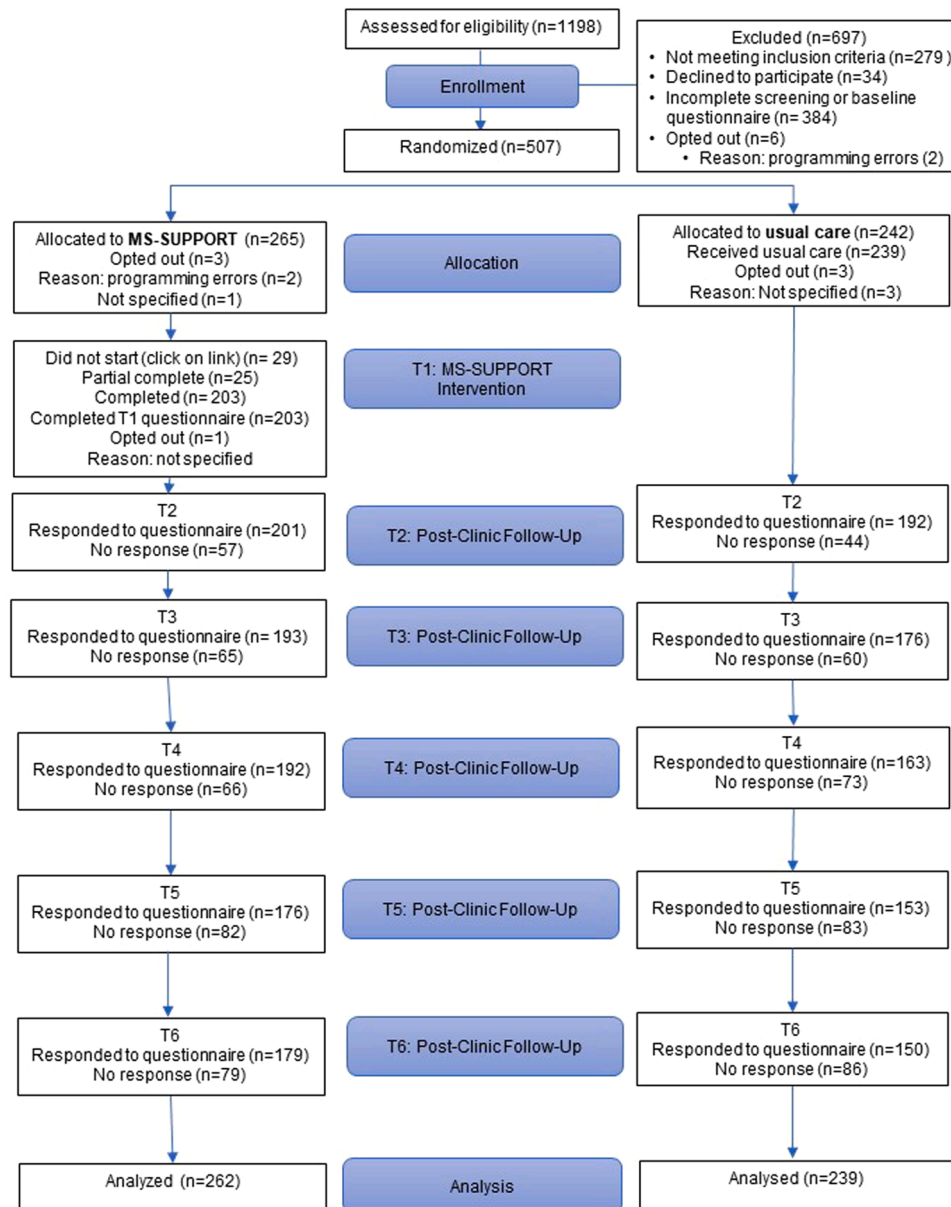


Fig. 2. CONSORT diagram.

### 3.1.5. DMT utilization

At enrollment, 99 (19.8%) participants were not currently using a DMT; 81 of those 99 non-users were past DMT users and 18 had never used a DMT. Among current DMT users at enrollment, 54.1% used infusion therapies, 26.3% oral, and 15.8% injectables.

Among DMT non-users at enrollment, the probability ratio of current DMT use was consistently higher in the MS-SUPPORT group (vs control) at all subsequent time points, with an overall effect of 1.30 (95% CI, 0.86-1.96). The probability ratio was highest (1.59) after the clinical appointment (Fig. 3).

### 3.1.6. Stratified longitudinal analyses

Longitudinal analyses stratified non-users at enrollment into never-users and past-users (Fig. 4). At T2, 57.1% (4 out of 7) never-users in the MS-SUPPORT group started a DMT compared to 0% (0/2) in controls (Fishers exact p-value=0.444). For past-users, 43.3% (13/30) started a DMT in the MS-SUPPORT group versus 33.3% (8 of 24) in controls

(p=0.454). Stratified longitudinal analyses according to type of clinician (neurologist vs Advanced Practice Provider) found no differences in starting a DMT (Supplement, Figure 2).

### 3.1.7. Time-to-start a DMT

The median DMT time-to-start for those who were not on a DMT at baseline was shorter among the MS-SUPPORT group than control (45.9 vs 89.9 days, p=0.25). The comparable times for people under age 40 was 60.53 vs 73.43 days; for those 40 years or older, 42.42 vs 95.01 days. Kaplan-Meier analysis (Fig. 5) shows that within 4 months of observation, the cumulative probability of starting a DMT trended consistently higher in the MS-SUPPORT group (p=0.25). At 30 days, the cumulative probability of starting a DMT was 28% in the MS-SUPPORT group vs 12% in controls. At 6-months, these probabilities were 55% vs 50%, respectively (See Supplement, Figure 3).

DMT users at T0 in the MS-SUPPORT group trended more likely to continue DMT at 3-month follow-up (but not beyond), compared to controls (97.3% vs 93.8%, p=0.17).

**Table 1**  
Participant Demographics (N=501)

	Intervention (MS-SUPPORT) (N=262) No. (%)	Control (Usual care) (N=239) No. (%)
<b>Mean age, years (SD)</b>	48.1 (11.4)	48.7 (11.9)
Range	22-76	19-78
<b>Gender</b>		
Female	225 (85.9)	199 (83.3)
<b>Race/ethnicity</b>		
White/Caucasian	211 (80.5)	205 (85.8)
Black or African American	29	21
Latino or Hispanic	13	8
Asian	2	1
Native American or Alaska native	2	2
Native Hawaiian/Pacific Islander	0	0
Other/Choose not to respond	8	3
<b>Highest level of education</b>		
Less than high school	2 (0.8)	2 (0.8)
High school graduate/GED	19 (7.3)	22 (9.2)
Some college, 2-year college, or technical school	106 (41.2)	87 (36.4)
College graduate	80 (30.5)	82 (34.3)
Graduate school or professional degree	53 (20.2)	46 (19.3)
<b>Health literacy</b>		
No issues with health literacy	208 (79.4)	213 (89.1)
Moderate issues with health literacy	54 (20.6)	26 (10.9)
<b>Type of MS</b>		
Relapsing-remitting MS	239 (91.2)	220 (92.1)
Active Secondary Progressive MS	15 (5.7)	12 (5.0)
CIS	0 (0)	1 (0.4)
Unsure (with relapses)	8 (3.1)	6 (2.5)
<b>Duration of MS (years) (n=499)</b>	Mean: 11.1 (8.4)	Mean: 12.7 (9.05)
Mean (SD)	Median: 9 (0-50)	Median: 12 (0-46)
Median (range)		
Diagnosed within the last 12 months	13 (5.0)	16 (6.8)
Diagnosed within 1-2 years	24 (9.2)	19 (8.0)
<b>DMT use</b>		
Current DMT use	202 (77.1)	200 (82.4)
Past but not current	48 (18.3)	33 (13.8)
Never used a DMT	12 (4.6)	6 (2.5)
<b>Type of DMT (n=399)</b>		
Injection	30 (14.9)	33 (16.8)
Oral	51(25.2)	54 (27.4)
Infusion	113 (55.9)	104 (52.8)
Other (IVIG, rituximab, methotrexate, monthly steroids)	8 (4.0)	6 (3.0)
Unknown	0	3
<b>Depression</b>	72 (27.48)	60 (25.10)
<b>Stage of decision-making (n=372)</b>		
Have not begun to think about options	84 (44.7)	76 (41.3)
Have not begun to think about options, but interested in starting	33 (17.6)	25 (13.6)
Considering options now	23 (12.2)	21 (11.4)
Close to selection	3 (1.6)	4 (2.2)
Already decided but willing to reconsider	21 (11.2)	23 (12.5)
Already decided and unlikely to change	24 (12.8)	35 (19.0)
<b>Role preference in decision-making</b>		
Make the final selection myself	11 (4.2)	16 (6.7)
Make the final selection myself after considering my clinician's opinion	110 (42.0)	106 (44.4)
Share responsibility with clinician	125 (47.7)	107 (44.8)

**Table 1 (continued)**

	Intervention (MS-SUPPORT) (N=262) No. (%)	Control (Usual care) (N=239) No. (%)
Have clinician make the final decision after considering my opinion	14 (5.3)	8 (3.4)
Leave all decisions to my clinician	2 (0.76)	2 (0.8)
<b>Referral source (n=417)</b>		
Clinician	112 (49.6)	96 (50.5)
Patient advocacy group	105 (46.5)	83 (43.7)
Private Facebook page	3 (1.3)	3 (1.6)
Unsure or other	5 (2.2)	8 (4.2)

**Abbreviations:** CIS: Clinically Isolated Syndrome; DMT: disease modifying treatment; GED: General Educational Development Test; IVIG: Intravenous Immunoglobulin; MS: multiple sclerosis; SD: standard deviation.

**Table 2**  
Participant Evaluation of MS-SUPPORT Immediately after Viewing (n= 203)

Attributes	MS-SUPPORT Group <sup>1</sup> (%) <sup>2</sup>
Recommend it to others with MS	88.2
Trust the information provided	93.1
Contains the right amount of information	89.7
Made me aware of the different treatment options available for MS	82.3
Helped me understand my goals and priorities regarding MS	85.7
Helped me understand the importance of taking DMTs as prescribed	82.3
Addressed topics that are important in communicating with my doctor	92.1
Helped me talk to my doctor about what matters most to me	85.2
Makes me more likely to take a DMT as prescribed	62.6
Helped me think about how involved I want to be in decisions about MS	80.8
Changed the way I think about DMTs	43.8
Will help me prepare for my next MS appointment	80.8
Motivated me to make lifestyle changes (e.g. quit smoking, exercise, lose weight)	64.0

DMT: disease modifying therapy; MS: multiple sclerosis.

<sup>a</sup> Data only available for the MS-SUPPORT group because controls did not view the tool.

<sup>b</sup> Percent who strongly agree or somewhat agree on a 5-point Likert scale, from strongly agree to strongly disagree.

**Table 3**  
Clinician-reported evaluations (n=222 responses)

	MS-SUPPORT (108) N (%)	Control (109) N (%)	P-value
<b>Recommend change in DMT</b>			
Start DMT	9 (8.33)	5 (4.59)	0.26
Change DMT	14 (12.96)	9 (8.26)	0.26
Stop DMT	0	1 (0.92)	
<b>Clinician Evaluation % reporting as excellent (n=219)</b>			
Communication with patient	91 (84.26)	86 (79.28)	0.34
Ability to engage patient in decision-making	93 (86.11)	89 (81.98)	0.40
Ability to tailor discussion about DMTs to what's important to the patient	92 (85.19)	88 (81.08)	0.42
Knowledge about patient's adherence to DMT	90 (83.33)	93 (85.32)	
Efficiency of the visit	83 (76.85)	85 (77.98)	

DMT: disease modifying therapy; MS: multiple sclerosis.

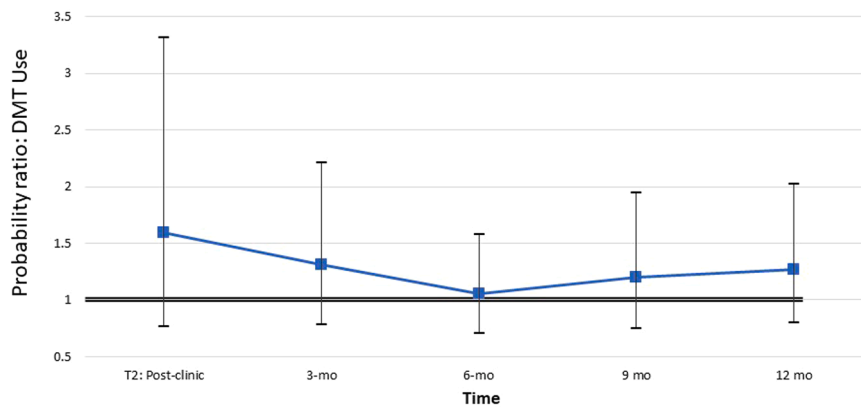


Fig. 3. Probability ration of DMT use over 1 year follow-up. DMT: disease modifying therapy.

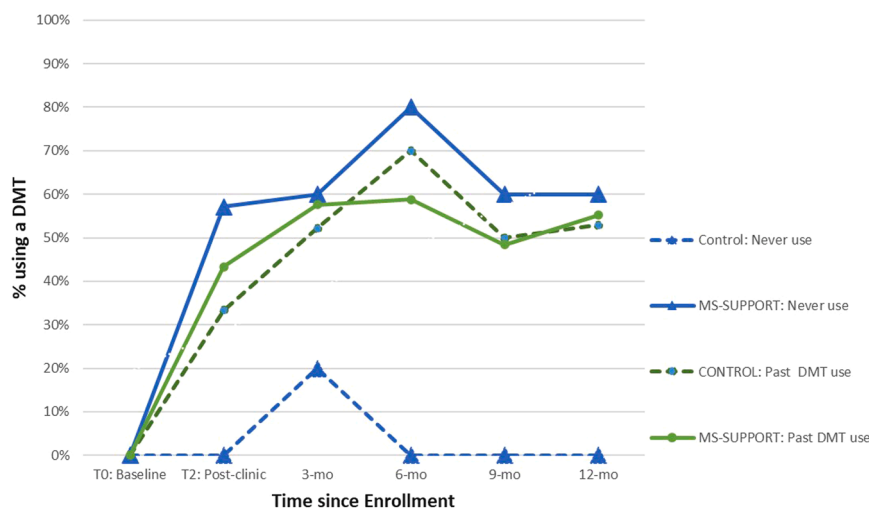


Fig. 4. Stratified longitudinal analyses This figure depicts the percentage of patients in each study group using a DMT over the 1-year follow-up, according to whether the patient had previously used a DMT (Past DMT use) or not (Never use). DMT: disease modifying therapy.

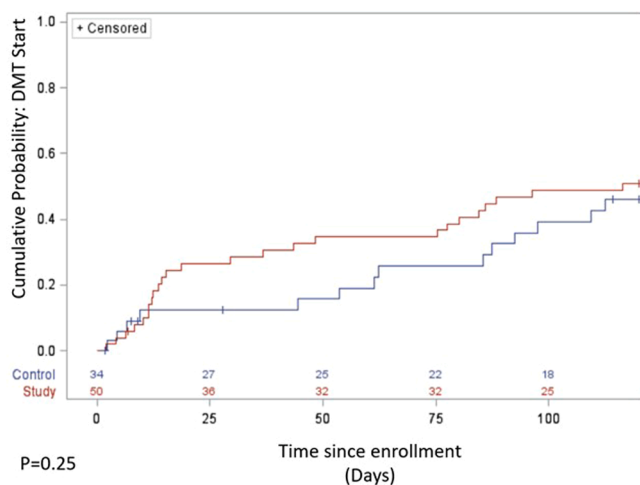


Fig. 5. Cumulative probability of starting a DMT. This Kaplan-Meier analysis depicts the cumulative probability of starting a DMT over the first 120 days for each study group, among those who were not using a DMT at the time of enrollment. The number of people in each study group is shown just above the horizontal axis. The p-value for the difference between study groups is 0.25. DMT: disease modifying therapy.

### 3.1.8. Adherence

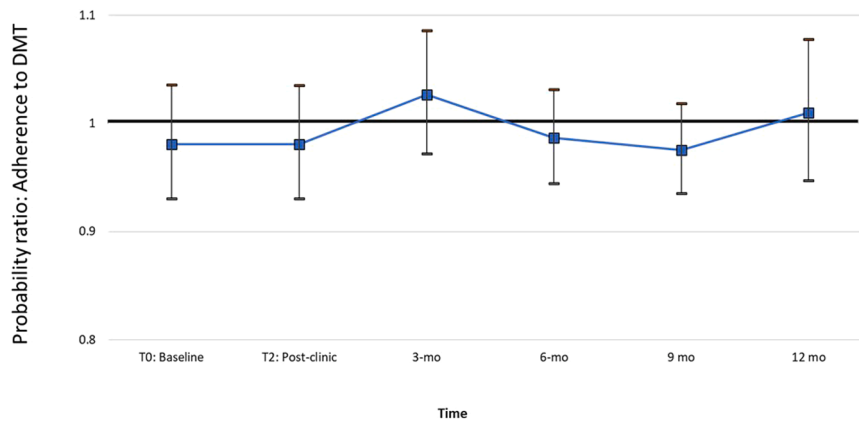
At enrollment, 96.7% of all DMT users (including all formulations) reported taking their last scheduled dose, 84.9% reported 100% adherence (not missing any doses), and 93.3% were adherent (taking 80% or more of the recommended dose). Among those taking daily-dosed DMTs, 96% took their last dose, 66.7% had 100% adherence, and 93.1% were adherent.

Among the 385 taking any DMT, longitudinal probability ratios for adherence and 100% adherence (study vs control group) trended higher at 3-month follow-up, with nearly identical results for both metrics of adherence (1.03 95% CI 0.97-1.09 and 1.03 (0.95-1.13), respectively (Figs. 6 and 7).

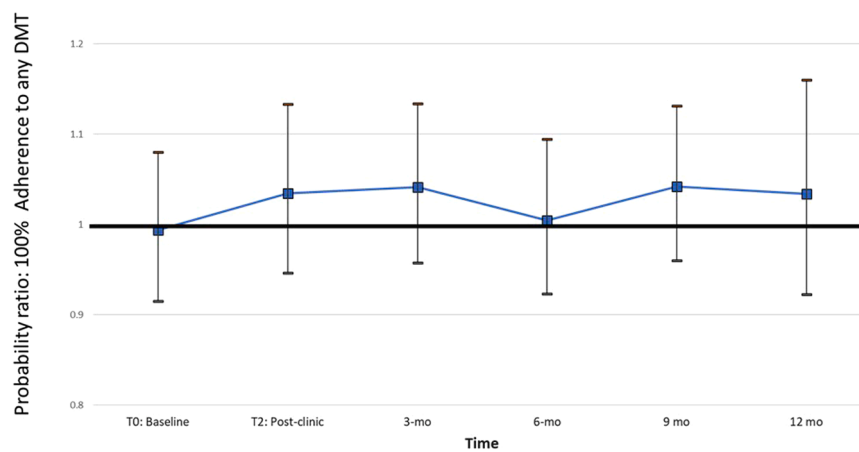
Among those taking daily-dosed DMTs (n=102), the MS-SUPPORT group was more likely than controls to be 100% adherent at T2 (81.3% vs 56.4%, p=0.026). When analyzed longitudinally, the MS-SUPPORT group was 26% more likely to be adherent than controls at T2, but this finding was no longer statistically significant (Fig. 8).

In cross-sectional analyses, the MS-SUPPORT group tended to miss a smaller proportion of daily-dosed DMT doses than the control group over the first 3 months, while the control group became more adherent over the first 6 months (See Supplement, Figure 4).

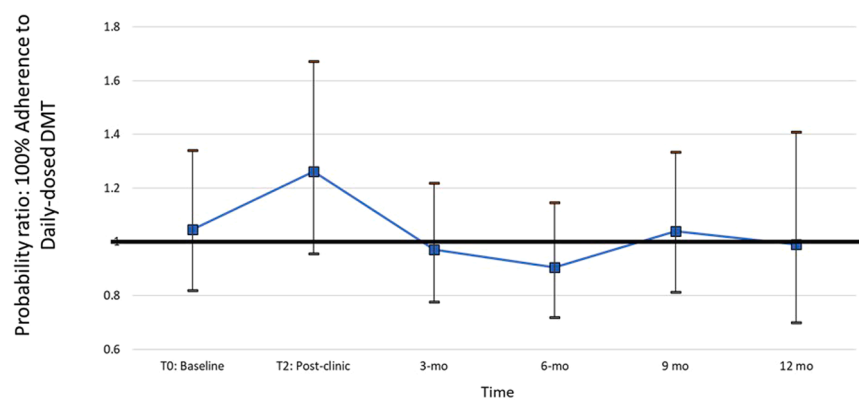
Among the 185 participants who reported reasons for DMT non-adherence, 91 (49%) forgot, 21 (11.4%) had concerns about COVID, and 16 (8.6%) had issues with insurance or affordability (Table 4). The MS-SUPPORT group was less likely to forget than controls (36 vs 55,



**Fig. 6. Longitudinal probability ratios of adherence to DMT.** This figure depicts the longitudinal probability ratios for adherence (study vs control group) over time.  
DMT: Disease modifying therapy, Mo: month



**Fig. 7. Longitudinal probability ratios of 100% adherence to DMT.** This figure depicts the longitudinal probability ratios for perfect (100%) adherence to DMT (study vs control group) over time.  
DMT: Disease modifying therapy, Mo: month



**Fig. 8. Probability ratio of perfect (100%) adherence to daily-dosed DMT over time.** These analyses are restricted to those taking daily dosed DMTs. DMT: disease modifying therapy, Mo: month

p=0.046, Fig. 9).

3.1.9. SDM, quality of care, and quality of life

In longitudinal analyses comparing changes between baseline and T2 between the MS-SUPPORT and control groups, the MS-SUPPORT group

trended towards preferring a more active role in decision-making, were closer to making a treatment decision, had less decisional conflict, and made a higher-quality decision, though differences were not significant (Table 5).

Similarly, the MS-SUPPORT group improved their understanding of their symptoms more than controls (p=0.07), and trended toward

**Table 4**  
**Reasons for Nonadherence** (N=185 responses across all surveys)

Reason	Number (%) <sup>*</sup>
I forgot	91 (49.2)
I had concerns about COVID	21 (11.4)
I had issues with insurance	16 (8.6)
I couldn't afford it	3 (1.6)
I didn't like the side-effects	8 (4.3)
I didn't have access to it (transportation, scheduling, etc)	8 (4.3)
I wasn't sure it was working	2 (1.1)
I was feeling better and didn't think I needed it	2 (1.1)
Other (not specified)	(26.5)

<sup>\*</sup> Participants could list more than one reason for nonadherence. The proportion is per number of respondents

perceiving more control and concern over their MS and thinking that treatments can help their MS.

Mental health quality of life improved significantly among those in the MS-SUPPORT group at 3 months and was sustained at 12-month follow-up. The MS-SUPPORT group reported 1.7 fewer days per month in which mental health was 'not good' (p=0.02).

We observed no differences at T2 between the MS-SUPPORT and control groups in communication or confidence subscales (COMRADE), nor in quality-of-care measures (Table 6). Most scale items were at their upper limit. Those who completed all of MS-SUPPORT trended towards higher COMRADE scores than non-completers (See Supplement, Figure 5).

**4.1. Discussion**

This study establishes the feasibility and acceptability of MS-SUPPORT for patients and their clinicians in diverse settings. We found consistent trends in favor of MS-SUPPORT in 9 of the 11 outcomes examined, including DMT utilization and adherence. These findings, coupled with statistically significant and clinically meaningful improvements in long-term mental health quality-of-life, with no negative impact on the efficiency of patient visits, provide evidence of net beneficial impact.

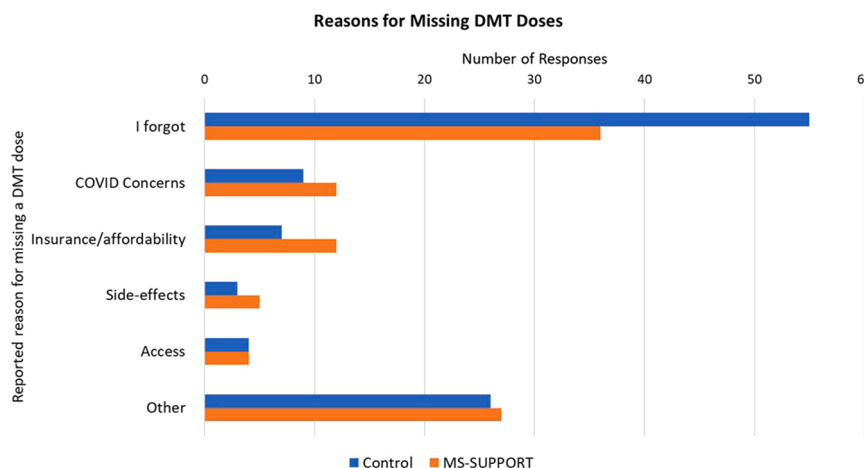
People who are involved in choosing a treatment may be more adherent to that treatment. MS-SUPPORT's impact on adherence likely results from coupling SDM with a comprehensive adherence module and sharing patients' adherence behaviors with clinicians via the summary report. Most patients reported that MS-SUPPORT helped them understand the importance of adherence and feel more likely to take their DMT as prescribed. Higher adherence in the MS-SUPPORT group was due to fewer people forgetting to take their DMT, consistent with specific content in MS-SUPPORT (*Tips about forgetting*). MS-SUPPORT was

most effective within a few months of exposure. Waning over time is expected, given that the intervention was sent only once. Follow-up and reinforcement would be expected to lead to a more sustained impact. (Bouton, 2014)

The observed improvement in mental health-related quality-of-life may have been mediated by changing the patient's understanding of their MS and the benefits of treatment, becoming more engaged in decision-making, and feeling less conflicted that their treatment plan is helping their MS. Treatment outcomes depend not only on bio-physiological treatment effects but also on the patient's trust and hopes that treatment will work, beliefs that their disease can be slowed, and the therapeutic alliance between patients and their clinicians. (Grootens and Sommer, 2022) Greater trust in clinicians increases adherence to their recommendations, improving outcomes. (Lafata et al., 2013) Observed improvements in mental health are statistically significant and clinically meaningful, corresponding to 1-2 fewer days of poor mental health each month. Other decision aids have not conclusively improved health-related quality of life, overall (Rutherford et al., 2019) or for pwMS. (Köpke et al., 2014) This finding confirms that the value of SDM is not just helping patients find the 'best' treatment but helping them feel comfortable with their treatment. (Colligan et al., 2017)

The contrast between participants' initial strongly positive reactions to MS-SUPPORT and the more nuanced impact observed when compared to controls may reflect response shifts. Interventions that alter peoples' understanding of the concepts about which they are surveyed can result in more critical evaluations, (Yank et al., 2013) which can underestimate the intervention's impact. Write-in comments support this shift in perspective: "Doing this study helped me realize that my [MS] provider is not the best fit for me." This phenomenon was found in another MS study, where the intervention group evaluated immunotherapy more critically than controls. (Heesen et al., 2011)

Our study had limitations. Launched during the COVID-19 pandemic lock-down, the intermittent closures of practices and infusion sites, cancelled appointments, and new telehealth visits affected retention and delivery of summary reports to clinicians. Additionally, participating clinicians, who referred half of our participants, likely had strong SDM skills at the start of the study. Participants' behaviors may have changed in response to knowing that they are being observed, potentially explaining improvements in the control group over time. Additionally, a desire to please their clinicians, (McCambridge et al., 2012) social desirability bias, recall bias, and prior relationship with their clinician (Wunderlich et al., 2010) help explain our high baseline scores for SDM processes, DMT use, and adherence. Patient-reported adherence is less accurate than pharmacy records or medication count, but patient-report enabled us to understand reasons for nonadherence. Self-report



**Fig. 9. Reasons for nonadherence.** Patient-reported reasons for missing DMT doses over the course of the study are shown for each study group.

**Table 5**  
Impact of MS-SUPPORT on Other Outcomes: Change in Scores between baseline and follow-up

	MS-SUPPORT Mean difference (SD)	CONTROL Mean difference (SD)	P- value <sup>2</sup>
<b>Role preference (T2-T0, Total score)</b>	-0.8 (0.69)	0.02 (0.65)	0.17
(-)			
% shifted to a collaborative role, T2 vs T0 (+)	75%	50%	0.37
<b>Decisional Conflict (SURE) (+)</b>	0.47 (1.17)	0.34 (0.96)	0.19
<b>Stage of Decision-Making (+)</b>	1.32 (1.83)	0.88 (1.36)	0.25
<b>Perception of illness (BIPQ) (T2-T0)</b>			
How much does your MS affect your life? (-)	3.35 (2.98)	3.62 (2.83)	0.32
How long do you think your MS will continue?	0.09 (.85)	0.09 (1.38)	0.79
How much control do you feel you have over your MS? (+)	0.21 (2.50)	-0.07 (2.52)	0.34
How much do you think your treatment can help your MS? (+)	0.27 (2.16)	0.03 (1.99)	0.11
How much do you experience symptoms from your MS? (-)	0.02(1.66)	-0.06 (1.56)	0.87
How concerned are you about your MS? (+)	0.11 (2.01)	-0.32 (1.97)	0.12
How well do you feel you understand your MS? (+)	0.55 (1.88)	0.25 (1.48)	<b>0.07</b>
How much does your MS affect you emotionally? (-)	0.1 (1.97)	0.06 (2.09)	0.84
<b>HR QoL at 3 months (compared to T0)</b>			
HRQoL1 General Health (+)	-0.02 (0.68)	-0.05 (0.63)	0.64
HRQoL2 Physical Health (# bad days) (-)	-1.02 (8.22)	-0.32 (8.96)	0.47
HRQoL3 Mental Health (# bad days) (-)	-1.68 (7.72)	0.1 (8.54)	<b>0.05</b>
HRQoL4-Function (# bad days) (-)	-1.35 (7.79)	-0.76 (9.36)	0.50
<b>HR QoL at 12 months (compared to T0)</b>			
HRQoL1 General Health (+)	0.03 (0.73)	-0.03 (0.68)	0.26
HRQoL2 Physical Health (# bad days) (-)	-1.25 (8.85)	-1.09 (8.72)	0.61
HRQoL3 Mental Health (# bad days) (-)	-1.67 (7.46)	-0.13 (8.14)	<b>0.02</b>
HRQoL4-Function (# bad days) (-)	-1.22 (9.05)	-1.84 (9.09)	0.89
<b>Decision Quality (T2-T0)</b>			
My treatment plan is helping me achieve my treatment goals (-)	-0.22 (1.40)	-0.10 (1.45)	0.20
My treatment plan reflects what's important to me when I think about the pros and cons of treatment (-)	-0.22 (1.48)	-0.05 (1.39)	0.15

(+) : higher scores signify better outcomes; greater differences indicate improvement

(-) higher scores signify worse outcomes; smaller (or more negative) differences indicate improvement.

<sup>2</sup> . P-values that achieved statistical or borderline statistical significance appear in bold.

**Abbreviations:** BIPQ: Brief Illness Perception Questionnaire; DMT: disease modifying therapy; HR QoL: Health-related Quality of life MS: multiple sclerosis; SD: standard deviation; SURE: a 4-item checklist for detecting decisional conflict (derived from “are you SURE?”); T0: Baseline assessment; T2: Assessment just after the clinical encounter.

adherence measures have been found to be a fairly accurate. (Fahrni et al., 2022) At baseline, COMRADE scores were 10-20 points higher than other studies, (Hamann et al., 2006) 80% used a DMT (compared to 48% in a recent study) (Colligan et al., 2017) and 93% were adherent (compared to 58.6%- 61.4% in other studies). (Burks et al., 2017, Ben-Zacharia et al., 2018) High baseline rates (higher than those used for power analyses) reduced our power to detect an effect. Our finding that non-completers of MS-SUPPORT tended to be less educated with lower health literacy suggests that MS-SUPPORT may not be appropriate for all patients; modifications or assistance for those with lower health

**Table 6**  
Measures assessed at post-clinic appointment (MS-SUPPORT vs Control)

Patient Outcomes (T2) *	MS-SUPPORT		Control		P- value	% at ceiling
	Mean	SD	Mean	SD		
<b>COMRADE Total (raw) (+)</b>	88.44	12.96	89.19	11.48	0.62	60.51%
<b>Communication Subscale (+)</b>	68.51	11.75	67.71	12.64	0.98	
<b>Confidence Subscale (+)</b>	71.52	10.26	73.03	8.54	0.48	
<b>Quality of Care (CAHPS)</b>						
Global rating of clinician (+)	9.29	1.16	9.272	1.27	0.9216	62.36%
Explain things in a way that was easy to understand (+)	2.78	0.54	2.78	0.54	0.9562	85.61%
Listen carefully to you (+)	2.79	0.52	2.81	0.54	0.7181	87.58%
Show respect for what you had to say (+)	2.86	0.47	2.86	0.49	0.6783	93.24%
Spend enough time (+)	2.72	0.62	2.79	0.56	0.2881	85.00%

\* +: higher scores signify better outcomes.

Abbreviations: CAHPS: Consumer Assessment of Healthcare Providers & Systems; COMRADE: Combined outcome measure for risk communication and treatment decision-making effectiveness; SD: standard deviation.

literacy may be needed.

Strengths of our study include a robust study design, long follow-up with multiple assessments, large national sample, inclusion of patient and clinician perspectives in real-world settings, and a theory-based intervention.

MS-SUPPORT adds to the growing number of SDM interventions for MS. (Köpke et al., 2014, Ben-Zacharia et al., 2018, Rahn et al., 2020) Previous interventions target a range of decision points, with most delivered as booklets or in-person programs. Integrating SDM into routine care, as guidelines recommend, will require interventions that support rapid dissemination and updating, suggesting web-based formats. Disseminating MS-SUPPORT to patients was simple and straightforward (requiring only a weblink) but delivering the patient’s summary report to the clinician at point-of care required more effort by patients or clinic staff. Embedding MS-SUPPORT into electronic health records should expedite dissemination and clinical integration.

The totality of our findings suggest that MS-SUPPORT is beneficial to patients and clinicians, facilitates SDM, and may increase DMT initiation, shorten time-to-start treatment, improve DMT adherence, and improve long-term mental health. Exploring approaches to reinforcement and monitoring its implementation in real-world settings should provide further insights into the value and utility of this new SDM tool.

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**Role of funding source**

The external authors’ independence in designing the study, interpreting the data, writing, and publishing the report was explicitly granted by the funding agreement.

The sponsor-investigator (Dr. Col) and study team were responsible for initiating and conducting the study and writing the final manuscript. The sponsor-investigator was responsible for ensuring the quality and integrity of data, following all applicable international and national guidelines. The manuscript was reviewed and approved by the funder.

## CRedit authorship contribution statement

**Nananda F Col:** Conceptualization, Methodology, Project administration, Investigation, Supervision, Software, Formal analysis, Writing – original draft, Writing – review & editing, Funding acquisition. **Andrew J Solomon:** Conceptualization, Investigation, Resources, Methodology, Writing – review & editing. **Enrique Alvarez:** Investigation, Methodology, Resources, Writing – review & editing. **Lori Pbert:** Methodology, Resources, Writing – review & editing. **Carolina Ionete:** Investigation, Resources, Project administration, Writing – review & editing. **Idanis BerriosMorales:** Investigation, Software, Writing – review & editing. **Jennifer Chester:** Resources, Project administration, Writing – review & editing. **Christen Kutz:** Resources, Project administration, Writing – review & editing. **Crystal Iwuchukwu:** Resources, Project administration, Writing – review & editing. **Terrie Livingston:** Funding acquisition, Writing – review & editing. **Vicky Springmann:** Conceptualization, Supervision, Investigation, Visualization, Software, Writing – review & editing, Funding acquisition. **Hannah V. Col:** Software, Formal analysis, Visualization, Data curation. **Long H. Ngo:** Conceptualization, Methodology, Formal analysis, Supervision, Visualization, Data curation, Writing – original draft, Writing – review & editing, Funding acquisition.

## Declaration of Competing Interest

Funding for this research was provided by EMD Serono Inc., USA, an affiliate of Merck KGaA, Darmstadt, Germany, through MS-LINK, a scientific consortium with a mission to improve patient outcomes by advancing MS science to generate actionable real-world data and patient-centered solutions. Further research supported by MS-LINK is designed to close existing scientific gaps identified by the MS community to advance discovery, care, and outcomes for patients with MS. **NC:** reports research grants and payment for participation in Advisory Board from EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany, during the conduct of the study; grants from Pfizer, grants from Biogen, grants from Edwards Lifesciences, LLC, and grants from MSAA (Multiple Sclerosis Association of America). **EA:** reports consultation or advisory fees for Alexion, Biogen, Celgene/BMS, EMD Serono/Merck, Genentech/Roche, Horizon, Motric Bio, Novartis, Sanofi, and TG Therapeutics; and funding or grants from: Biogen, Genentech/Roche, Novartis, TG Therapeutics, Patient-Centered Outcomes Research Institute, National Multiple Sclerosis Society, National Institutes of Health, and Rocky Mountain MS Center, **LP:** has nothing to disclose. **CI (Carolina)** has received research support from Riccio Neuroscience Fund and compensation from Sanofi Genzyme and Bristol Myers Squibb for advisory board participation. **IBM:** has nothing to disclose. **AJS:** reports funding by NIH/NINDS K02NS109340; compensation for consulting or advisory boards from EMD Serono, Genentech, Biogen, Alexion, Celgene, Octave Bioscience, and Greenwich Biosciences, compensation for nonpromotional speaking from EMD Serono, and research support from Biogen; and participated in contracted research with Biogen, Novartis, Actelion, and Genentech. **CK:** Consultant for EMD Serono, Biogen, Genzyme, BMS, Amgen, Teva, and Alexion. **TL:** is an employee of EMD Serono, Inc., Rockland, MA, USA, an affiliate of Merck KGaA, Darmstadt, Germany, **JC:** reports personal fees from EMD Serono, Inc., an affiliate of Merck KGaA, Darmstadt, Germany, Biogen, Allergan, and Biohaven, **CIw (Crystal):** has nothing to disclose. **HC:** has nothing to disclose. **LN:** has nothing to disclose.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.msard.2023.105092](https://doi.org/10.1016/j.msard.2023.105092).

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