MS and Family Planning

Everything You Need To Know

CAN DO MULTIPLE SCLEROSIS

WEBINAR WEDNESDAYS

THIS WEBINAR IS SPONSORED BY:

UPCOMING PROGRAMS

Wednesday, October 30
MS MOVES

Wednesday, November 6
SPECIAL WEBINAR ALERT:
Car-T Therapy – An Emerging Treatment for MS

Wednesday, November 13
COACHING SERIES
Expert Tips for Effective Relief From MS Pain

CANDO-MS.ORG

How to Ask Questions During the Webinar

Type in your questions
using the Questions Box

Provide comments and engage with the speakers and audience using the **Chat Box**

NEW! Closed captioning

YOUR SPEAKERS

Riley Bove

Neurologist

California

Roz Kalb

Psychologist & Health Coach

Maine

“You’ve Come A Long Way, Baby!”

The New York Times

Women Are Calling Out ‘Medical Gaslighting’

Studies show female patients and people of color are more likely to have their symptoms dismissed by medical providers. Experts say: Keep asking questions.

Give this story 2.7K

Marta Monteiro

By Melinda Wenner Moyer

Published March 28, 2022 Updated March 31, 2022

The Atlantic Sign In Subscribe

The Doctor Doesn’t Listen to Her. But the Media Is Starting To.

Physicians have long dismissed or downplayed women's sexual- and reproductive-health concerns—but in 2018, stories about "health-care gaslighting" are consistently breaking through to the mainstream.

By Ashley Fetters

Bettmann / Getty / The Atlantic

AUGUST 10, 2018 SHARE

Key Points: A Preview

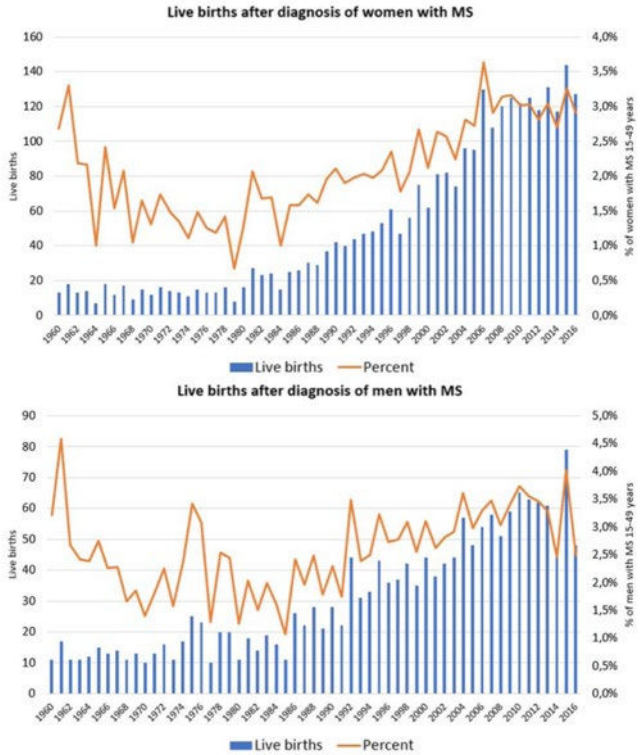
- **Pregnancy planning (or prevention) is an essential aspect of caring for young women and men with MS**
    - Counseling, contraception, vaccination, DMT discussion, diverse populations, (in)fertility questions
- **Hormonal immune suppression during pregnancy is followed by rebound disease activity**
- **Disease control can be achieved throughout the pregnancy period**
- **"4th Trimester": postpartum period as a critical period in the MS course**
- **The risk of MS in the general population is 0.1%; the risk for a person with a first-degree relative is about 3%.**

Reproductive Decision-Making: Evolving Mores

Counseling Starts at Diagnosis: Key Messages

- *You can plan for the family that you would want if you did not have MS*
- *Your MS will not hurt your children*
  - *Mental health*
  - *Financial planning*
- *Your neurology team will work with you and your obstetrical/fertility team to manage your MS during childbearing*

Thanks to the work of many, Decisions are changing



Moberg et al, MSJ 2019

Should we stabilize disease activity during the pregnancy period?

Proactive: "Active Management"

- **Prevent injury before it happens**
- Reduce worry about relapses and allow patient to focus on pregnancy, rehabilitation, mood, and newborn
- Optimize DMT window before, during and after pregnancy

Reactive Management

- **Some patients may not need or want DMT optimization**
- Monitor for new activity
  - MRI:
    - Preconception "baseline" MRI
    - During pregnancy: MRI for safety monitoring (PML) and to evaluate new neurological symptoms; gad only if would change management
    - Postpartum: first 3M, gad ok with lactation
- Biomarkers (eg NFL or panels of markers)
  - ?

Understanding the Guidance: Three Frameworks for DMT Discontinuation

Follow the label

Wait 5 maximal half-lives (exponential decay)

Limitations
- Teriflunomide
- Rebound risk (S1P, NTZ)
- Patient's disease control

Weigh known risks and benefits to patient and fetus

Informed by: real-world data, class effects, physiological principles

Note: evolving, real-world

If unintentional exposure, stop DMT, consider fetal U/S, refer urgently to MFM and to pregnancy-informed neurologist

Problems with Labels: Inconsistencies

		FDA	EMA
PREGNANCY	RITUXIMAB	Avoid pregnancy for 12 months after last infusion	Avoid pregnancy for 12 months after last infusion
	OCRELIZUMAB	Avoid pregnancy for 6 months after last infusion	Avoid pregnancy for 12 months after last infusion
	OFATUMUMAB	Avoid pregnancy for 6 months after the last injection	Avoid pregnancy for 6 months after the last injection
	UBLITUXIMAB	Avoid pregnancy for 6 months after last dose	Avoid pregnancy for 4 months after the last infusion
	INEBILIZUMAB	Avoid pregnancy for 6 months after last dose	Avoid pregnancy for 6 months after last dose
LACTATION	RITUXIMAB	No BF during treatment and for 6 months following infusion	BF not recommended and optimally for 12 months following infusion
	OCRELIZUMAB	Consider developmental and health benefits of BF, along with mother's clinical need for OCR, and any potential adverse effects on breastfed infant from OCR or from underlying maternal condition.	Discontinue BF during therapy.
	OFATUMUMAB	Consider developmental and health benefits of BF, along with mother's clinical need for OFA, and any potential adverse effects on breastfed infant from OFA or from underlying maternal condition.	In humans, excretion of IgG antibodies in milk occurs during the first few days after birth, which decreases to low concentrations soon afterwards. A risk to the breastfed child cannot be excluded during this short period. Afterwards, OFA could be used during BF if clinically needed. If the patient was treated with OFA up to the last few months of pregnancy, breastfeeding can be started immediately after birth.
	UBLITUXIMAB	Consider developmental and health benefits of BF, along with mother's clinical need for UBLI , and any potential adverse effects on breastfed infant from Ubli or from underlying maternal condition.	It is unknown whether ublituximab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which decreases to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period. Afterwards, ublituximab could be used during breast-feeding if clinically needed.
	INEBELIZUMAB	There are no data on the presence of inebilizumab-cdon in human milk, the effects on a breastfed infant, or the effects on milk production. Human IgG is excreted in human milk, and the potential for absorption of UPLIZNA to lead to B-cell depletion in the breastfed infant is unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for UPLIZNA and any potential adverse effects on the breastfed infant from UPLIZNA or from the underlying maternal condition.	The use of inebilizumab in women during lactation has not been studied. It is unknown whether inebilizumab is excreted in human milk. In humans, excretion of IgG antibodies in milk occurs during the first few days after birth, which is decreasing to low concentrations soon afterwards. Consequently, a risk to the breast-fed child cannot be excluded during this short period. Afterwards, Uplizna could be used during breast feeding if clinically needed. However, if the patient was treated with Uplizna up to the last few months of pregnancy, breast feeding can be started immediately after birth.

Example of a Framework Supporting Patient, Infant and Family

Risks of treatment continuation

Baby

- Effect of treatment exposure; potential teratogenicity
- Long-term effects of treatment—eg, on developing immune system
- Treatment associated adverse events—eg, alemtuzumab-associated thyroid disorders
- Risks around live vaccination in first 6 months of life

Mother

- Dual immunosuppression during pregnancy
- Treatment-associated risk—eg, natalizumab and JCV-associated PML
- Reduced maternal and neonatal vaccine response

Risks of treatment discontinuation

Baby

- Impact of maternal disability
- Potential need for rescue treatment during pregnancy

Mother

- Relapses or disease reactivation
- Rebound (selected DMT)
- Long-term disability which might be substantial
- Treatment-associated risk might not reverse during pregnancy—eg, impact of anti-CD20 on maternal vaccine response
- Adverse effect on wellbeing due to worry regarding untreated disease

Benefits of treatment continuation

- Ability to achieve control of disease activity and reduce post-partum relapse risk; can minimise exposure in pregnancy
- Long-term effects on disability

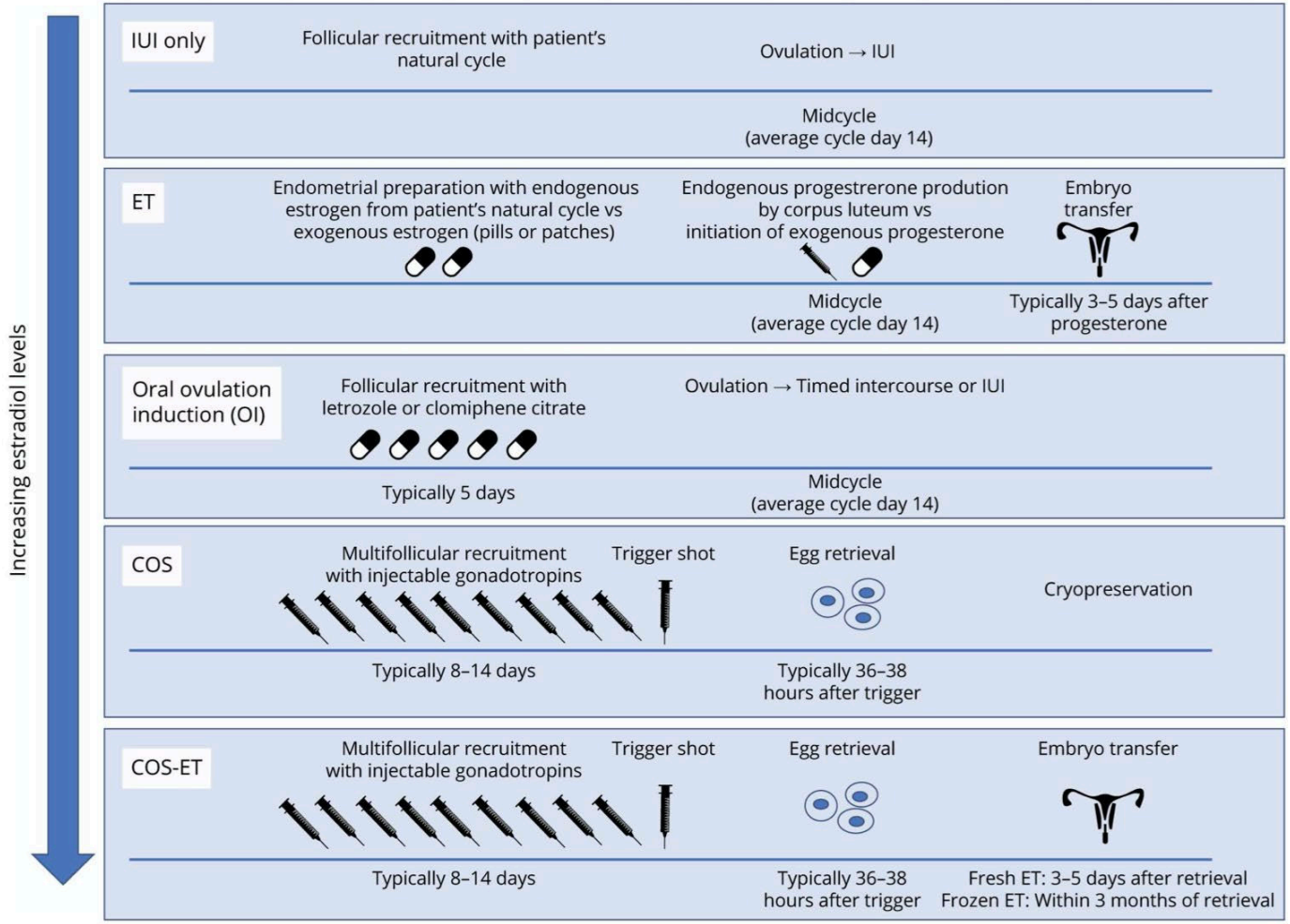
Benefits of treatment discontinuation

- Safety for baby
- Might not affect disease control in individuals with mild disease

Krysko, Dobson, et al, Lancet Neurology 2023

Fertility Treatments and Relapse Risk

Figure 1 Overview of Common Fertility Treatments, Organized Based on Hypothetical Risk of MS Inflammatory Activity



MS = multiple sclerosis.

Graham et al, N2 2023

- Meta-analysis of 5 small studies suggest increased risk of relapses (Bove et al, MSJ 2020)
- But more modern DMT-era cohorts **suggest no increased risk**, regardless of treatment type
  - Mainguy et al, Neurology2022; Graham et al, N2 2023
- **Continuing DMT during this time period may be key**
- **Coordination of care between neurologic and obstetric clinicians!**
  - Consider referral at 6M

MS – Predictors of Inflammatory Activity Postpartum

INCREASED RISK

- Withdrawal of highly effective DMTs
- Disease pre-conception
  - Higher EDSS
  - Higher relapse rate
  - Active MRI

PROTECTIVE

- Breastfeeding
- Early resumption of therapy?

Early
Effective
Minimal therapeutic lag

Bsteh MSJ 2020; Yeh et al, Neurology 2021; Anderson et al N2 2021; Razaz N2 2020; Krysko et al JAMA Neuro 2019; Lorefice Neurol Ther 2022; Ostrem et al MSJ ETC 2022; Lehmann et al MSJ 2021; Hughes et al MSJ 2014

The Fourth Trimester:

Need for Comprehensive Care, Self management, and Support

MS Management:

- Repeat MRI especially if patient not planning on resuming DMT
- Review lactation plan (+ consult)
- Screen for endocrine abnormalities (e.g. thyroid)

Comprehensive functional evaluation

MENTAL: Mood, Sleep, Fatigue, Thinking

PHYSICAL: Gait, Balance, Endurance, Falls

BLADDER, BOWEL

SOCIAL: work, support, stress

Perinatal Depression and Anxiety in Women With Multiple Sclerosis

A Population-Based Cohort Study

Karine Eid, MD, Øivind Fredvik Torkildsen, MD, PhD, Jan Aarseth, PhD, Heidi Øyen Flemmen, MD, Trygve Holmøy, MD, PhD, Åslaug Rudjord Lorentzen, MD, PhD, Kjell-Morten Myhr, MD, PhD, Trond Riise, PhD, Cecilia Simonsen, MD, Cecilie Fredvik Torkildsen, MD, Stig Wergeland, MD, PhD, Johannes Sverre Willumsen, MD, Nina Øksendal, MD, Nils Erik Gilhus, MD, PhD, and Marte-Helene Bjørk, MD, PhD

Correspondence
Dr. Eid
karine.eid@uib.no

Neurology® 2021;96:e2789-e2800. doi:10.1212/WNL.0000000000012062

Conclusion

Women diagnosed with MS have increased risk of perinatal depression. Women with MS symptom onset within 5 years after pregnancy have increased risk of both depression and anxiety during pregnancy.

Established risk factors

Older age, primiparity, prior depression

MULTIPLE SCLEROSIS JOURNAL | MSJ

Original Research Paper

Risk factors for peripartum depression in women with multiple sclerosis

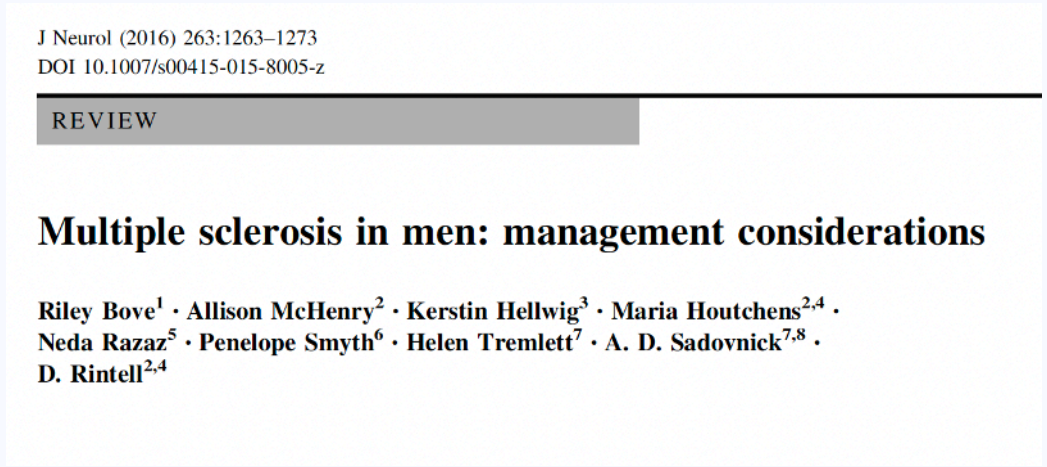
Kristen M Krysko, Annika Anderson, Jessica Singh, Kira McPolin, Alice Rutatangwa, William Rowles, A Dessa Sadovnick, Maria K Houtchens and Riley Bove

Table 2. Demographic, pregnancy-related and mood-related factors and association with peripartum depression (n = 143 pregnancies in 111 women).

	Peripartum depression		OR, 95% CI (univariable)	*p value*	OR, 95% CI (multivariable)*	*p value*
	PPD present (n = 18)	PPD absent (n = 125)				
Demographics						
Maternal age, mean years (SD), per 1-year increase	35.4 (4.5)	32.7 (4.6)	**1.16, 1.03–1.32**	**0.016***	**1.17, 1.02–1.34**	**0.029**
Marital status, n (%)				0.29		
Married	15 (83.3)	111 (88.8)	1 (reference)			
Long-term partner	1 (5.6)	3 (2.4)	2.47, 0.24–25.44	0.45		
Single	2 (11.1)	4 (3.2)	3.67, 0.62–21.84	0.15		
Unknown	0 (0)	7 (5.6)	–			
Pregnancy-related factors						
Primiparity, n (%)[a], vs multiparity	15 (83.3)	66 (54.1)	**4.02, 1.14–14.23**	**0.031***	**8.10, 1.38–47.40**	**0.020**
Unplanned pregnancy, n (%)[a] vs planned	2 (13.3)	16 (17.6)	0.69, 0.14–3.45	0.65		
Season of delivery, n (%)				0.76		
Fall	4 (22.2)	32 (25.6)	1 (reference)			
Winter	6 (33.3)	28 (22.4)	1.73, 0.45–6.58	0.43		
Spring	4 (22.2)	34 (27.2)	0.90, 0.20–3.93	0.88		
Summer	4 (22.2)	31 (24.8)	1.02, 0.34–4.42	0.98		
Preterm (<37 weeks), n (%)	2 (11.1)	11 (8.8)	1.17, 0.22–6.18	0.86		
Low birth weight (<2500 g), n (%)[a]	1 (7.1)	6 (8.6)	0.95, 0.14–6.21	0.95		
Delivery mode, n (%)[a]						
Spontaneous vaginal delivery	10 (58.8)	65 (67.0)	1 (reference)			
Cesarean section or assisted delivery	7 (41.2)	32 (33.0)	1.42, 0.51–3.98	0.50		
Postpartum sleep disturbance, n (%)[a]	6 (33.3)	16 (13.4)	**3.23, 1.17–8.91**	**0.024***	1.58, 0.42–5.99	0.50
Breastfeeding exclusively for ≥3 months, n (%)	7 (38.9)	46 (36.8)	1.09, 0.41–2.93	0.86		
Breastfeeding difficulty, n (%)[a]	7 (41.2)	18 (16.5)	**3.58, 1.27–10.08**	**0.016***	1.94, 0.46–8.13	0.36
Mood-related factors						
Pre-pregnancy depression, n (%)[a]	13 (72.2)	51 (41.5)	**3.70, 1.27–10.01**	**0.017***	**3.89, 1.04–14.60**	**0.044**
Pre-pregnancy anxiety, n (%)[a]	9 (50.0)	39 (31.5)	2.14, 0.82–5.56	0.12		
Antidepressant discontinuation, n (%)[a]	2 (11.1)	12 (9.8)	1.04, 0.20–5.54	0.96		

Potential MS related factors:
not significant
(relapse, EDSS, DMT, etc)

Men: Gendered Experiences



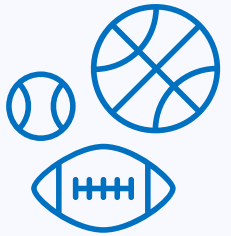
J Neurol (2016) 263:1263–1273
DOI 10.1007/s00415-015-8005-z

REVIEW

Multiple sclerosis in men: management considerations

Riley Bove[1] · Allison McHenry[2] · Kerstin Hellwig[3] · Maria Houtchens[2,4] · Neda Razaz[5] · Penelope Smyth[6] · Helen Tremlett[7] · A. D. Sadovnick[7,8] · D. Rintell[2,4]

- Sex differences in risk and course
- Mental health
  - Self-medication, substance use
  - Social support/isolation
- Specific symptoms and concerns
  - Sexual function
  - Urological concerns
  - Role of exogenous androgens
- Societal role
  - Work
  - Parenting
  - Impact, stigma of visible, invisible disability
- Specific DMT guidance



Men With MS

- Male fertility is unimpaired in MS
  - If erectile dysfunction or inability to reach orgasm interferes with intercourse, help is available
- The impact of most DMTs on sperm have not been studied.
- Teriflunomide (Aubagio®) has been found in women whose husbands are taking it. Men are advised to use barrier contraception during treatment and for two years after stopping treatment.
- Cladribine (Mavenclad®) reduces sperm quality. Men and women should use effective contraception for 6 months after taking this drug.

Gender Inclusivity

- Neurologist expertise and cultural competence – pick the right provider for you!
- Effect of gender affirming hormone treatments on MS risk
- Surgeries, hormones could influence pregnancy/lactation/ infection risk
- Gaps in comprehensive management of MS symptoms: mood, bowel, bladder, sexual function

To Answer Your Genetics Questions

- The risk of MS in the general population is **0.1%-0.3%**
- **2%** In a person whose parent has MS
  - Significantly higher if both parents have MS
- **4%** in a person who has a sibling with MS
- **25%** in an identical twin of a person with MS (environment matters too!)
- **2%** in a parent of a child with MS

At this time, there is no test that can determine whether a child will develop MS

Key Points – A Summary

Pregnancy planning (or prevention) is an essential aspect of caring for young women with MS

- Counseling, contraception, vaccination, DMT discussion, diverse populations, (in)fertility questions

Hormonal immune suppression during pregnancy is followed by rebound disease activity

Disease control can be achieved throughout the pregnancy period

- Proactive strategy – reduce risk of EDSS progression and patient worry
- Reactive strategy – some patients may not require treatment
  - Monitoring: MRI (MRI and Gad OK during lactation; MRI OK but no gad during pregnancy)
- **DMT choices: several frameworks to interpret risk during pregnancy and lactation**

"4th Trimester": postpartum period as a critical period in the MS course

- Rehabilitation, mood, fatigue, disease stabilization, social needs
- Lactation is a scientific question we can and should address
- Prioritizing needs of patient, infant, family

Q+A

THIS WEBINAR IS SPONSORED BY:

CONNECT WITH US

TIKTOK

@CanDoMultipleSclerosis

FACEBOOK

@CanDoMultipleSclerosis

TWITTER

@CanDoMS

INSTAGRAM

@CanDoMultipleSclerosis