

## Supplementary Appendix

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**eTable 1: Number of contributed pregnancies in the modern epoch by country**

	<b>Term &amp; pre-term pregnancies (n = 1640)</b>	<b>Miscarriages &amp; abortions (n = 358)</b>
<b>Country of residence, n (%)</b>		
<b>Czech Republic</b>	323 (19.7)	99 (27.7)
<b>Australia</b>	313 (19.1)	72 (20.1)
<b>Italy</b>	239 (14.6)	39 (10.9)
<b>Turkey</b>	211 (12.9)	44 (12.3)
<b>Spain</b>	146 (8.9)	25 (7.0)
<b>Canada</b>	126 (7.7)	30 (8.4)
<b>Kuwait</b>	104 (6.3)	18 (5.0)
<b>Other European countries</b>	111 (6.8) <sup>a</sup>	14 (3.9) <sup>c</sup>
<b>Other</b>	67 (4.1) <sup>b</sup>	17 (4.7) <sup>d</sup>

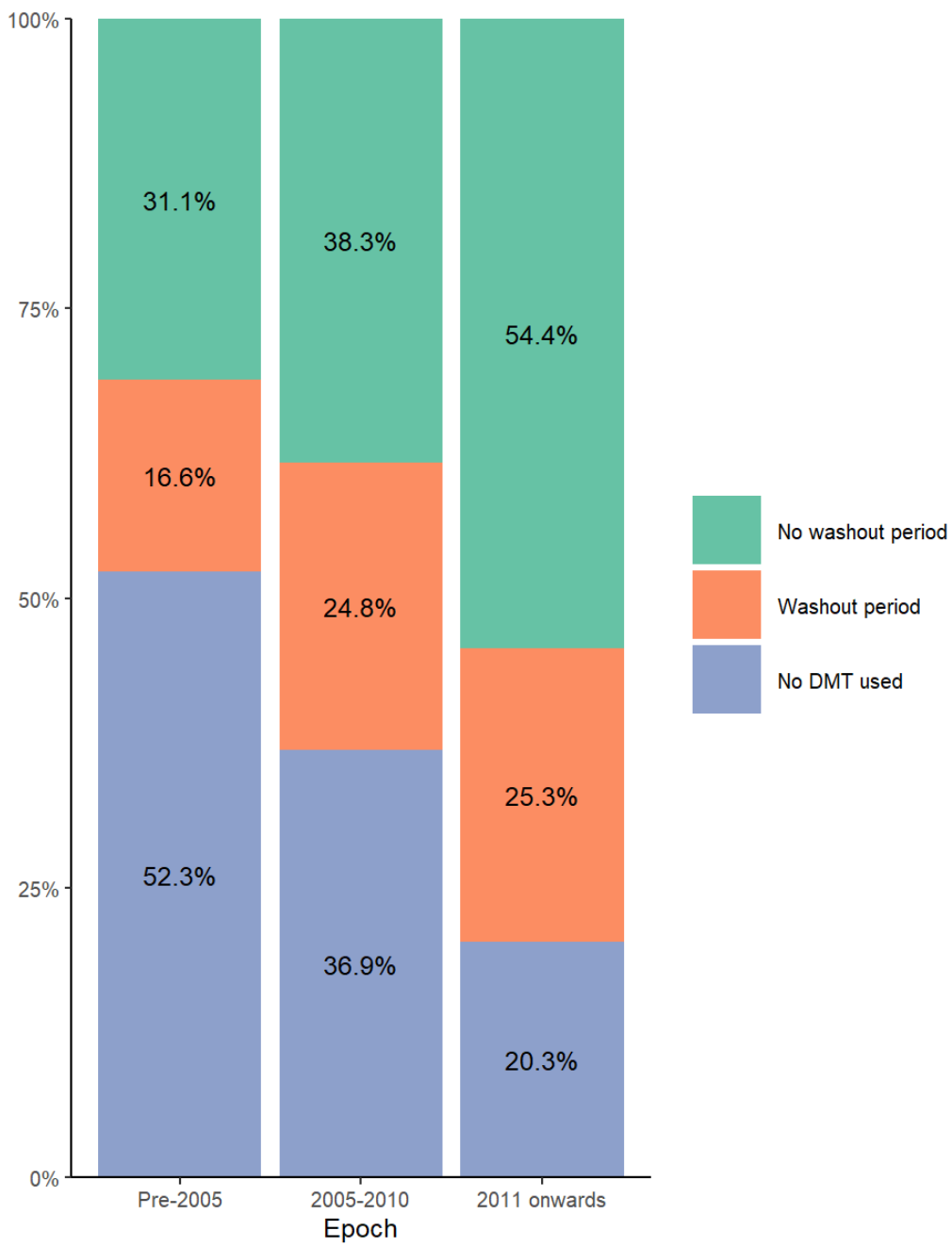
<sup>a</sup>Other European countries include Belgium (n = 45), Portugal (n = 30), Netherlands (n = 20), Ireland (n = 8), United Kingdom (n = 5), Hungary (n = 3).

<sup>b</sup>Other countries include Lebanon (n = 45), Brazil (n = 7), Tunisia (n = 10), Argentina (n = 2), Oman (n = 2), Saudi Arabia (n = 1).

<sup>c</sup>Other European countries include Belgium (n = 2), Portugal (n = 6), Netherlands (n = 4), Hungary (n = 2).

<sup>d</sup>Other countries include Lebanon (n = 10), Tunisia (n = 4), Cuba (n = 1), Egypt (n = 1), New Zealand (n = 1).

**eFigure: Preconception disease-modifying therapy use and behavior across epochs**



Abbreviations: DMT = disease-modifying therapy.

**eTable 2: Characteristics of term/preterm pregnancies in the modern epoch by disease-modifying therapy class used preconception**

	<b>High-efficacy (n = 242)</b>	<b>Medium-efficacy (n = 207)</b>	<b>Low-efficacy (n = 845)</b>	<b>None (n = 346)</b>	<i>p</i>
<b>Age at conception, years, median (IQR)</b>	31.9 (28.7-35.0)	31.9 (28.3-35.2)	31.8 (28.7-34.7)	32.9 (29.5-35.4)	0.014
<b>Time from first symptoms to conception, years, median (IQR)</b>	6.69 (4.10-11.3)	8.20 (4.73-10.9)	5.92 (3.21-9.88)	5.55 (2.42-9.19)	<0.0001
<b>Phenotype at conception, No. (%)</b>					
<b>Relapsing-remitting MS</b>	241 (99.6)	204 (98.6)	780 (92.3)	274 (79.2)	<0.0001
<b>Clinically isolated syndrome</b>	1 (0.4)	3 (1.4)	65 (7.7)	72 (20.8)	
<b>EDSS at conception, median (IQR)</b>	1.5 (1-2)	1 (0-2)	1 (0-1.5)	1 (0-1.5)	<0.0001
<b>EDSS at conception, median (IQR)</b>					
<b>0-1.5</b>	128 (52.9)	130 (62.8)	579 (68.5)	227 (65.6)	<0.0001
<b>2.0-3.5</b>	86 (35.5)	48 (23.2)	165 (19.5)	62 (17.9)	
<b>≥ 4.0</b>	14 (5.8)	11 (5.3)	24 (2.8)	8 (2.3)	
<b>Missing</b>	14 (5.8)	18 (8.7)	77 (9.1)	49 (14.2)	
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.299 (0.587)	0.338 (0.653)	0.288 (0.571)	0.253 (0.642)	0.18
<b>DMT washout period, months, median (IQR)</b>	0 (0-0.452)	1.18 (0-3.99)	0 (0-0.493)	-	<0.0001
<b>DMT continued into pregnancy, No. (%)</b>					
<b>No</b>	97 (40.1)	144 (69.6)	349 (41.3)	-	<0.0001
<b>Yes</b>	145 (59.9)	63 (30.4)	496 (58.7)	-	
<b>Duration of DMT</b>	0.378 (0-1.73)	0 (0-0.296)	0.427 (0-1.12)	-	<0.0001

<b>continued into pregnancy, months, median (IQR)</b>					
<b>DMT class re-initiated postpartum, No. (%)</b>					
<b>High</b>	187 (77.3)	13 (6.3)	17 (2.0)	16 (4.6)	<0.0001
<b>Medium</b>	20 (8.3)	143 (69.1)	75 (8.9)	30 (8.7)	
<b>Low</b>	6 (2.5)	16 (7.7)	571 (67.6)	63 (18.2)	
<b>None</b>	29 (12.0)	35 (16.9)	182 (21.5)	237 (68.5)	
<b>Time until DMT re-initiation after delivery, months, median (IQR)<sup>a</sup></b>	1.08 (0.230-2.46)	2.09 (0.813-4.51)	2.86 (1.08-5.06)	5.59 (2.60-7.95)	<0.0001

<sup>a</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum. DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IQR = interquartile range; MS = multiple sclerosis; SD = standard deviation.

**eTable 3: Characteristics of term/preterm pregnancies in the modern epoch associated with preconception natalizumab, fingolimod and dimethyl fumarate use**

	<b>Natalizumab (n = 219)</b>	<b>Fingolimod (n = 147)</b>	<b>Dimethyl fumarate (n = 57)</b>	<b>p</b>
<b>Age at conception, years, median (IQR)</b>	31.6 (28.5- 34.9)	32.0 (28.5- 35.4)	30.7 (28.1- 33.6)	0.34
<b>Time from first symptoms to conception, years, median (IQR)</b>	6.61 (4.10- 11.2)	8.25 (5.58- 11.0)	7.64 (3.63- 9.77)	0.091
<b>Phenotype at conception, No. (%)</b>				
<b>Relapsing-remitting MS</b>	218 (99.5)	147 (100)	54 (94.7)	0.0084
<b>Clinically isolated     syndrome</b>	1 (0.5)	0	3 (5.3)	
<b>EDSS at conception, median (IQR)</b>	1.5 (1-2)	1 (0-2)	1 (0-1.75)	0.0044
<b>EDSS at conception, median (IQR)</b>				
<b>0-1.5</b>	118 (53.9)	91 (61.9)	38 (66.7)	0.10
<b>2.0-3.5</b>	78 (35.6)	36 (24.5)	12 (21.1)	
<b>≥ 4.0</b>	11 (5.0)	9 (6.1)	1 (1.8)	
<b>Missing</b>	12 (5.5)	11 (7.5)	6 (10.5)	
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.275 (0.559)	0.366 (0.680)	0.230 (0.538)	0.30
<b>DMT washout period, months, median (IQR)</b>	0 (0-0.312)	1.48 (0-4.04)	0 (0-3.42)	<0.0001
<b>DMT continued into pregnancy, No. (%)</b>				
<b>No</b>	85 (38.8)	105 (71.4)	36 (63.2)	<0.0001
<b>Yes</b>	134 (61.2)	42 (28.6)	21 (36.8)	
<b>Duration of DMT continued into pregnancy, months, median (IQR)</b>	0.394 (0-1.30)	0 (0-0.444)	0 (0-0.263)	<0.0001
<b>DMT class re-initiated postpartum, No. (%)</b>				
<b>Natalizumab</b>	166 (75.8)	3 (2.0)	4 (7.0)	-
<b>Rituximab</b>	1 (0.5)	0	0	
<b>Ocrelizumab</b>	4 (1.8)	1 (0.7)	1 (1.8)	
<b>Alemtuzumab</b>	4 (1.8)	4 (2.7)	0	
<b>Fingolimod</b>	16 (7.3)	109 (74.1)	2 (3.5)	
<b>Dimethyl fumarate</b>	4 (1.8)	3 (2.0)	28 (49.1)	
<b>Low</b>	5 (2.3)	5 (3.4)	10 (17.5)	
<b>None</b>	19 (8.7)	22 (15.0)	12 (21.1)	
<b>Time until DMT re- initiation after delivery, months, median (IQR)<sup>a</sup></b>	1.18 (0.298- 2.60)	2.10 (0.854- 4.63)	2.00 (0.657- 3.15)	0.00033

<sup>a</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum.  
DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IQR = interquartile range; MS = multiple sclerosis; SD = standard deviation.

**eTable 4: Characteristics of term and preterm pregnancies associated with preconception natalizumab use**

	<b>NAT with washout (n = 79)</b>	<b>NAT up to first trimester (n = 90)</b>	<b>NAT beyond first trimester (n = 38)</b>	<b><i>p</i></b>
<b>Age at conception, years, median (IQR)</b>	31.5 (29.3-34.3)	31.7 (28.0-34.3)	30.3 (28.1-36.0)	0.93
<b>Time from first symptoms to conception, years, median (IQR)</b>	6.94 (4.26-10.8)	6.00 (3.59-11.3)	8.27 (4.01-11.1)	0.80
<b>EDSS at conception, median (IQR)</b>	1.5 (1-2)	1.5 (1-2.5)	2 (1-2)	0.34
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.291 (0.581)	0.292 (0.591)	0.211 (0.474)	0.79
<b>DMT washout period, months, median (IQR)</b>	0.526 (0.0657-2.32)	0 (0-0)	0 (0-0)	-
<b>Duration of DMT continued into pregnancy, months, median (IQR)</b>	0 (0-0)	0.624 (0.394-0.953)	6.60 (5.95-8.17)	-
<b>DMT class re-initiated postpartum, No. (%)</b>				
<b>High</b>	57 (72.2)	73 (81.1)	35 (92.1)	0.18
<b>Medium</b>	11 (13.9)	7 (7.8)	1 (2.6)	
<b>Low</b>	1 (1.3)	2 (2.2)	1 (2.6)	
<b>None</b>	10 (12.7)	8 (8.9)	1 (2.6)	
<b>Time until DMT re-initiation after delivery, months, median (IQR)<sup>a</sup></b>	1.84 (0.789-3.35)	1.46 (0.756-2.78)	0.0986 (0-1.25)	<0.0001

<sup>a</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum. IQR = interquartile range; NAT = natalizumab; SD = standard deviation.



**eTable 5: Characteristics of term and preterm pregnancies associated with preconception dimethyl fumarate use**

	<b>DMF with washout (n = 34)</b>	<b>DMF into pregnancy (n = 20)</b>	<b><i>p</i></b>
<b>Age at conception, years, median (IQR)</b>	30.1 (27.4-33.0)	32.1 (29.9-35.5)	0.090
<b>Time from first symptoms to conception, years, median (IQR)</b>	7.30 (3.47- 10.2)	8.66 (3.80- 9.66)	0.73
<b>EDSS at conception, median (IQR)</b>	1.5 (1-1.63)	1 (0-2)	0.90
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.180 (0.394)	0.250 (0.639)	0.93
<b>DMT washout period, months, median (IQR)</b>	2.79 (0.123-4.69)	0 (0-0)	-
<b>Duration of DMT continued into pregnancy, months , median (IQR)</b>	0 (0-0)	0.674 (0.263-1.28)	-
<b>DMT class re-initiated postpartum, No. (%)</b>			
<b>High</b>	3 (8.8)	2 (10.0)	0.82
<b>Medium</b>	18 (52.9)	12 (60.0)	
<b>Low</b>	4 (11.8)	3 (15.0)	
<b>None</b>	9 (26.5)	3 (15.0)	
<b>Time until DMT re-initiation after delivery, months, median (IQR)<sup>a</sup></b>	2.00 (1.05-3.45)	2.63 (0.657-3.02)	0.83

<sup>a</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum. DMF = dimethyl fumarate; IQR = interquartile range; SD = standard deviation.

**eTable 6: Characteristics of term and preterm pregnancies associated with preconception fingolimod use**

	<b>FIN with washout (n = 102)</b>	<b>FIN into pregnancy (n = 41)</b>	<i>p</i>
<b>Age at conception, years, median (IQR)</b>	31.9 (28.3-35.1)	32.0 (29.1-36.0)	0.21
<b>Time from first symptoms to conception, years, median (IQR)</b>	8.23 (5.67- 11.9)	8.39 (4.58- 10.2)	0.21
<b>EDSS at conception, median (IQR)</b>	1.5 (1-2)	1 (0-2)	0.14
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.361 (0.710)	0.366 (0.623)	0.72
<b>DMT washout period, months, median (IQR)</b>	3.04 (1.35-4.81)	0 (0-0)	-
<b>Duration of DMT continued into pregnancy, months , median (IQR)</b>	0 (0-0)	1.15 (0.690-3.02)	-
<b>DMT class re-initiated postpartum, No. (%)</b>			
<b>High</b>	6 (5.9)	2 (4.9)	0.71
<b>Medium</b>	75 (73.5)	34 (82.9)	
<b>Low</b>	3 (2.9)	1 (2.4)	
<b>None</b>	18 (17.6)	4 (9.8)	
<b>Time until DMT re-initiation after delivery, months, median (IQR)<sup>a</sup></b>	2.63 (1.13-5.45)	1.08 (0.657-3.55)	0.0045

<sup>a</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum. FIN = fingolimod; IQR = interquartile range; SD = standard deviation.

**eTable 7: Characteristics of term/preterm pregnancies with or without relapse during pregnancy**

	Term/preterm pregnancies (n = 1640)		
	With relapse (n = 194)	Without relapse (n = 1446)	<i>p</i>
<b>Age at conception, years, median (IQR)</b>	30.4 (26.9-33.5)	32.2 (29.2-35.3)	<0.0001
<b>Time from first symptoms to conception, years, median (IQR)</b>	6.06 (3.54-9.83)	6.22 (3.36-10.2)	0.70
<b>EDSS at conception, median (IQR)</b>	1.5 (1-2) <sup>a</sup>	1 (0-2) <sup>b</sup>	0.12
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.497 (0.757)	0.260 (0.570)	<0.0001
<b>DMT class used preconception, No. (%)</b>			
<b>High</b>	46 (23.7)	196 (13.6)	<0.0001
<b>Medium</b>	41 (21.1)	166 (11.5)	
<b>Low</b>	78 (40.2)	767 (53.0)	
<b>None</b>	29 (14.9)	317 (21.9)	
<b>DMT washout period, months, median (IQR)</b>	0.591 (0-4.66)	0 (0-8.25)	0.22
<b>DMT continued into pregnancy, No. (%)</b>			
<b>No</b>	124 (63.9)	812 (56.2)	0.048
<b>Yes</b>	70 (36.1)	634 (43.8)	
<b>DMT duration continued into pregnancy, months, median (IQR)</b>	0 (0-0.690)	0 (0-0.986)	0.026

<sup>a</sup>175 pregnancies with recorded EDSS within one year of conception.

<sup>b</sup>1307 pregnancies with recorded EDSS within one year of conception.

DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IQR = interquartile range; SD = standard deviation.

**eTable 8: Predictors of relapse during pregnancy for term/preterm pregnancies (only patients with RRMS at conception; CIS excluded)**

	<b>Adjusted OR (95% CI)</b>	<b><i>p</i></b>
<b>Age at conception</b>		
<b>&lt; 35 years</b>	1.00	
<b>≥ 35 years</b>	0.385 (0.235-0.630)	0.00015
<b>EDSS at conception</b>		
<b>&lt; 2</b>	1.00	
<b>≥ 2</b>	1.15 (0.771-1.73)	0.49
<b>Missing</b>	1.14 (0.620-2.11)	0.67
<b>Annualized relapse rate in one-year preconception</b>	1.50 (1.17-1.93)	0.0015
<b>DMT used preconception</b>		
<b>Natalizumab</b>	3.26 (1.94-5.48)	<0.0001
<b>Fingolimod</b>	2.31 (1.31-4.07)	0.0037
<b>Dimethyl fumarate</b>	1.47 (0.541-3.98)	0.45
<b>Low-efficacy</b>	1.00	
<b>None</b>	0.593 (0.259-1.36)	0.22
<b>DMT washout period, months</b>	1.06 (1.00-1.13)	0.051
<b>Natalizumab continued into pregnancy, months</b>	0.755 (0.599-0.952)	0.018
<b>Fingolimod continued into pregnancy, months</b>	0.952 (0.753-1.20)	0.68
<b>Dimethyl fumarate continued into pregnancy, months</b>	0.325 (0.0290-3.65)	0.36
<b>Low efficacy-DMT continued into pregnancy, months</b>	0.991 (0.871-1.13)	0.89

**eTable 9: Characteristics of abortions/miscarriages/stillbirths with or without relapse during pregnancy**

	Abortions/miscarriages/stillbirths (n = 358)		
	With relapse (n = 16)	Without relapse (n = 342)	<i>p</i>
<b>Pregnancy duration, months, median (IQR)</b>	1.72 (1.12-2.53)	1.84 (1.35-2.43)	0.89
<b>Age at conception, years, median (IQR)</b>	33.9 (31.2-36.7)	34.1 (29.9-37.2)	0.65
<b>Time from first symptoms to conception, years, median (IQR)</b>	6.12 (4.37-13.0)	6.74 (3.55-10.4)	0.64
<b>EDSS at conception, median (IQR)</b>	1.75 (1-3)	1.5 (1-2)	0.099
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.750 (0.856)	0.272 (0.608)	0.0021
<b>DMT class used preconception, No. (%)</b>			
<b>High</b>	2 (12.5)	62 (18.1)	0.81
<b>Medium</b>	2 (12.5)	49 (14.3)	
<b>Low</b>	8 (50.0)	175 (51.2)	
<b>None</b>	4 (25.0)	56 (16.4)	
<b>DMT washout period, months, median (IQR)</b>	0.0986 (0-7.93)	0 (0-3.29)	0.26
<b>DMT continued into pregnancy, No. (%)</b>			
<b>No</b>	8 (50.0)	131 (38.3)	0.50
<b>Yes</b>	8 (50.0)	211 (61.7)	
<b>DMT duration continued into pregnancy, months, median (IQR)</b>	0.131 (0-1.31)	0.772 (0-1.40)	0.56

DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IQR = interquartile range; SD = standard deviation.

**eTable 10: Characteristics of term/preterm pregnancies with and without relapse in the early postpartum period**

	Term/preterm pregnancies (n = 1640)		
	With relapse (n = 223)	Without relapse (n = 1417)	<i>p</i>
<b>Age at conception, years, median (IQR)</b>	31.7 (27.9-34.1)	32.0 (29.0-35.3)	0.032
<b>Time from first symptoms to conception, years, median (IQR)</b>	6.47 (3.80-10.2)	6.14 (3.28-10.2)	0.33
<b>EDSS at conception, median (IQR)</b>	1.5 (1-2.375) <sup>a</sup>	1 (0-2) <sup>b</sup>	<0.0001
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.481 (0.755)	0.258 (0.566)	<0.0001
<b>Annualized relapse rate in pregnancy, mean (SD)</b>	0.540 (1.31)	0.157 (0.508)	<0.0001
<b>DMT class used preconception, No. (%)</b>			
<b>Natalizumab</b>	46 (20.6)	173 (12.2)	-
<b>Rituximab</b>	2 (0.9)	5 (0.4)	
<b>Alemtuzumab</b>	0	15 (1.1)	
<b>Mitoxantrone</b>	0	1 (0.1)	
<b>Fingolimod</b>	29 (13.0)	118 (8.3)	
<b>Dimethyl fumarate</b>	11 (4.9)	46 (3.2)	
<b>Daclizumab</b>	0	3 (0.2)	
<b>Low</b>	96 (43.0)	749 (52.9)	
<b>None</b>	39 (17.5)	307 (21.7)	
<b>DMT washout period, months, median (IQR)</b>	0 (0-3.47)	0 (0-8.74)	0.055
<b>DMT continued into pregnancy, No. (%)</b>			
<b>No</b>	114 (51.1)	822 (58.0)	0.063
<b>Yes</b>	109 (48.9)	595 (42.0)	
<b>DMT duration continued into pregnancy, months, median (IQR)</b>	0 (0-0.986)	0 (0-0.953)	0.17
<b>DMT class re-initiated postpartum, No. (%)</b>			
<b>Natalizumab</b>	45 (20.2)	157 (11.1)	-
<b>Rituximab</b>	1 (0.4)	4 (0.3)	
<b>Ocrelizumab</b>	2 (0.9)	5 (0.4)	
<b>Alemtuzumab</b>	3 (1.3)	16 (1.1)	
<b>Fingolimod</b>	45 (20.2)	141 (10.0)	
<b>Dimethyl fumarate</b>	15 (6.7)	67 (4.7)	
<b>Low</b>	84 (37.7)	572 (40.4)	
<b>None</b>	28 (12.6)	455 (32.1)	

<b>Time until DMT re-initiation after delivery, months, median (IQR)<sup>c</sup></b>	2.14 (1.00-3.42)	2.55 (0.789-5.29)	0.088
<b>Breastfeeding, No. (%)</b>			
<b>No</b>	157 (70.4)	1034 (73.0)	0.47
<b>Yes</b>	66 (29.6)	383 (27.0)	
<b>Duration of breastfeeding, months, median (IQR)<sup>d</sup></b>	1.91 (0.986-3.10)	3.48 (1.77-6.03)	<0.0001

<sup>a</sup>202 pregnancies with recorded EDSS within 1 year of conception.

<sup>b</sup>1280 pregnancies with recorded EDSS within 1 year of conception.

<sup>c</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum.

<sup>d</sup>Of pregnancies following which patient breastfed.

DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IQR = interquartile range; SD = standard deviation.

**eTable 11: Predictors of time-to-relapse in early postpartum for term/preterm pregnancies (only patients with RRMS at conception; CIS excluded)**

	<b>Adjusted HR (95% CI)</b>	<b><i>p</i></b>
<b>Age at conception</b>		
< 35 years	1.00	
≥ 35 years	0.706 (0.496-1.01)	0.054
<b>EDSS at conception</b>		
< 2	1.00	
≥ 2	1.71 (1.23-2.37)	0.0012
Missing	1.34 (0.770-2.34)	0.30
<b>ARR in one-year preconception</b>	1.26 (1.03-1.53)	0.024
<b>ARR in pregnancy</b>	1.20 (1.03-1.41)	0.023
<b>DMT used preconception</b>		
Natalizumab	2.02 (1.36-3.01)	0.00054
Fingolimod	1.36 (0.813-2.29)	0.24
Dimethyl fumarate	2.04 (1.03-4.03)	0.040
Low-efficacy	1.00	
None	2.67 (1.21-5.89)	0.015
<b>DMT washout period, months</b>	0.924 (0.868-0.984)	0.014
<b>DMT continued into pregnancy, months</b>	1.04 (0.943-1.15)	0.43
<b>DMT class re-initiated postpartum</b>		
Natalizumab	0.112 (0.0385-0.323)	<0.0001
Alemtuzumab	0.320 (0.0686-1.49)	0.15
Anti-CD20	2.44 (0.264-22.7)	0.43
Fingolimod	0.478 (0.204-1.12)	0.089
Dimethyl fumarate	1.03 (0.406-2.61)	0.95
Low	0.394 (0.208-0.748)	0.0040
None	1.00	
<b>Breastfeeding</b>		
No	1.00	
Yes	0.548 (0.357-0.841)	0.0059



**eTable 12: Characteristics of abortions/miscarriages/stillbirths with or without relapse in the early postpartum period**

	Abortions/miscarriages/stillbirths (n = 358)		
	With relapse (n = 35)	Without relapse (n = 323)	<i>p</i>
<b>Pregnancy duration, months, median (IQR)</b>	1.38 (1.02-2.30)	1.84 (1.38-2.46)	0.063
<b>Age at conception, years, median (IQR)</b>	32.9 (27.8-36.1)	34.2 (30.2-37.2)	0.099
<b>Time from first symptoms to conception, years, median (IQR)</b>	5.67 (2.90-8.37)	6.87 (3.82-11.0)	0.040
<b>EDSS at conception, median (IQR)</b>	1.5 (1-2.5) <sup>a</sup>	1.5 (1-2) <sup>b</sup>	0.15
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.490 (0.712)	0.272 (0.615)	0.021
<b>Annualized relapse rate in pregnancy, mean (SD)</b>	0.298 (1.76)	0.445 (2.99)	0.64
<b>DMT class used preconception, No. (%)</b>			
<b>High</b>	6 (17.1)	58 (18.0)	0.23
<b>Medium</b>	7 (20.0)	44 (13.6)	
<b>Low</b>	20 (57.1)	163 (50.5)	
<b>None</b>	2 (5.7)	58 (18.0)	
<b>DMT washout period, months, median (IQR)</b>	0 (0-2.60)	0 (0-3.47)	0.61
<b>DMT continued into pregnancy, No (%)</b>			
<b>No</b>	14 (40.0)	125 (38.7)	1.00
<b>Yes</b>	21 (60.0)	198 (61.3)	
<b>DMT duration continued into pregnancy, months, median (IQR)</b>	0.624 (0-1.20)	0.821 (0-1.41)	0.26
<b>DMT class re-initiated during postpartum period, No. (%)</b>			
<b>High</b>	6 (17.1)	60 (18.6)	0.098
<b>Medium</b>	8 (22.9)	31 (9.6)	
<b>Low</b>	16 (45.7)	148 (45.8)	
<b>None</b>	5 (14.3)	84 (26.0)	
<b>Time until DMT re-initiation after delivery, months, median (IQR)<sup>c</sup></b>	0.772 (0-2.47)	0 (0-0.904)	0.0058

<sup>a</sup>31 pregnancies with recorded EDSS within one year of conception.

<sup>b</sup>302 pregnancies with recorded EDSS within one year of conception.

<sup>c</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum.

DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IQR = interquartile range; SD = standard deviation.

**eTable 13: Predictors of time-to-relapse during the early postpartum period for abortions/miscarriages/stillbirths**

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	p value	HR (95% CI)	p
<b>Age at conception</b>				
< 35 years	1.00		1.00	
≥ 35 years	0.576 (0.280-1.18)	0.13	0.489 (0.201-1.19)	0.11
<b>EDSS at conception</b>				
< 2	1.00		1.00	
≥ 2	1.77 (0.875-3.59)	0.11	1.68 (0.681-4.12)	0.26
Missing	2.53 (0.850-7.52)	0.096	2.55 (0.570-11.4)	0.22
<b>Annualized relapse rate in one-year preconception</b>	1.60 (1.07-2.39)	0.021	1.89 (1.12-3.18)	0.017
<b>Annualized relapse rate in pregnancy</b>	0.975 (0.851-1.12)	0.71	0.839 (0.628-1.12)	0.23
<b>DMT class used preconception</b>				
Natalizumab	0.920 (0.379-2.23)	0.85	1.32 (0.364-4.77)	0.68
Fingolimod	1.52 (0.597-3.87)	0.38	1.65 (0.364-7.50)	0.52
Dimethyl fumarate	0.700 (0.0851-5.76)	0.74	0.904 (0.0663-12.3)	0.94
Low-efficacy	1.00		1.00	
None	0.296 (0.0694-1.26)	0.10	0.134 (0.0163-1.10)	0.061
<b>DMT washout period, months</b>	0.971 (0.903-1.04)	0.43	1.10 (0.938-1.28)	0.25
<b>DMT continued into pregnancy</b>				
No	1.00		-	-
Yes	0.947 (0.480-1.87)	0.87	-	-
<b>DMT continued into pregnancy, months</b>	0.744 (0.523-1.06)	0.099	0.629 (0.339-1.17)	0.14
<b>DMT class re-initiated in the postpartum period</b>				
High	0.584 (0.181-1.88)	0.37	0.318 (0.0565-1.79)	0.19
Medium	0.810 (0.184-3.57)	0.78	0.687 (0.116-4.08)	0.68
Low	0.868 (0.414-1.82)	0.71	1.25 (0.426-3.65)	0.69
None	1.00		1.00	

DMT re-initiation postpartum was encoded as a time-varying covariate. Multivariable model included the presented variables and was adjusted for country of residence and number of clinic visits during one-year postpartum (not shown). Akaike Information Criterion of multivariable model was 418 and Global Schoenfeld test p=0.94.

DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; HR = hazard ratio.

**eTable 14: Characteristics of term and preterm pregnancies with or without a confirmed disability progression event**

	Term/preterm pregnancies (n = 850)		
	With CDP event (n = 48)	Without CDP event (n = 802)	<i>p</i>
<b>Age at conception, years, median (IQR)</b>	31.4 (28.2-33.6)	31.9 (28.9-34.8)	0.42
<b>Time from first symptoms to conception, years, median (IQR)</b>	7.81 (4.49-9.80)	6.06 (3.42-10.1)	0.30
<b>EDSS at conception, median (IQR)</b>	1 (0-1.5)	1.5 (1-2)	0.15
<b>Annualized relapse rate in one-year preconception, mean (SD)</b>	0.586 (0.825)	0.295 (0.600)	0.0051
<b>Annualized relapse rate in pregnancy, mean (SD)</b>	0.775 (0.931)	0.172 (0.569)	<0.0001
<b>Relapse occurrence in postpartum, No. (%)<sup>a</sup></b>			
<b>No</b>	24 (50)	624 (77.8)	<0.0001
<b>Yes</b>	24 (50)	178 (22.2)	
<b>DMT class used preconception, No. (%)</b>			
<b>High</b>	10 (20.8)	110 (13.7)	0.054
<b>Medium</b>	10 (20.8)	87 (10.8)	
<b>Low</b>	23 (47.9)	468 (58.4)	
<b>None</b>	5 (10.4)	137 (17.1)	
<b>DMT washout period, months, median (IQR)</b>	0.312 (0-3.26)	0 (0-4.45)	0.30
<b>DMT continued into pregnancy, No. (%)</b>			
<b>No</b>	31 (64.6)	415 (51.7)	0.11
<b>Yes</b>	17 (35.4)	387 (48.3)	
<b>DMT duration continued into pregnancy, months, median (IQR)</b>	0 (0-0.879)	0 (0-1.02)	0.20
<b>DMT class re-initiated during postpartum period, No. (%)</b>			
<b>High</b>	10 (20.8)	113 (14.1)	0.0070
<b>Medium</b>	15 (31.2)	129 (16.1)	
<b>Low</b>	19 (39.6)	386 (48.1)	
<b>None</b>	4 (8.3)	174 (21.7)	
<b>Time until DMT re-initiation after delivery, months, median (IQR)<sup>b</sup></b>	2.27 (0.854-4.63)	2.48 (1.08-4.54)	0.74
<b>Breastfeeding, No. (%)</b>			
<b>No</b>	35 (72.9)	514 (64.1)	0.28
<b>Yes</b>	13 (27.1)	288 (35.9)	

<b>Duration of breastfeeding, months, median (IQR)<sup>c</sup></b>	2.43 (0.526-4.07)	3.02 (1.47-5.03)	0.33
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<sup>a</sup>in first six months, and before CDP event (in women who experienced CDP event).

<sup>b</sup>Of pregnancies following which the patient restarted a DMT within 12-months postpartum.

<sup>c</sup>Of pregnancies following which patient breastfed.

CDP = confirmed disability progression; DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; IQR = interquartile range; SD = standard deviation.

**eTable 15: Predictors of time-to-confirmed disability progression event for term and preterm pregnancies**

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	<i>p</i>	HR (95% CI)	<i>p</i>
<b>Age at conception</b>				
< 35 years	1.00		1.00	
≥ 35 years	0.650 (0.305-1.39)	0.27	0.893 (0.396-2.01)	0.78
<b>EDSS at conception</b>	0.846 (0.582-1.23)	0.38	0.659 (0.434-0.999)	0.049
<b>Annualized relapse rate in one-year preconception</b>	1.66 (1.23-2.24)	0.00090	1.42 (0.942-2.13)	0.095
<b>Annualized relapse rate in pregnancy</b>	1.80 (1.45-2.24)	<0.0001	1.67 (1.25-2.22)	0.00052
<b>Relapse occurrence in postpartum<sup>a</sup></b>	3.34 (1.88-5.94)	<0.0001	2.54 (1.21-5.33)	0.014
<b>DMT class used preconception</b>				
<b>High</b>	1.83 (0.872-3.85)	0.11	1.40 (0.606-3.25)	0.43
<b>Medium</b>	2.30 (1.11-4.75)	0.025	1.90 (0.766-4.70)	0.17
<b>Low</b>	1.00		1.00	
<b>None</b>	0.757 (0.286-2.00)	0.57	0.542 (0.170-1.73)	0.30
<b>DMT class re-initiated in the postpartum period</b>				
<b>High</b>	1.45 (0.543-3.84)	0.46	0.786 (0.232-2.65)	0.70
<b>Medium</b>	0.813 (0.180-3.68)	0.79	0.121 (0.0116-1.26)	0.077
<b>Low</b>	0.791 (0.333-1.88)	0.60	0.697 (0.256-1.90)	0.48
<b>None</b>	1.00		1.00	
<b>Breastfeeding</b>				
<b>No</b>	1.00		1.00	
<b>Yes</b>	0.494 (0.227-1.08)	0.19	0.659 (0.282-1.538)	0.33

DMT re-initiation postpartum and breastfeeding were encoded as time-varying covariates. Multivariable model included the presented variables and was adjusted for country of residence and number of clinic visits during one-year postpartum (not shown). Akaike Information Criterion of multivariable model was 626 and Global Schoenfeld test  $p=0.08$ .

<sup>a</sup>in first six months and before CDP event.

CI = confidence interval; CDP = confirmed disability progression; DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; HR = hazard ratio.