eMethods

Determining DMT status

Participants were asked to select which specific DMT they were actively on from a list of all DMTs. Those endorsed being on a DMT were asked to provide the date of their last DMT. Unfortunately, several participants reported their last DMT date after their first vaccine shot, therefore, we could not determine their DMT status at vaccination and they were subsequently excluded from the final data set. For all others reporting a date for their last DMT prior their first vaccine shot, we evaluated whether they were therapeutically compliant (i.e., the time between their last DMT and their first vaccination was within the recommended treatment window). The following rubric was used to determine DMT status at first vaccination:

Rubric used to determine DMT status at vaccination

DMT	Time preceding first vaccine shot to be considered "treated" at vaccination
Aubagio (teriflunomide)	>30 days
Avonex (Interferon beta-1a)	>30 days
Betaseron (interferon beta-1b)	>30 days
Cellcept (mycophenolate mofetil)	>30 days
Copaxone (glatiramer acetate)	>30 days
Extavia (interferon beta-1b)	>30 days
Gilenya (fingolimod)	>30 days
Glatopa (glatiramer acetate)	>30 days
Imuran (azathioprine)	No observations
Lemtrada (alemtuzumab)	>3 years
Mavenclad (cladribine)	>5 years (range in data: 7 to 388 days)
Mayzent (siponimod)	>30 days
Monomethyl fumarate	No observations
Novantrone (mitoxantrone)	No observations
Ocrevus (ocrelizumab)	>40 weeks
Ofatumumab (Kesimpta)	>90 days
Ozanimod (Zeposia)	>30 days
Plegridy (peginterferon beta-1a)	>30 days
Rebif (interferon beta-1a)	>30 days
Rituxan (rituximab)	>40 weeks
Tecfidera (dimethyl fumarate)	>30 days
Tysabri (natalizumab)	>90 days
Vumerity (diroximel fumarate)	>30 days

Source population and response rate

iConquerMS launched their REAL MS surveys on 11/17/2014, including surveys capturing demographics, well-being, quality of life, and MS symptomatology. Researchers can use the iConquerMS portal to launch their specific research surveys (i.e., program satisfaction with an exercise intervention, experiences with telemedicine early in the pandemic, COVID-19 awareness). Existing participants are notified of a new survey launch via e-mail and are regularly invited to complete a new research survey or update their REAL MS survey (i.e., quality of life). New participants informed of the study through other avenues (i.e., regional recruitment by a specific researcher), can register and complete the specific research survey of interest – these new participants are also invited to complete REAL MS surveys and all other active research surveys. Of the 7,580 individuals registered with iConquerMS, 4,861 individuals have participated in at least one survey – 71.3% (N=3,467) have also completed the REAL MS demographic survey.

In the one and two years prior the launch of the current study (3/22/2021), there were 1,849 and 547 active participants, respectively (completed at least one survey during the relevant interval; a total of 2,396 participants completed a survey in the prior two years). Of the 825 participants in the current study (before quality control criteria were imposed), 530 were active in the year prior the launch of the study, 31 were active in the two years prior, 32 were active prior two years, and the remaining 232 participants were new registrants. As a result, the response rate for the current study based on participants active in the preceding year was 28.7% (530/1849), for the preceding two years was 23.4% (561/2396), and since the launch of iConquerMS to 6/9/2021 was 17.0% (825/4861).

REAL MS demographic data was available for 72.6% (1332/1835) of participants active in the two years prior the launch of the current study and who were not a part of the current baseline study population, of whom 1,314 self-reported a diagnosis of MS or CIS (see Table).

Attribute (Mean [SD] or %)		**All MS cases**
N		1314
Age (years)		53.2 (12.0)
Female		79.2%
Latinx		4.2%
Race	White	90.9%
	Non-white	8.5%
	Unknown	0.6%
Subtype (N=1,297)	Relapsing remitting	62.8%
	Secondary progressive	21.8%
	Primary progressive	10.5%
	Clinically isolated syndrome	2.7%
	Unknown	2.0%
Disease duration (N=1,292)		14.5 (10.1)
Patient Determined Disease Steps (N=1,044)		3.1 (2.3)

eTable 1. Vaccine reactions after the first vaccination in all PwMS, PwMS not on a DMT, and PwMS on a S1PR DMT. Percentages are reported.

%	Reaction	Itch	Pain	Redness	Swelling	Warmth	Chills	Fatigue	Fever	Headache	Joint Pain	Malaise	Muscle Ache	Nausea	Allergic	Other
All PwMS (N=719)	None	91.79 (n=660)	45.62 (n=328)	89.15 (n=641)	87.76 (n=631)	86.23 (n=620)	84.28 (n=606)	66.48 (n=478)	85.26 (n=613)	72.32 (n=520)	84.7 (n=609)	78.86 (n=567)	81.64 (n=587)	92.21 (n=663)	97.22 (n=699)	93.46 (n=672)
	Mild	6.12 (n=44)	21.14 (n=152)	5.15 (n=37)	6.4 (n=46)	7.37 (n=53)	5.56 (n=40)	8.62 (n=62)	4.73 (n=34)	10.85 (n=78)	4.87 (n=35)	6.68 (n=48)	5.42 (n=39)	4.03 (n=29)	1.67 (n=12)	2.5 (n=18)
	Moderate	1.95 (n=14)	28.51 (n=205)	5.01 (n=36)	5.15 (n=37)	5.84 (n=42)	7.23 (n=52)	14.19 (n=102)	7.37 (n=53)	11.96 (n=86)	8.07 (n=58)	10.85 (n=78)	9.18 (n=66)	3.34 (n=24)	0.83 (n=6)	2.78 (n=20)
	Severe	0.14 (n=1)	4.73 (n=34)	0.7 (n=5)	0.7 (n=5)	0.56 (n=4)	2.92 (n=21)	10.71 (n=77)	2.64 (n=19)	4.87 (n=35)	2.36 (n=17)	3.62 (n=26)	3.76 (n=27)	0.42 (n=3)	0.28 (n=2)	1.25 (n=9)
PwMS not on a DMT (N=178)	None	92.78 (n=167)	52.78 (n=95)	88.89 (n=160)	88.33 (n=159)	87.22 (n=157)	84.44 (n=152)	67.22 (n=121)	83.33 (n=150)	75 (n=135)	85 (n=153)	77.78 (n=140)	80 (n=144)	91.11 (n=164)	96.11 (n=173)	91.11 (n=164)
	Mild	5 (n=9)	20.56 (n=37)	5 (n=9)	4.44 (n=8)	7.78 (n=14)	3.33 (n=6)	6.67 (n=12)	4.44 (n=8)	6.67 (n=12)	3.89 (n=7)	5.56 (n=10)	4.44 (n=8)	5 (n=9)	1.67 (n=3)	5 (n=9)
	Moderate	2.22 (n=4)	22.22 (n=40)	4.44 (n=8)	6.11 (n=11)	3.89 (n=7)	8.89 (n=16)	15 (n=27)	10.56 (n=19)	12.78 (n=23)	9.44 (n=17)	13.33 (n=24)	11.67 (n=21)	3.33 (n=6)	2.22 (n=4)	3.33 (n=6)
	Severe	0 (n=0)	4.44 (n=8)	1.67 (n=3)	1.11 (n=2)	1.11 (n=2)	3.33 (n=6)	11.11 (n=20)	1.67 (n=3)	5.56 (n=10)	1.67 (n=3)	3.33 (n=6)	3.89 (n=7)	0.56 (n=1)	0 (n=0)	0.56 (n=1)
PwMS on a S1PR DMT (N=56)	None	100 (n=56)	55.36 (n=31)	92.86 (n=52)	91.07 (n=51)	94.64 (n=53)	92.86 (n=52)	76.79 (n=43)	92.86 (n=)52	80.36 (n=45)	91.07 (n=51)	89.29 (n=50)	92.86 (n=52)	96.43 (n=54)	98.21 (n=55)	92.86 (n=52)
	Mild	0 (n=0)	16.07 (n=9)	7.14 (n=4)	7.14 (n=4)	3.57 (n=2)	3.57 (n=2)	5.36 (n=3)	1.79 (n=1)	12.5 (n=7)	1.79 (n=1)	5.36 (n=3)	1.79 (n=1)	1.79 (n=1)	1.79 (n=1)	1.79 (n=1)
	Moderate	0 (n=0)	26.79 (n=15)	0 (n=0)	1.79 (n=1)	1.79 (n=1)	3.57 (n=2)	12.5 (n=7)	5.36 (n=3)	3.57 (n=2)	3.57 (n=2)	3.57 (n=2)	1.79 (n=1)	1.79 (n=1)	0 (n=0)	3.57 (n=2)
	Severe	0 (n=0)	1.79 (n=1)	0 (n=0)	0 (n=0)	0 (n=0)	0 (n=0)	5.36 (n=3)	0 (n=0)	3.57 (n=2)	3.57 (n=2)	1.79 (n=1)	3.57 (n=2)	0 (n=0)	0 (n=0)	1.79 (n=1)

eTable 2. Vaccine reactions after the second vaccination in all PwMS, PwMS not on a DMT, and PwMS on a S1PR DMT. Percentages are reported.

%	Reaction	Itch	Pain	Redness	Swelling	Warmth	Chills	Fatigue	Fever	Headache	Joint Pain	Malaise	Muscle Ache	Nausea	Allergic	Other
All PwMS (N=442)	None	90.5 (n=400)	38.91 (n=172)	88.01 (n=389)	87.33 (n=386)	85.29 (n=377)	74.21 (n=328)	46.83 (n=207)	69.91 (n=309)	59.73 (n=264)	80.09 (n=354)	65.16 (n=288)	68.33 (n=302)	86.2 (n=381)	97.74 (n=432)	91.4 (n=404)
	Mild	6.56 (n=29)	28.51 (n=126)	6.79 (n=30)	7.01 (n=31)	7.92 (n=35)	9.28 (n=41)	10.63 (n=47)	12.22 (n=54)	15.84 (n=70)	4.52 (n=20)	8.37 (n=37)	7.47 (n=33)	7.24 (n=32)	1.58 (n=7)	2.49 (n=11)
	Moderate	2.04 (n=9)	28.05 (n=124)	4.07 (n=18)	4.75 (n=21)	6.33 (n=28)	12.9 (n=57)	28.28 (n=125)	13.12 (n=58)	18.1 (n=80)	11.31 (n=50)	20.59 (n=91)	19 (n=84)	5.2 (n=23)	0.45 (n=2)	4.3 (n=19)
	Severe	0.9 (n=4)	4.52 (n=5)	1.13 (n=5)	0.9 (n=4)	0.45 (n=2)	3.62 (n=16)	14.25 (n=63)	4.75 (n=21)	6.33 (n=28)	4.07 (n=18)	5.88 (n=26)	5.2 (n=23)	1.36 (n=6)	0.23 (n=1)	1.81 (n=8)
PwMS not on a DMT (N=110)	None	91.82 (n=101)	47.27 (n=52)	90 (n=99)	89.09 (n=98)	88.18 (n=97)	80.91 (n=89)	51.82 (n=57)	75.45 (n=83)	70 (n=77)	85.45 (n=94)	70.91 (n=78)	73.64 (n=81)	88.18 (n=97)	99.09 (n=109)	92.73 (n=102)
	Mild	5.45 (n=6)	22.73 (n=25)	5.45 (n=6)	3.64 (n=4)	3.64 (n=4)	8.18 (n=9)	11.82 (n=13)	10.91 (n=12)	10.91 (n=12)	1.82 (n=2)	4.55 (n=5)	2.73 (n=3)	5.45 (n=6)	0.91 (n=1)	1.82 (n=2)
	Moderate	1.82 (n=2)	23.64 (n=26)	2.73 (n=3)	5.45 (n=5)	7.27 (n=8)	9.09 (n=10)	23.64 (n=26)	11.82 (n=13)	11.82 (n=13)	10.91 (n=12)	19.09 (n=21)	19.09 (n=21)	5.45 (n=6)	0 (n=0)	4.55 (n=5)
	Severe	0.91 (n=1)	6.36 (n=7)	1.82 (n=2)	1.82 (n=2)	0.91 (n=1)	1.82 (n=2)	12.73 (n=14)	1.82 (n=2)	7.27 (n=8)	1.82 (n=2)	5.45 (n=6)	4.55 (n=5)	0.91 (n=1)	0 (n=0)	0.91 (n=1)
PwMS on a S1PR DMT (N=33)	None	100 (n=33)	48.48 (n=16)	90.91 (n=30)	90.91 (n=30)	93.94 (n=31)	90.91 (n=30)	60.61 (n=20)	87.88 (n=29)	66.67 (n=22)	93.94 (n=31)	87.88 (n=29)	81.82 (n=27)	96.97 (n=32)	100 (n=33)	100 (n=33)
	Mild	0 (n=0)	21.21 (n=7)	6.06 (n=2)	3.03 (n=1)	3.03 (n=1)	0 (n=0)	18.18 (n=6)	6.06 (n=2)	18.18 (n=6)	0 (n=0)	0 (n=0)	3.03 (n=1)	3.03 (n=1)	0 (n=0)	0 (n=0)
	Moderate	0 (n=0)	30.3 (n=10)	3.03 (n=1)	6.06 (n=2)	3.03 (n=1)	6.06 (n=2)	18.18 (n=6)	3.03 (n=1)	15.15 (n=5)	6.06 (n=2)	12.12 (n=4)	12.12 (n=4)	0 (n=0)	0 (n=0)	0 (n=0)
	Severe	0 (n=0)	0 (n=0)	0 (n=0)	0 (n=0)	0 (n=0)	3.03 (n=1)	3.03 (n=1)	3.03 (n=1)	0 (n=0)	0 (n=0)	0 (n=0)	3.03 (n=1)	0 (n=0)	0 (n=0)	0 (n=0)

eTable 3. Frequency of vaccine reactions by study enrollment in relation to participants' receipt of their first vaccine dose.

		All PwMS	Enrolled before 1st vaccine dose	Enrolled 14 days after 1st vaccine dose	Enrolled 15-30 days after 1st vaccine dose	Enrolled 31-60 days after 1st vaccine dose	Enrolled 61+ days after 1st vaccine dose
First Vaccine Dose	**N**	**719**	**102**	**127**	**136**	**197**	**157**
	Any reaction	63.84%	60.78%	62.99%	58.09%	67.01%	67.52%
	Any local reaction	56.27%	51.96%	55.12%	51.47%	60.41%	58.97%
	Any systemic reaction	45.68%	42.16%	46.46%	44.85%	45.18%	48.72%
	Any severe reaction	16.99%	11.76%	14.17%	20.59%	18.27%	17.95%
	Any severe local reaction	5.43%	1.96%	3.15%	6.62%	5.58%	8.33%
	Any severe systemic reaction	14.35%	10.78%	11.81%	19.12%	15.23%	13.46%
Second Vaccine Dose	**N**	**442**	**50**	**62**	**92**	**127**	**111**
	Any reaction	73.98%	78.00%	72.58%	67.39%	74.02%	78.38%
	Any local reaction	62.22%	64.00%	59.68%	54.35%	67.72%	63.06%
	Any systemic reaction	64.25%	72.00%	66.13%	61.96%	59.06%	67.57%
	Any severe reaction	22.40%	12.00%	24.19%	27.17%	20.47%	24.32%
	Any severe local reaction	5.20%	2.00%	1.61%	4.35%	7.09%	7.21%
	Any severe systemic reaction	20.81%	12.00%	24.19%	25.00%	19.69%	20.72%