
International Organization of MS Nurses

Pregnancy and Breastfeeding in MS

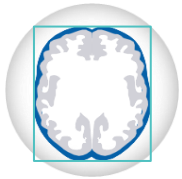
Supported by Novartis Pharmaceuticals Corporation



Background



MS is the most common neurologic disability in women of childbearing age and affects **women 3 times** more frequently **than men**¹⁻³



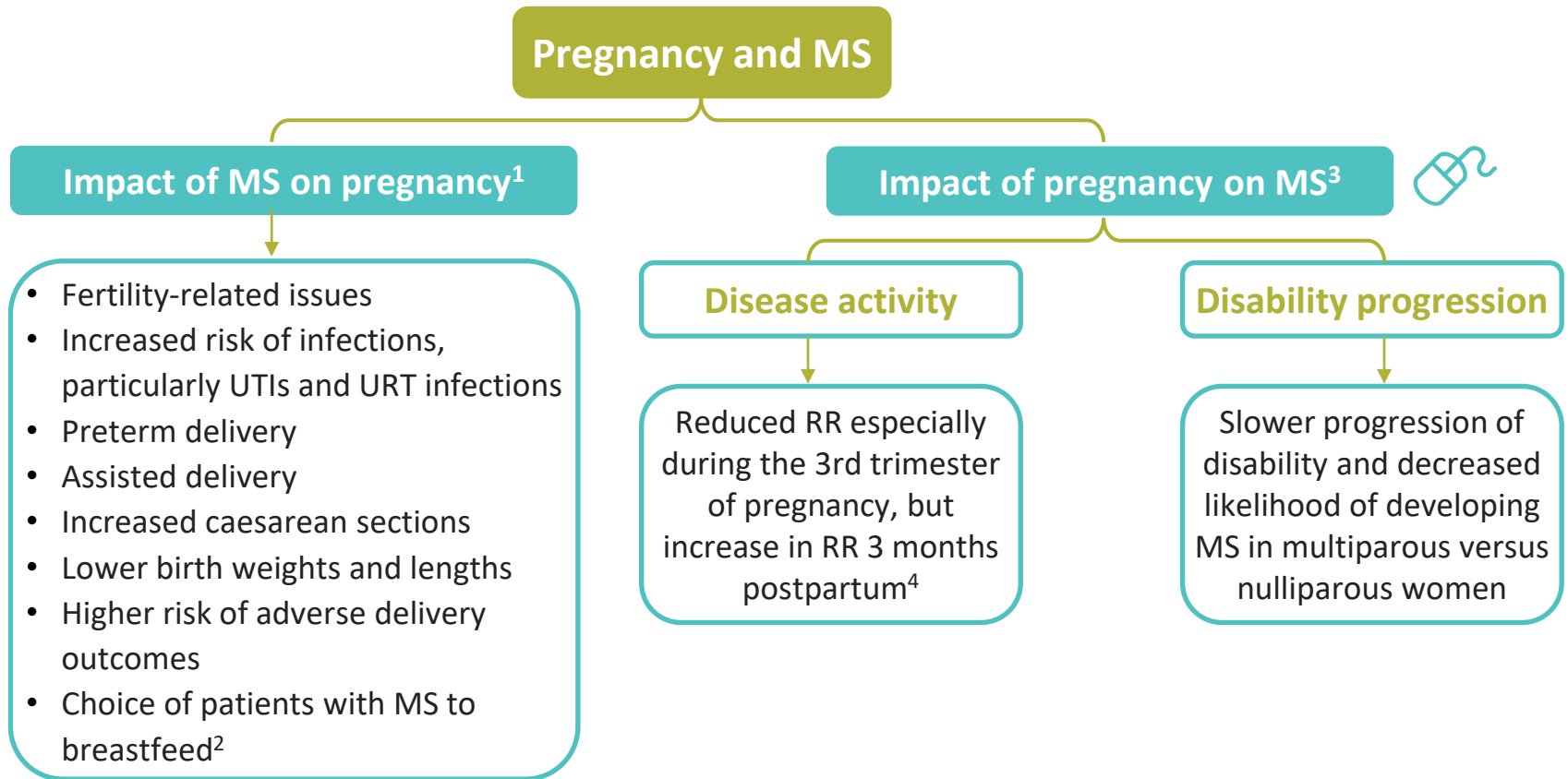
MRI findings revealed that female patients with MS have **higher inflammatory activity** and therefore have a **higher relapse rate and more inflammatory lesions**⁴



Historically, women with MS were **discouraged from becoming pregnant** as pregnancy was thought to worsen disease course^{5,6}

1. Wallin MT et al. *Neurology* 2019;92:e1029-e1040;
2. Sellner J et al. *Autoimmun Rev.* 2011;10:495-502;
3. MacDonald SC et al. *Am J Epidemiol.* 2019;188:57-66;
4. Villaverde-González R. *Degener Neurol Neuromuscul Dis.* 2022;12:1-21;
5. Lamaita R et al. *JBRA Assist Repro.* 2021;25:493-499;
6. Confavreux C et al. *N Engl J Med.* 1998;339:285-291.

Pregnancy and MS



RR=relapse rates; URT=upper respiratory tract; UTIs=urinary tract infections.

1. Villaverde-González R. *Degener Neurol Neuromuscul Dis.* 2022;12:1-21;

2. Krysko KM et al. *JAMA Neurol.* 2020;77:327-338;

3. Simone IL et al. *Front Neurol.* 2021;12:697974;

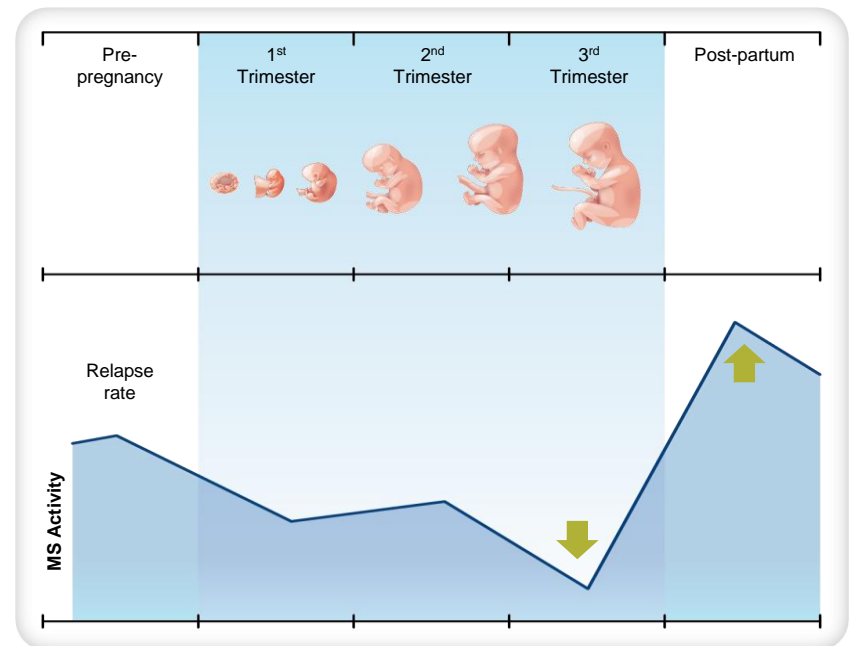
4. Vukusic S et al. *Brain.* 2004;127:1353-1360.



IMPACT OF PREGNANCY ON WOMEN WITH MS

Impact of Pregnancy on MS Disease Activity

- Pregnancy is a natural disease modifier in MS associated with significantly^{1,2}
 - Decreased RR in 3rd trimester and
 - Increased RR in first 3 months postpartum
- Changes in frequency of relapse risk during pregnancy and postpartum are associated with fluctuations in endocrine hormones³
- Women with greater disease activity in the year before pregnancy and during pregnancy have a higher risk of relapse in 3 months postpartum⁴

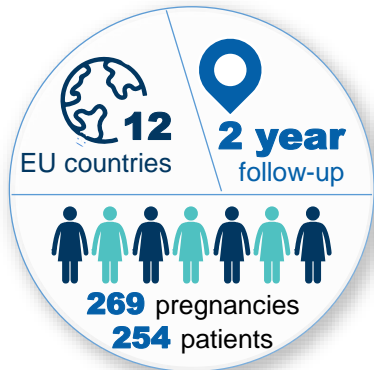


Reproduced with permission from Patas K et al. Elsevier⁵

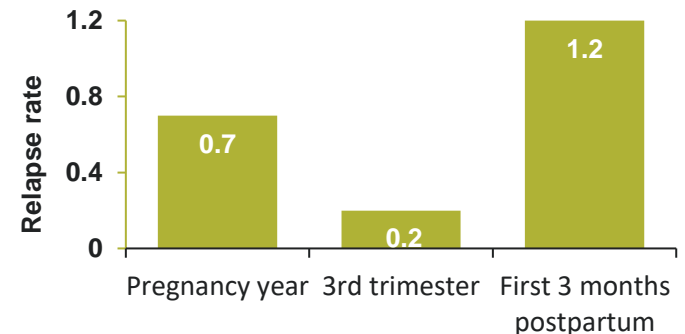
1. Confavreux C et al. *N Engl J Med*. 1998;339:285-291;
2. Modrego PJ et al. *J Comp Eff Res*. 2021;10:175-186;
3. Voskuhl R, Momtazee C. *Neurotherapeutics*. 2017;14:974-984;
4. Vukusic S et al. *Brain*. 2004;127(Pt 6):1353-1360;.
5. Patas K et al. *J Reprod Immunol*. 2013;97:140-146.

Pregnancy in Multiple Sclerosis (PRIMS) Study

Objective: To determine the effect of pregnancy on relapses and disability progression¹



- Pregnancy ARR decreased by >70% during the 3rd trimester and increased during the first 3 months postpartum²
- Overall ARR in the pregnancy year* was similar to the antepartum rate^{1,2}
- Only 28% of women experienced a postpartum relapse²
- No change in disability progression during the study^{1,2}



*Pregnancy year=9 months of pregnancy + 3 months postpartum.

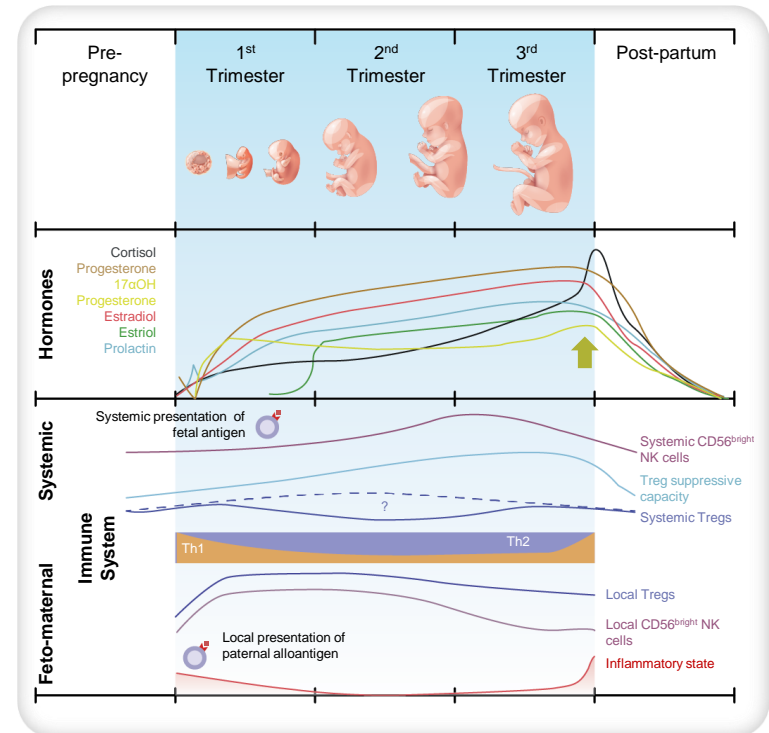
ARR=annualized relapse rate; EU=European Union.

1. Confavreux C et al. *N Engl J Med.* 1998;339:285-291;

2. Vukusic S et al. *Brain.* 2004;127(Pt 6):1353-1360.

Effect of Pregnancy on MS Relapses

- **Reduced risk of relapses during pregnancy may be explained by^{1,2}**
 - Fluctuations in immunoregulatory endocrine hormones (estrogen and progesterone)
 - Th1 (pro-inflammatory) to Th2 (anti-inflammatory) switch in Th cells
 - Immunotolerance induced by exposure to fetal antigens



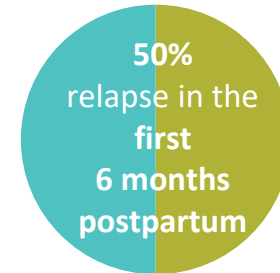
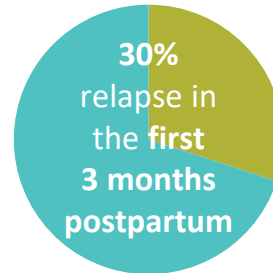
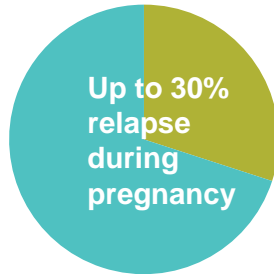
Reproduced with permission from Patas K et al. Elsevier²

CD=cluster of differentiation; NK=natural killer; Th=T-helper; Treg=T regulatory.

1. Villaverde-González R. *Degener Neurol Neuromuscul Dis*. 2022;12:1-21;

2. Patas K et al. *J Reprod Immunol*. 2013;97:140-146.

Risk of Relapses During Pregnancy and Postpartum



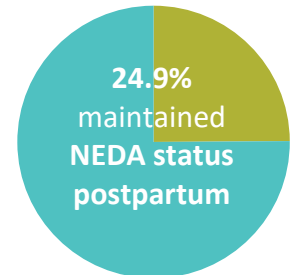
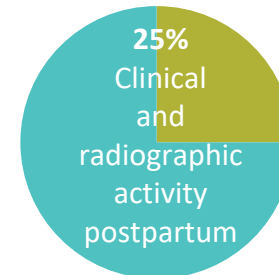
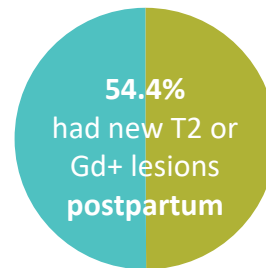
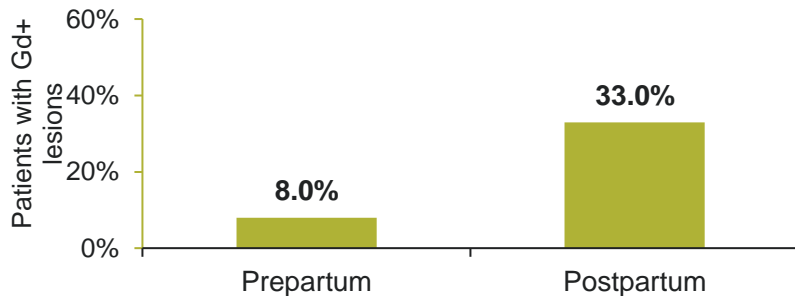
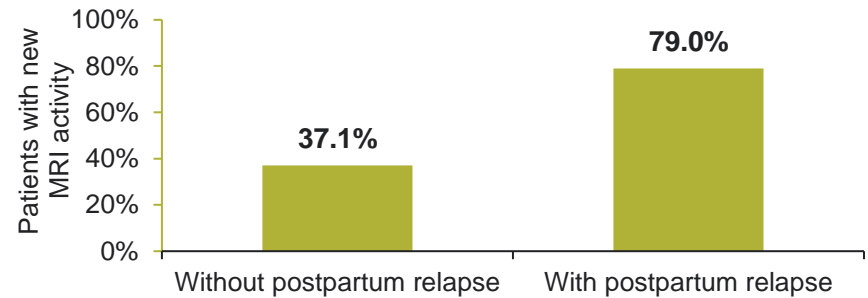
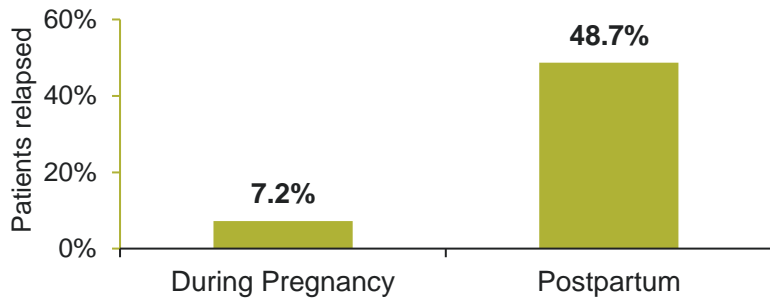
Factors associated with risk of relapse	
During pregnancy	During postpartum
<ul style="list-style-type: none">• Age <35 years	<ul style="list-style-type: none">• Presence of relapses during pregnancy• Younger age group
<ul style="list-style-type: none">• Relapses in the year before pregnancy• Greater disability at the time of conception• Relapses following DMT cessation before conception	

DMT=disease modifying therapy.

Villaverde-González R. *Degener Neurol Neuromuscul Dis.* 2022;12:1-21.

Risk of Relapses During Pregnancy and Postpartum

- Between 2006 and 2015 a total of 123 pregnancies from a tertiary care MS center were analyzed



Gd+=gadolinium-enhancing; NEDA=no evidence of disease activity.
Houtchens M et al. *Neurol Neuroimmunol Neuroinflamm.* 2020;7:e890.



MANAGEMENT OF MS DURING PREGNANCY

Management of MS During Prepregnancy



Family planning

Discuss family planning and pregnancy-related issues to help make informed treatment decisions on medication choices



Disease stabilization

Achievement of disease stability (absence of relapses, and/or sustained progression of disability, and/or radiological activity) before pregnancy



Contraceptive use

Patients should be advised about available contraceptive methods especially during treatment with high-efficacy DMTs



Safety of DMTs

DMTs safety assessments should be considered



Clinical and MRI monitoring

Managing women with MS includes clinical and MRI examination before conception



Mandatory Precautions

Preconceptional vitamin D and folic acid supplementation. Avoid alcohol and smoking

Management of MS During Pregnancy



DMT precautions

Consider discontinuing all the DMTs



Routine care

Clinical monitoring should continue, and laboratory monitoring as needed per clinician (gynecologist and obstetrician) discretion



Disabling relapse

Standard high-dose IVMP can be used to treat relapse, especially in the 2nd and 3rd trimesters. Plasma exchange may be preferred early in pregnancy due to risks of high-dose IVMP on the early fetus



MRI scans

MRI without Gd could be obtained. Schedule a visit to evaluate the patient neurologically and make plans for the postpartum period



Breastfeeding

Encourage exclusive breastfeeding if the patient would like to breastfeed

IVMP=intravenous methylprednisolone.

Villaverde-González R. *Degener Neurol Neuromuscul Dis.* 2022;12:1-21.

Management of MS Postpartum



Monitor for MRI activity

Patients should be closely monitored in the postpartum period. MRI without Gd could be obtained. If maternal Gd is administered, conservative advice recommends a pause of 4 hours before breastfeeding



Breastfeeding

If the patient would like to breastfeed, then exclusive breastfeeding should be recommended as this is less associated with relapses than intermittent breastfeeding

MRI=magnetic resonance imaging.

Villaverde-González R. *Degener Neurol Neuromuscul Dis.* 2022;12:1-21; Bruen D. Personal communication.

Family Planning Is Pivotal for MS Management

Prepregnancy



- Family planning
- Disease stabilization
- Contraceptive use
- Discuss pregnancy issues
- Non-teratogenic DMTs
- Clinical and MRI monitoring
- Individualized treatment
- Vitamin D and folic acid supplement

Pregnancy



- Monitor every trimester
- Advised on UTI infection common in pregnancy
- Vitamin D and folic acid supplement
- MRI without Gd+ in case of disease reactivation
- Discontinue all DMTs
- Corticosteroid for relapses, especially in the 2nd and 3rd trimester
- Discuss patient's wishes regarding breastfeeding
- Vaccines recommendations

Postpartum



- Monitor for increased clinical and MRI activity
- Breastfeeding considerations
- Resuming DMTs soon after delivery, with breastfeeding considerations
- Corticosteroid for postpartum relapse treatment
- MRI not contraindicated

Considerations for Relapse Management During Pregnancy



Not to delay DMT onset

DMT versus no DMT during preconception prevents postpartum relapses.¹ Initiate DMT preconception to achieve disease stability at least 1 year before an attempt for pregnancy²

Corticosteroid treatment

IVMP is the first-line therapy for severe relapses during pregnancy.³ Avoid IVMP during the 1st trimester due to the risk of fetal malformations (eg, cleft palate)⁴

Breastfeeding

Women who exclusively breastfed in the first 6 months postpartum had a fewer relapses than those who had partially breastfed/did not breastfeed at all⁵

Resuming DMTs postpartum

In patients who do not wish to breastfeed should immediately resume DMTs soon after delivery as it is associated with decreased risk of postpartum relapse^{1,6}

MP=methylprednisolone.

1. Yeh WZ et al. *Neurology*. 2021;96:e2989-3002;
2. Canibaño B et al. *J Drug Assess*. 2020;9:20-36;
3. Coyle PK et al. *Mult Scler Relat Disord*. 2019;32:54-63;
4. Park-Wyllie L et al. *Teratology*. 2000;62:385-92;
5. Hellwig K et al. *JAMA Neurol*. 2015;72:1132-8;
6. Bsteh G et al. *Mult Scler*. 2020;26:69-78.



USE OF DMTs DURING PREGNANCY AND BREASTFEEDING

FDA Recommendations for Use of DMTs During Pregnancy and Breastfeeding

Pregnancy and Breastfeeding

Interferon-β	<ul style="list-style-type: none">• No clear relationship between use and major congenital malformations• Animal data: may cause fetal harm
Glatiramer acetate	<ul style="list-style-type: none">• Human data: not sufficient to support conclusions about drug-associated risk for major birth defects and miscarriage
Monoclonal antibodies	<ul style="list-style-type: none">• Animal data: may cause fetal harm
Fumarates	<ul style="list-style-type: none">• Animal data: may cause fetal harm• Fumarates appear to be safe to use while breastfeeding
S1PR modulators	<ul style="list-style-type: none">• Animal data: may cause fetal harm• Females of reproductive potential should use effective birth control during treatment and after stopping treatment (from 1 week to 2 months for different S1PR modulators)
Pyrimidine synthesis inhibitors	<ul style="list-style-type: none">• Contraindicated for use in pregnant women and in females of reproductive potential who are not using effective contraception because of the potential for fetal harm
Purine antimetabolite	<ul style="list-style-type: none">• Contraindicated for use in pregnant women and in women and men of reproductive potential who are not using effective contraception because of the risk of fetal harm• It is unknown if it passes into breast milk. Do not breastfeed on the days, during treatment, and for 10 days after the last dose

S1PR=sphingosine-1-phosphate receptor.

<https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-The-MS-Disease-Modifying-Medications.pdf>; Drugs.com, Dimethyl fumarate while breastfeeding, 2022.

Unmet Needs

- Need for more accurate biomarkers for disease activity and prognosis
- Accumulating accurate data on fetal risks and breast milk exposure
- Need for patient awareness and appropriate information to MS patients planning parenthood and receiving DMT

Conclusion



Historically, women with MS were **discouraged from becoming pregnant** as pregnancy was thought to worsen disease course^{1,2}

Pregnancy is a naturally occurring disease modifier of MS associated with **reduced RR in the 3rd trimester** followed by a rebounding RR postpartum^{3,4}

MS management during pregnancy and postpartum is challenging as **all DMTs are not indicated during pregnancy**⁵

Prevention of relapses and disability postpartum through shared decision-making related to family planning and therapeutic strategies to be considered before, during, and after pregnancy⁶

1. Lamaita R et al. *JBRA Assist Repro*. 2021;25:493-499;
2. Confavreux C et al. *N Engl J Med*. 1998;339:285-291;
3. Voskuhl R, Momtazee C. *Neurotherapeutics*. 2017;14:974-984;
4. Patas K et al. *J Reprod Immunol*. 2013;97:140-146;
5. Varytè G et al. *Curr Opin Obstet Gynecol*. 2021;33:378-383;
6. Villaverde-González R. *Degener Neurol Neuromuscul Dis*. 2022;12:1-21.

Nursing Implications

- Nurses are uniquely qualified to educate and counsel women with MS about the impact of pregnancy and breastfeeding on their MS—and the impact of their MS on pregnancy and breastfeeding
- At or soon after diagnosis, it is important to review family planning issues and contraception with women of childbearing age
- Discontinuation of disease-modifying therapies should be discussed once pregnancy is confirmed
- Exclusive breastfeeding is encouraged