Supplemental Online Content

Hellwig K, Tokic M, Thiel S, et al. Multiple sclerosis disease activity and disability following discontinuation of natalizumab for pregnancy. *JAMA Netw Open*. 2022;5(1):e2144750. doi:10.1001/jamanetworkopen.2021.44750

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

eTable 1: GLMM Poisson model for relapses postpartum in 252 pregnancies with known timing of NTZ-restart

	GLMM Poisson: year postpartum		
Coeffcient	*Incidence Rate Ratios*	*CI (95%)*	*P-Value*
Pre-preg.-group	1.46	0.99 – 2.17	.06
1st-Tri-group	1.33	0.95 – 1.87	.10
late NTZ restart	0.76	0.40 – 1.41	.38
early NTZ restart	0.42	0.19 – 0.93	**.032**
year post. Trim. 2	0.60	0.42 – 0.87	**.006**
year post. Trim. 3	0.45	0.30 – 0.67	**<.001**
year post. Trim. 4	0.22	0.13 – 0.37	**<.001**
Relapse in pregnancy	1.43	1.05 – 1.96	**.025**
late NTZ restart * 1st-Tri-group	0.91	0.43 – 1.95	.81
early NTZ restart * 1st-Tri-group	1.40	0.56 – 3.55	.47
Random Effects			
σ^2	1.89		
$\tau_{00\ ID}$	0.00		
N_{ID}	252		
Observations	990		
Marginal R^2 / Conditional R^2	0.169 / NA		

We analyzed an interaction term of NTZ cessation group and timing of the DMT restart, controlled for having had any relapse in pregnancy. No NTZ restart in one year postpartum was chosen as the reference category to display here.

GLMM, generalized linear mixed model; CI, Confidence Interval; LMP, date of last menstrual period; preg., pregnancy; Pre-preg – group, pregnancies, where NTZ was withdrawn prior to the LMP; 1st-Tri-Group, Pregnancies, where NTZ was withdrawn within the first trimester of pregnancy; NTZ, Natalizumab; year post Trim.1-4, quarter of 91.25 days of postpartum year; No NTZ restart, 99 pregnancies where no NTZ was reintroduced during the postpartum year; late NTZ restart, 83 pregnancies, where NTZ was reintroduced later than 4 weeks postpartum; early NTZ restart, 70 pregnancies, where NTZ was reintroduced up to 4 weeks postpartum

eTable 2: Results of the GLMM Poisson model from which the contrasts throughout the results are drawn

	GLMM Poisson: year prior to pregnancy - year postpartum		
Coeffcient	*Incidence Rate Ratios*	*CI (95%)*	*P-Value*
Pre preg. group	0.96	0.35 – 2.61	.93
1stTri-group	1.16	0.49 – 2.76	.74
year pre. Trim. 2	1.10	0.47 – 2.58	.83
year pre. Trim. 3	1.20	0.52 – 2.77	.68
year pre. Trim. 4	1.31	0.57 – 2.99	.52
preg. Trim. 1	1.95	0.90 – 4.23	.09
preg. Trim. 2	1.95	0.93 – 4.08	.08
preg. Trim. 3	1.58	0.69 – 3.60	.28
year post. Trim. 1	2.82	1.37 – 5.80	**.005**
year post. Trim. 2	1.02	0.43 – 2.46	.96
year post. Trim. 3	1.65	0.75 – 3.65	.21
year post. Trim. 4	1.17	0.49 – 2.81	.73
Disease duration (years)	0.99	0.96 – 1.01	.33
Age at LMP (years)	0.98	0.95 – 1.00	.08
GW at entry into registry	1.01	1.00 – 1.01	.12
year pre. Trim. 2 * 1stTri-group	0.91	0.33 – 2.48	.85

year pre. Trim. 3 * 1stTri-group	0.60	0.22 – 1.65	.32
year pre. Trim. 4 * 1stTri-group	0.44	0.16 – 1.23	.12
preg. Trim. 1 * 1stTri-group	0.10	0.03 – 0.34	**<.001**
preg. Trim. 2 * 1stTri-group	0.76	0.32 – 1.81	.53
preg. Trim. 3 * 1stTri-group	0.85	0.32 – 2.25	.75
year post. Trim. 1 * 1stTri-group	0.74	0.32 – 1.74	.5
year post. Trim. 2 * 1stTri-group	1.32	0.48 – 3.61	.59
year post. Trim. 3 * 1stTri-group	0.40	0.15 – 1.07	.07
year post. Trim. 4 * 1stTri-group	0.21	0.06 – 0.74	**.015**
Random Effects			
σ^2	2.09		
$\tau_{00\ ID}$	0.18		
ICC	0.08		
$N_{\ ID}$	271		
Observations	2930		
Marginal R^2 / Conditional R^2	0.159 / 0.226		

We analyzed an interaction term of NTZ cessation group and timeframe, controlled for disease duration at LMP, age at LMP, and gestational week at entry into the cohort.
GLMM, generalized linear mixed model; CI, Confidence Interval; LMP, date of last menstrual period; preg., pregnancy; Pre preg – group, pregnancies, where NTZ was withdrawn prior to the LMP; 1st-Tri Group, Pregnancies, where NTZ was withdrawn within the first trimester of pregnancy; NTZ, Natalizumab; year pre Trim.1-4, quarter of 91.25 days of the year prior to LMP; preg Trim. 1-3, trimester of pregnancy; year post Trim.1-4, quarter of 91.25 days of postpartum year.

eTable 3: Recurrent event analysis using the Andersen-Gill extension of the cox proportional hazards model

	Recurrent Event Analysis: From 100 days prior to NTZ cessation to DOD		
Coeffcient	*Estimates*	*CI (95%)*	*P-Value*
1st-Tri-group	0.68	0.31 – 1.48	.36
Trimester1	1.21	0.73 – 2.02	.40
Trimester2	0.78	0.48 – 1.27	.26
Trimester3	0.87	0.45 – 1.67	.66
Age at LMP (years)	0.96	0.93 – 1.00	**.044**
Disease duration at LMP (years)	1.02	0.98 – 1.05	.33
1st-Tri-group * Trimester1	0.38	0.10 – 1.43	.16
1st-Tri-group * Trimester2	1.14	0.45 – 2.88	.79
1st-Tri-group * Trimester3	1.04	0.37 – 2.96	.94
Observations	1317		
R^2 Nagelkerke	0.018		

T0 was chosen to be 100 days prior to NTZ cessation, censoring occurred at the day of the delivery. We modeled a time-dependent covariate for the pregnancy status (prior to pregnancy, trimester 1-3) and controlled for age at LMP and, disease duration at LMP. An interaction term was included for the NTZ cessation group and the pregnancy status.
CI, Confidence Interval; LMP, date of last menstrual period; Pre preg – group, pregnancies, where NTZ was withdrawn prior to the LMP; 1st Tri-Group, Pregnancies, where NTZ was withdrawn within the first trimester of pregnancy; NTZ, Natalizumab; Trimester 1-3, trimester of pregnancy; DOD, day of delivery.

eTable 4: Survival analysis using the cox proportional hazards model of time to first relapse in pregnancy

	Survival Analysis: t0= LMP, censored at day of delivery		
Coeffcient	*Estimates*	*Conf. Int (95%)*	*P-Value*
1st Trim. group	0.60	0.40 – 0.88	**.009**
Observations	274		
R^2 Nagelkerke	0.024		

T0 was chosen to be the LMP, censoring occurred at the day of delivery.
CI, Confidence Interval; LMP, date of last menstrual period; Pre preg – group, pregnancies, where NTZ was withdrawn prior to the LMP; 1st Tri-Group, Pregnancies, where NTZ was withdrawn within the first trimester of pregnancy; NTZ, Natalizumab

eTable 5: Survival analysis using cox proportional hazards model of time to first relapse from 2nd pregnancy trimester

	Survival Analysis: t0= start of 2nd trimester, censored at day of delivery		
Coeffcient	*Estimates*	*Conf. Int (95%)*	*P-Value*
Time since NTZ cessation (days)	1.00	1.00 – 1.00	.302
Observations	274		
R^2 Nagelkerke	0.005		

T0 was chosen to be the start of the 2nd trimester of pregnancy, censoring occurred at the day of delivery.
CI, Confidence Interval; LMP, date of last menstrual period; Pre preg – group, pregnancies, where NTZ was withdrawn prior to the LMP; 1st Tri-Group, Pregnancies, where NTZ was withdrawn within the first trimester of pregnancy; NTZ, Natalizumab

eTable 6: Demographic and clinical characteristics of women in the prepregnancy and first-trimester group

	All N= 274	**Pre-Preg-group N=85**	**1st-Tri-group N=189**
	n (%)	n (%)	n (%)
Age at LMP (years), mean (SD)	31.25 (4.27)	31.50 (4.28)	31.14 (4.28)
Disease Duration (years), median [IQR]	5.98 [3.90;10.02]	5.97 [3.92;10.15]	5.98 [3.87;10.01]
Any relapse in year prior to pregnancy	96 (35.04)	35 (41.18)	61 (32.28)
MS related Disability at baseline (N=227[a])			
missing	47 (17.15)	28 (32.94)	19 (10.05)
no disability (EDSS 0-2.0)	95/227 (41.85)	25/57 (43.86)	70/170 (41.18)
some disability, (EDSS 2.5-3.5)	109/227 (48.02)	30/57 (52.63)	79/170 (46.47)
some ambulatory impairment, no assist device (EDSS 4.0-5.5)	21/227 (9.25)	2/57 (3.51)	19/170 (11.18)
cane required (EDSS 6.0-6.5)	1/227 (0.44)	0/57 (0.00)	1/170 (0.59)
wheelchair required (EDSS >=7.0)	1/227 (0.44)	0/57 (0.00)	1/170 (0.59)
Total duration NTZ treatment pre-pregnancy (years), median [IQR]	2.63 [1.91;3.90]	2.50 [1.43;3.12]	3.14 [2.09;4.05]
Any relapse under NTZ treatment	44 (16.06)	15 (17.65)	29 (15.34)
Any prior attempt to stop NTZ	14 (5.11)	3 (3.53)	11 (5.82)
Any relapses with prior stopping attempts	8 (2.92)	2 (2.35)	6 (3.17)
Gestational week at enrollment (weeks), median [IQR]	11.71 [7.14;21.14]	11.79 [6.43;21.14]	11.57 [7.57;21.14]

Pre-Preg-group, pregnancies with last NTZ infusion prior to LMP but within 2 years of conception; 1stTri-group, pregnancies with last NTZ infusion within 1st trimester of pregnancy; LMP, last menstrual period; SD, standard deviation; IQR, interquartile range; n, number in group; MS, multiple sclerosis; baseline, within three months prior to conception; EDSS, expanded disability status scale; NTZ, natalizumab; N, denominator.

[a]For all disability related analysis pregnancies with less than 3 EDSS values are counted as missing. Denominator for this subgroup analysis is the number of pregnancies with 3 available EDSS values (N=227).

eTable 7: Disease activity during pregnancy and the postpartum period in the prepregnancy and first-trimester group

	All N= 274	**Pre-Preg. N=85**	**1st Trim. N=189**	***P* overall**
	n (%)	n (%)	n (%)	
Pregnancy				
Any relapse in pregnancy	109 (39.78)	41 (48.24)	68 (35.98)	.07
More than one pregnancy relapse	42 (15.33)	17 (20.00)	25 (13.23)	.21
Any relapse in 1st trimester	24 (8.76)	19 (22.35)	5 (2.65)	<.001
Any relapse in 2nd trimester	75 (27.37)	23 (27.06)	52 (27.51)	>.99
Any relapse in 3rd trimester	44 (16.06)	13 (15.29)	31 (16.40)	.96
Any severe relapse in pregnancy[a]	31 (11.31)	10 (11.76)	21 (11.11)	<.001
Restarted NTZ in pregnancy	5 (1.82)	2 (2.35)	3 (1.59)	.65
Disability during pregnancy (N=227[b])				
Information missing	47 (17.2)	28 (32.9)	19 (10.1)	
Disability progression in pregnancy	40/227 (17.62)	12/57 (21.05)	28/170 (16.47)	<.001
Persistent severe Relapse related disability in pregnancy	31/227 (13.66)	10/57 (17.54)	21/170 (12.35)	<.001
Postpartum period				
Any relapse postpartum	135 (49.27)	45 (52.94)	90 (47.62)	.49
Lost to follow up postpartum[c]				
Up to 1st trimester	4 (1.46)	1 (1.18)	3 (1.59)	
Up to 2nd trimester	6 (2.19)	2 (2.35)	4 (2.12)	
Up to 3rd trimester	13 (4.74)	5 (5.88)	8 (4.23)	
Up to 4th trimester	36 (13.14)	13 (15.29)	23 (12.17)	
Timing of any relapse postpartum[c]				
1st trimester postpartum	86/270 (31.85)	28/84 (33.34)	58/186 (31.18)	.91
2nd trimester postpartum	48/268 (17.91)	10/83 (12.05)	38/185 (20.54)	.24
3rd trimester postpartum	35/261 (13.41)	16/80 (20.00)	19/181 (10.50)	.09
4th trimester postpartum	16/238 (6.72)	10/72 (13.89)	6/166 (3.61)	.016
Any severe relapse postpartum[a]	15 (5.47)	7 (8.24)	8 (4.23)	<.001
Disability postpartum (N=227[b])				
Information missing	47 (17.2)	28 (32.9)	19 (10.1)	
Disability progression postpartum	39/227 (17.18)	14/57 (24.56)	25/170 (14.71)	<.001
Persistent severe Relapse related disability postpartum	29/227 (12.78)	12/57 (21.05)	17/170 (10.00)	<.001

	All N= 274	**Pre-Preg. N=85**	**1st Trim. N=189**	***P* overall**
Breastfeeding (N=260[d])				
Information missing	14 (5.11)	6 (7.06)	8 (4.23)	
Exclusively	81/260 (31.15)	25/79 (31.65)	56/181 (30.94)	.77
No breastfeeding	103/260 (39.62)	32/79 (40.51)	71/181 (39.23)	
Some, but not exclusively	76/260 (29.23)	22/79 (27.85)	54/181 (29.83)	
NTZ restart postpartum (N=252)				
Missing due to LFU before NTZ restart	22 (8.03)	11 (12.94)	11 (5.82)	
no NTZ restart in one year pp	99/252 (39.29)	40/74 (54.05)	59/178 (33.15)	
Resumed NTZ post-partum	153/252 (60.71)	34/74 (45.95)	119/178 (66.85)	.001
> 4 weeks/later	83/153 (54.25)	18/34 (52.94)	65/119 (54.62)	.004
0-4 weeks/early	70/153 (45.75)	16/34 (47.06)	54/119 (45.38)	
Postpartum *weeks of NTZ restart, mean (SD)*	9.37 (12.35)	7.77 (11.39)	9.82 (12.61)	.37

Pre-Preg-group, pregnancies with last NTZ infusion prior to LMP but within 2 years of conception; 1stTri-group, pregnancies with last NTZ infusion within 1st trimester of pregnancy; LMP, last menstrual period; SD, standard deviation; IQR, interquartile range; n, number in group; MS, multiple sclerosis, baseline, within three months prior to conception; EDSS, expanded disability status scale; NTZ, natalizumab; n, number; N, denominator; LFU, lost to follow up

[a]36 pregnancies with relapses in pregnancy or one-year post-partum and missing EDSS value were categorized as “non-severe”. 33 relapses in pregnancy and 43 relapses post-partum could not be rated for severity

[b] For all disability related analysis pregnancies with less than 3 EDSS values are counted as missing. Denominator for this subgroup analysis is the number of pregnancies with 3 available EDSS values (n=227)

[c]36 pregnancies are lost to follow up during the first year postpartum, 4 during the first trimester, 2 during the second trimester, 7 during the third trimester and 23 during the fourth trimester. Denominators for this subgroup analysis is the number of pregnancies with completed follow up per postpartum trimester (first trimester N=270, second trimester N=268, third trimester N=261, fourth trimester N=238)

[d]Breastfeeding: Exclusively, pregnancies followed for at least 8 weeks without introduction of supplemental feedings; No breastfeeding, pregnancies without any breastfed meal after delivery; Breastfeeding: Some, but not exclusively, pregnancies with follow up < 8 weeks or with supplemental feeding during the first 2 months. Denominator for this subgroup analysis is the number of pregnancies with available breastfeeding data (n=260)

eTable 8: Relapse risk and expanded disability status scale change during pregnancy and past-partum

		All	Joined later in pregnancy	Joined in 1st trimester	*P* value
		N=274	***N=129***	***N=145***	
		n (%)	***n (%)***	***n (%)***	
	Pregnancies with SRDCS at 3rd trimester	31 (11.31)	20 (15.50)	11 (7.59)	.07
SRDCS[a] at 3rd trimester, one year pp and newly at one year pp, n (%)	Pregnancies with SRDCS at one year pp	29 (10.58)	18 (13.95)	11 (7.59)	.16
	Pregnancies newly with SRDCS at one year pp	13 (4.74)	6 (4.65)	7 (4.83)	>.99
Median (IQR) EDSS at 3rd trimester and one year pp	EDSS 3rd trimester, median (IQR)	2.00 [1.00;3.50]	3.00 [1.00;4.00]	2.00 [1.00;3.00]	.13
	EDSS at one year pp, median (IQR)	2.00 [1.00;3.50]	3.00 [1.00;3.50]	2.00 [1.00;3.00]	.13
Median (IQR) change EDSS at 3rd trimester and one year pp	Delta EDSS between baseline and 3rd trimester, median (IQR)	0.00 [0.00;0.00]	0.00 [0.00;0.50]	0.00 [0.00;0.00]	.09
	Delta EDSS between baseline and one year pp, median (IQR)	0.00 [0.00;0.50]	0.00 [0.00;0.50]	0.00 [0.00;0.38]	.04
	missing	47 (17.15)	23 (17.83)	24 (16.55)	
Significant clinical worsening (N=227[b]) at 3rd trimester and one year pp, n (%)	Pregnancies with significant clinical worsening at 3rd trimester	26/227 (11.45)	16/106 (15.09)	10/121 (8.26)	.21
	Pregnancies with significant clinical worsening at one year pp	23/227 (10.13)	15/106 (14.15)	8/121 (6.61)	.13
	missing	47 (17.15)	23 (17.83)	24 (16.55)	
Categorical EDSS (N=227[b]) at 3rd trimester and one year pp, n (%)	Pregnancies with EDSS >= 2 at 3rd trimester	145/227 (63.88)	70/106 (66.04)	75/121 (61.98)	.60
	Pregnancies with EDSS >= 2 at one year pp	147/227 (64.76)	72/106 (67.92)	75/121 (61.98)	.45
	Pregnancies with EDSS >= 3 at 3rd trimester	96/227 (42.29)	54/106 (50.94)	42/121 (34.71)	.03
	Pregnancies with EDSS >= 3 at one year pp	95/227 (41.85)	53/106 (50.00)	42/121 (34.71)	.04
	Pregnancies with EDSS >= 4 at 3rd trimester	45/227 (19.82)	27/106 (25.47)	18/121 (14.88)	.1
	Pregnancies with EDSS >= 4 at one year pp	41/227 (18.10)	22/106 (20.75)	19/121 (15.70)	.48

		All	Joined later in pregnancy	Joined in 1st trimester	*P* value
		N=274	***N=129***	***N=145***	
		n (%)	***n (%)***	***n (%)***	
	Pregnancies with EDSS >= 8 at 3rd trimester	2/227 (0.88)	1/106 (0.94)	1/121 (0.83)	.82
	Pregnancies with EDSS >= 8 at one year pp	2/227 (0.88)	2/106 (1.89)	0/121 (0.00)	.28
	missing	47 (17.15)	23 (17.83)	24 (16.55)	
Categorical EDSS change (N=227[b]) at 3rd trimester and one year pp, n (%)	Pregnancies with delta EDSS >= 2 points between baseline and 3rd trimester	25/227 (11.01)	16/106 (15.09)	9/121 (7.44)	.14
	Pregnancies with delta EDSS >= 2 points between baseline and one year pp	23/227 (10.13)	15/106 (14.15)	8/121 (6.61)	.13
	Pregnancies with delta EDSS >= 3 points between baseline and 3rd trimester	11/227 (4.85)	9/106 (8.49)	2/121 (1.65)	.04
	Pregnancies with delta EDSS >= 3 points between baseline and one year pp	5/227 (2.20)	4/106 (3.77)	1/121 (0.83)	.26
	Pregnancies with delta EDSS >= 4 points between baseline and 3rd trimester	3/227 (1.32)	3/106 (2.83)	0/121 (0.00)	.15
	Pregnancies with delta EDSS >= 4 points between baseline one year pp	3/227 (1.32)	2/106 (1.89)	1/121 (0.83)	.64
	missing	47 (17.15)	23 (17.83)	24 (16.55)	
Disability progression (N=227[b]) at 3rd trimester and one year pp, n (%)	Pregnancies with disability progression at 3rd trimester	40/227 (17.62)	23/106 (21.70)	17/121 (14.05)	.24
	Pregnancies with disability progression at one year pp	39/227 (17.18)	24/106 (22.64)	15/121 (12.40)	.09
	missing	47 (17.15)	23 (17.83)	24 (16.55)	
Newly reaching EDSS (N=227[b]) Milestones at 3rd trimester and one year pp, n (%)	Pregnancies with new walking limitation (EDSS >= 4) at 3rd trimester	22/227 (9.69)	15/106 (14.15)	7/121 (5.79)	.08
	Pregnancies with new walking limitation (EDSS >= 4) at one year pp	9/227 (3.96)	3/106 (2.83)	6/121 (4.96)	.62
	Pregnancies newly requiring walking aid (EDSS >= 6 during) at 3rd trimester	7/227 (3.08)	5/106 (4.72)	2/121 (1.65)	.33
		All	**Joined later in pregnancy**	**Joined in 1st trimester**	***P* value**

		N=274	***N=129***	***N=145***	
		n (%)	***n (%)***	***n (%)***	
	Pregnancies newly requiring walking aid (EDSS >= 6) at one year pp	2/227 (0.88)	1/106 (0.94)	1/121 (0.83)	.82
	Pregnancies newly bedbound (EDSS >= 8) at 3rd trimester	2/227 (0.88)	1/106 (0.94)	1/121 (0.83)	.82
	Pregnancies newly bedbound (EDSS >= 8) at one year pp	1/227 (0.44)	1/106 (0.94)	0/121 (0.00)	.52
Relapses in pregnancy and pp year	Pregnancies with at least one relapse during pregnancy	109 (39.78)	59 (45.74)	50 (34.48)	.08
	Pregnancies with at least one relapse during 1st trimester	24 (8.76)	9 (6.98)	15 (10.34)	.44
	Pregnancies with at least one relapse during 2nd trimester	75 (27.37)	43 (33.33)	32 (22.07)	.05
	Pregnancies with at least one relapse during 3rd trimester	44 (16.06)	24 (18.60)	20 (13.79)	.36
	Number relapses during pregnancy, median (IQR)	0.00 [0.00;1.00]	0.00 [0.00;1.00]	0.00 [0.00;1.00]	.06
	Number relapses during 1st Trim, median (IQR)	0.00 [0.00;0.00]	0.00 [0.00;0.00]	0.00 [0.00;0.00]	.36
	Number relapses during 2nd Trim, median (IQR)	0.00 [0.00;1.00]	0.00 [0.00;1.00]	0.00 [0.00;0.00]	.03
	Number relapses during 3rd Trim, median (IQR)	0.00 [0.00;0.00]	0.00 [0.00;0.00]	0.00 [0.00;0.00]	.27
	Lost to follow up postpartum[c]				
	Up to 2nd trimester	6 (2.19)	5 (3.88)	1 (0.69)	
	Up to 4th trimester	36 (13.14)	15 (11.63)	21 (14.48)	
	Pregnancies with at least one relapse during first 6 months pp (N=268[c])	115/268 (42.91)	62/124 (50.00)	53/144 (36.81)	.13
	Pregnancies with at least one relapse during first 12 months pp (N=238[c])	135/238 (56.72)	68/114 (59.65)	67/124 (54.03)	.34

Stratified in pregnancies that joined in 1st trimester (median gestation week of enrollment (IQR): 7.3 (1.9 - 11.9)) and in pregnancies that joined later in pregnancy (median gestation week of enrollment (IQR): 21.9 (12.0 – 37.9)). All *P*-values from univariate comparisons. N, denominator; n, number in group; SRDCS, Severe Relapse Disability Composite Score; pp, post-partum; EDSS, Expanded Disability Status Scale; baseline, 3 months prior to conception; IQR, interquartile range; Trim, trimester

[a]36 pregnancies with relapses in pregnancy or one-year postpartum and missing EDSS value were categorized as “non-severe”. 33 relapses in pregnancy and 43 relapses postpartum could not be rated for severity.

[b]For all disability related analysis pregnancies with less than 3 EDSS values are counted as missing. Denominator for this subgroup analysis is the number of pregnancies with 3 available EDSS values (N=227).

[c]36 pregnancies are lost to follow up during the first year postpartum, 4 during the first trimester, 2 during the second trimester, 7 during the third trimester and 23 during the fourth trimester. Denominators for this subgroup analysis is the number of pregnancies with completed follow up per postpartum trimester (first trimester N=270, second trimester N=268, third trimester N=261, fourth trimester N=238)

eTable 9: Clinical characteristics of women with EDSS increase ≥3 or absolute EDSS ≥7.5 during pregnancy or the postpartum year

	BASELINE				DURING PREGNANCY					POSTPARTUM						
No	**Joined in 1st trimester**	**Disease duration, years**	**NTZ exposure duration, days**	**Baseline EDSS**	**No rel in preg**	**Time to first rel after last NTZ, months**	**Worst EDSS and relapse treatment**	**EDSS 3rd trimester**	**Delta EDSS between baseline and 3rd trimester**	**BF**	**DMT resumption**	**Time to pp DMT start, months**	**No rel up to 12 months pp**	**Time to first rel pp after last NTZ, days**	**EDSS at one year pp**	**Delta EDSS between baseline and one year pp**
1	yes	13.65	-16	1	2	5.27 7.47	EDSS unk 3.000 mg CS i.v.	6.5	5.5	no	NTZ	0	1	2	1	0
2	no	7.29	17	0	3	3.67 6.54 7.54	EDSS 5.5 20.000 mg CS i.v. 7xIVIG	5.5	5.5	yes	NTZ	0.70	1	271	1	1
3	no	3.25	14	0	2	4.57 7.64	EDSS 5.5 10.000 mg CS i.v.	5.5	5.5	no	NTZ	0.54	0		0	0
4	no	1.95	31	4	2	3.07 4.20	EDSS 9.5 10.000 mg CS i.v. 3xPLEX NTZ 300 mg 3x10g IVIG mechanical ventilation	8.5	4.5	no	NTZ	0.64	0		9	5
5	no	13.01	-75	3.5	2	3.00 5.04	EDSS 8.5 13.000 mg CS i.v. 2x40 mg CS i.th. 5xPLEX 4xIA 5x300 mg NTZ	7.5	4	no	NTZ	0.17	0		6	2.5

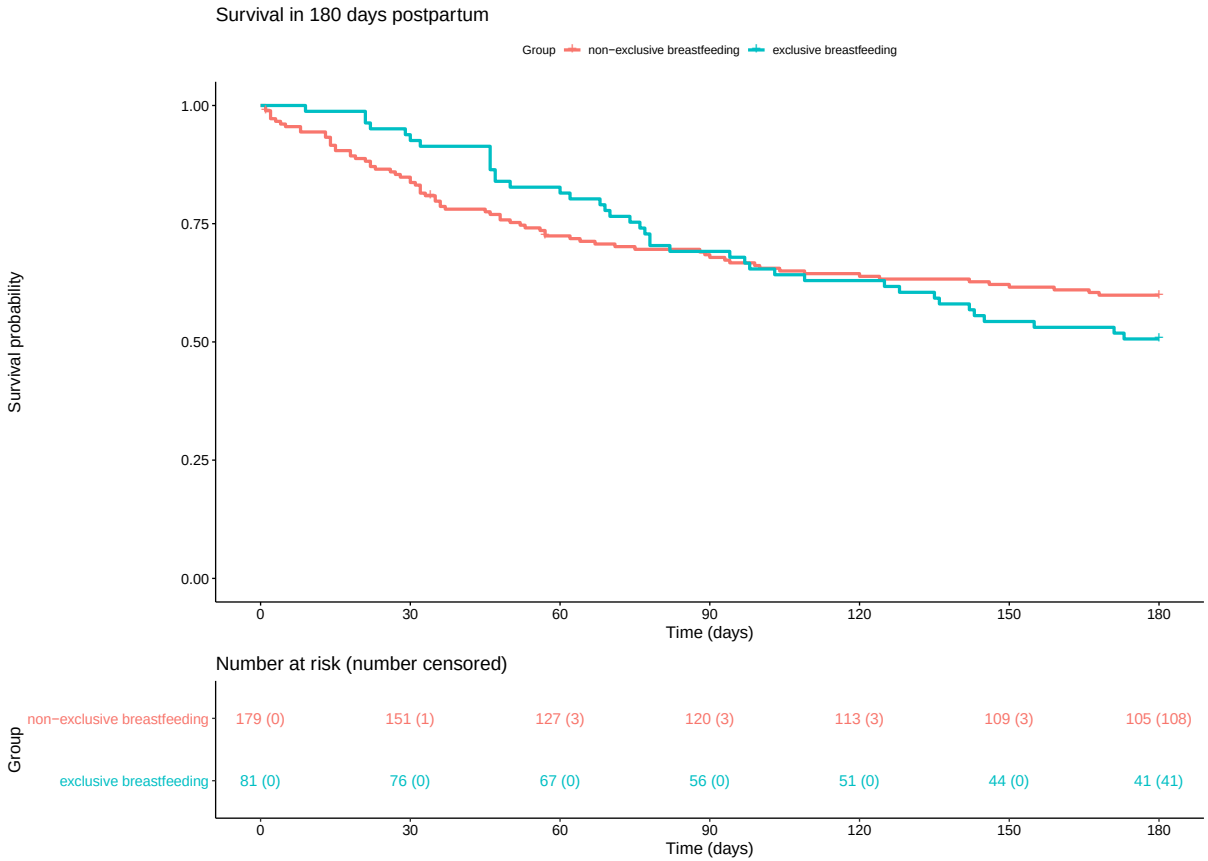
	BASELINE				**DURING PREGNANCY**					**POSTPARTUM**						
No	**Joined in 1st trimester**	**Disease duration, years**	**NTZ exposure duration, days**	**Baseline EDSS**	**No rel in preg**	**Time to first rel after last NTZ, months**	**Worst EDSS and relapse treatment**	**EDSS 3rd trimester**	**Delta EDSS between baseline and 3rd trimester**	**BF**	**DMT resumption**	**Time to pp DMT start, months**	**No rel up to 12 months pp**	**Time to first rel pp after last NTZ, days**	**EDSS at one year pp**	**Delta EDSS between baseline and one year pp**
6	no	6.88	16	2	3	5 6.17 7.17	EDSS 6 8.000 mg CS i.v. 4x25g IVIG 2x60 mg CS i.th.	6	4	no	NTZ	0.24	1	13	4	2
7	no	11.94	23	3	3	3.57 5.6 6.64	EDSS unk 13.000 mg CS i.v.	6.5	3.5	no	NTZ	0.24	1	118	6.5	3.5
8	no	3.56	21	2	3	3.07 5.10 6.80	EDSS 5.5 9.000 mg CS i.v. 5xIA/PLEX	5.5	3.5	no	unk	unk	minimum 3	unk	9.5/8	7.5
9	no	3.43	-295	1.5	4	12.17 14.20	EDSS 5.5 500 mg CS	5	3.5	no	DAC	5.24	1	748	3	1.5
10	yes	4.45	19	1	1	4.54	EDSS unk 3.000 mg CS i.v.	4	3	yes	NTZ	5.04	2	351	1	0
11	no	7.05	17	1	2	3.47 4.5	EDSS unk 8.000 mb CS i.v. 2x300mg NTZ	4	3	no	NTZ	0.27	2	265	1	0
12	yes	2.61	7	2	2	1.50 5.40	EDSS 7.0 8.000 mg CS 5xIA	4.5	2.5	no	NTZ	7.40	2	304	6.5	4.5
	BASELINE				**DURING PREGNANCY**					**POSTPARTUM**						

No	Joined in 1st trimester	Disease duration, years	NTZ exposure duration, days	Baseline EDSS	No rel in preg	Time to first rel after last NTZ, months	Worst EDSS and relapse treatment	EDSS 3rd trimester	Delta EDSS between baseline and 3rd trimester	BF	DMT resumption	Time to pp DMT start, months	No rel up to 12 months pp	Time to first rel pp after last NTZ, days	EDSS at one year pp	Delta EDSS between baseline and one year pp
13	yes	12.76	47	7.5	1	2.74	EDSS 9.5 10.000 mg CS i.v. 3x30 g IVIG 300 mg NTZ	8.5	2	no	NTZ	0.74	0		7.5	0
14	no	16.26	7	1	0			1	0	yes	NTZ	2.80	1	341	4	3

*Worst EDSS during relapse postpartum 9.5 recovered to 8 at the end of the postpartum year.

No, Number; NTZ, natalizumab; baseline, up to 3 months prior to conception; EDSS, expanded disability status scale; rel, relapse; preg, pregnancy; BF, breastfeeding; DMT, disease modifying therapy; pp, postpartum; unk, unkown; mg, milligrams; CS, corticosteroids; i.v., intravenous; IVIG, intravenous immunoglobulins; PLEX, plasma exchange; g, grams; i.th., intrathecal; IA, immunoadsorption; DAC, daclizumab.

eFigure: Time to first relapse postpartum split by breastfeeding behavior



The turquoise curve depicts the survival probability of the exclusive breastfeeding group in the first 180 days postpartum, the red curve the survival probability of the non-exclusive breastfeeding group. The light-colored contours indicate the respective confidence intervals. The red and turquoise numbers depict the number of cases at risk of suffering from a relapse in the respective group at the given timepoints. t_0, date of delivery; exclusive breastfeeding, exclusive breastfeeding for at least 8 weeks after delivery with no supplemental feeding; non-exclusive breastfeeding, not breastfeeding or breastfeeding plus formula meals or early reintroduction of disease modifying therapies