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Disease-modifying drug treatment before, during, and after pregnancy in women with multiple sclerosis and a live birth

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INTRODUCTION

- Multiple sclerosis (MS) is up to three times more common in women than in men,[1] and the clinical onset is often during childbearing years.[2]
- MS is more commonly diagnosed in women of childbearing age than in any other group.[3]
- More evidence to support decision making in women with MS of childbearing age is needed.[4]
- A better understanding of the 'real-world' disease-modifying drug (DMD) treatment patterns in women with MS and a pregnancy is essential in order to improve available clinical support, healthcare services, and quality of life for women with MS of childbearing age.[2]

OBJECTIVES

- To evaluate DMD treatment before, during, and after pregnancy in women with MS and a live birth using US administrative claims data.
- To determine rates of, and time to, DMD initiation in women with MS and a live birth and no DMD treatment during the third trimester.

METHODS

Data description

- This was a retrospective administrative claims database study using IMS Health Real World Data Adjudicated Claims – US data from between January 1, 2006 and June 30, 2015.
- The database comprises complete, adjudicated, plan-level data including a complete inventory of a patient's prescriptions, inpatient hospital claims, and outpatient medical claims.
- The database consists primarily of commercial Preferred Provider Organization plans and can thus under-represent the patients on Medicaid or Medicare relative to patients on commercial plans (ie, the population aged >65 years).
- Approximately 150 million patients with a medical benefit, and a subset of 95 million patients with both medical and pharmacy benefits, are included in the database.

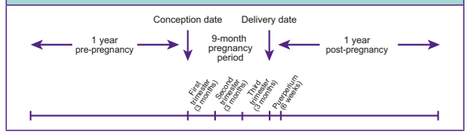
Study population

- Patients were required to have at least one encounter with a diagnosis of MS (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code: 340.xx), be female, and be aged 18–64 years as of the index date.
- Women with MS were required to have at least one clinical encounter with a diagnosis of pregnancy or a pregnancy-related procedure (ie, applicable ICD-9-CM and Current Procedural Terminology codes[5,6]) from the index date to June 30, 2014.
- Continuous eligibility was required from the pregnancy diagnosis minus 1 year to 1 year post-pregnancy diagnosis with no gaps in coverage.
- Patients were required to have a live birth procedure code to be included in the live birth sample.[6]
  - The date of the live birth procedure was used to estimate the date of conception and the pregnancy periods. Continuous eligibility from 1 year before conception to 1 year after the live birth were required inclusion criteria for this cohort.
- For the analysis of DMD initiation post live birth, patients were required to have no claims for a DMD during the third trimester.

Data analysis

- Baseline demographic and clinical characteristics were evaluated.
  - Baseline characteristics evaluated included age, region, and payer type.
  - Clinical characteristics evaluated included overall comorbidity as measured by the Charlson Comorbidity Index and the individual rates of the most common comorbidities in MS.[7]
- DMD treatment was evaluated during the year prior to pregnancy (at 3-month intervals), during the three trimesters of pregnancy, during the puerperium (6 weeks post-pregnancy), and at 1 year post-pregnancy (7–12 weeks post-pregnancy and 3–6, 6–9, and 9–12 months post-pregnancy) (**Figure 1**).

Figure 1. Time periods evaluated for women with MS and a live birth[a]



MS, multiple sclerosis.
[a]Conception date and pregnancy periods are estimated based on the date of the live birth claim.

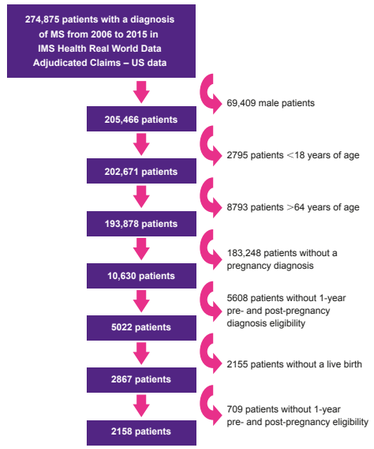
- The proportion of women exposed to DMD treatment during the 12 time periods was evaluated.
- Results were stratified by the number of relapses women experienced in the year prior to pregnancy.
- For descriptive analyses, categorical variables were summarized using percentages. Continuous variables were summarized using means, standard deviations, and medians.

RESULTS

Sample selection

- Of the 205,466 women with MS in the claims database, a total of 2158 women fulfilled the inclusion criteria (ie, a pregnancy diagnosis claim, 1 year of continuous eligibility pre- and post-pregnancy diagnosis, and a live birth) and were included in the analysis (**Figure 2**).

Figure 2. Sample selection for the analysis of DMD treatment in women with MS and a live birth



DMD, disease-modifying drug; **MS**, multiple sclerosis.

Baseline characteristics

- The baseline demographics and clinical characteristics of women with MS and a live birth from 2006 to 2015 are presented in **Table 1**.

DMD treatment patterns in women with MS and a live birth

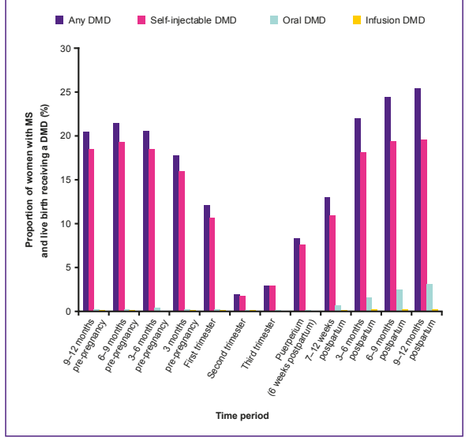
- The proportions of women receiving self-injectable, oral, or infusion DMD treatment before, during, and after their pregnancy are presented in **Figure 3**.
  - Overall, the proportion of women with MS and a live birth receiving DMD treatment was low (range: 1.9–25.5%).
  - The rate of DMD treatment declined during the pre-pregnancy and pregnancy periods.
  - DMD treatment increased during the puerperium and postpartum periods, rising to pre-pregnancy treatment rates 3–6 months after a live birth.
  - Most patients were treated with self-injectable DMDs (range: 1.7–19.6%); the use of oral and infusion DMDs in this sample was low (range: 0.1–3.1% and 0–0.2%, respectively).
- The rate of DMD treatment was higher in women who experienced a greater number of relapses during the year prior to pregnancy (range: 0 relapses, 1.4–21.7%; 1 relapse, 5.7–48.5%; 2 relapses, 4.6–46.1%; ≥3 relapses, 0–66.7%) (**Figure 4**).
  - The rate of DMD treatment was low during the second and third trimesters of pregnancy (range: 0 relapses, 1.4–2.3%; 1 relapse, 5.7–7.4%; 2 relapses, 4.6–6.2%; ≥3 relapses, 0–4.2%).
  - Up to two-thirds of women experiencing ≥3 relapses in the year prior to pregnancy received DMD treatment during the pre-pregnancy and postpartum periods (range: 37.5–66.7% and 29.2–58.3%, respectively).

Table 1. Baseline demographics and clinical characteristics of women with MS and a live birth (2006–2015)

Characteristic	Value
Age	
n	2158
Mean, years (SD)	30.26 (4.68)
Median, years	30
Age grouping, years, %[a]	
18–24	10.5
25–29	33.8
30–34	37.6
35–39	15.6
40–44	2.6
≥45	0.05
Geographic region, %	
Midwest	32.2
Northeast	29.0
South	30.6
West	8.2
Insurance, %[a]	
Commercial	98.6
Medicaid	1.3
Medicare	0.2
Charlson Comorbidity Index score[b]	
Mean (SD)	0.21 (0.59)
Median	0
Comorbidity, %	
Gastrointestinal diseases	13.1
Anxiety	12.3
Thyroid disease	10.8
Depression	10.1
Hyperlipidemia	7.8
Hypertension	5.7
Chronic lung disease	5.6
Diabetes	2.6
Arthritis	2.1
Alcohol disorder	0.2

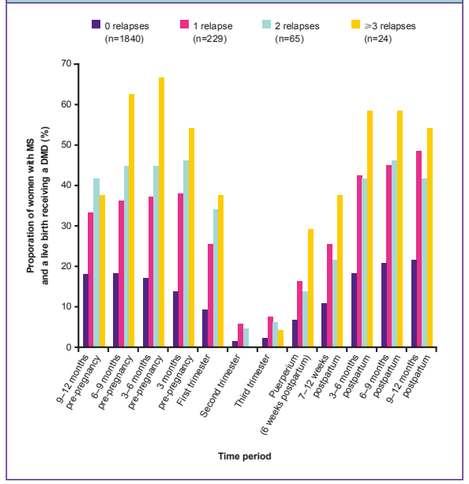
MS, multiple sclerosis; **SD**, standard deviation.
[a]Due to rounding, percentages do not equal 100.0%.
[b]Pre-pregnancy diagnosis.

Figure 3. Proportion of women with MS and a live birth receiving DMD treatment before, during, and after pregnancy



DMD, disease-modifying drug; **MS**, multiple sclerosis.

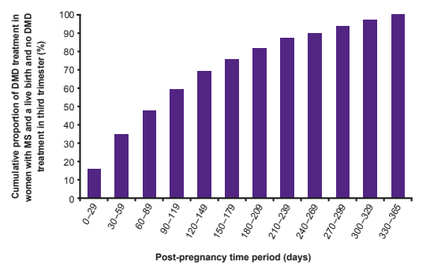
Figure 4. Proportion of women with MS and a live birth receiving DMD treatment before, during, and after pregnancy by number of pre-pregnancy relapses[a]



DMD, disease-modifying drug; **MS**, multiple sclerosis.
[a]Stratified by the number of relapses women experienced in the year prior to conception, as estimated by the date of the live birth.

- Of the 2094 women who did not receive DMD treatment in the third trimester, 596 (28.5%) initiated DMD treatment during the year after pregnancy.
  - The cumulative rate of DMD treatment steadily increased during the postpartum period (**Figure 5**).
    - Approximately 50% of women initiated DMD treatment in the first 90 days after pregnancy.
  - The proportion of women initiating DMD treatment was highest in those who experienced a greater number of relapses in the year prior to pregnancy (0 relapses, 24.5%; 1 relapse, 50.9%; 2 relapses, 54.1%; ≥3 relapses, 60.9%).
  - Women were more likely to initiate DMD treatment if they were exposed to DMD treatment in the pre-pregnancy period, compared with women who did not receive DMD treatment in the pre-pregnancy period (72.6% vs 12.4%, respectively).
    - The median time to DMD initiation was shorter in women exposed to DMD treatment pre-pregnancy compared with women not exposed to DMD treatment pre-pregnancy (84 days vs 122 days, respectively).

Figure 5. Cumulative rate of DMD treatment in the year after pregnancy in women with MS and a live birth who did not receive DMD treatment in the third trimester (n=596)



DMD, disease-modifying drug; **MS**, multiple sclerosis.

LIMITATIONS

- Claims data are not specifically collected for research purposes and missing information may limit the inferences that can be made from the data.
- The ICD-9-CM code for MS does not differentiate between different types of MS (eg, primary progressive MS, relapsing–remitting MS, or secondary progressive MS).
- Administrative claims databases provide information on patients with health insurance administered by regional health plans in the US and results may not be generalizable to patients who self-pay or patients without employer-sponsored commercial health insurance.

CONCLUSIONS

- **Per our knowledge, this is the first claims database study to evaluate DMD treatment in women with MS before, during, and after pregnancy in the US.**
- **The proportion of women with MS with a live birth receiving DMD treatment was low and declined during the pre-pregnancy and pregnancy periods.**
- **The proportion of those receiving DMD treatment was greater in women with MS and a live birth who experienced ≥1 relapse in the pre-pregnancy period.**
- **In women who did not receive DMD treatment in the third trimester, approximately one-quarter initiated DMD treatment in the year after pregnancy; the proportion initiating treatment was greater in women with prior exposure to DMDs in the pre-pregnancy period.**
- **Claims data can be a valuable resource for examining a variety of health services research questions.**

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