

Supplemental Online Content

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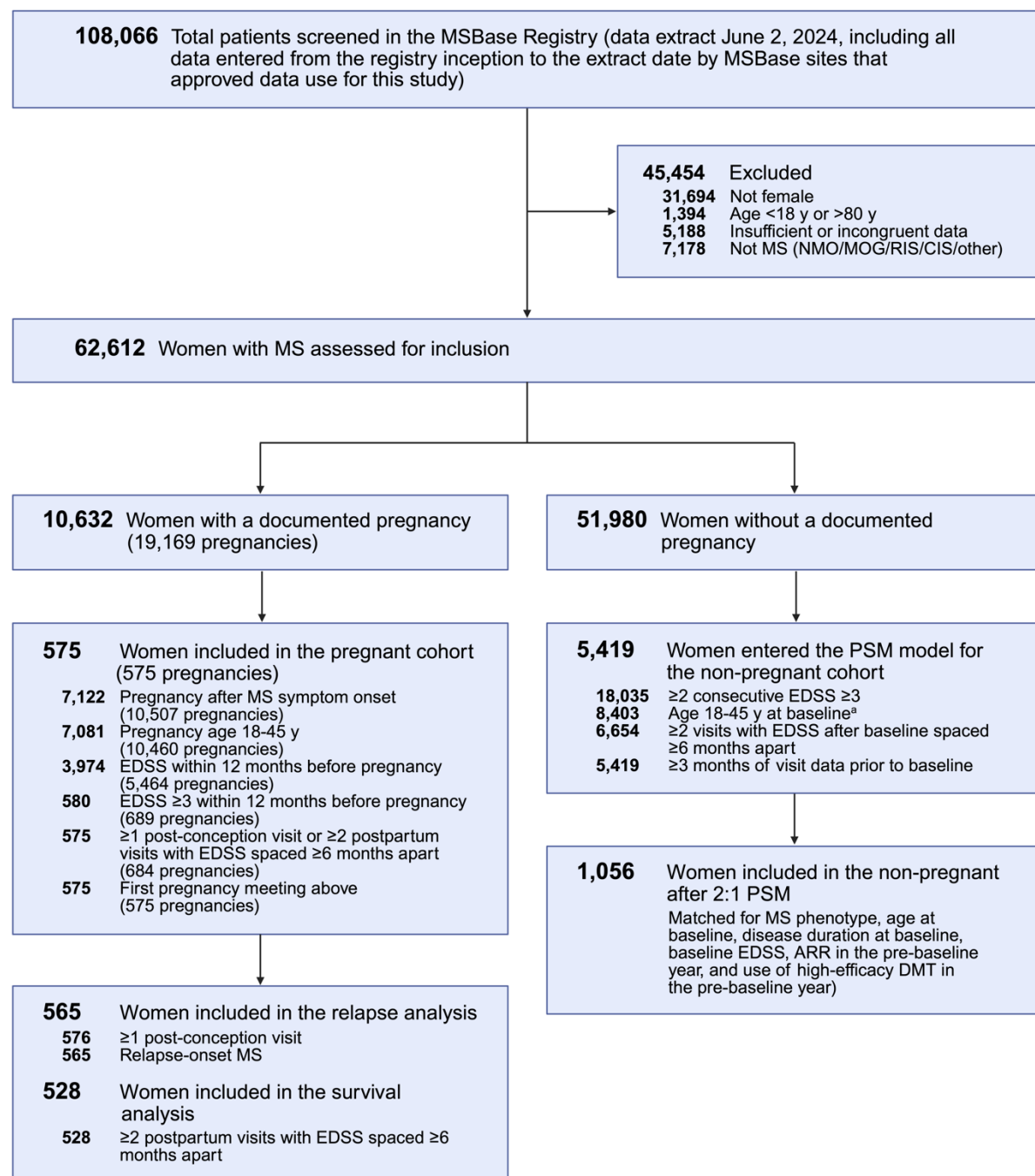
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This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1. Inclusion and Exclusion Flow Diagram



Abbreviations: ARR, annualised relapse rate; CIS, clinically isolated syndrome; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; MOG, myelin-oligodendrocyte glycoprotein antibody-associated disease; NMO, neuromyelitis optica spectrum disorder; PSM, propensity score matching; RIS, radiologically isolated syndrome.

^a Baseline in the non-pregnant group was defined as the first consecutive EDSS score of at least 3

eTable 1. Characteristics of Women in the Pregnant Cohort

Characteristic	n = 575
Age at MS symptom onset, median (IQR), y	23.33 (19.50-27.14)
MS phenotype, n (%)	
Relapsing-remitting MS	536 (93.2)
Secondary progressive MS	29 (5.0)
Primary progressive MS	10 (1.7)
Age at included pregnancy, median (IQR), y	32.50 (29.14-36.10)
Disease duration at included pregnancy, median (IQR), y	8.17 (4.50-12.36)
Pregnancy duration, median (IQR), w	38.57 (34.79-39.86)
Live births, n (%)	477 (82.96)
Days between preconception visit and conception, median (IQR)	73 (30.5-140.5)
Preconception EDSS, median (range)	3.5 (3.0-7.5)
ARR in the preconception year, median (IQR)	0.00 (0.00-1.00)
DMTs used in the preconception year, n (%) ^a	469 (81.6)
Interferon	141 (24.5)
Natalizumab	104 (18.1)
Glatiramer acetate	76 (13.2)
Fingolimod	46 (8.0)
Anti-CD20 therapy	40 (7.0) ^b
Dimethyl fumarate	31 (5.4)
Alemtuzumab	9 (1.6)
Teriflunomide	8 (1.4)
Cladribine	4 (0.7)
Other	10 (1.7) ^c
Women on high-efficacy DMT in the preconception year, n (%)	205 (25.7)
Months between DMT withdrawal and pregnancy, median (IQR) ^d	-0.99 (-1.77-0.39)
DMT used in the postpartum year, n (%) ^e	438 (76.2)
Interferon	131 (22.8)
Natalizumab	103 (17.9)
Glatiramer acetate	62 (10.8)
S1P receptor modulator	50 (8.7) ^f
Anti-CD20 therapy	36 (6.3) ^g
Dimethyl fumarate	31 (5.4)
Alemtuzumab	9 (1.6)
Teriflunomide	8 (1.4)
Cladribine	4 (0.7)
Other	4 (0.7) ^h
Women on high-efficacy DMT in the postpartum year, n (%)	201 (35.0)
Months to reinitiation of DMT postpartum, median (IQR) ⁱ	1.46 (0.00-3.90)
Documentation of breastfeeding, n (%)	195 (33.9)
Breastfeeding duration, median (IQR), mo	2.46 (1.12-5.03)
Follow-up duration from the preconception visit, median (IQR), y	13.09 (8.20-7.67)

Abbreviations: DMT, disease-modifying therapy; IQR, interquartile range; mo, months; S1P, sphingosine-1-phosphate; w, weeks; y, years.

^a For individuals who used more than one DMT type in the preconception year, only the DMT commenced closest to conception was included

^b Ocrelizumab (n = 33), rituximab (n = 7)

^c Mitoxantrone (n = 3), trial (n = 3), AHSCT (n = 2), daclizumab (n = 2)

^d Positive values indicate withdrawal of the DMT prior to pregnancy, and negative values indicate continuation after conception. In some cases, a DMT may have been withdrawn for pregnancy, but the temporary discontinuation and reinitiation dates may not have been entered in the registry, which may influence the accuracy of the data

^e For individuals who used more than one DMT type in the postpartum year, only the first DMT initiated after pregnancy was included

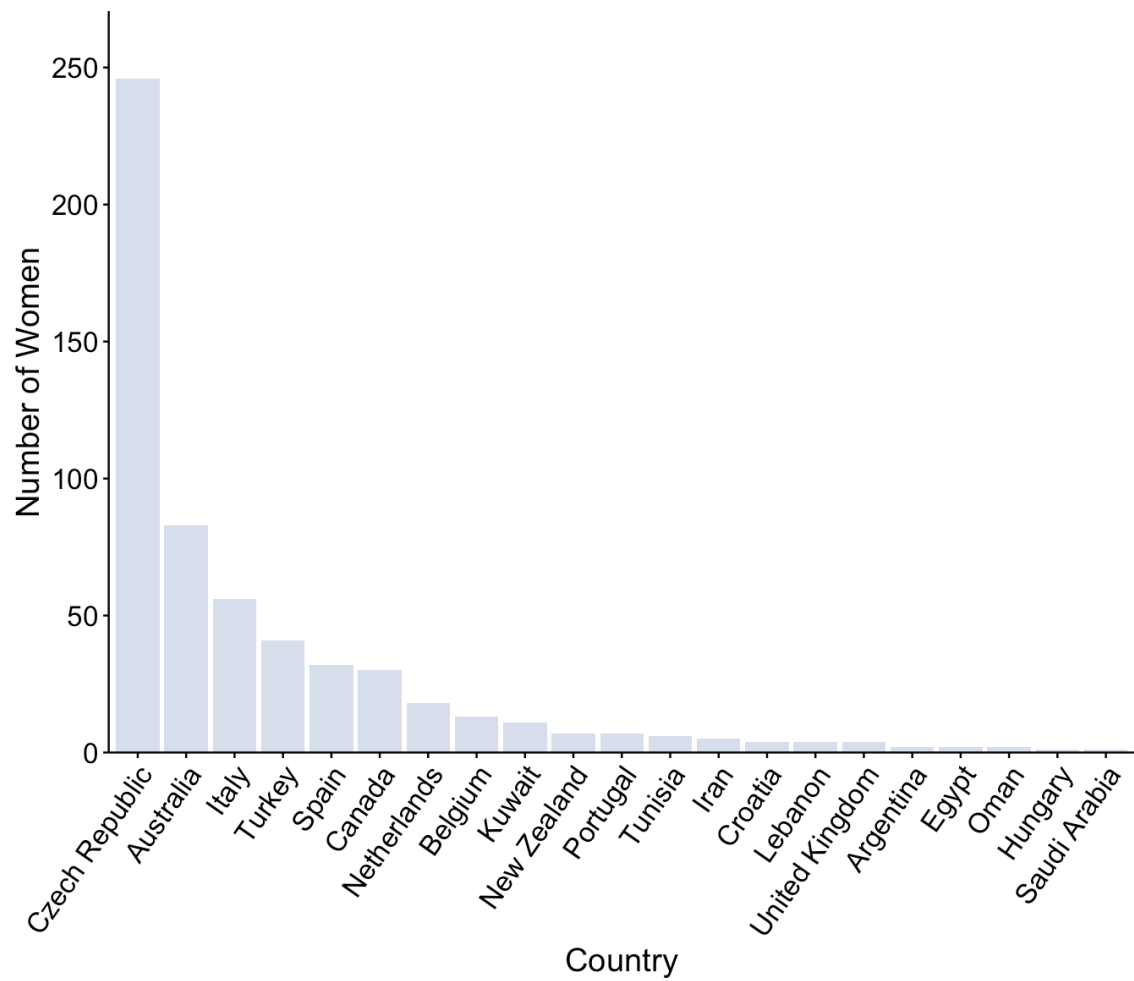
^f Fingolimod (n = 48), ozanimod (n = 1), siponimod (n = 1)

^g Ocrelizumab (n = 29), rituximab (n = 6), ofatumumab (n = 1)

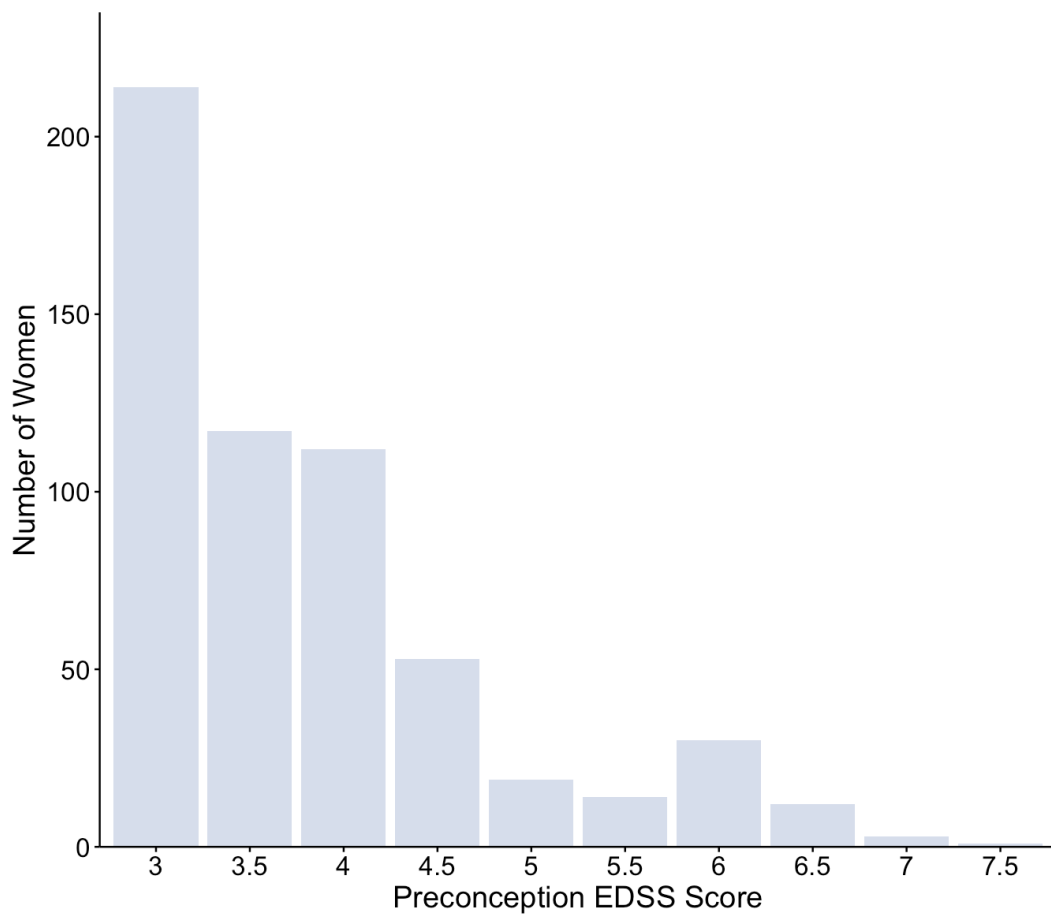
^h Mitoxantrone (n = 2), cyclophosphamide (n = 1), trial (n = 1)

ⁱ For DMT reinitiated within 12 months postpartum. The reinitiation time was set to 0 if a DMT was continued during pregnancy without an interval off treatment, or if it was recommenced prior to the end date of pregnancy

eFigure 2. Countries of Women in the Pregnant Cohort



eFigure 3. Preconception EDSS Scores of Women in the Pregnant Cohort



eTable 2. Washout Periods of Preconception Disease-Modifying Therapies

DMT Type	n (n = 575)	Months Before Pregnancy, median (IQR)
DMTs used in the preconception year	469	-0.99 (-1.77-0.39)
Interferon	141	-1.12 (-1.94-0.00)
Natalizumab	104	-1.07 (-2.78--0.07)
Glatiramer acetate	76	-0.99 (-1.54-0.00)
Fingolimod	46	-0.59 (-1.32-2.19)
Anti-CD20 therapy	40 ^a	0.84 (-0.90-3.43)
Dimethyl fumarate	31	-1.18 (-1.84--0.76)
Alemtuzumab	9	7.00 (1.84-8.94)
Teriflunomide	8	-0.87 (-1.27-2.01)
Cladribine	4	8.80 (6.82-9.17)

Abbreviations: DMT, disease-modifying therapy; IQR, interquartile range.

For the most common DMTs used in the 12 months prior to conception. For individuals who used more than one DMT type in the preconception year, only the DMT commenced closest to conception was included. Positive values indicate withdrawal of the DMT prior to pregnancy, and negative values indicate continuation after conception. In some cases, a DMT may have been withdrawn for pregnancy, but the temporary discontinuation and reinitiation dates may not have been entered in the registry, which may influence the accuracy of the data.

^a Ocrelizumab (n = 33), rituximab (n = 7)

eTable 3. Timing of Reinitiation of Disease-Modifying Therapies After Pregnancy

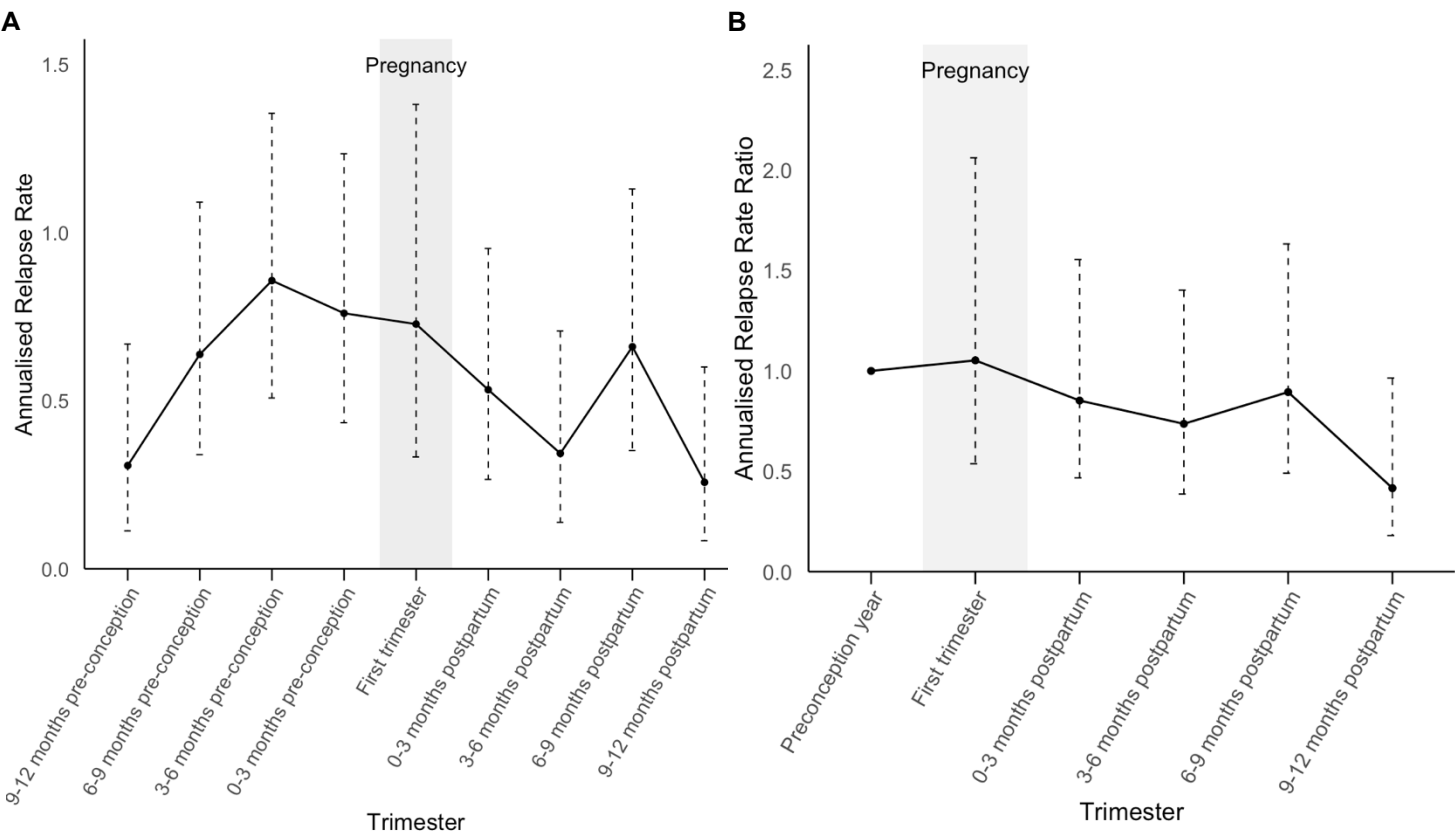
DMT Type	n (n = 575)	Months to Reinitiation, median (IQR)
DMT used in the postpartum year	438	1.46 (0.00-3.90)
Interferon	131	2.43 (0.34-5.17)
Natalizumab	103	0.56 (0.00-1.69)
Glatiramer acetate	62	1.84 (0.01-5.89)
S1P receptor modulator	50 ^a	1.61 (0.11-3.49)
Anti-CD20 therapy	36 ^b	1.46 (0.07-3.60)
Dimethyl fumarate	31	2.17 (0.77-3.12)
Alemtuzumab	9	1.54 (0.85-2.33)
Teriflunomide	8	1.58 (0.39-2.67)
Cladribine	4	7.79 (5.69-8.63)
Mitoxantrone	2	4.01 (2.30-5.72)
Cyclophosphamide	1	7.88 (7.88-7.88)

Abbreviations: DMT, disease-modifying therapy; IQR, interquartile range; S1P, sphingosine-1-phosphate. For the most common DMTs reinitiated within 12 months postpartum. For individuals who used more than one DMT type in the postpartum year, only the first DMT initiated after pregnancy was included. The reinitiation time was set to 0 if a DMT was continued during pregnancy without an interval off treatment, or if it was recommenced prior to the end date of pregnancy.

^a Fingolimod (n = 48), ozanimod (n = 1), siponimod (n = 1)

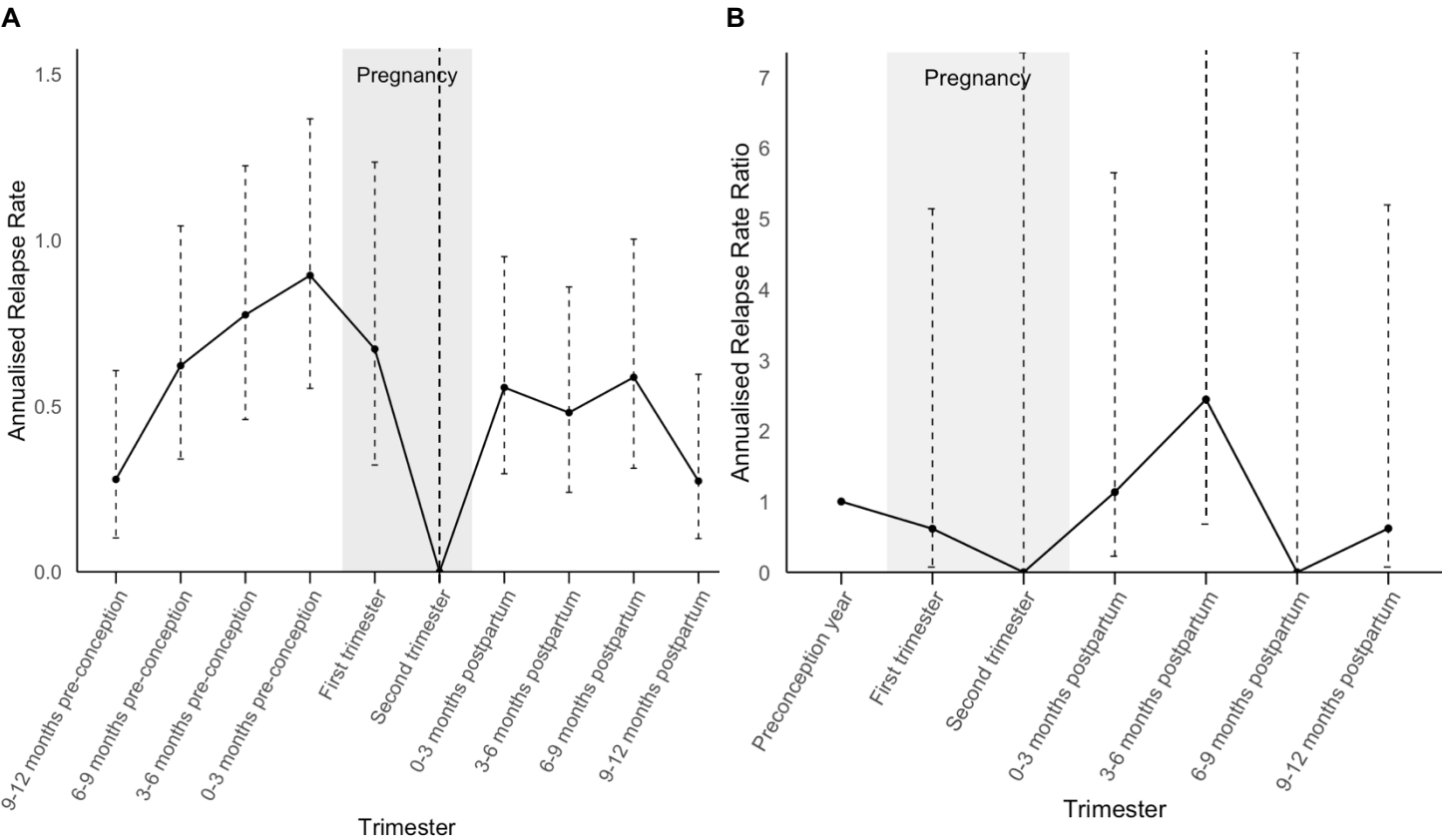
^b Ocrelizumab (n = 29), rituximab (n = 6), ofatumumab (n = 1)

eFigure 4. Annualised Relapse Rates and Rate Ratios for First-Trimester Pregnancy Losses



n = 85 first-trimester pregnancy losses (miscarriage or termination)
A: Absolute peri-pregnancy annualised relapse rates; B: Rate ratios for relapses relative to the preconception year calculated using a mixed-effects Poisson regression model

eFigure 5. Annualised Relapse Rates and Rate Ratios for First-Trimester and Second-Trimester Pregnancy Losses



n = 85 first-trimester pregnancy losses (miscarriage or termination) and n = 11 second-trimester pregnancy losses. There were no reported events during the second trimester.
A: Absolute peri-pregnancy annualised relapse rates; B: Rate ratios for relapses relative to the preconception year calculated using a mixed-effects Poisson regression model

eTable 4. Annualised Relapse Rate Ratios for Live Births by Disease-Modifying Therapy and Treatment Epoch

Category	n	Time Period	Annualised Relapse Rate Ratio (95% CI) ^a	P value
All live births	469	Preconception year	1.00	-
		First trimester	0.25 (0.15-0.43)	<0.001
		Second trimester	0.41 (0.28-0.60)	<0.001
		Third trimester	0.36 (0.23-0.56)	<0.001
		0-3 months postpartum	1.36 (1.06-1.75)	0.01
		3-6 months postpartum	0.79 (0.58-1.08)	0.14
		6-9 months postpartum	1.01 (0.76-1.34)	0.94
		9-12 months postpartum	0.88 (0.65-1.19)	0.39
Live births, excluding rebound disease activity ^b	346	Preconception year	1.00	-
		First trimester	0.20 (0.10-0.40)	<0.001
		Second trimester	0.21 (0.12-0.39)	<0.001
		Third trimester	0.15 (0.07-0.32)	<0.001
		0-3 months postpartum	1.39 (1.05-1.85)	0.02
		3-6 months postpartum	0.86 (0.61-1.22)	0.40
		6-9 months postpartum	0.95 (0.68-1.33)	0.76
		9-12 months postpartum	1.01 (0.73-1.41)	0.94
Most common preconception DMTs				
Interferon	117	Preconception year	1.00	-
		First trimester	0.22 (0.08-0.61)	0.004
		Second trimester	0.29 (0.12-0.66)	0.003
		Third trimester	0.21 (0.08-0.59)	0.003
		0-3 months postpartum	1.57 (1.02-2.40)	0.04
		3-6 months postpartum	1.05 (0.64-1.73)	0.84
		6-9 months postpartum	1.20 (0.74-1.93)	0.46
		9-12 months postpartum	1.33 (0.84-2.11)	0.23
Natalizumab	84	Preconception year	1.00	-
		First trimester	0.10 (0.01-0.71)	0.02
		Second trimester	0.75 (0.37-1.55)	0.44
		Third trimester	0.59 (0.25-1.37)	0.22
		0-3 months postpartum	0.83 (0.40-1.69)	0.60
		3-6 months postpartum	0.55 (0.24-1.30)	0.18
		6-9 months postpartum	0.76 (0.36-1.61)	0.48
		9-12 months postpartum	0.49 (0.19-1.24)	0.13
Glatiramer acetate	63	Preconception year	1.00	-
		First trimester	0.28 (0.07-1.17)	0.08
		Second trimester	0.36 (0.11-1.18)	0.09
		Third trimester	0.00 (0.00-Inf)	0.92
		0-3 months postpartum	1.41 (0.71-2.83)	0.33
		3-6 months postpartum	0.64 (0.25-1.66)	0.36
		6-9 months postpartum	0.90 (0.39-2.05)	0.80
		9-12 months postpartum	1.03 (0.47-2.25)	0.95
Fingolimod	31	Preconception year	1.00	-
		First trimester	0.94 (0.32-2.79)	0.92
		Second trimester	1.01 (0.38-2.73)	0.98
		Third trimester	2.23 (1.03-4.83)	0.04
		0-3 months postpartum	1.74 (0.76-4.00)	0.19
		3-6 months postpartum	1.10 (0.41-2.97)	0.85
		6-9 months postpartum	1.56 (0.65-3.74)	0.32
		9-12 months postpartum	0.23 (0.03-1.72)	0.15
Anti-CD20 therapy	31 ^c	Preconception year	1.00	-
		First trimester	0.00 (0.00-Inf)	1.00
		Second trimester	0.00 (0.00-Inf)	1.00
		Third trimester	0.00 (0.00-Inf)	1.00
		0-3 months postpartum	0.75 (0.15-3.71)	0.72
		3-6 months postpartum	0.42 (0.05-3.73)	0.44

Dimethyl fumarate	27	6-9 months postpartum	0.00 (0.00-Inf)	1.00
		9-12 months postpartum	0.95 (0.19-4.71)	0.95
		Preconception year	1.00	-
		First trimester	0.00 (0.00-Inf)	0.97
		Second trimester	0.07 (0.04-2.77)	0.32
		Third trimester	0.00 (0.00-Inf)	0.98
		0-3 months postpartum	2.30 (0.84-6.34)	0.11
		3-6 months postpartum	0.40 (0.05-3.08)	0.38
		6-9 months postpartum	0.79 (0.17-3.60)	0.76
None	89	9-12 months postpartum	0.79 (0.17-3.60)	0.76
		Preconception year	1.00	-
		First trimester	0.25 (0.08-0.81)	0.02
		Second trimester	0.07 (0.01-0.52)	0.009
		Third trimester	0.16 (0.04-0.65)	0.01
		0-3 months postpartum	1.24 (0.70-2.20)	0.46
		3-6 months postpartum	0.88 (0.45-1.71)	0.71
		6-9 months postpartum	0.97 (0.51-1.84)	0.93
		9-12 months postpartum	0.74 (0.36-1.53)	0.42
Natalizumab strategy				
Natalizumab discontinued preconception	23	Preconception year	1.00	-
		First trimester	0.00 (0.00-Inf)	1.00
		Second trimester	1.24 (0.44-3.52)	0.68
		Third trimester	0.96 (0.27-3.43)	0.95
		0-3 months postpartum	1.07 (0.34-3.32)	0.91
		3-6 months postpartum	0.55 (0.12-2.50)	0.44
		6-9 months postpartum	1.39 (0.49-3.95)	0.53
		9-12 months postpartum	1.15 (0.37-3.59)	0.81
		Natalizumab discontinued during the first or second trimester	42	Preconception year
First trimester	0.23 (0.03-1.70)			0.15
Second trimester	0.78 (0.27-2.29)			0.65
Third trimester	0.43 (0.10-1.85)			0.26
0-3 months postpartum	0.88 (0.30-2.57)			0.81
3-6 months postpartum	0.44 (0.10-1.88)			0.27
6-9 months postpartum	0.66 (0.19-2.22)			0.50
9-12 months postpartum	0.22 (0.03-1.67)			0.14
Natalizumab continued into the third trimester	19			Preconception year
		First trimester	0.00 (0.00-Inf)	1.00
		Second trimester	0.00 (0.00-Inf)	1.00
		Third trimester	0.41 (0.05-3.25)	0.40
		0-3 months postpartum	0.39 (0.05-3.08)	0.37
		3-6 months postpartum	0.25 (0.17-3.59)	0.75
		6-9 months postpartum	0.00 (0.00-Inf)	1.00
		9-12 months postpartum	0.00 (0.00-Inf)	1.00
		Treatment epoch ^d		
Modern epoch	343	Preconception year	1.00	-
		First trimester	0.22 (0.11-0.44)	<0.001
		Second trimester	0.49 (0.31-0.77)	0.002
		Third trimester	0.49 (0.31-0.79)	0.004
		0-3 months postpartum	1.54 (1.14-2.07)	0.005
		3-6 months postpartum	0.82 (0.55-1.20)	0.31
		6-9 months postpartum	0.89 (0.61-1.30)	0.55
		9-12 months postpartum	0.77 (0.52-1.16)	0.21
		Middle epoch	98	Preconception year
First trimester	0.24 (0.09-0.65)			0.005
Second trimester	0.30 (0.13-0.70)			0.005
Third trimester	0.18 (0.06-0.56)			0.003
0-3 months postpartum	1.14 (0.70-1.86)			0.61
3-6 months postpartum	0.87 (0.51-1.51)			0.63
6-9 months postpartum	1.11 (0.67-1.84)			0.68
9-12 months postpartum	1.02 (0.60-1.71)			0.95

Early epoch	28	Preconception year	1.00	-
		First trimester	0.55 (0.16-1.85)	0.33
		Second trimester	0.16 (0.02-1.17)	0.07
		Third trimester	0.00 (0.00-Inf)	0.97
		0-3 months postpartum	0.84 (0.32-2.24)	0.73
		3-6 months postpartum	0.34 (0.08-1.44)	0.14
		6-9 months postpartum	1.35 (0.60-3.05)	0.47
		9-12 months postpartum	1.01 (0.41-2.51)	0.98

Abbreviations: CI, confidence interval; DMT, disease-modifying therapy.

Infinite CIs were generated for certain time intervals due to no recorded events, preventing the model from estimating finite coefficients.

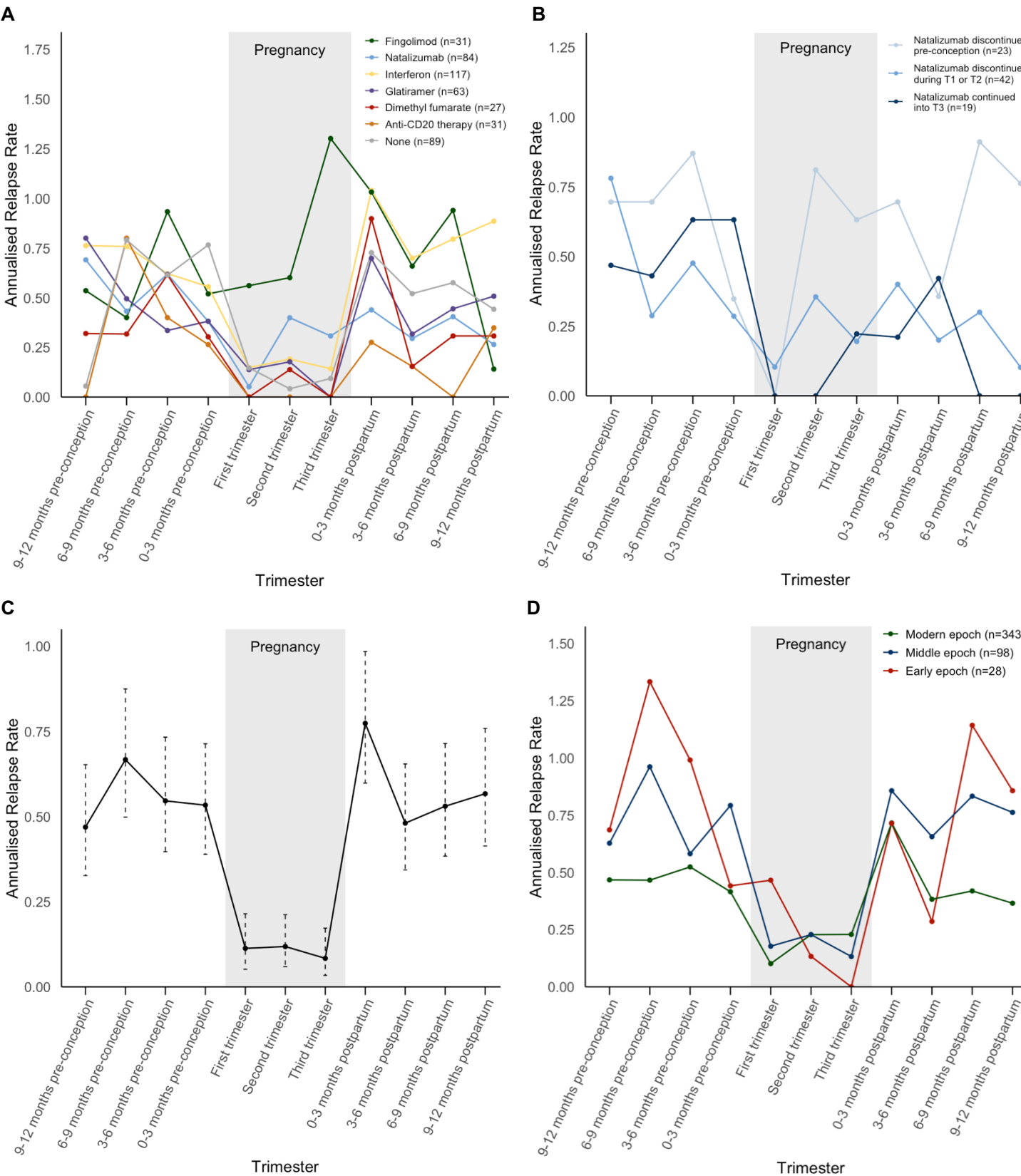
^a Relative to the preconception year

^b Excluding fingolimod use and natalizumab discontinuation prior to the third trimester of pregnancy

^c Ocrelizumab (n = 25), rituximab (n = 6)

^d The early epoch was defined as the period before 2005, the middle epoch as 2005 to 2010, and the modern epoch as the period after 2010

eFigure 6. Annualised Relapse Rates for Live Births by Disease-Modifying Therapy and Treatment Epoch



Abbreviations: T1, first trimester of pregnancy; T2, second trimester of pregnancy; T3, third trimester of pregnancy. A: Peri-pregnancy annualised relapse rates (ARRs) by most common preconception DMTs. Anti-CD20 therapy included ocrelizumab (n = 25) or rituximab (n = 6); B: Peri-pregnancy ARR by natalizumab prescribing strategy; C: Peri-pregnancy ARR for live births, excluding the rebound effect associated with fingolimod use or natalizumab

discontinuation prior to the third trimester (n = 346); D: Peri-pregnancy ARRs by treatment epoch. The early epoch was defined as the period before 2005, the middle epoch as 2005 to 2010, and the modern epoch as the period after 2010

eTable 5. Covariate Balance Between Pregnant and Non-Pregnant Cohorts Before and After 2:1 Propensity Score Matching

Covariate	Type	Unadj. Mean (SD)		Unadj. SMD	Balance Status Pre-Matching ^a	Adj. Mean (SD)		Adj. SMD	Balance Status Post-Matching
		Pregnant (n = 528)	Non-pregnant (n = 5419)			Pregnant (n = 528)	Non-pregnant (n = 1056)		
Distance				0.729	Not balanced			0.004	<i>Balanced</i>
MS phenotype^b	Binary	-	-	0.041	<i>Balanced</i>	-	-	-0.002	<i>Balanced</i>
Age at baseline	Cont	32.38 (4.91)	36.58 (6.24)	-0.748	Not balanced	32.38 (4.91)	32.38 (6.03)	0.002	<i>Balanced</i>
Disease duration at baseline	Cont	8.86 (5.48)	8.72 (6.25)	0.024	<i>Balanced</i>	8.86 (5.48)	9.00 (6.14)	-0.039	<i>Balanced</i>
Baseline EDSS	Cont	3.81 (0.96)	4.19 (1.23)	-0.345	Not balanced	3.81 (0.96)	3.83 (0.99)	-0.021	<i>Balanced</i>
ARR in the pre-baseline year	Cont	0.56 (0.81)	0.76 (1.10)	-0.216	Not balanced	0.56 (0.81)	0.56 (0.85)	-0.008	<i>Balanced</i>
Use of high-efficacy DMT in the pre-baseline year^c	Binary	-	-	0.119	Not balanced	-	-	0.015	<i>Balanced</i>

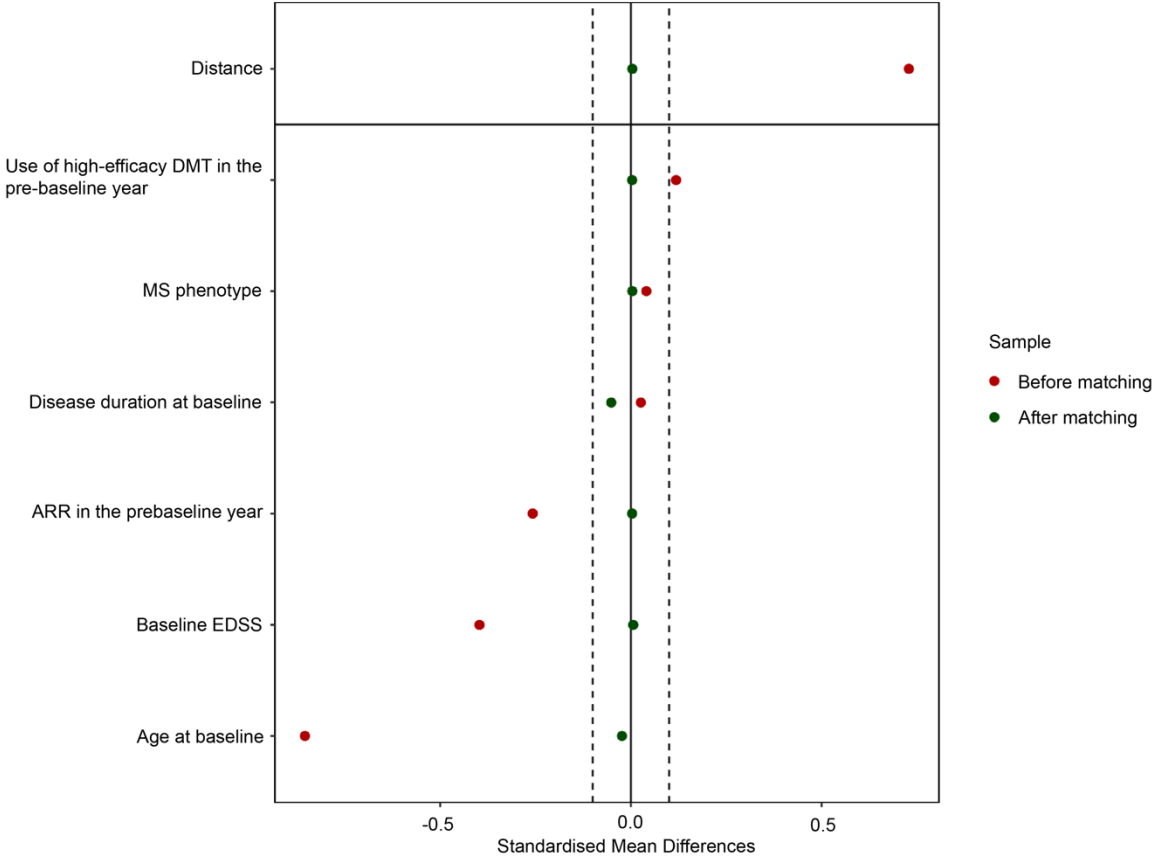
Abbreviations: Adj, adjusted; ARR, annualised relapse rate; cont, continuous; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; SD, standard deviation; SMD, standardized mean difference; unadj, unadjusted.

^a A variable was considered balanced if the absolute SMD was less than 0.1

^b Relapse-onset or progressive-onset

^c High-efficacy DMT was defined as alemtuzumab, anti-CD20 monoclonal antibodies, natalizumab, cladribine, sphingosine-1-phosphate receptor inhibitors, cyclophosphamide, and autologous haematopoietic stem cell transplant

eFigure 7. Covariate Balance Between Pregnant and Non-Pregnant Cohorts Before and After 2:1 Propensity Score Matching



Abbreviations: ARR, annualised relapse rate; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale.
Dashed vertical lines represent the commonly accepted threshold values of ± 0.1 .

eTable 6. Survival Analysis of Time to 6-Month Confirmed Disability Worsening for All Pregnancies

Covariate	Unadj. HR (95% CI 0.67-1.05)	Unadj. P value	Adj. HR (95% CI 0.67-1.05)	Adj. P value
Pregnancy history	1.15 (0.96-1.38)	0.13	1.15 (0.96-1.38)	0.13
High-efficacy DMT exposure (time- varying covariate)	-	-	1.00 (0.90-1.12)	0.98

Abbreviations: Adj, adjusted; CI, confidence interval; DMT, disease-modifying therapy; HR, hazard ratio; unadj, unadjusted.

Comparing women with MS with pregnancies of any duration and meeting other inclusion criteria for the survival analysis (n = 528) and a non-pregnant cohort (n = 1056) matched with 2:1 propensity score matching.

eTable 7. Assessment of Proportional Hazards Assumption Using Schoenfeld Residuals

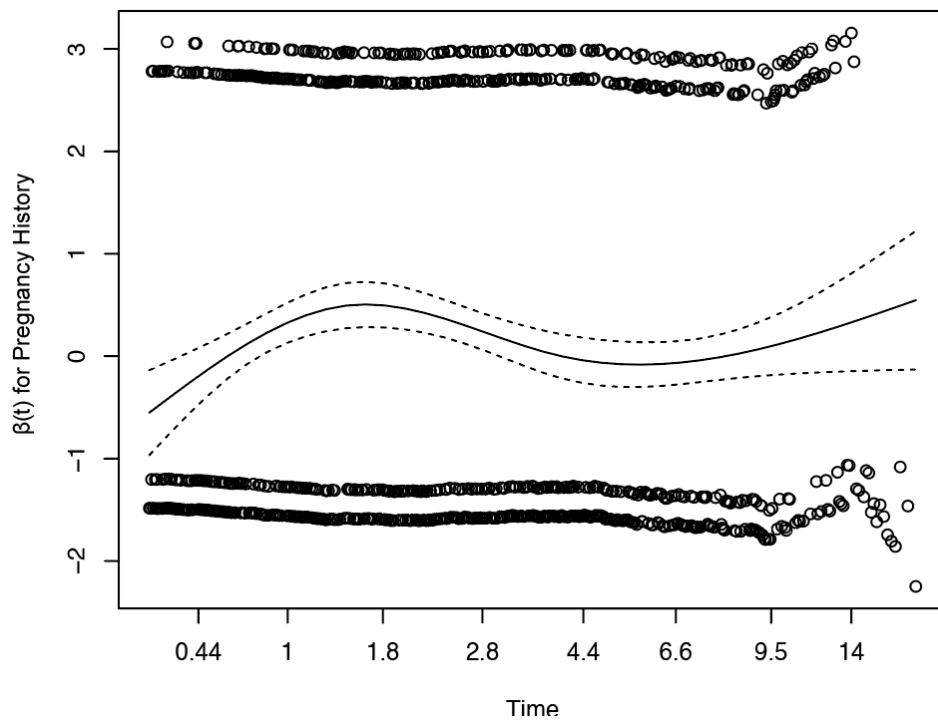
Covariate	Chi-square	Degrees of Freedom	P value
Pregnancy history	0.002	1	0.96
High-efficacy DMT exposure (time-varying covariate)	0.054	1	0.82
Global	0.055	2	0.97

Abbreviations: DMT, disease-modifying therapy.

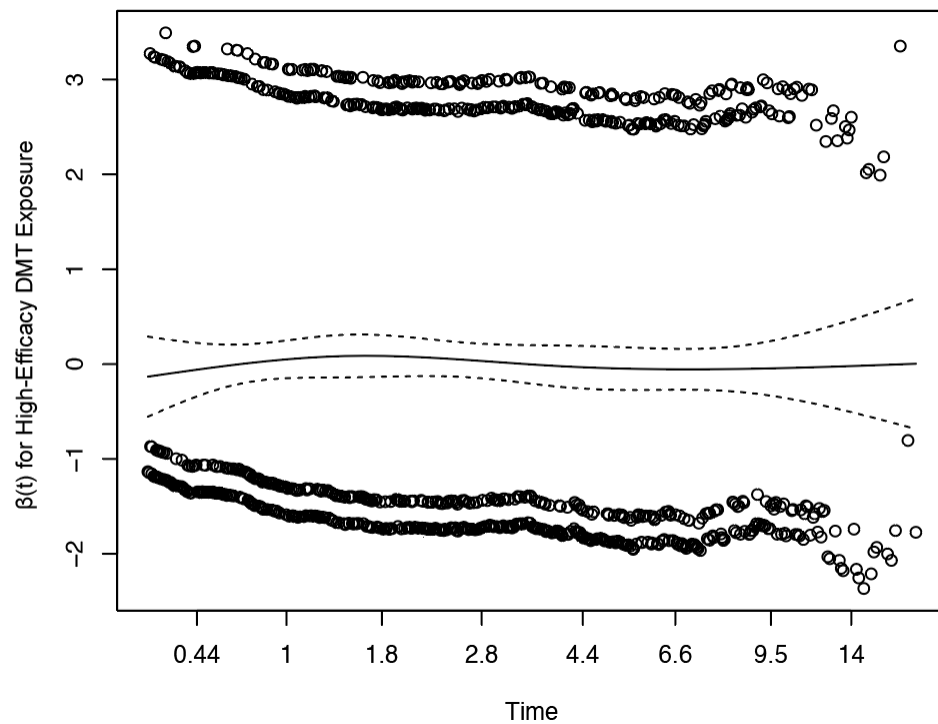
Results of the proportional hazards assumption test using Schoenfeld residuals for the Cox regression model assessing the association between pregnancy history and time to 6-month confirmed disability worsening. A non-significant P value indicates that the proportional hazards assumption is not violated for the corresponding covariate or the overall model.

eFigure 8. Assessment of Proportional Hazards Assumption Using Scaled Schoenfeld Residual Plots

A



B



Abbreviations: DMT, disease-modifying therapy.

A: Scaled Schoenfeld residual plot for pregnancy history; B: Scaled Schoenfeld residual plot for high-efficacy DMT exposure as a time-varying covariate

eTable 8. Predictors of Time to 6-Month Confirmed Disability Worsening for Pregnant Women with Live Births

Variable	n (n = 439)	Unadj. HR (95% CI)	Unadj. P value	Adj. HR (95% CI)	Adj. P value
Age at conception		1.01 (0.98-1.04)	0.46	1.00 (0.96-1.04)	0.89
Disease duration at conception		1.00 (0.98-1.03)	0.88	0.98 (0.94-1.02)	0.32
Preconception EDSS >4	94	1.68 (1.23-2.30)	0.001	0.94 (0.61-1.45)	0.78
ARR in the preconception year		1.18 (1.01-1.39)	0.04	1.20 (0.99-1.47)	0.06
ARR during pregnancy		1.40 (1.15-1.71)	0.001	1.37 (1.13-1.65)	0.001
DMT continuation into pregnancy	219	0.70 (0.53-0.93)	0.01	0.74 (0.53-1.05)	0.09
Monoclonal antibody therapy in the preconception year	116	1.15 (0.83-1.61)	0.40	NA	NA
First postpartum EDSS >4	114	2.49 (1.87-3.32)	<0.001	2.69 (1.80-4.03)	<0.001
ARR in the first 6 months postpartum		1.17 (1.04-1.31)	0.008	1.10 (0.96-1.26)	0.16
Time to DMT reinitiation	344	1.00 (1.00-1.00)	0.86	1.00 (1.00-1.00)	0.93
Monoclonal antibody therapy in the postpartum year	108	1.10 (0.78-1.55)	0.60	NA	NA
Breastfeeding duration	182	0.93 (0.88-0.98)	0.01	0.93 (0.85-1.01)	0.08

Abbreviations: Adj, adjusted; ARR, annualised relapse rate; CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; HR, hazard ratio; unadj, unadjusted.

eTable 9. Predictors of Relapse During Pregnancy for Live Births in the Modern Epoch

Variable	n (n = 343)	Unadj. OR (95% CI)	Unadj. P value	Adj. OR (95% CI)	Adj. P value
Age at conception		0.93 (0.86-1.00)	0.05	0.87 (0.79-0.96)	0.005
Disease duration at conception		1.05 (0.99-1.11)	0.14	1.13 (1.04-1.23)	0.004
Preconception EDSS >4	73	0.98 (0.43-2.25)	0.97	0.87 (0.33-2.09)	0.76
ARR in the preconception year		1.63 (1.08-2.46)	0.02	1.60 (1.00-2.54)	0.05
DMT used within 1 month of conception ^a					
Natalizumab	75	15.34 (1.93-1983.83)	0.005	13.88 (1.69-1807.66)	0.009
Interferon	62	8.17 (0.92-1077.4)	0.06	7.65 (0.82-1017.75)	0.08
Anti-CD20 therapy ^b	27	1.29 (0.01-241.84)	0.90	0.74 (0.00-141.93)	0.88
Dimethyl fumarate	24	4.53 (0.23-673.01)	0.32	8.87 (0.44-1341.29)	0.15
Fingolimod	16	33.96 (3.43-4587.97)	0.001	51.13 (4.73-7070.63)	<0.001
None	94	10.76 (1.35-1392.22)	0.02	4.53 (0.50-603.29)	0.22
Monoclonal antibody therapy in the preconception year	122	1.06 (0.53-2.14)	0.86	NA	NA
Natalizumab exposure relative to conception					
Natalizumab discontinued preconception	20	6.83 (1.20-39.05)	0.03	NA	NA
Natalizumab discontinued during T1 or T2	41	4.22 (0.82-21.67)	0.08	NA	NA
Natalizumab use during T3	19	1.14 (0.10-13.38)	0.92	NA	NA
DMT washout period	88	1.00 (0.99-1.01)	0.31	NA	NA
DMT continuation into pregnancy	190	0.55 (0.28-1.08)	0.08	0.29 (0.11-0.78)	0.01

Abbreviations: Adj, adjusted; ARR, annualised relapse rate; CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; OR, odds ratio; unadj, unadjusted.

Glatiramer acetate was designated as the reference DMT for DMT variables.

^a DMT administration dates within 1 month of conception, or estimated infusion date within 6 months of conception for anti-CD20 therapies

^b Ocrelizumab (n = 21), rituximab (n = 6). Firth's correction was used in both the univariable and multivariable models to generate confidence intervals for anti-CD20 therapies due to complete separation caused by the absence of relapses during pregnancy in this group

eTable 10. Predictors of Relapse Within 3 Months Postpartum for Live Births in the Modern Epoch

Variable	n (n = 343)	Unadj. OR (95% CI)	Unadj. P value	Adj. OR (95% CI)	Adj. P value
Age at conception		0.97 (0.91-1.03)	0.33	0.98 (0.91-1.06)	0.67
Disease duration at conception		0.97 (0.92-1.03)	0.33	0.99 (0.92-1.05)	0.68
Preconception EDSS >4	73	0.84 (0.41-1.72)	0.64	1.02 (0.46-2.23)	0.96
ARR in the preconception year		1.29 (0.89-1.87)	0.18	1.25 (0.83-1.87)	0.29
ARR during pregnancy		1.28 (0.87-1.87)	0.21	1.18 (0.76-1.84)	0.47
DMT continuation into pregnancy	190	0.91 (0.52-1.6)	0.74	0.83 (0.44-1.58)	0.58
Natalizumab exposure relative to conception					
Natalizumab discontinued preconception	20	0.67 (0.16-2.79)	0.58	NA	NA
Natalizumab discontinued during T1 or T2	41	0.3 (0.07-1.19)	0.09	NA	NA
Natalizumab use during T3	19	0.21 (0.03-1.79)	0.15	NA	NA
Pregnancy duration		1.00 (0.98-1.02)	0.85	NA	NA
Breastfeeding	154	1.00 (0.57-1.76)	0.99	0.83 (0.44-1.59)	0.58
DMT reinitiation within 1 month	103	0.45 (0.23-0.89)	0.02	0.43 (0.20-0.91)	0.03
Monoclonal antibody therapy reinitiated within 1 month postpartum	54	0.45 (0.17-1.2)	0.11	NA	NA
Timing of natalizumab reinitiation					
Early natalizumab reinitiation (≤14 days postpartum)	27	0.42 (0.07-2.35)	0.32	NA	NA
Late natalizumab reinitiation (>14 days postpartum)	49	1.17 (0.35-3.88)	0.80	NA	NA

Abbreviations: Adj, adjusted; ARR, annualised relapse rate; CI, confidence interval; DMT, disease-modifying therapy; EDSS, Expanded Disability Status Scale; OR, odds ratio; T1, first trimester of pregnancy; T2, second trimester of pregnancy; T3, third trimester of pregnancy; unadj, unadjusted.
Glatiramer acetate was designated as the reference DMT for DMT variables.

eTable 11. Survival Analysis of Time to 6-Month Confirmed Disability

Worsening for Live Births Only

Covariate	Unadj. HR (95% CI 0.67-1.05)	Unadj. P value	Adj. HR (95% CI 0.67-1.05)	Adj. P value
Pregnancy history	0.88 (0.70-1.10)	0.25	1.10 (0.91-1.33)	0.33
High-efficacy DMT exposure (time- varying covariate)	-	-	0.93 (0.82-1.05)	0.21

Abbreviations: Adj, adjusted; CI, confidence interval; DMT, disease-modifying therapy; HR, hazard ratio; unadj, unadjusted.

Comparing women with MS with live births and meeting other inclusion criteria for the survival analysis (n = 439) and a non-pregnant cohort (n = 878) matched with 2:1 propensity score matching.