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CONy & Teva Neuroscience MS Matters live webinar series

MS Matters: Managing patients through their pregnancy journey

Thank you for joining. The webinar will begin shortly

This webinar is organised and funded by Teva Pharmaceuticals Europe B.V.
Date of Preparation: April 2019 | **HQ/MS/19/0003a**

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Welcome and Introduction

Prof. Sven Schippling

Faculty

Prof. Sven Schippling, Moderator

Deputy Head of the Department of Neuroimmunology and Clinical Multiple Sclerosis Research (nims) at the University Hospital Zürich, Switzerland

Dr Kerstin Hellwig, Co-presenter

Senior Consultant, Department of Neurology, St. Josef-Hospital/Ruhr University, Bochum, Germany

Agenda

Time (CEST)	Title	Speaker
17:00–17:05	**Welcome and introduction**	Sven Schippling
17:05–17:10	**Family planning with MS**	Sven Schippling
17:10–17:20	**Pre-pregnancy: Starting out on the family planning path**	Kerstin Hellwig
17:20–17:25	**Ask the audience**	All
17:25–17:35	**Pregnancy: The continuing journey**	Sven Schippling
17:35–17:40	**Ask the audience**	All
17:40–17:50	**Post-pregnancy: Looking to the future**	Kerstin Hellwig
17:50–17:55	**Ask the audience**	All
17:55–18:00	**Closing remarks**	Sven Schippling

Family planning with MS

Prof. Sven Schippling

Conflicts of interest

- Sven Schippling is supported by the Swiss National Science Foundation (SNF), the Swiss Multiple Sclerosis Society, the Betty and David Koetser Foundation for Brain Research and the Myelin Repair Foundation (USA)
- He is the Co-Director of the Clinical Research Priority Program for Multiple Sclerosis ($CRPP^{MS}$) supported by the University of Zurich, Switzerland
- He is a member of the International Clinical Consortium of the Guthy Jacksson NMO Charitable Foundation, California, USA
- He sits on the Steering committees of the OCTIMS, PASSOS, BENEFIT, REFINE, EMPIRE, ENSEMBLE and CLARIFY-MS trials, the MS in the 21st Century and the ParadigMS initiatives
- He is a founding member of the Neuromyelitis Optica Study Group (NEMOS), Germany, and the Drug Development Network (DDNZ), Zurich, Switzerland
- He received travel support as well as speaker´s fees from Actelion, Almirall, Bayer Healthcare, Biogen, Sanofi/Genzyme, Merck, Novartis, Roche, Santen, Teva

Why are we here?

- MS is a disease of young women[1]
- MS is increasingly diagnosed in women[1]
- More women with MS are getting pregnant[2]

1. Coyle P. Ther Adv Neurol Disord 2016; 9(3):198-210; 2. Houtchens et al. Neurology 2018;91(17):e1559–e69

Pre-pregnancy: Starting out on the family planning approach

Dr Kerstin Hellwig

Disclosures of interest

- Kerstin Hellwig
  - Research support and speaker honoraria from:
    - Almirall
    - Bayer Healthcare
    - Biogen Idec
    - Genzyme-Sanofi
    - Merck-Serono
    - Novartis
    - Teva

What do you need to consider pre-pregnancy?

Genetic risk

Fertility and foetal development

Basic counselling

Pre-pregnancy

Contraception choice

Impact of pregnancy on MS prognosis

DMT use/washout periods

ART

ART=assisted reproductive techniques; DMT=disease modifying therapy

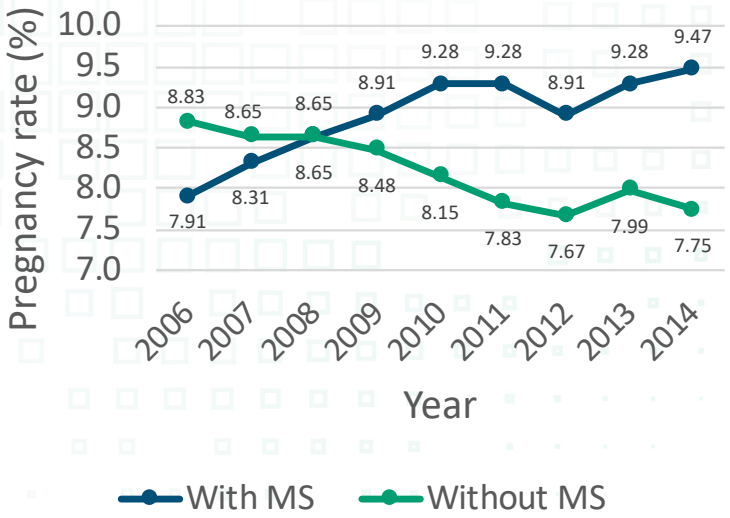
Coyle P. Ther Adv Neurol Disord 2016;9:198–210.

Getting pregnant: Women with MS

- In general, MS does not seem to have a significant impact on the ability to conceive[1]
- Scarce data on time to pregnancy in patients with MS, but:
  - Diminished sexual activity by 40%–80% vs the general population[2,3]
  - In US, maternal age of MS patients tend to be higher vs controls: ~32.5 vs 29.3 years[4]
  - Swiss survey: often >6 months between stopping DMD therapy and conception[5]
  - Calgary MS database: mean of 4 years to initiate DMT after deferring DMT for family planning[6]

Pregnancy rates among women with MS are rising[4]

Adjusted proportion of women with and without MS and with a pregnancy, by year (data from US)[4]

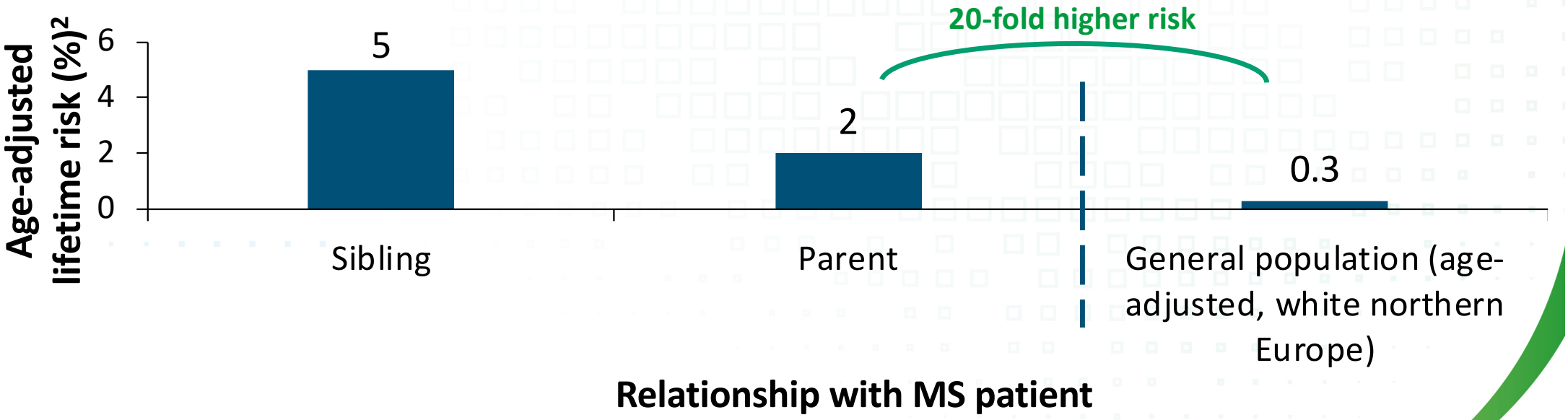


DMD=disease modifying drug

1. Coyle P, Ther Adv Neurol Disord 2016;9(3):198-210; 2. Demirkiran et al . Mult Scler. 2006;12:209-214; 3. Miller AE. Mult Scler. 2016;22:715-716; 4. Houtchens et al. Neurology 2018;91(17):e1559–e69. 5. Kamm et al, Front Neurol 2018;9 821. 6. Makkawi S et al. ePoster presented at ECTRIMS-ACTRIMS, Paris, France, October 2017; EP1355.

Heritability of MS is considered to be relatively low

- MS is not an inheritable disease, but the genetic make-up contributes to the life-long risk of MS[1]
- Children with 1 MS parent have a 2% risk to develop MS themselves[1,2]



1. Vukusic S, et al. Nat Rev Neurol 2015;11:280-9; 2. Compston A, et al. Lancet 2008;372:1502-17

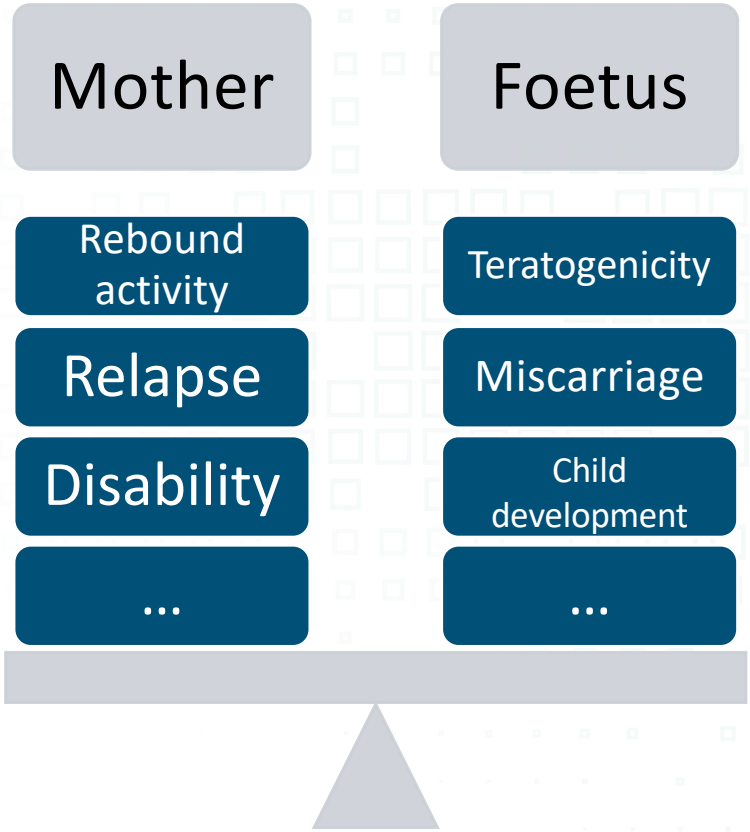
Relapses before and during pregnancy predict the risk of postpartum relapses

- Two-year postpartum follow up of PRIMS study
  - Women with greater disease activity in the year before pregnancy and during pregnancy have higher risk of relapse in postpartum 3 months
  - Indicators of the occurrence of ≥1 postpartum relapse in 1st 3 months:

	Odds ratio (95% CI)	p
# relapses in pre-pregnancy year	1.94 (1.35–2.80)	<0.0001
# relapses during pregnancy	1.87 (1.12–3.13)	0.02
MS duration (years)	1.11 (1.03–1.20)	0.01

Vukusic S, et al. Brain 2004;127:1353-60

Pregnancy and MS treatment



Coyle P. Ther Adv Neurol Disord 2016;9:198–210.

When to stop DMTs in women with MS wishing to conceive

MS neurologists were almost equally divided on when to stop DMTs for a woman wishing to conceive:

49% said stop DMTs after conception

50% said stop DMTs immediately

Fernandez O, et al. Eur Journ Neurol. 2018;25:739–46.

General recommendations to address the topic

1. Ask early/preferentially with first diagnosis if family planning is an issue
2. Discuss treatment approaches in case of short- or medium-term family planning
3. No interaction with hormonal contraception for current DMTs
4. Counsel about a low genetic risk (3–5%) if one parent has MS
5. Counsel that the risk of complication in pregnancy is not increased by MS
6. **Most important recommendation**: Try to counsel your patients 6–12 months prior to planned conception to allow for the best short-term medication approach
7. Recommend taking folic acid before pregnancy

Neurologists should continuously talk to and counsel their patients

Personal communication of the speaker

Pregnancy: The continuing journey

Prof. Sven Schippling

What do you need to consider during pregnancy?

Evaluation and treatment of relapses and disease symptoms

DMT use

Pregnancy

Disease activity

Delivery and anaesthesia choices

DMT=disease modifying therapy

Coyle et al. Ther Adv Neurol Disord 2016;9:198–210.

Pregnancy is not harmful, it might have a protective effect

- Retrospective, 2-centre study in 445 MS patients (184 parous*, 261 nulliparous)
- Longer time to reach EDSS 4 and 6 in parous vs nulliparous patients:

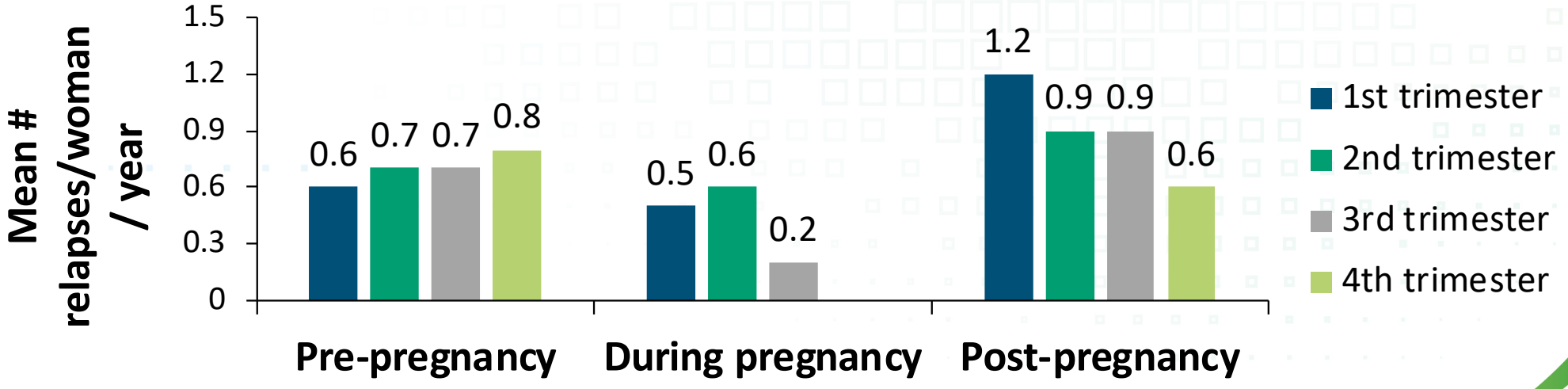
Disability milestone	Parous (N=184)	Nulliparous (N=261)	p
EDSS 4 • Median time to reach EDSS 4 (years) • HR (vs nulliparous)	 13 0.552	 9 Ref	 <0.001 0.008
EDSS 6 • Median time to reach EDSS 6 (years) • HR (vs nulliparous)	 15 0.422	 12 Ref	 0.02 0.012

EDSS=Expanded Disability Status Scale. *Those with pregnancies after MS onset

Masera S, et al. Mult Scler 2015;21:1291-7

Reduced disease activity during pregnancy

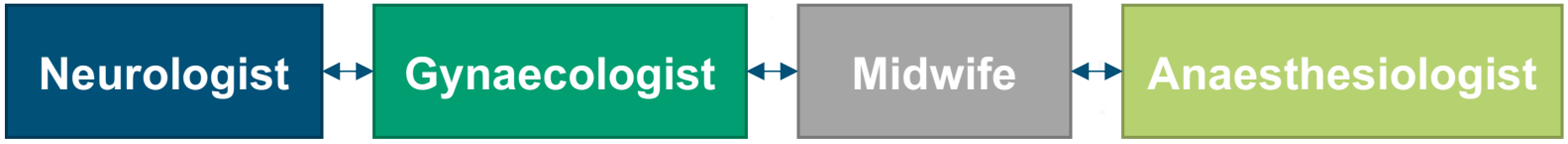
- Until the 1980s: women were advised against pregnancy
- Major change: Pregnancy in MS (PRIMS) study - 1998
  - 254 MS patients with 269 pregnancies
  - Annualised relapse rate (ARR) declines during pregnancy (especially 3rd trimester)
  - ARR increases in 1st trimester postpartum, and then returns to the pre-pregnancy rate



Confavreux C, et al. N Engl J Med 1998;339:285-91

Pregnancies in MS have a normal course

- Pregnancies in women with MS have a **normal course**:[1,2]
  - Foetal outcomes: no ≠ in gestational age and birth weight
  - Delivery: no ≠ in frequency of assisted vaginal delivery or caesarean section
  - Epidurals and caesarean section are not associated with adverse effects on MS course
- Regular counselling is important to:[2]
  - Discuss pregnancy-related issues
  - Alleviate fears that might persist
- DMTs and symptomatic treatments should only be continued if the balance of benefit and risk is in their favour[1]
- Communication and collaboration is essential:[2]



1. Miller DH, et al. Mult Scler 2014;20:527–36; 2. Vukusic S, et al. Nat Rev Neurol 2015;11:280–9

Post-pregnancy: Looking to the future

Dr. Kerstin Hellwig

What do we need to consider postpartum?

Breastfeeding

Impact on infant/child development

Postpartum

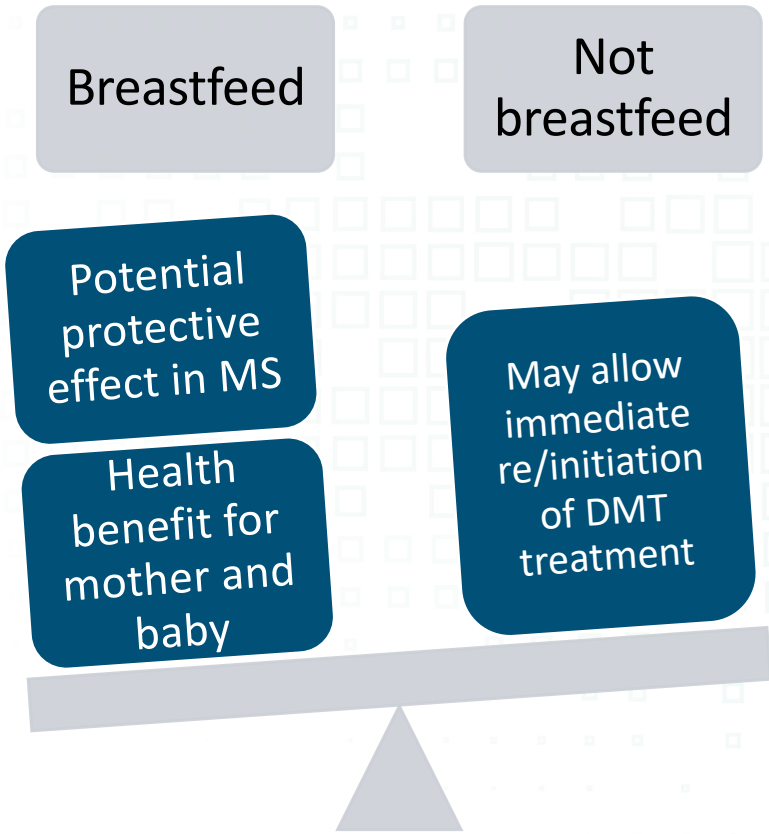
Disease activity

DMT use

DMT=disease modifying therapy

Coyle et al. Ther Adv Neurol Disord 2016;9:198–210.

To breastfeed or not to breastfeed?



Vukusic S, et al. Nat Rev Neurol 2015;11:280–9

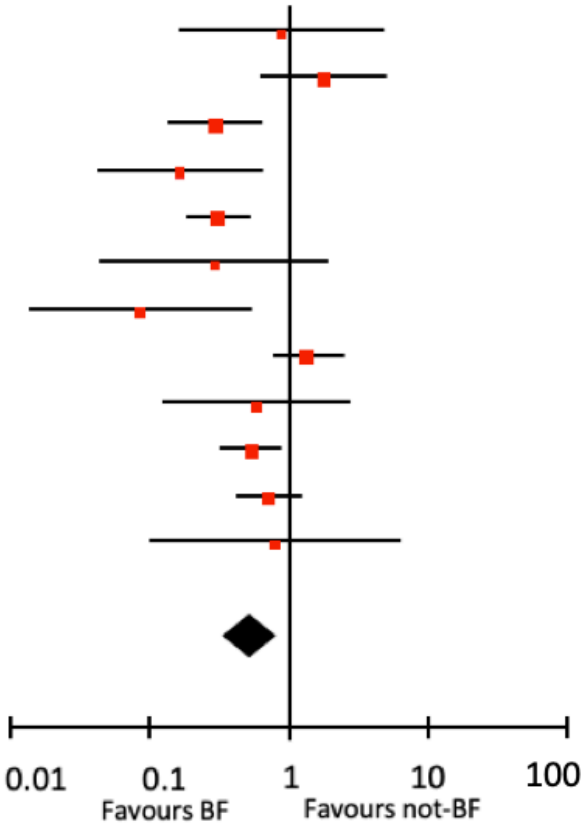
Breastfeeding vs non-breastfeeding

Comparison of breastfeeding MS patients vs non-breastfeeding MS patients

	Favours BF		Favours not-BF			Odds Ratio	Odds Ratio,
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Airas 2010	26	55	3	6	4.8%	0.90 [0.17, 4.84]	
Fernandez Liguori 2009	30	79	6	24	8.6%	1.84 [0.66, 5.14]	
Gulick 2002	47	140	22	35	10.8%	0.30 [0.14, 0.65]	
Hellwig 1	3	34	14	38	6.3%	0.17 [0.04, 0.64]	
Hellwig 2	31	171	61	147	13.3%	0.31 [0.19, 0.52]	
Iorio 2009	2	8	8	15	4.0%	0.29 [0.04, 1.94]	
Langer-Gould 2009	5	14	13	15	4.2%	0.09 [0.01, 0.54]	
Nelson 1988	36	96	29	95	12.5%	1.37 [0.75, 2.49]	
Neuteboom 2011	6	24	4	11	5.4%	0.58 [0.13, 2.71]	
Portaccio 2011	35	103	97	199	13.5%	0.54 [0.33, 0.89]	
Vukusic 2004	52	137	45	97	13.2%	0.71 [0.42, 1.20]	
Worthington 1994	3	8	3	7	3.5%	0.80 [0.10, 6.35]	
Total (95% CI)		**869**		**689**	**100.0%**	**0.53 [0.34, 0.82]**	
Total events	276		305				

Heterogeneity: $Tau^2 = 0.31$; $Chi^2 = 29.89$, df = 11 (P = 0.002); $I^2 = 63\%$

Test for overall effect: Z = 2.83 (P = 0.005)



BF=breastfeeding; IV=inverse variance; CI=confidence interval; df=degrees of freedom

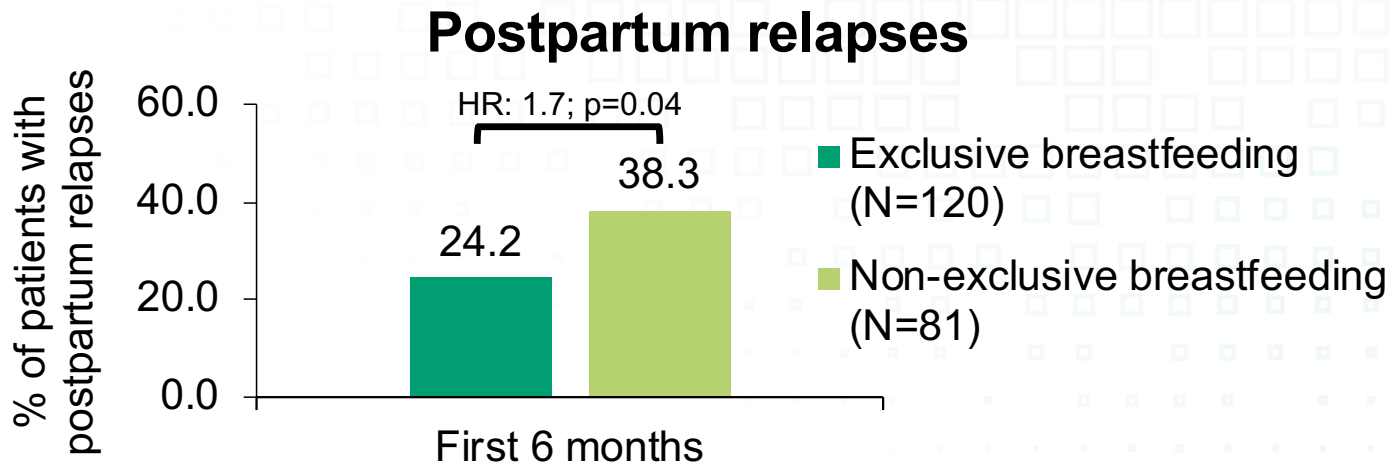
Pakpoor J. et al. J Neurol 2012;259:2245–8

Breastfeeding: No increased risk of postpartum relapse

- Before breastfeeding, evaluate:

Risk of postpartum relapse	MS symptoms	Wish to restart DMT

- Among 201 pregnant RRMS patients from the German MS and Pregnancy Registry:



HR=hazard ratio

Hellwig K, et al. JAMA Neurol 2015;72:1132–8

When to restart DMT?

- No data available
- Only recommendation:
  - A decision should be made as to whether to restart DMT or to breastfeed
  - Limited information is available on DMT excretion in milk
- Always use INDIVIDUAL, shared decision-making. Consider each case on an individual basis that takes into account:

Disease activity before pregnancy	Breastfeeding?	Patient's wish

Vukusic S, et al. Nat Rev Neurol 2015;11:280–9

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Pregnancy and postpartum summary and recommendations:

1. More information on pharmacological treatment in pregnancy is needed; include pharmacologically treated pregnancies in registries
2. Pregnancy might have a protective effect
3. Most women with MS will not experience an increase in disability from a postpartum relapse
4. DMT use after pregnancy should consider: disease activity, breastfeeding risk/benefit analysis and patient's wish
5. Breastfeeding in itself not harmful – exclusive breastfeeding may be beneficial in women with milder disease. Breastfeeding should NOT be discouraged in favour of resuming MS medications in most women
6. If a women does not want to breastfeed, it is recommended that they start early (7–14 days) with MS treatment

Personal communication of the speaker

Closing Remarks

Prof. Sven Schippling

Closing remarks

- Heritability of MS is considered to be relatively low[1,2]
- Potential risk of drugs damaging the foetus should be weighed against risk of relapse and disability[3]
- Most pregnancies in women with MS have a normal course, including normal delivery[1,4]
- Patients should be counselled at every stage, from pregnancy planning to breast-feeding and re-starting DMTs[1]
- Decisions on when to restart DMTs should be based on the individual[1]

1. Vukusic S, et al. Nat Rev Neurol 2015;11:280-9; 2. Compston A, et al. Lancet 2008;372:1502-17; 3. Coyle P. Ther Adv Neurol Disord 2016;9:198–210; 4. Miller DH, et al. Mult Scler 2014;20:527–36;

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Thank you!