Adverse Pregnancy Outcomes in Myasthenia Gravis: A Retrospective Cohort Study in a US Health Insurance Claims Database

Melanie H. Jacobson[1], Rupa Makadia[1], John Sheehan[2*], Nathan Hall[1], Jill Hardin[1], Sicong Huang[3], Ran Sun[4], Rebecca Zaha[4], Alexis A. Krumme[1]

[1]Janssen Research & Development, LLC, Global Epidemiology; [2]Janssen Global Services, LLC, Medical Affairs, Immunology; [3]Janssen Research & Development, LLC, Immunology; [4]Janssen Research & Development, LLC, R&D Data Science.

*Presenting author

Introduction

- Pregnancy is common among individuals with autoantibody conditions and adverse perinatal outcomes have been documented.[1]

- However, previous studies in myasthenia gravis (MG) have produced mixed results.

Objective

- To determine the burden of adverse perinatal outcomes in MG
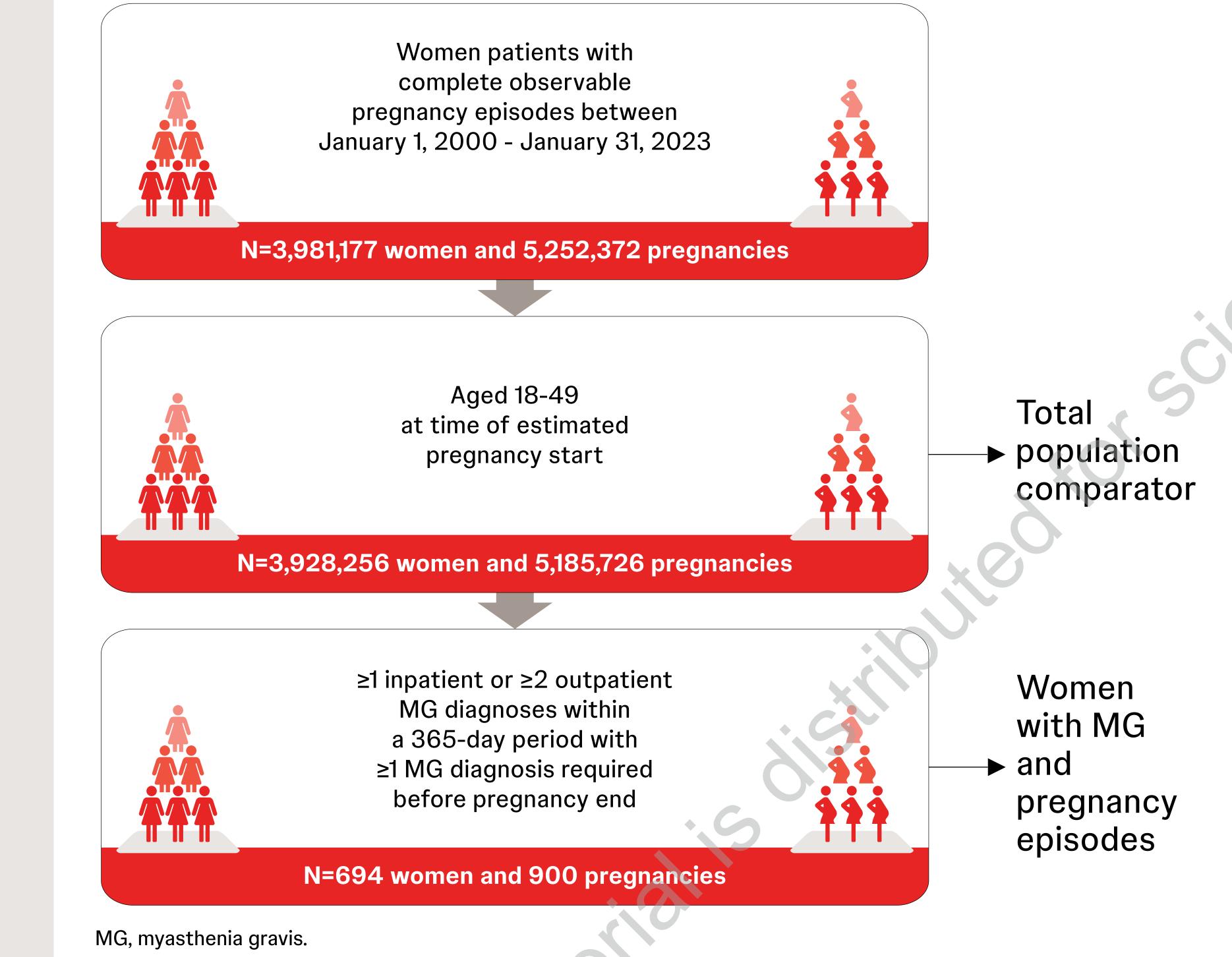
Methods

- We conducted a retrospective cohort study in the United States (US) Merative(R) MarketScan(R) Commercial Database between 2000–2023 (**Figure 1**).

- Pregnancies in women aged 18-49 years were identified and dated using a validated algorithm that establishes a hierarchy of routine healthcare encounters in pregnancy.[1]

- Among live births, maternal and infant records were linked using an algorithm that relies on a shared family insurance identification number.[2]

- Two cohorts of pregnancies were created: one with evidence of MG diagnosis and one of the total population.

- MG was defined by ≥1 inpatient or ≥2 outpatient diagnoses within a 365-day period, with ≥1 diagnosis required before pregnancy end.

- The prevalence of six perinatal outcomes was calculated in the MG and total populations: live birth, spontaneous abortion, Cesarean (C-) section, preeclampsia, preterm birth, and small for gestational age (SGA). Outcome definitions were based on diagnosis and procedure codes.

- For comparisons, outcome prevalence in the total population was age-standardized to the MG population age distribution.

Results

- A total of 694 individuals with MG had 900 pregnancies and 3,928,256 individuals in the total population had 5,185,726 pregnancies (**Figure 1**).

- The prevalence of live birth (75.0% vs 72.6%, p=0.10) and spontaneous abortion (20.4% vs 22.2%, p=0.20) was similar in the MG and age-adjusted total population, respectively (**Table 1; Figure 2**).

- Preeclampsia (10.7% vs 7.1%, p<0.01) and C-section (42.9% vs. 36.7%, p<0.01) were more frequent among MG than the total population (**Table 1; Figure 2**).

- The largest relative differences were noted for preterm birth (18.0% vs. 9.9%, p<0.01) and SGA (4.3% vs. 1.7%, p<0.01), which were more prevalent among MG than the total population (**Table 1; Figure 2**).

Figure 1. Patient inclusion flow chart

Women patients with complete observable pregnancy episodes between January 1, 2000 - January 31, 2023

N=3,981,177 women and 5,252,372 pregnancies

Aged 18-49 at time of estimated pregnancy start

N=3,928,256 women and 5,185,726 pregnancies

Total population comparator

≥1 inpatient or ≥2 outpatient MG diagnoses within a 365-day period with ≥1 MG diagnosis required before pregnancy end

N=694 women and 900 pregnancies

Women with MG and pregnancy episodes

MG, myasthenia gravis.

- On average, women with MG were older than those in the total population (mean age: 32 vs 30 years, respectively).

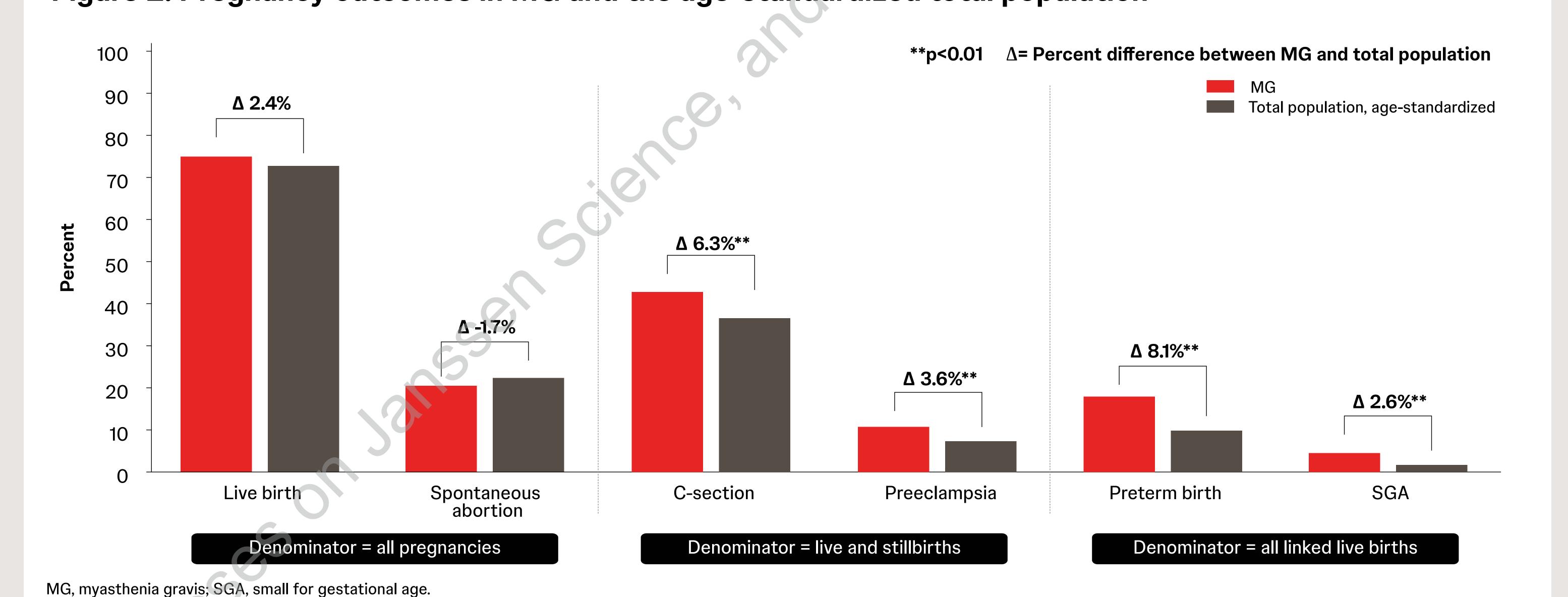### Figure 2. Pregnancy outcomes in MG and the age-standardized total population

**p<0.01   Δ= Percent difference between MG and total population

Legend: MG (red), Total population, age-standardized (dark gray)

Δ 2.4% (Live birth); Δ -1.7% (Spontaneous abortion); Δ 6.3%** (C-section); Δ 3.6%** (Preeclampsia); Δ 8.1%** (Preterm birth); Δ 2.6%** (SGA)

Denominator = all pregnancies (Live birth, Spontaneous abortion)
Denominator = live and stillbirths (C-section, Preeclampsia)
Denominator = all linked live births (Preterm birth, SGA)

MG, myasthenia gravis; SGA, small for gestational age.

Table 1. Pregnancy outcomes in MG and the age-standardized total population

Pregnancy outcome[a]	MG			Total Population		Age-standardized total population	
	N with outcome	N denominator	Percent	N with outcome	N denominator	Percent	p values[b]
Live birth	675	900	75.0	3,832,613	5,185,726	72.6	0.10
Spontaneous abortion	184	900	20.4	1,078,896	5,185,726	22.2	0.20
C-Section	292	680	42.9	1,347,071	3,853,754	36.7	<0.01
Preeclampsia	73	680	10.7	271,997	3,853,754	7.1	<0.01
Preterm birth	87	483	18.0	264,122	2,713,667	9.9	<0.01
SGA	21	483	4.3	45,648	2,713,667	1.7	<0.01

[a]The denominator for live birth and spontaneous abortion is all pregnancies. The denominator for C-section and preeclampsia is live births. The denominator for preterm birth and small for gestational age is all linked live births. [b]Proportions with pregnancy outcomes were compared using chi-square tests.
C-section, caesarean section; MG, myasthenia gravis; SGA, small for gestational age.

Conclusions

- In this study, MG was associated with a greater burden of certain adverse perinatal outcomes, occurring in both mother and infant.

- Further research is needed to understand drivers of pregnancy outcomes in MG.

Strengths and Limitations

- This study used a large US claims database spanning 23 years that contains comprehensive, longitudinal capture of patient encounters with the healthcare system.

- We examined a broad suite of outcomes in both the mother and infant.

- Pregnant individuals with MG may be more closely monitored than the total population, potentially leading to larger observed differences in certain pregnancy outcomes.

- Insurance claims databases lack clinical information on disease severity, potentially limiting the ability to identify determinants of adverse pregnancy outcomes.

Autoantibody: MG

References:
1. Matcho A, Ryan P, Fife D, Gifkins D, Knoll C, Friedman A. Inferring pregnancy episodes and outcomes within a network of observational databases. *PLoS One*. 2018 Feb 1;13(2):e0192033. doi: 10.1371/journal.pone.0192033.
2. Weaver J, Hardin JH, Blacketer C, Krumme AA, Jacobson MH, Ryan PB. Development and evaluation of an algorithm to link mothers and infants in two US commercial healthcare claims databases for pharmacoepidemiology research. *BMC Medical Research Methodology*. 2023 Oct 21;23(1):246.