Impact of race and social determinants of health on exacerbations in generalized myasthenia gravis

Louis Jackson[1], Zhiwen Liu[1], Jacqueline Pesa[1], Alicia K Campbell[1], Ashley Anderson[2]

[1]Janssen Scientific Affairs, LLC, Titusville, NJ, USA; [2]Department of Neurology, Houston Methodist, Houston, TX, USA

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Introduction

- Generalized myasthenia gravis (gMG) is a rare, chronic autoantibody disease characterized by muscle weakness and fatigue
- Individuals with gMG bear a substantial burden from their disease. In a retrospective study, 38.6% of patients experienced a myasthenia gravis (MG)-related hospitalization, 18.4% a myasthenic crisis, and 24.6% MG exacerbations, with most occurring within 2–3 years of diagnosis[1]
- Limited research has identified differences in disease presentation and clinical outcomes in MG among different racial/ethnic patient populations[2–4]

Objective

- To estimate the association of race/ethnicity and MG exacerbation among individuals with gMG

Methods

Study design

- This was a retrospective cohort study using data from HealthVerity, consisting of a large, de-identified, US closed medical and pharmacy insurance claims database and data collected directly from large, nationally representative diagnostic laboratories
- Additional social determinants of health (SDOH) variables were linked from the Agency for Healthcare Research and Quality (AHRQ)[5] based on residential ZIP codes for a subset of patients to evaluate the robustness of the effects of race/ethnicity on MG exacerbation after adjusting for SDOH factors

Patient selection criteria

- Inclusion criteria included:
  - ≥1 claim with a diagnosis code for MG in the primary billing position for an inpatient visit or ≥2 claims on separate days within a 60-day period with a diagnosis code for MG in any billing position for an outpatient, emergency department, or other type of visit between January 1, 2017, and June 30, 2023
    - The index date was defined as the date of the first qualifying diagnosis (as defined earlier) when ≥1 MG diagnosis occurred in the prior 12 months (patients had ≥2 MG diagnoses when entering the cohort)
  - ≥12 months of continuous health plan enrollment prior to the index date
  - Age ≥18 years on the index date
  - Race/ethnicity data available
- Exclusion criteria included:
  - Claims with MG diagnosis codes for visits to ophthalmologic specialists only during the entire cohort identification period

Definitions and variables

- MG diagnosis was based on International Classification of Diseases, 10th Revision, Clinical Modification diagnosis codes G70.00 and G70.01
- MG exacerbation was defined as an inpatient episode with MG diagnosis at admission

- Patients were followed until the earlier of the end of continuous enrollment or the end of the study period
- Patient race/ethnicity data were captured from the dataset and categorized as Asian, Black, Hispanic, or White
- SDOH data (percentage with health insurance, income) from the AHRQ database between 2017 and 2020 were linked using residential ZIP codes for an available subset of the study cohort in the HealthVerity dataset
  - For the percentage of the population with health insurance coverage, thresholds described were <5.3%, ≤11.3%, and >11.3%
  - For income per capita (US dollars, inflation-adjusted to data file year), thresholds described were ≤US$29,999, <US$50,000, and ≥US$50,000[6]

Statistical analysis

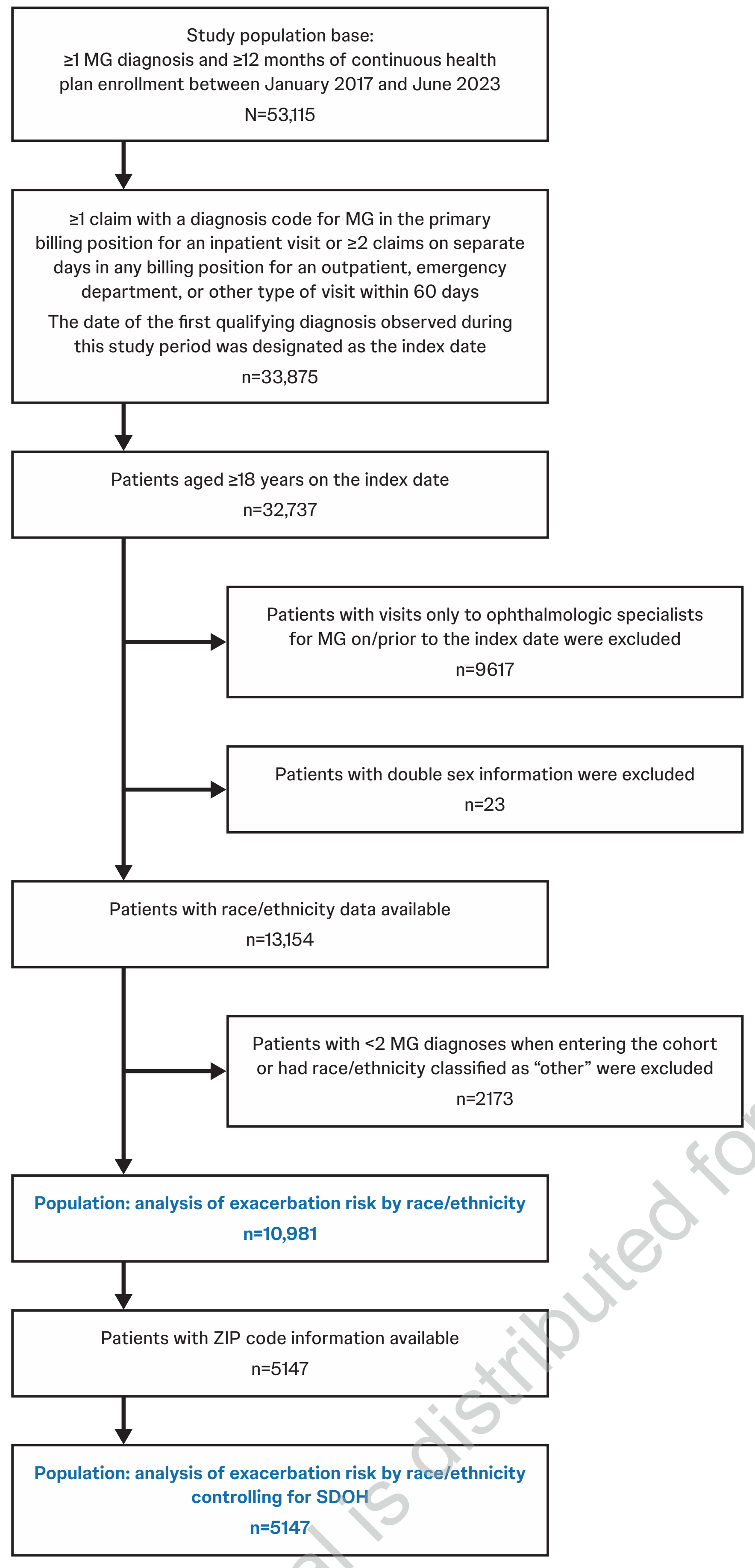
- Baseline patient characteristics were summarized using descriptive statistics
- To control for confounding factors, the inverse probability of treatment weighting (IPTW) using baseline variables was constructed with multinomial distribution for race/ethnicity—Asian, Black, Hispanic, or White. The application of these weights to the study population created a pseudo-population in which confounders were equally distributed across comparison groups
- Risk of exacerbation (i.e., incidence rate ratio for the occurrence of ≥1 exacerbation during follow-up) was calculated in the IPTW population using White patients as the reference group
- To further assess the robustness of the association between race/ethnicity and MG exacerbation, risk of exacerbation was further adjusted for SDOH factors for the subset of patients with data available. Three successive analyses were conducted, adjusting for percentage of population with health insurance coverage (<5.3% reference, <11.3%, >11.3%), for income, and for both percentage of population with health insurance coverage and income

Results

Patients

- 10,981 patients with gMG were included in this analysis (**Figure 1**)

FIGURE 1: Patient attrition flowchart



Study population base:
≥1 MG diagnosis and ≥12 months of continuous health plan enrollment between January 2017 and June 2023
N=53,115

≥1 claim with a diagnosis code for MG in the primary billing position for an inpatient visit or ≥2 claims on separate days in any billing position for an outpatient, emergency department, or other type of visit within 60 days
The date of the first qualifying diagnosis observed during this study period was designated as the index date
n=33,875

Patients aged ≥18 years on the index date
n=32,737

Patients with visits only to ophthalmologic specialists for MG on/prior to the index date were excluded
n=9617

Patients with double sex information were excluded
n=23

Patients with race/ethnicity data available
n=13,154

Patients with <2 MG diagnoses when entering the cohort or had race/ethnicity classified as “other” were excluded
n=2173

Population: analysis of exacerbation risk by race/ethnicity
n=10,981

Patients with ZIP code information available
n=5147

Population: analysis of exacerbation risk by race/ethnicity controlling for SDOH
n=5147

MG, myasthenia gravis; **SDOH**, social determinants of health.

- Overall, 63.8% were White, 19.4% were Black, 12.0% were Hispanic, and 4.8% were Asian (**Table 1**)

- Baseline demographics and clinical characteristics for the groups of Black and White patients (**Table 1**) included:
  - Mean age was 50.0 years among Black and 62.4 years among White patients
  - 71.9% of Black and 57.9% of White patients were female
  - 61.3% of Black and 31.7% of White patients were recipients of Medicaid
  - Prior MG exacerbations were reported among 13.2% of Black and 8.6% of White patients
  - Comorbidities, including hypertension and diabetes, occurred at a numerically similar rate in the Black and White patient groups, despite Black patients being generally younger
- Weighted baseline patient demographics and clinical characteristics are provided in **Table 1**

TABLE 1: Patient demographics and clinical characteristics

Characteristic	Unweighted				Weighted			
	Asian (n=529)	Black (n=2130)	Hispanic (n=1317)	White (n=7005)	Asian (n=559)	Black (n=2130)	Hispanic (n=1330)	White (n=7001)
Female, n (%)	321 (60.7)	1531 (71.9)	872 (66.2)	4054 (57.9)	336 (60.2)	1334 (62.6)	806 (60.6)	4332 (61.9)
Mean age, years (SD)	57.8 (17.7)	50.0 (16.9)	55.2 (19.5)	62.4 (18.1)	58.4 (18.1)	57.0 (17.1)	57.9 (19.2)	59.4 (18.7)
Age group, n (%)								
18–44 years	125 (23.6)	840 (39.4)	385 (29.2)	1182 (16.9)	123 (22.0)	502 (23.6)	313 (23.5)	1611 (23.0)
45–54 years	82 (15.5)	442 (20.8)	233 (17.7)	943 (13.5)	109 (19.5)	328 (15.4)	205 (15.4)	1090 (15.6)
55–64 years	145 (27.4)	427 (20.0)	269 (20.4)	1725 (24.6)	129 (23.1)	486 (22.8)	309 (23.2)	1632 (23.3)
>65 years	177 (33.5)	421 (19.8)	430 (32.6)	3155 (45.0)	198 (35.4)	813 (38.2)	504 (37.9)	2667 (38.1)
Quan-Charlson Comorbidity Index score, mean (SD)	1.4 (1.9)	1.6 (2.2)	1.6 (2.1)	1.7 (2.1)	1.9 (2.3)	1.6 (2.2)	1.7 (2.1)	1.6 (2.1)
Health plan insurance, n (%)								
Commercial	200 (37.8)	313 (14.7)	314 (23.8)	2018 (28.8)	143 (25.6)	567 (26.6)	346 (26.0)	1807 (25.8)
Medicare Advantage	107 (20.2)	476 (22.3)	367 (27.9)	2634 (37.6)	187 (33.5)	635 (29.8)	429 (32.3)	2274 (32.5)
Medicaid	213 (40.3)	1306 (61.3)	615 (46.7)	2219 (31.7)	218 (39.0)	885 (41.5)	532 (40.0)	2792 (39.9)
Unknown	9 (1.7)	35 (1.6)	21 (1.6)	134 (1.9)	10 (1.8)	42 (2.0)	23 (1.7)	128 (1.8)
Prior MG exacerbation, n (%)	32 (6.0)	281 (13.2)	112 (8.5)	602 (8.6)	59 (10.6)	188 (8.8)	133 (10.0)	639 (9.1)
Comorbidity (in >20% of individuals), n (%)								
Hypertension	273 (51.6)	1287 (60.4)	770 (58.5)	4315 (61.6)	342 (61.2)	1285 (60.3)	811 (61.0)	4235 (60.5)
Diabetes	119 (22.5)	567 (26.6)	407 (30.9)	1686 (24.1)	140 (25.1)	535 (25.1)	336 (25.3)	1772 (25.3)
Hypothyroidism	114 (21.6)	352 (16.5)	330 (25.1)	1942 (27.7)	152 (27.2)	521 (24.5)	336 (25.3)	1746 (24.9)
Deficiency anemia	116 (21.9)	630 (29.6)	323 (24.5)	1626 (23.2)	118 (21.1)	527 (24.7)	335 (25.2)	1716 (24.5)
Autoimmune condition	123 (23.3)	573 (26.9)	373 (28.3)	1894 (27.0)	163 (29.2)	589 (27.7)	353 (26.5)	1903 (27.2)
Other neurological disorders	92 (17.4)	401 (18.8)	257 (19.5)	1672 (23.9)	138 (24.7)	497 (23.3)	308 (23.2)	1562 (22.3)
Chronic pulmonary disease	105 (19.8)	655 (30.8)	344 (26.1)	2129 (30.4)	199 (35.6)	632 (29.7)	413 (31.1)	2072 (29.6)
Obesity	82 (15.5)	873 (41.0)	499 (37.9)	2580 (36.8)	215 (38.5)	785 (36.9)	489 (36.8)	2557 (36.5)
Depression	92 (17.4)	533 (25.0)	331 (25.1)	2010 (28.7)	185 (33.1)	621 (29.2)	367 (27.6)	1910 (27.3)
Treatment received, n (%)								
Acetylcholinesterase inhibitor	259 (49.0)	1077 (50.6)	666 (50.6)	3100 (44.3)	245 (43.8)	986 (46.3)	615 (46.2)	3248 (46.4)
Corticosteroid	209 (39.5)	983 (46.2)	577 (43.8)	3032 (43.3)	260 (46.5)	939 (44.1)	586 (44.1)	3053 (43.6)
Nonsteroidal immunosuppressant	88 (16.6)	431 (20.2)	224 (17.0)	1232 (17.6)	91 (16.3)	386 (18.1)	237 (17.8)	1249 (17.8)
Rescue treatment	43 (8.1)	287 (13.5)	124 (9.4)	684 (9.8)	61 (10.9)	232 (10.9)	136 (10.2)	721 (10.3)
MG-related thymectomy	2 (0.4)	8 (0.4)	2 (0.2)	21 (0.3)	16 (2.9)	6 (0.3)	2 (0.2)	23 (0.3)

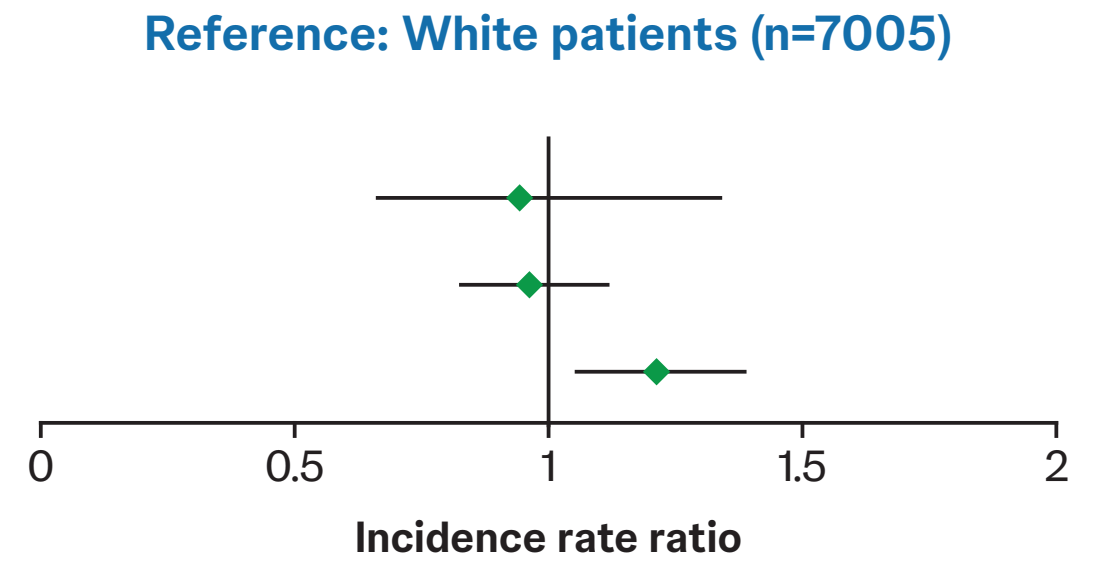
MG, myasthenia gravis; **SD**, standard deviation.

Risk of exacerbation by race/ethnicity

- During follow-up, the risk of MG exacerbation was significantly higher among Black versus White patients (**Figure 2**)
- There was no significant difference in risk of exacerbation among White versus Hispanic or White versus Asian patients (**Figure 2**)

FIGURE 2: Weighted risk of MG exacerbation during follow-up for Asian, Hispanic, and Black patients with gMG, relative to White patients (n=10,981)

Race/ethnicity	Incidence rate ratio	95% CI
Asian (n=529)	0.94	0.66–1.34
Hispanic (n=1317)	0.96	0.82–1.12
Black (n=2130)	1.21	1.05–1.39

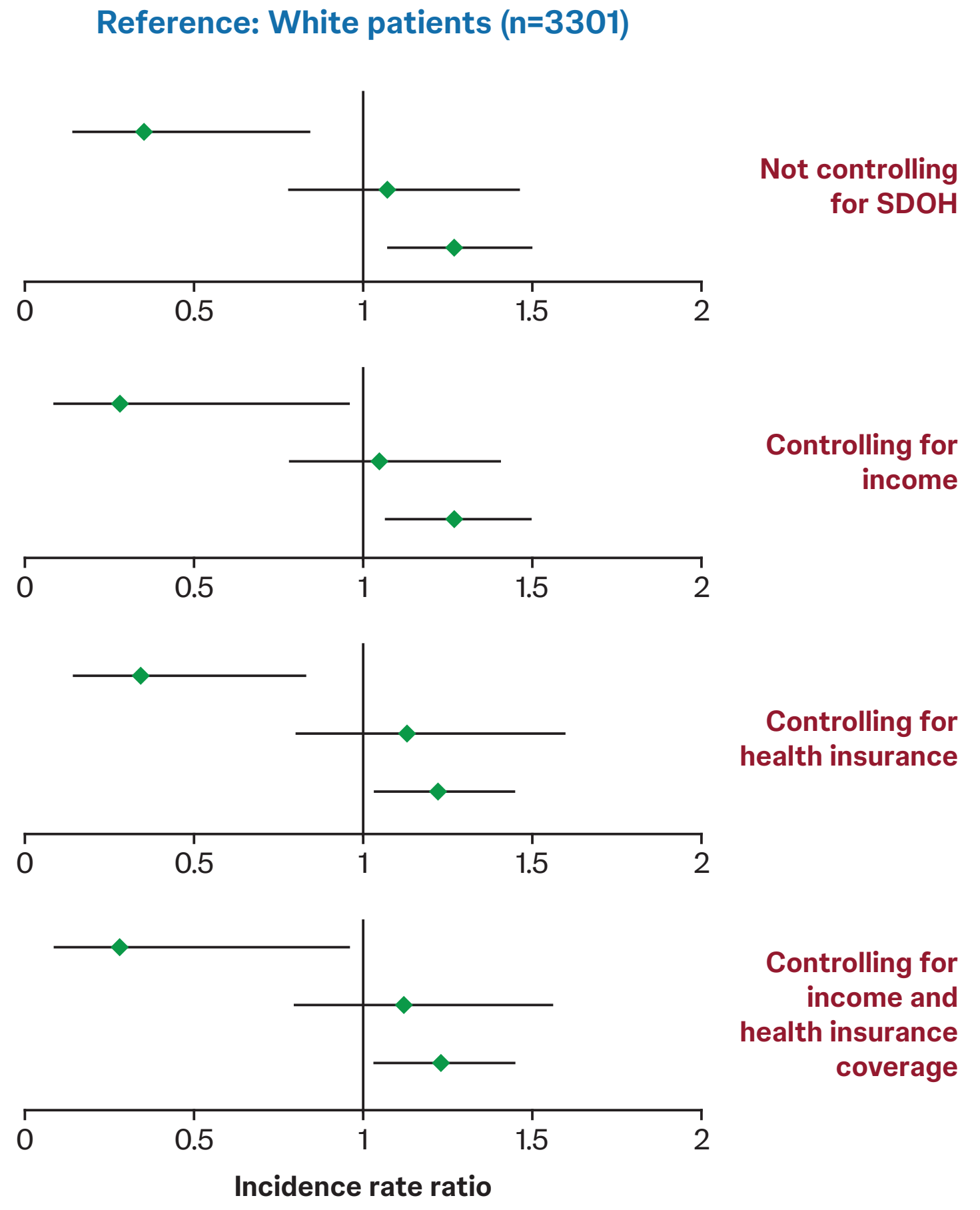


Model was weighted for all demographics, health insurance plans, comorbidities (congestive heart failure, valvular heart disease, pulmonary circulation disorders, hypertension, paralysis, other neurological disorders, chronic pulmonary disease, diabetes, hypothyroidism, renal failure, liver disease, chronic peptic ulcer disease, lymphoma, metastatic cancer, coagulation deficiency, obesity, weight loss, fluid and electrolyte disorders, blood loss anemia, deficiency anemia, alcohol abuse, drug abuse, psychoses, and depression), and MG treatments at baseline.
CI, confidence interval; **gMG**, generalized myasthenia gravis; **MG**, myasthenia gravis.

- In the subset of patients who could be linked to SDOH data (n=5147), the observed association remained consistent
  - After controlling for percentage of population with health insurance coverage and for income, as individual measures and combined, the risk of MG exacerbation remained higher among Black versus White patients (**Figure 3**)

FIGURE 3: Weighted risk of MG exacerbation during follow-up for Asian, Hispanic, and Black patients with gMG, relative to White patients, among a subset of patients who could be linked to SDOH data (n=5147)

Race/ethnicity	Incidence rate ratio	95% CI
Asian (n=174)	0.35	0.14–0.84
Hispanic (n=395)	1.07	0.78–1.46
Black (n=1277)	1.27	1.07–1.50
Asian (n=174)	0.28	0.08–0.96
Hispanic (n=395)	1.05	0.78–1.41
Black (n=1277)	1.27	1.06–1.50
Asian (n=174)	0.34	0.14–0.83
Hispanic (n=395)	1.13	0.80–1.60
Black (n=1277)	1.22	1.03–1.45
Asian (n=174)	0.28	0.08–0.96
Hispanic (n=395)	1.12	0.79–1.56
Black (n=1277)	1.23	1.03–1.45



Model was weighted for all demographics, insurance plans, comorbidities (congestive heart failure, valvular heart disease, pulmonary circulation disorders, hypertension, paralysis, other neurological disorders, chronic pulmonary disease, diabetes, hypothyroidism, renal failure, liver disease, chronic peptic ulcer disease, lymphoma, metastatic cancer, coagulation deficiency, obesity, weight loss, fluid and electrolyte disorders, blood loss anemia, deficiency anemia, alcohol abuse, drug abuse, psychoses, and depression), and MG treatments at baseline, in addition to the variables listed on the right-hand side of each panel. <5% threshold of linked zip code having health insurance was used to determine ‘low’ health insurance coverage.
CI, confidence interval; **gMG**, generalized myasthenia gravis; **MG**, myasthenia gravis; **SDOH**, social determinants of health.

Limitations

- The number of Asian patients was low; therefore, no conclusions can be drawn about this population based on our analysis
- “Hispanic” describes a person who is descended from a Spanish-speaking population and that person may be of any race. This is a limitation of the HealthVerity data
- SDOH data were not measured at the patient level and served only as proxies

Conclusions

- These results suggest potential racial disparities in MG care as evidenced by a higher risk of MG exacerbation among Black vs White patients with gMG, even after controlling for select SDOH variables
- This finding warrants further investigation into the potential mechanisms and factors associated with varying clinical outcomes for patients with gMG who belong to different racial/ethnic groups
- At-risk populations should be a focus for healthcare providers, disease management efforts, and patient support entities

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Disclosures

LJ, **ZL**, **JP**, and **AKC** are employees of Janssen Scientific Affairs, LLC, a Johnson & Johnson Company, the sponsor of this study. **AA** is a speakers bureau member for Alexion Pharmaceuticals and consultant for Janssen Pharmaceuticals.

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References available upon request