

Pregnancy and multiple sclerosis: Risk of unplanned pregnancy and drug exposure in utero

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Abstract

Background: Multiple sclerosis is a central nervous system demyelinating disease that affects women of reproductive potential. It is important to identify the frequency and risk factors of unplanned or disease-modifying therapy-exposed pregnancies to create interventions to reduce these.

Methods: This retrospective, single-center, observational chart review study aims to identify risk factors for unplanned pregnancy to identify a target population for family counseling.

Results: In total, 63 live births in 45 patients (20 unplanned and 43 planned) were analyzed. The percentage of unplanned pregnancy was 32%. The proportion of those receiving family planning counseling was lower in the patients with unplanned pregnancies ($p < 0.001$). The main risk factors for unplanned pregnancy were younger age ($p = 0.004$), disease-modifying therapy exposure ($p < 0.001$), and being unmarried ($p < 0.001$). Overall, 16 pregnancies had disease-modifying therapy exposure and in a subsequent study the risk for disease-modifying therapy exposure was unplanned status ($p < 0.001$). Birth outcomes were not different between groups. There were more enhancing lesions in the post-partum magnetic resonance imaging of women with planned pregnancy ($p < 0.04$).

Conclusion: Prevention of unplanned pregnancy could lead to less disease-modifying therapy exposed pregnancies. This study suggests a targeted intervention of family planning counseling in younger, unmarried multiple sclerosis patients could potentially lead to less unintended in utero disease-modifying therapy exposure.

Keywords: Multiple sclerosis, pregnancy

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Introduction

Multiple sclerosis (MS) is a chronic immune-mediated demyelinating disease of the central nervous system that leads to progressive permanent disability in most patients. In the USA, approximately 700,000 people live with MS¹ and the prevalence is increasing.^{2,3} This increasing prevalence appears to be due to an increase mainly of the relapsing–remitting (RR) phenotype in women.^{2,4,5} The RR phenotype of MS is highly treatable, with regulatory approval of 16 disease-modifying therapies (DMT) that reduce relapses and potentially prevent or delay permanent neurologic disability.^{6,7} Evidence suggests early initiation of effective DMT leads to better outcomes in RRMS patients.^{8–10} Whereas emerging data suggest that some DMTs, particularly

glatiramer acetate and interferon-beta, may be safe in the earliest stages of pregnancy, most DMT and symptomatic treatments being used in MS are not considered completely safe in women who are attempting to conceive, are pregnant, or nursing.^{11–15} Management of MS with DMT needs to be balanced with reproductive goals.

Several studies looking at unplanned pregnancy rates in various populations have been conducted in the teenage and military populations. In these studies, women who were younger than 30, unmarried, attained lower educational levels, economically disadvantaged, depressed, non-Caucasian, and used birth control incorrectly were more likely to have an unplanned pregnancy.^{16–19} Due to perceived stress,

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psychosocial problems, and lack of adequate prenatal care, these women were more likely to have preterm deliveries and infants with low birth rates.¹⁶ Moreover, women with unplanned pregnancies were more likely to have obstetric complications and infections.²⁰

Limited data exist exploring the rate of unplanned pregnancy in MS patients. From a paper published by Henshaw et al. in 1998, estimates suggest that as many as 50% of pregnancies in the general population in the US are unplanned.²¹ Most citations in the literature source this study to quote a 50% unplanned pregnancy rate in MS.²² A few notable exceptions are the recently published studies that utilized population-based surveys and chart review techniques from Denmark, Germany, and Spain suggesting the unplanned pregnancy rates was as low as 10% and 16.6%, respectively.^{23,24} The rate of unplanned pregnancy is considered to be lower in western Europe compared to the USA.²⁵ Therefore, it becomes important to look at the unplanned pregnancy rate in a US population. If the unplanned pregnancy rates in the USA also apply to the MS population, then there is reason for concern. Unintended in utero exposure to MS medications potentially can lead to teratogenic effects, long-term disability, and intellectual impairment in the offspring.^{26–29} It is critical that women are adequately counseled about family planning issues, especially while on DMT.^{30–33} By simply providing education and family planning counseling, the rate of contraceptive usage increased with a corresponding drop in the rate of unplanned pregnancies.¹⁷

A previous study showed that family planning issues are brought up by only 57% of physicians when starting a DMT in women of child-bearing potential.³⁴ This retrospective, single-center, observational chart review study aims to identify risk factors for unplanned pregnancy to identify a target population for family counseling. Secondary aims are to examine the use of DMT during pregnancy, to determine the effect of unplanned pregnancy on the course of MS, and to determine outcomes of unplanned pregnancy in an MS population in the USA.

Methods

Patient identification

The study population comprised patients who received medical care at the Cleveland Clinic Mellen Center in Cleveland, Ohio, a large, quaternary MS specialty clinic that sees over 20,000 patient

visits per year. Cleveland Clinic Institutional Research Board (IRB) approval was received to conduct a data query and chart review. After IRB approval, an automated electronic medical record (EMR) data search identified 181 pregnancies in 150 patients with International Classification of Diseases (ICD) 9 and 10 codes for both pregnancy and MS from 2000 to 2016. Comprehensive review was undertaken of the EMR of these 150 patients, including all office visits, telephone calls, and direct patient provider EMR messaging encounters. These data were extracted by a single reviewer (AS) to create a database. Patients were excluded from analysis if they did not have MS, the pregnancy occurred prior to being diagnosed with MS, they did not receive their obstetrics care within the Cleveland Clinic network, the pregnancy did not result in a live birth or they did not have a neurologic appointment at the Mellen Center before and after the pregnancy, resulting in 63 pregnancies in 43 women in the final analysis (Figure 1).

Measurements of outcomes of interest

A pregnancy was defined as unplanned if it met one of the following two criteria. The first criterion required that pregnancy was documented as unplanned in the first obstetrics note. If this criterion was not met, then additional information in the chart was considered, including documentation elsewhere in the medical record indicating pregnancy was unplanned, evidence the patient required instruction on starting prenatal vitamins or folic acid, or asked the doctor what she needed to do after the discovery of the pregnancy. If either criterion were met, then the pregnancy was considered unplanned, otherwise, the pregnancy was considered planned. A pregnancy was also considered planned if there was documentation in the chart specifically stating that it was planned.

Measurement of exposure of interest

The primary exposure of interest was the presence of family planning counseling as documented in the EMR. If there was no documented family planning counseling, then it was assumed to have not occurred. Additionally, when family planning counseling occurred, the narrative of the note was explored to see if the counseling occurred after a patient inquiry about the topic. If it was not specified who initiated the conversation, then it was assumed that the provider initiated the conversation.

Measurement of covariates

For both analyses, several covariates were extracted from the patient's EMR to determine their effects on outcome of interests for the purposes of modeling,

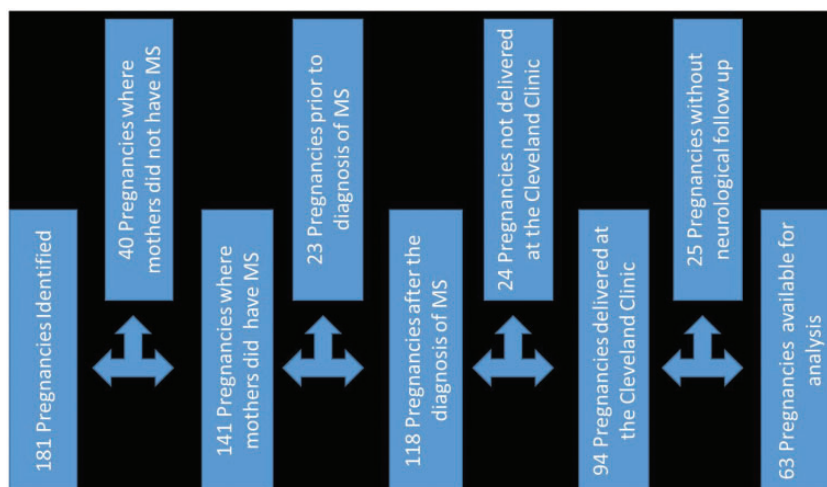


Figure 1. Study population. For the study, 181 pregnancies in 150 patients with International Classification of Diseases (ICD) 10 codes for both pregnancy and multiple sclerosis (MS) from 2000 to 2016 were identified. Patients were excluded from analysis if they did not have MS, the pregnancy occurred prior to being diagnosed with MS, they did not deliver within the Cleveland Clinic network, or they did not have neurologic follow-up at the Mellen Center. These inclusion and exclusion criteria resulted in 63 pregnancies in 43 women for the final analysis.

specifically, demographic factors (age, race, marital status), obstetric history (pregnancy outcome, infant delivery weight, infant APGAR scores, previous pregnancies, previous pregnancy outcomes, complication with delivery, need for caesarian section, breast feeding choice, and breast feeding duration), age at delivery, smoking status, last measured pre-pregnancy body mass index, use of birth control prior to pregnancy, and MS-related clinical information (age of diagnosis of MS, use of DMT during pregnancy, time to restarting DMT post pregnancy, number of relapses the year before pregnancy, number of relapses during the pregnancy, number of relapses the year after and the number of new T2 and enhancing lesions on magnetic resonance imaging (MRI) pre-pregnancy and post-partum MRI).

Statistical analysis

Data were de-identified by removing all health-protected information. Characteristics of patients who had planned versus unplanned pregnancies were compared using Chi-square analysis and *t*-tests for categorical and continuous variables, respectively. Spearman plots with all the collected covariates were constructed from which a model was created with the variables that had the highest five correlation coefficients. From that model, a bidirectional stepwise logistic regression was performed to generate a model with the lowest Akaike information criterion value. Subsequently, the *p*-values of the natural log of the odds (Logit) were calculated

using a *t*-test and Chi-squared test depending on the variable type. The Logit was used to calculate the odds ratio and 95% confidence intervals (CI) that each model component had on the likelihood of unplanned pregnancy. For each analysis, the statistical significance was defined as $p < 0.05$ and a Bonferroni correction was conducted to account for multiple comparisons.

A secondary aim was to explore the proportion of DMT-exposed pregnancies in all planned and unplanned pregnancies. A Chi-squared test was done on the total pool of analyzed pregnancies in this study to compare DMT-exposed and non-DMT-exposed pregnancies. A logistic regression comparing DMT-exposed pregnancies to planning status and birth control usage was conducted. Next, a logistic regression analysis comparing pregnancy outcomes in planned versus unplanned pregnancies and DMT-exposed and non-DMT-exposed pregnancies was undertaken. Pregnancy outcomes were also compared between planned and unplanned pregnancies. R Studio was utilized to perform all statistical analysis.³⁵

Results

Unplanned pregnancy rate and risk factors

Baseline characteristics are summarized in Table 1. Compared to patients with planned pregnancies, patients with unplanned pregnancies were more frequently younger than 30 years old at delivery

Table 1. Baseline demographics comparing unplanned versus planned pregnancies.

	Unplanned	Planned	<i>p</i> value
<i>N</i>	20	43	
Married (<i>n</i> , (%))	12 (60)	42 (98)	<0.001
Pre-pregnancy body mass index (mean (sd))	26.74 (9.12)	25.80 (5.83)	0.63
Age at MS diagnosis (mean (sd))	25.32 (4.96)	27.41 (5.07)	0.13
Age at delivery (mean (sd))	29.48 (5.55)	33.04 (4.33)	0.007
Number of women who had at least one relapse in the pre-pregnancy year (<i>n</i> (%))	6 (30)	17 (40)	0.472
Average ARR pre-pregnancy year (mean (sd))	0.55 (0.83)	0.63 (0.98)	0.759
Number of women who had at least one relapse within the first post-partum year (<i>n</i> (%))	12 (60)	21 (49)	0.417
Average ARR post-partum year (mean (sd))	0.60 (0.68)	0.65 (0.90)	0.822
Duration of maternal MS at delivery (mean (sd))	4.16 (3.53)	5.63 (3.64)	0.139
Assisted reproductive therapy (<i>n</i> (%))	0.0 (0.0)	5 (12)	0.116
In vitro fertilization (<i>n</i> (%))	0 (0.0)	2 (5.0)	0.335
On DMT during pregnancy (<i>n</i> (%))	13 (65)	3 (7)	<0.001
DMT (<i>n</i> (%))			<0.001
None	7 (35.0)	40 (93.0)	
Interferon beta-1a intramuscular	5 (25.0)	0 (0.0)	
Interferon beta-1a subcutaneous	1 (5.0)	0 (0.0)	
Interferon beta-1b subcutaneous	0 (0.0)	1 (2.3)	
Glatiramer acetate	3 (15.0)	2 (4.7)	
Azathioprine	1 (5.0)	0 (0.0)	
Dimethyl fumarate	1 (5.0)	0 (0.0)	
Natalizumab	2 (10.0)	0 (0.0)	
Caesarean section (<i>n</i> (%))	5 (25)	19 (44)	0.149
Birth weight (mean (sd))	3.31 (0.51)	3.13 (0.55)	0.244
Gestational age (mean (sd))	38.75 (1.21)	38.52 (1.69)	0.59
Age of menarche (mean (sd))	12.78 (1.64)	12.04 (1.24)	0.17
Gravida (mean (sd))	1.95 (1.15)	1.77 (1.07)	0.539
Breast feed (<i>n</i> (%))	7 (35)	27 (63)	0.04
Duration of breastfeeding in days (mean (sd))	44 (87)	100 (128)	0.079
Time to restart DMT in days after delivery (mean (sd))	392 (684)	389 (525)	0.984
Smoking (<i>n</i> (%))	6 (30)	5 (12)	0.076
Race (<i>n</i> (%))			0.792
Black	1 (5.0)	4 (9.3)	
Hispanic	1 (5.0)	3 (7.0)	
White	18 (90.0)	36 (83.7)	
EDSS pre-pregnancy (median [IQR])	2.25 [1.00, 2.50]	2 [0.50, 2.50]	0.319
Post-partum EDSS (median [IQR])	2 [1.38, 3.00]	2 [1.50, 2.50]	0.712
Change in EDSS (mean (sd))	0.07 (0.86)	0.31 (0.89)	0.319
New T2 lesions on post-partum MRI (mean (sd))	1.20 (1.74)	2.05 (1.78)	0.082
Enhancing lesions (mean (sd))	0.30 (0.80)	1.10 (1.54)	0.034
New T2 lesions prior to conception (mean (sd))	0.89 (1.45)	1.45 (1.70)	0.22
Enhancing lesions pre-pregnancy (mean (sd))	0.68 (1.38)	0.43 (1.06)	0.431

ARR: annualized relapse rate; DMT: disease modifying therapies; EDSS: Expanded Disability Status Scale; IQR: interquartile range; MRI: magnetic resonance imaging; MS: multiple sclerosis.

(11 (55%) versus seven (17%), $p = 0.004$, Figure 2), unmarried (12 (60%) versus 42 (98%), $p < 0.001$, Figure 3), treated with DMT at the time of conception (13 (65%) versus three (9%), $p < 0.001$), and

reportedly on birth control (five (25%) versus 0 (0%), $p < 0.001$). Additionally, the proportion of those receiving family planning counseling was lower in patients with unplanned pregnancies

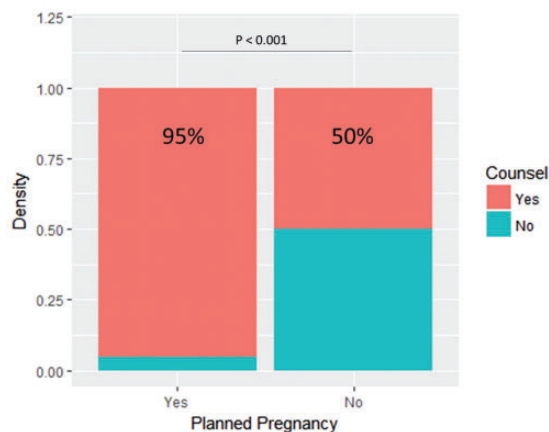


Figure 2. Proportion of planned pregnancies depending on whether the patient received family planning counseling. The number of people who had received family planning and had an unplanned pregnancy versus those who had not received family planning.

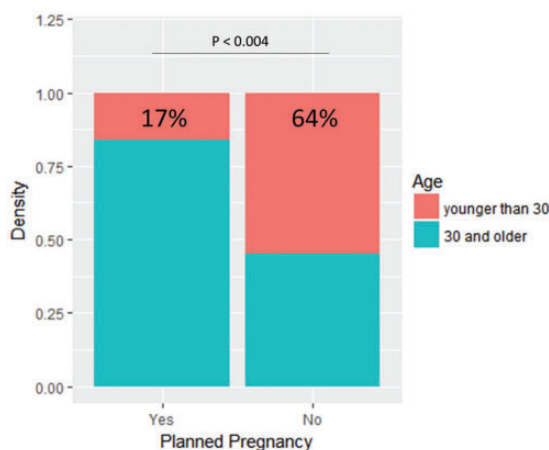


Figure 3. Proportion of planned pregnancies based on age. The rate of planned pregnancy based on whether the patient was younger or older than 30 years of age.

(10 (50%) versus 41 (95%), $p < 0.001$, Figure 4). Of those who received family planning counseling, women with unplanned pregnancies were less likely to initiate the conversation about reproductive goals than those who had planned pregnancies (four (40%) versus 38 (93%) $p < 0.001$). No other differences were significant after Bonferroni correction.

Starting with the simplest logistic regression models, those patients who did not receive family planning counseling had a substantially greater likelihood of having an unplanned pregnancy than those who received counseling (odds ratio (OR) = 20, 95% CI

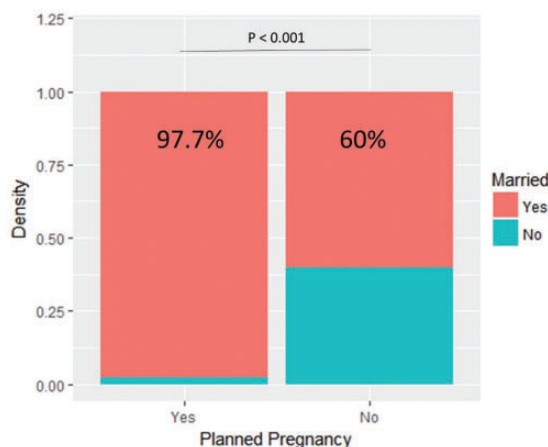


Figure 4. Proportion of planned pregnancies based on marital status. The number of planned pregnancies based on whether the patient was married.

Table 2. Odds ratio of model components that predict planned pregnancies

	Odds ratio (95% CI)
No family planning counseling	0.028 (0.0024, 0.20)
Married at first prenatal visit	17.4 (1.30, 664)
Age ≥ 30	13.9 (2.57, 105)
Prior pregnancy	0.20 (0.03, 1.03)
CI: confidence interval.	

4.5–148, $p < 0.0001$). The correlation coefficient from this model was $R^2 = 0.339$ ($p < 0.001$).

For the more complex model, the four covariates with the highest Spearman correlation coefficients were chosen: pregnancy number of the current pregnancy, counseling, marital status, and age ≥ 30 years at the time of delivery. In final models, those who did not receive family planning counseling had 0.028 times the odds of having a planned pregnancy than those who received counseling ($p < 0.0011$, Table 2 and Figure 5). Patients who were married at their first prenatal visit had 17.4 times the odds of having a planned pregnancy than those who were not married ($p = 0.06$). Those who entered their fourth decade of life had 13.9 times the odds of having a planned pregnancy compared to those who were younger ($p < 0.01$). Finally, patients who were pregnant for the first time had 0.2 times the odds of having a planned pregnancy compared to their multigravida counterparts ($p = 0.07$). The final model

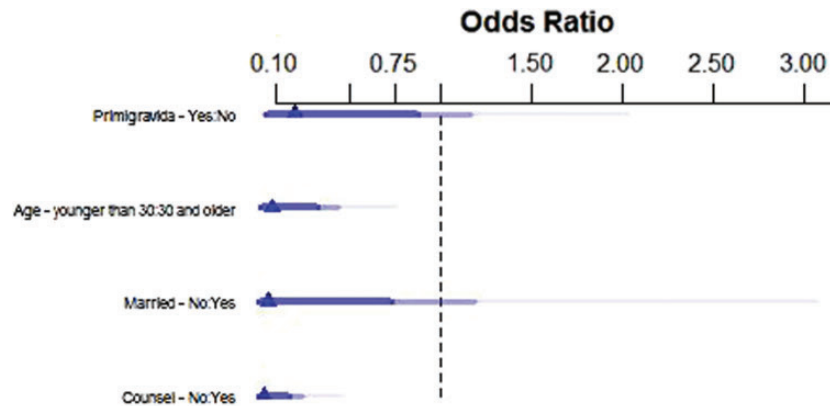


Figure 5. Odds ratios for unplanned pregnancy from the complex post stepwise regression model predicting planned pregnancies. The triangle represents the odds ratio, dark blue line represents 90% confidence interval, medium blue line represents 95% confidence interval, and light blue line represents 99% confidence interval.

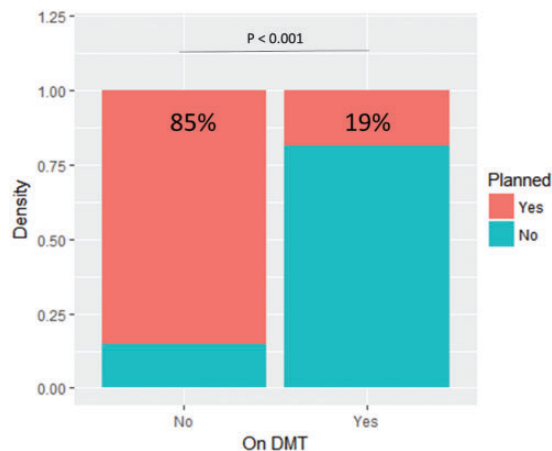


Figure 6. Proportion of individuals on disease-modifying therapies (DMT) depending on their pregnancy status. The number of pregnancies exposed to DMT relative to whether the pregnancy was planned.

after a stepwise regression had a better predictive ability of unplanned pregnancy risk than the original model. The final model had an R^2 of 0.634. This demonstrates that counseling was associated with a lower proportion of unplanned pregnancies.

When examining the secondary outcome of being on DMT at pregnancy onset, those whose pregnancies were unplanned were 25 times (95% CI, 6.25–131) more likely to be on DMT while pregnant than those whose pregnancies were planned ($p < 0.0001$) (Figure 6). The DMTs used in the unplanned group consisted of nine patients on injectable therapies, one patient on azathioprine, one patient on dimethyl fumarate, and two on natalizumab. The three planned pregnancies were all exposed to injectable

therapies. Of the 16 patients who became pregnant while on DMT, four were on birth control. When examining the birth outcomes of unplanned versus planned pregnancy status and DMT exposed and non-exposed patients, there were no statistically significant differences between the comparative groups.

Finally, when comparing the post-relapse rate and MRI outcomes, there was no difference in the rate of relapse whether the pregnancy was planned or unplanned ($p = 0.11$). Roughly 47% of women in the unplanned pregnancy group and 49% of women in the planned pregnancy group had an MRI within 1 year of their delivery. Among those receiving MRIs, there was an increased number of enhancing lesions in women with planned pregnancies ($p = 0.034$). Additionally, a higher percentage of women with planned pregnancies developed either new T2 lesions ($p = 0.04$) or enhancing lesions ($p = 0.015$) within a year after giving birth.

Discussion

MS is a disease that disproportionately affects women of reproductive potential. Therefore, research looking into reproductive health is a critical but sometimes forgotten aspect of clinical research and practice of medicine in general.³⁶ The goal of the present study was to add to existing information concerning pregnancy and the importance of family planning for MS patients in a US population.

These results suggest an association exists between women who were counseled prior to becoming pregnant after an MS diagnosis and a lower proportion of unplanned pregnancies. One possible interpretation of the data would be that family planning counseling

may lead to conscious choices by the patients to take steps to reduce their risk of unplanned pregnancies. However, the reverse interpretation may also be true, that MS patients who are already planning to become pregnant may be more likely to seek out family planning counseling. Given the retrospective design of this study and the limitations of a chart review, it is difficult to determine the temporal relationship between these variables.

The overall proportion of unplanned pregnancies in this cohort was 32%. Prior to this study, the number of unplanned pregnancies was assumed to be 50% in the US,³⁷ based on the national average from non-MS patients. Given the make-up of this cohort, the age-corrected unplanned pregnancy rate in US MS patients should be 28.2%.³⁸ Other known risk factors for unplanned pregnancy, such as age, race, marital status, and whether there was a prior pregnancy, were included in the model. Still, the importance of counseling patients remained. However, half of those patients with unplanned pregnancies were counseled. This observation suggests that either counseling alone is not effective, or that effective counseling needs to be discussed multiple times with the patient instead of mainly just at initial diagnosis and start of a new DMT. In this sample, most of those with unplanned pregnancies who were counseled only had family planning counseling documented once in the chart. Therefore, a possible intervention to address infrequent family planning counseling would be to include a brief review of reproductive goals during all clinical follow-up visits of reproductively able MS patients.

Another important result is the low proportion of birth control use among women on DMT who became pregnant. Of those who were on DMT when they became pregnant, 81% of those pregnancies were unplanned. Only four of 16 women who had DMT exposure during pregnancy were documented as being on highly effective forms of birth control (the pill or an intra-uterine device). This probably underestimates the true birth control usage rate in the unplanned pregnancy group due to not counting the use of barrier methods. This observation highlights the importance of not only discussing family planning and use of birth control when they are placed on DMT but also ensuring patients are using birth control correctly. Although neurologists may not be familiar with all of the options for birth control and their correct usage, they can either encourage patients to discuss these issues with their gynecologist or primary-care physician or make an

appropriate referral. With most clinics implementing EMRs in regular practice, ensuring adequate birth control use while on DMT could be automated. For example, an automated alert could be triggered during an encounter when a woman is on or is prescribed a DMT or other teratogenic medication to remind the physician to provide family planning counseling.

We also found the rate of MRI activity within a year after giving birth appeared to be higher in the patients who had planned pregnancies. This result could suggest that women who stop DMT prior to pregnancy in order to conceive are more likely to have a relapse post-partum. Another explanation could be secondary to the higher rate of breastfeeding in the group with planned pregnancies as opposed to unplanned pregnancies. However, this question warrants further study. Additionally, we also found the percentage of patients having a relapse was greater in the year post partum when compared to the year prepartum in the studied population (37% versus 52%). Potential explanations of this difference could be due to multiple factors. The first was that 25% of the patients were on DMT at the time of pregnancy. The second is that the delay to restarting DMT was on average over a year. Considering that the pre- and post-annual relapse rate (ARR) were 0.605 and 0.634 respectively, this could suggest that annualized relapse rates were not substantially different between the two time epochs. Finally, there was no difference between planned and unplanned groups in regards to the percentage of patients who relapsed in the post-partum year and the ARR.

Another finding is that there were no differences in birth outcomes between the unplanned and planned pregnancies and between DMT exposed versus non-exposed pregnancies. This finding is unexpected due to the previously reported literature of the negative consequences of unplanned pregnancies.¹⁶ This may be due to the study being underpowered to detect these effects.

This study has several limitations. The most critical is that this was a single-center, retrospective chart review. The analysis depended on data available in the chart, which might be incomplete or inaccurate, thus leading to misclassification bias. For example, published evidence suggests that preventive counseling rates may be underreported in the medical chart by as much as 30% compared to what is observed during a clinical encounter.³⁹⁻⁴¹ Similarly,

the difference in patient-initiated reproductive goals discussion may have led to a recording bias in charting family planning counseling among those actively planning to conceive. Another issue is that, although this was an extensive chart review, it only included the records in the Cleveland Clinic Health system. Moreover, because the charts were selected by ICD 9 and 10 codes for pregnancy and MS, this may have caused pregnancies that did not lead to live birth to be excluded. Some of the non-live birth outcomes, if they occurred early enough in the pregnancy, could have been coded only under ICD codes related to spontaneous or elective abortions and not under pregnancy ICD codes and therefore were missed in this retrospective data collection. Additionally, these non-live births could also have been missed if the care for these pregnancies occurred at an outside facility. Another issue was that it was not possible to measure any family planning counseling that the patient may have received from outside sources, such as a pharmaceutical company patient assistance program, pharmacist, or other provider. It is also possible the relationship between family planning and unplanned pregnancy is non-causal. The presence of family planning as noted in the medical records analyzed may be a confounder related to women who are planning a pregnancy. Besides the concerns of errors and bias in the medical record notation when using chart extraction to measure the rate of preventative counseling done in the clinic, some data were impossible to extract from the chart review. Ideally, these issues could be addressed by following a prospective cohort, which would allow data to be collected in a more controlled and systematic fashion. Furthermore, it would allow for increased recruitment due to patients not being required to receive all of their care within one medical system. Another limitation is that the cohort was small, and may have been underpowered to detect an effect for some of the exposures of interest such as birth outcomes and disease state outcomes. However, it should be noted that national pregnancy databases in patients with MS generally only number hundreds of patients, with Brazil's database including 142 patients and Germany's database including 335 patients.^{42,43} Therefore, for a single-center study to include data on 63 pregnancies in patients with MS does not seem too far out of line. The lower pregnancy number may be secondary to various issues such as women having completed their family goals prior to the diagnosis of MS or deciding not to become pregnant because of their disease or other social reasons.⁴⁴ A final issue is that the study population that comes to a tertiary center may differ from the general MS

clinic. In this retrospective study, approximately 26% of identified pregnancies were excluded due to lack of neurologic follow-up data. The relatively high drop-out rate reduces the overall strength of study findings. The fact that many patients had to be censored due to incomplete records could also introduce selection bias. These data did not allow estimation of population-based incidence and prevalence rates and the results therefore may suffer from selection bias, due to this patient population having potentially more aggressive disease, limiting generalizability.

To address these shortcomings, the next step would be to validate the results in a broader clinical setting. Replicating these data in different centers would strengthen the generalizability of the results. Ultimately, a prospective multicenter study in the USA would be optimal to define and control factors of interest in patients with MS with planned or unplanned pregnancies. Ideally, this can be accomplished by establishing a new pre-pregnancy registry in patients with MS or partnering with an existing research collaborative.

Conflict of Interests

Dr Andrew Smith serves as a consultant or speaker for Bayer, Biogen, Genentech, Genzyme, EMD Serono and Novartis.

Jeffrey Cohen reports personal compensation for consulting for Alkermes, Biogen, Convelo, EMD Serono, ERT, Gossamer Bio, Mapi, Novartis, Pendopharm, and ProValuate; speaking for Mylan and Synthon; and serving as a Co-Editor of *Multiple Sclerosis Journal – Experimental, Translational and Clinical*.

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