

Use of Multiple Sclerosis Drugs Among Live Birth Pregnancies in the U.S.

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Disclaimer

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Background

- Multiple sclerosis (MS)
 - An immune-mediated chronic disease affecting ~ 947,000 people (U.S.)
 - Preferentially affects women (3:1)
 - Typical onset is 20-40 years of age
 - Common cause of non-traumatic neurologic disability in young adults

- Safety issues related to MS in pregnancy became a concern over the past decade
 - Discovery of new treatments transformed MS into a manageable disease
 - Time-to-MS diagnosis and time-to-treatment significantly decreased

Background

- Decreased risk of MS relapse in pregnancy, especially in 3rd trimester
 - The postpartum period is characterized by a significant increase in the MS relapse rate

- Many concerns among women with MS regarding the prepregnancy, pregnancy, and postpartum period
 - Multiple treatment options for MS available, but none recommended for use in women who are pregnant, trying to become pregnant, or who are breastfeeding
 - ~50% of pregnancies are unintended → exposure to MS drugs in early pregnancy still occurs

Objective

- To assess use of MS drugs before, during, and after pregnancy among a large commercially insured U.S. population of women delivering live births

Methods

- Data Source
 - 16 Data Partners from the Sentinel Distributed Database
 - Data from January 1, 2000 to Aug 31, 2017
- Pregnancies ending in live birth deliveries, identified using a validated algorithm
- Cohort Eligibility Criteria
 - Females in the following age groups: 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, and 45-49 years
 - Required to be enrolled in plans with medical and drug coverage for 484 days before their delivery date and 183 days after their delivery date, with gaps in coverage of up to 45 days



Methods

- Exposure identification during pregnancy
 - Prevalence of use during pregnancy of 12 MS drugs overall and individually
 - Dalfampridine, dimethyl fumarate, fingolimod, glatiramer acetate, interferon beta-1a, interferon beta-1b, peginterferon beta-1a, teriflunomide, alemtuzumab, natalizumab, daclizumab, mitoxantrone
 - National Drug Codes and Healthcare Common Procedure Coding System codes

Methods

- Assessed use by trimester and maternal age at delivery
 - Calculation of trimesters and pregnancy start with the validated algorithm
 - 183-91 days pre-pregnancy start, 90 days pre-pregnancy start, 1st, 2nd, and 3rd trimesters, 90 days post-delivery, and 91-183 days post-delivery
- Not all Data Partners contributed over the entire study period
 - 6/16 contributed data over the entire study period
 - 11/16 contributed data > 10 years

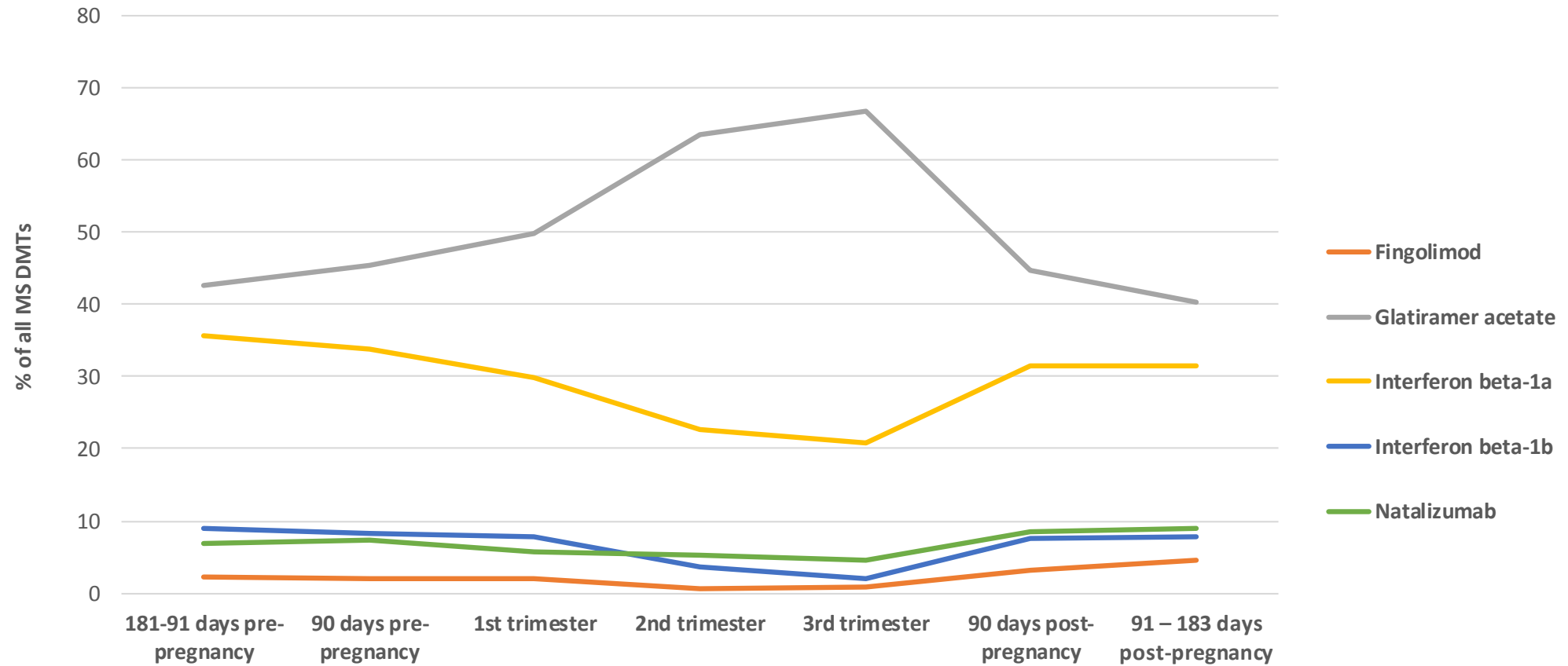
Results

Table 1. Prevalence of Multiple Sclerosis Drug Use among Women with Live Birth Deliveries, by Pregnancy Time Period

Pregnant Cohort	Use in the 183 – 91 Days Pre-pregnancy	Use in the 90 Days Pre-pregnancy	Any Use During Pregnancy	Any Use, 1st Trimester	Any Use, 2nd Trimester	Any Use, 3rd Trimester	Use in the 90 Days Post-pregnancy	Use in the 91 – 183 Days Post-pregnancy
Number of Pregnancies	2,205,383	2,205,383	2,205,383	2,205,383	2,205,383	2,203,324	2,205,383	2,205,383
Drug of Interest								
All multiple sclerosis drugs	1,407 (100.0%)	1,243 (100.0%)	1,011 (100.0%)	944 (100.0%)	269 (100.0%)	246 (100.0%)	958 (100.0%)	1,330 (100.0%)
Dalfampridine	9 (0.6%)	10 (0.8%)	6 (0.5%)	6 (0.6%)	1 (0.4%)	0 (0.0%)	7 (0.7%)	14 (1.0%)
Dimethyl fumarate	58 (4.1%)	54 (4.3%)	51 (5.0%)	45 (4.7%)	9 (3.3%)	11 (4.5%)	63 (6.6%)	113 (8.4%)
Fingolimod	33 (2.3%)	26 (2.0%)	20 (1.9%)	20 (2.1%)	2 (0.7%)	2 (0.8%)	30 (3.1%)	60 (4.5%)
Glatiramer acetate	602 (42.7%)	564 (45.3%)	501 (49.5%)	470 (49.7%)	171 (63.6%)	164 (66.7%)	427 (44.6%)	538 (40.4%)
Interferon beta-1a	502 (35.6%)	421 (33.8%)	307 (30.3%)	283 (29.9%)	61 (22.7%)	51 (20.7%)	302 (31.5%)	419 (31.5%)
Interferon beta-1b	126 (8.9%)	104 (8.3%)	78 (7.7%)	74 (7.8%)	10 (3.7%)	5 (2.0%)	72 (7.5%)	104 (7.8%)
Peginterferon beta-1a	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.2%)	6 (0.4%)
Teriflunomide	2 (0.1%)	3 (0.2%)	2 (0.1%)	2 (0.2%)	2 (0.7%)	2 (0.8%)	3 (0.3%)	7 (0.5%)
Alemtuzumab	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)
Natalizumab	99 (7.0%)	91 (7.3%)	61 (6.0%)	55 (5.8%)	14 (5.2%)	11 (4.5%)	81 (8.5%)	120 (9.0%)
Daclizumab	1 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mitoxantrone	3 (0.2%)	1 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	1 (0.0%)

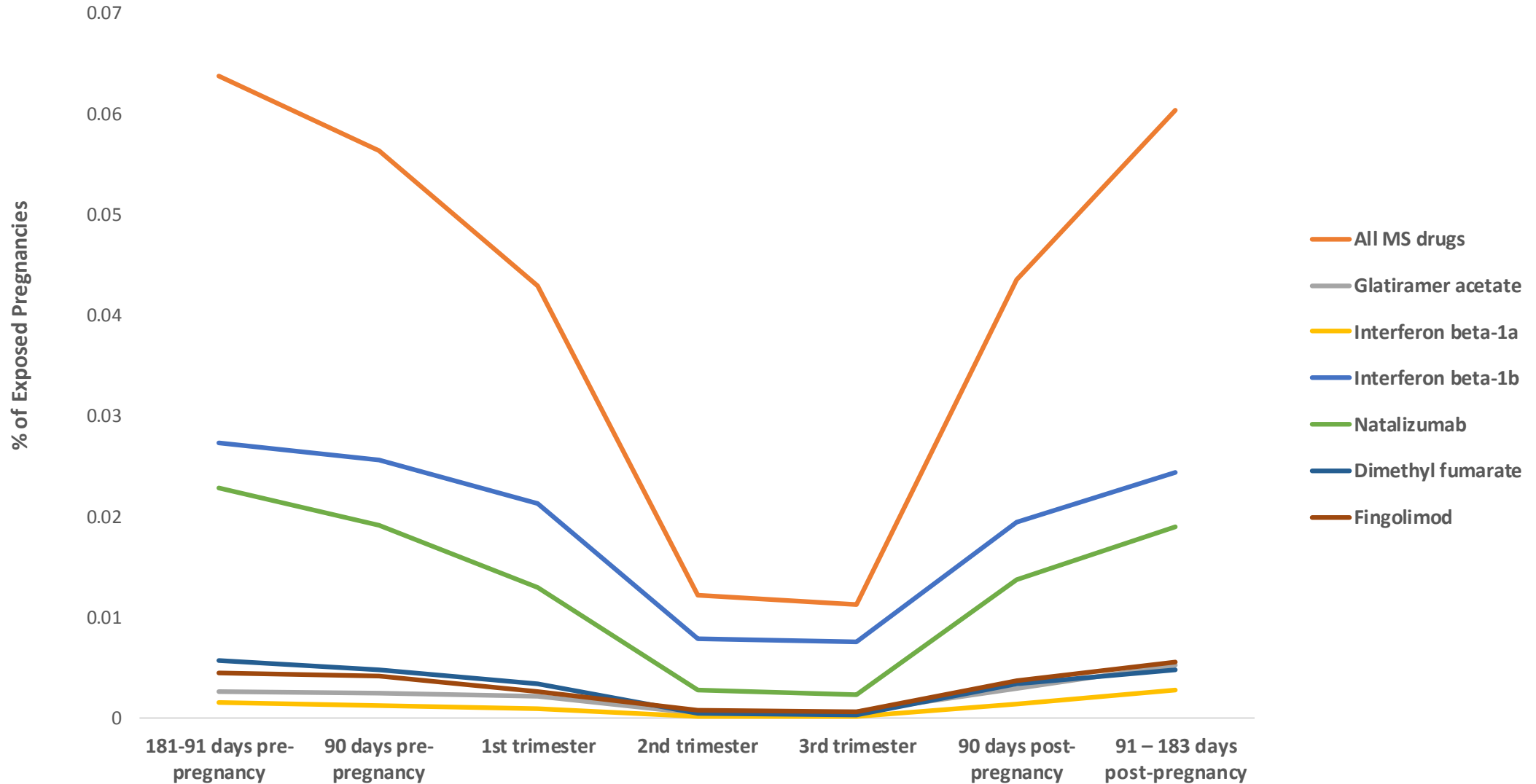
Results

Figure 1. Percent of DMTs Dispensed among Women with Live Birth Deliveries, by Pregnancy Time Period, Jan 2000-Aug 2017



Results

Figure 2. Prevalence of Multiple Sclerosis Drug Use among Women with Live Birth Deliveries, by Pregnancy Time Period, Jan 2000- Aug 2017



Results

Table 2. Prevalence of Multiple Sclerosis Drug Use among Women with Live Birth Deliveries, by Maternal Age at Delivery, Jan 2000- Aug 2017

Pregnant Cohort	15-19 years	20-24 years	25-29 years	30-34 years	35-39 years	40-44 years	45-49 years
Number of Pregnancies	116,609 (100.0%)	289,734 (100.0%)	547,521 (100.0%)	743,631 (100.0%)	406,602 (100.0%)	92,907 (100.0%)	8,379 (100.0%)
All multiple sclerosis drugs	7 (0.0%)	54 (0.0%)	211 (0.0%)	384 (0.1%)	273 (0.1%)	69 (0.1%)	13 (0.2%)

Discussion

- In Sentinel's pregnancy cohort, use of MS drugs in pregnancy was rare
 - Sentinel covers 66.9 million members
 - ~ 50% of all pregnancies in the U.S. are insured by Medicaid

- First generation MS drugs were the most commonly dispensed in pregnancy
 - More safety data

- A considerable decline in MS drug use use from six months before through the first trimester, followed by an increase in use post-delivery
 - Safety vs. MS relapse

Discussion

- The clinical guidelines are closely followed to discontinue MS drugs before planning pregnancy, unless the risk for MS activity outweighs the risks associated with their use in pregnancy
 - Capturing live births
 - Capturing unplanned pregnancies?
 - Capturing women with higher MS activity?
- Women with lower MS activity more likely to be pregnant
 - Lower MS drug use?

Conclusion

- Use of MS drugs was low overall
- Our results suggest that many women with MS drug use who deliver live births discontinue drugs by early pregnancy and resume use to near pre-pregnancy levels within 6 months
- The resumption of treatment within 6 months suggests the need for more research on safety during lactation

Acknowledgements

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