

Racial and Ethnic Differences in Antiseizure Medications Among People With Epilepsy on Medicaid

A Case of Potential Inequities

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Abstract

Background and Objectives

Being on a newer, second-, and third-generation antiseizure medication (ASM) may represent an important marker of quality of care for people with epilepsy. We sought to examine whether there were racial/ethnic differences in their use.

Methods

Using Medicaid claims data, we identified the type and number of ASMs, as well as the adherence, for people with epilepsy over a 5-year period (2010–2014). We used multilevel logistic regression models to examine the association between newer-generation ASMs and adherence. We then examined whether there were racial/ethnic differences in ASM use in models adjusted for demographics, utilization, year, and comorbidities.

Results

Among 78,534 adults with epilepsy, 17,729 were Black, and 9,376 were Hispanic. Overall, 25.6% were on older ASMs, and being solely on second-generation ASMs during the study period was associated with better adherence (adjusted odds ratio: 1.17, 95% confidence interval [CI]: 1.11–1.23). Those who saw a neurologist (3.26, 95% CI: 3.13–3.41) or who were newly diagnosed (1.29, 95% CI: 1.16–1.42) had higher odds of being on newer ASMs. Importantly, Black (0.71, 95% CI: 0.68–0.75), Hispanic (0.93, 95% CI: 0.88–0.99), and Native Hawaiian and Other Pacific Island individuals (0.77, 95% CI: 0.67–0.88) had lower odds of being on newer ASMs when compared with White individuals.

Discussion

Generally, racial and ethnic minoritized people with epilepsy have lower odds of being on newer-generation ASMs. Greater adherence by people who were only on newer ASMs, their greater use among people seeing a neurologist, and the opportunity of a new diagnosis point to actionable leverage points for reducing inequities in epilepsy care.

Antiseizure medications (ASMs) are the primary treatment for people living with epilepsy. There are dozens of ASMs available and the decision of which ASM may be best is based on the specific type of seizures and other clinical factors discussed between a patient and their physician. Broadly, ASMs can be put into 3 generations, based on the chronology of their availability in the United States.^{1–3} First-generation ASMs include drugs such as carbamazepine,

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phenytoin, and valproate. Second-generation ASMs include drugs such as gabapentin, levetiracetam, and zonisamide. Finally, third-generation ASMs include the newest drugs such as lacosamide and perampanel. These ASMs differ in efficacy and tolerability based on a variety of factors including type of epilepsy and side effect profile. Although there is substantial variation across and within drug generations, as well as patient-specific factors that affect tolerance, some newer-generation ASMs may have fewer side effects and may be more effective for seizure control.^{2,4,5} However, this is not universally true, and not all newer ASMs are the best choice for a given patient.⁶⁻⁸ Nonetheless, patterns of prescriptions may provide an interesting marker of quality of care and disparities in epilepsy treatment.

Finding the right medication is often a trial-and-error process that is ideally a careful collaboration between patients and their epilepsy care providers. Patients with limited access to quality care may not receive the benefit of thorough consideration of ASM regimen and response. It has been shown that “use of second-generation [ASMs], access to specialty care, and deliberate efforts to change medications following epilepsy-related hospital encounters improved outcomes.”⁹ This likely reflects closer follow-up and heightened efforts in finding proper therapy and indicates that in addition to generation being an important care outcome, switching ASMs is a critical part of this relationship.

Among the elderly, older-generation ASMs are more commonly prescribed, and people on older ASMs have lower adherence.¹⁰⁻¹³ Although the use of third-generation ASMs has increased, there are geographic differences in the use of these newer ASMs.^{5,14} Layered on these patterns of usage is the observation that there are racial and ethnic differences in adherence to ASMs, with minoritized populations having overall lower adherence. These differences in adherence can be driven by the combination of many factors, including potential structural barriers in access to optimal ASM management (e.g., access to specialty care and affordability of medications), mistrust of the health care system, and doctor-patient communication. However, to understand factors that affect usage patterns, it is first necessary to document them, and prior studies of usage patterns by generation of ASM use remain limited.¹⁵⁻²⁰ Of the work that evaluated the relationship between race and ASM use, there have been mixed findings. Although some studies have not found racial/ethnic differences in the overall use of ASMs, at least 1 identified that Black individuals have lower odds, compared with White individuals, of receiving an appropriate ASM.^{11,21-23} Thus, the careful evaluation of racial differences in ASM use can fill a critical gap in knowledge and allow us to identify correctable health inequities in people with epilepsy.

To improve our understanding of differences in ASM use, we undertook this study to determine (1) whether newer ASMs were associated with greater adherence, (2) whether some racial/ethnic groups were less likely to receive newer ASMs,

and (3) whether lower use of new ASMs might explain some portion of the racial/ethnic differences in adherence. We hypothesized that newer-generation ASMs would be associated with greater odds of adherence and that racial and ethnic minoritized populations would have lower odds of being prescribed newer-generation ASMs than nonminoritized people with epilepsy.

Methods

Data Source

This study uses 5 years (2010–2014) of Medicaid claims data from 15 states: California, Georgia, Iowa, Louisiana, Michigan, Minnesota, Missouri, Mississippi, New Jersey, Pennsylvania, South Dakota, Tennessee, Utah, Vermont, West Virginia, and Wyoming. These years and states were selected at the time of study initiation based on data availability, as other states and more recent years could not be obtained. The data included Medicaid enrollment, demographic information, inpatient claims, other services (that includes outpatient provider claims), and a file that includes all prescriptions filled during the study period while the individual was enrolled in Medicaid. Medicaid is a state-administered insurance program that covers some low-income individuals, those with disabilities, some children, and other potentially vulnerable groups. These data have been described previously.^{16,24}

Inclusion Criteria

We identified people with epilepsy in our data using a combination of diagnosis codes (either one epilepsy [345.xx] or 2 seizure [780.39], with an additional code at least 30 days later) and at least 2 fills of an ASM, as previously described.²⁵ We further limited our study population to those who were enrolled in Medicaid for the entire study period, had valid prescription data, and were in the 18–64 age range. Notably, all individuals included had a full 5 years of complete data. Our study focused on adults with epilepsy; therefore, we excluded children (<18 years old). Beyond age 64 individuals would also be enrolled in Medicare, which may affect billing and claims completeness. Similarly, we excluded individuals who were identified as being dually enrolled in Medicare and Medicaid as this is a unique study population warranting explicit exploration. Finally, we excluded patients who were in a nursing home.²⁶

Antiseizure Medications

We identified ASM prescription fills in the claims data by using a list published by the American Epilepsy Society to link the generic drug names listed in the historical files to the National Drug Code.²⁷ We then assigned each ASM to its respective generation (first, second, or third) based on its availability in the United States (Table 1).³ Importantly, some of the ASMs in our data were not yet fully approved during our study period; however, they still represent the most up-to-date and comprehensive list of ASMs that could have been used. For analysis purposes, we combined second

Table 1 List of Antiseizure Medications by Generation

First generation	Carbamazepine, clonazepam, diazepam, ethosuximide, phenobarbital, phenytoin, clorazepate, methsuximide, acetazolamide, primidone, divalproex sodium, lorazepam, and valproic acid
Second generation	Felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, topiramate, zonisamide, and tiagabine
Third generation	Clobazam, eslicarbazepine, ezogabine, lacosamide, perampanel, rufinamide, vigabatrin, fosphenytoin, and everolimus

and third generation into 1 category, representing newer ASMs, as is commonly done.^{4,9} We used the highest generation an individual was ever on during the study period to categorize their generation. We also identified patients who were on different generations of ASMs, either concurrently or consecutively, as a marker of ASM switching and quality of care and used these data in the analyses.

Outcomes of Interest

There were 2 main outcomes of interest in this study. The first was adherence to ASMs, as measured by the proportion of days covered (PDC), where <0.8 represents not adherent.^{28,29} The PDC represents the days' supply of medication that was dispensed divided by the total number of days in that calendar period. For example, if a patient were to fill 30-day prescriptions on January 1, January 29, March 1, and April 10, we would say that they had 120 days' supply/129 days or a PDC of 0.93. The second outcome of interest was being on a newer-generation (second or third) ASM.

Exposures

We aimed to assess 2 associations: (1) ASM generation and adherence and (2) race/ethnicity and ASM generation. Thus, we had 1 exposure and 1 outcome for each association. When using generation of ASM as the exposure, we created a new variable that combined the ASM generation with whether the individual was on multiple generations. This was done to capture ASM switching, a marker of quality of care and disease severity that may affect adherence and our measurement of it. This information had to be combined due to the high correlation between these 2 variables (i.e., because patients were classified based on their highest generation, there would be no patients coded as first generation who also had switched), and therefore, it was not valid to include them both independently in the model. Although this new variable adds complexity to interpretation, we nonetheless could identify patterns in the effect of generation on adherence. We also used the race/ethnicity categories provided to us in the Medicaid personal summary file, based on the patient's enrollment form that is submitted to Medicaid. We do not know who completes this information, and whether that is the beneficiary, a family member or caregiver or someone else on their behalf—an important limitation when studying

disparities. The categories were American Indian or Alaskan Native (AIAN), Asian or Pacific Islander, Black, Hispanic, Native Hawaiian or Other Pacific Islander (NHOPI), Other, and White. The 2 exposures of interest were being on a newer-generation ASM and race/ethnicity.

Covariates

We included several important covariates. First, we included the following demographics: age at epilepsy index date, sex (male/female; collected in a similar manner as race/ethnicity discussed above), county rurality from the Rural-Urban Continuum Code,³⁰ neurologists per 100,000 at the county level obtained from the Area Health Resources File,³¹ and index year (to account for those who are newly diagnosed). To adjust for disease severity, seizure control, and contact with the health care system, we determined whether an individual was treated by a neurologist (using the provider taxonomy on the claim) and whether they were in the top quartile of emergency department (ED) visits during the 5-year study period. We identified ED visits using revenue center codes, procedure codes, and place of service codes (Place of Service: 23; Revenue Center Codes: 0450, 0451, 0452, 0456, 0459, and 0981; Procedure Codes: 99281, 99282, 99283, 99284, 99285, and 99288). The provider taxonomy was unable to separate epileptologists from neurologists. We also included the Elixhauser comorbidities, a commonly used set of comorbidities, to account for overall morbidity.³² In previous work, we have identified injuries as an important aspect of care related to utilization.²⁴ Therefore, we also included injuries identified via the Clinical Classification Software (CCS) for other injuries and conditions due to external causes.³³ Finally, we included developmental disorders, as individuals with these may have more severe epilepsy, also identified from CCS codes.

Analyses

We created multilevel logistic regression models, to account for clustering by state, by allowing a random intercept by state. The 2 exposures and 2 outcomes were assessed in key combinations to address 3 research questions: (1) Do patients on newer generation ASMs have greater odds of being adherent? (2) Are there racial/ethnic differences in the use of newer-generation ASMs? (3) After accounting for generation of ASM, are there persistent racial/ethnic differences in adherence? This suite of questions and the models that flow from them were designed to address 1 overarching question: Do we find evidence that racial/ethnic differences in ASM adherence can be explained by avoidable differences in the quality of clinical management and thus represent inequities in care?

To address these 3 questions and the overarching theme, we constructed 2 unique regression model structures (see eAppendix 1 in the Supplement for the full equations, links.lww.com/CPJ/A390). The first model (model 1) examined the association between ASM generation and adherence to ASMs (the outcome), and model 2 examined the association between race/

Table 2 Study Population

n (%)	n = 78,534
Demographics	
Race/ethnicity	
White	41,975 (53.4)
Black	17,729 (22.6)
AIAN	505 (0.6)
Asian	1,246 (1.6)
Hispanic	9,376 (11.9)
NHOPI	1,154 (1.5)
Other	6,549 (8.3)
Age, y	
18–24	17,027 (21.7)
25–34	20,560 (26.2)
35–44	16,127 (20.5)
45–54	17,061 (21.7)
55+	7,759 (9.9)
Female	44,651 (56.9)
Rurality	
Nonrural	62,939 (80.1)
Rural	15,557 (19.8)
Missing	38 (0.0)
Neurologists per 100,000, median [interquartile range]	3.38 [1.57–5.41]
ASM use and adherence	
Generation of ASM	
First generation, no switch	20,115 (25.6)
Second generation, total	51,104 (65.1)
Second generation, switch	11,658 (14.8)
Second generation, no switch	39,446 (50.2)
Third generation	7,315 (9.3)
Third generation, switch	25 (0.03)
Third generation, no switch	7,290 (9.3)
Adherent	39,070 (49.7)
Utilization and neurologic care	
No. of ED visits, median [interquartile range]	5.00 [1.00–13.00]
Neurologist visit	35,794 (45.6)
Comorbidities	
Hypertension	27,791 (35.4)
Psychoses	27,367 (34.8)

Table 2 Study Population (*continued*)

n (%)	n = 78,534
Developmental disorders	24,312 (31.0)
Chronic lung disease	21,114 (26.9)
Injuries	20,826 (26.5)
Electrolyte disorder	15,187 (19.3)
Paralysis	14,362 (18.3)
Deficiency anemia	12,909 (16.4)
Diabetes	11,895 (15.1)
Drug abuse	9,939 (12.7)
Obesity	9,670 (12.3)
Depression	9,570 (12.2)
Hypothyroidism	9,130 (11.6)
Alcohol abuse	5,865 (7.5)
Weight loss	4,454 (5.7)
Liver disease	3,991 (5.1)
Diabetes w/complication	3,977 (5.1)
Congestive heart failure	3,275 (4.2)
Arthritis	3,258 (4.1)
Coagulopathy	3,229 (4.1)
Peripheral vascular disease	3,146 (4.0)
Tumor	2,971 (3.8)
Valvular disease	2,588 (3.3)
Renal failure	2,501 (3.2)
Pulmonary circulation disorder	1,444 (1.8)
Blood loss	986 (1.3)
HIV/AIDS	825 (1.1)
Metastatic cancer	410 (0.5)
Lymphoma	252 (0.3)
Peptic ulcer disease	98 (0.1)

Abbreviations: AIAN = American Indian or Alaskan Native; ASM = antiseizure medication; NHOPI = Native Hawaiian or Other Pacific Islander.

ethnicity and being on newer ASMs (the outcome). We report the adjusted odds ratios (aORs), with 95% confidence intervals (CIs), with the unadjusted odds ratios reported in eTable 1, links. www.com/CPJ/A390. We also conducted 2 sensitivity analyses. The first examined whether, among patients on newer ASMs, there were persistent inequities in the use of third-generation ASMs. Recognizing that second-generation ASMs are becoming increasingly used as first-line therapy, we sought to understand whether there were more specific inequities when evaluating second vs third generation. We also examined whether the

Table 3 ASM Generation and Adherence by Race/Ethnicity

n (%)	White, n = 41,975	Black, n = 17,729	AIAN, n = 505	Asian, n = 1,246	Hispanic, N = 9,367	NHOPI, n = 1,154	Other, n = 6,549
Generation of ASM							
First generation	9,788 (23.3)	5,271 (29.7)	101 (20.0)	382 (30.7)	2,519 (26.9)	398 (34.5)	1,656 (25.3)
Second generation	27,713 (66.0)	11,393 (64.3)	378 (74.9)	736 (59.1)	5,969 (63.7)	646 (56.0)	4,269 (65.2)
Third generation	4,474 (10.7)	1,065 (6.0)	26 (5.1)	128 (10.3)	888 (9.5)	110 (9.5)	624 (9.5)
Adherent	22,379 (53.3)	7,225 (40.8)	227 (45.0)	683 (54.8)	4,542 (48.4)	647 (56.1)	3,367 (51.4)

Abbreviations: AIAN = American Indian or Alaskan Native; ASM = antiseizure medication; NHOPI = Native Hawaiian or Other Pacific Islander.

observed inequities were consistent among just those individuals in our study who were newly diagnosed (2012, 2013, or 2014). Finally, we stratified the analysis to those who saw a neurologist vs those who did not to examine whether our findings were influenced by access to care. These supplemental analyses can be found in eTable 2 and eTable 3, links.lww.com/CPJ/A390. SAS version 9.3 was used for data cleaning, whereas R version 3.6.3 was used for analysis.

Standard Protocol Approvals, Registrations, and Patient Consents

This study was approved by the Institutional Review Board and the Privacy Board of the Centers for Medicare and Medicaid Services.

Data Availability

Access to these data is restricted under a Data Users Agreement from the Centers for Medicare & Medicaid Services.

Results

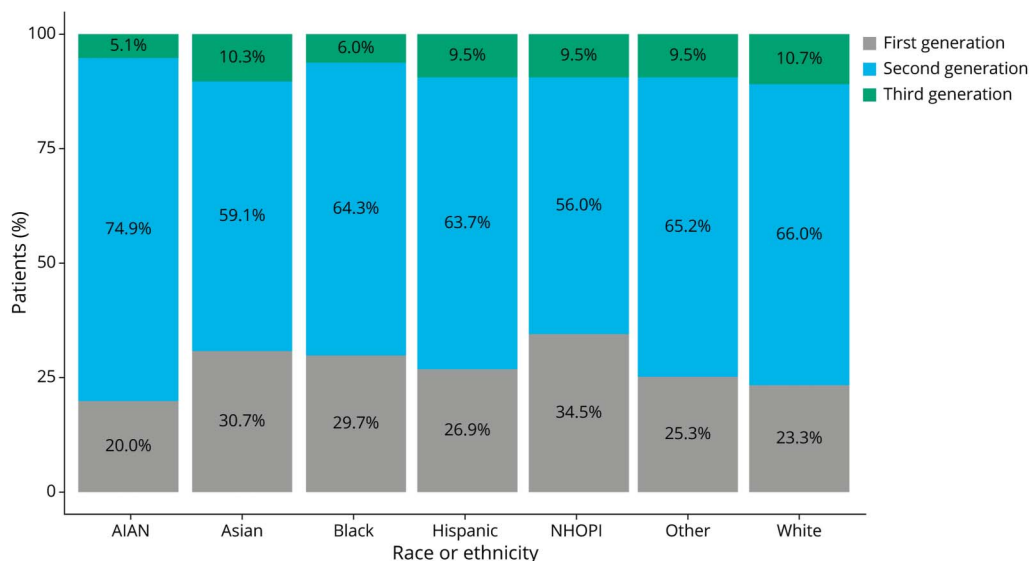
Overall, our study included 78,534 adult people with epilepsy, with 87.4% in a blind or disabled Medicaid eligibility status. Although a majority were White (41,975), there were 17,729 Black individuals, 505 AIAN, 1,246 Asians, 9,376 Hispanics, 1,154 NHOPI, and 6,549 Other (Table 2). Most included patients (80.1%) lived in nonrural areas. A quarter (25.6%) of patients were on first-generation ASMs, with 65.1% on second generation and 9.3% on third generation (Table 2). Nearly 60% of patients were on multiple generations of ASMs during the study period (Table 2). Only half (49.7%) of all patients were adherent to ASMs. Compared with White individuals, every other racial/ethnic group assessed had a higher proportion of individuals on first-generation ASMs, except for AIANs (Table 3 and Figure 1). The AIAN group is small, and thus, the estimates may not be stable. Furthermore, while 10.7% of White individuals were on third-generation ASMs, only 6.0% of Black individuals and 5.1% of AIAN were (Table 3 and Figure 1).

In our first logistic regression model, we observed that, compared with those on first-generation ASMs, those on newer (second or

third generation) ASMs, who did not switch generations, had greater odds of being adherent, although this effect was not significant for third-generation ASMs (Table 4, model 1). Those who were on newer generations, but had switched, had lower odds of being adherent compared with those who remained on first-generation ASMs (Table 4, model 1). We also observed racial and ethnic differences with respect to what ASMs a patient was taking. When compared with White individuals, Black (aOR: 0.71 [95% CI: 0.68–0.75]), Hispanic individuals (aOR: 0.93 [95% CI: 0.88–0.99]), and NHOPI individuals (aOR: 0.77 [95% CI: 0.67–0.88]) all had lower odds of being on newer-generation ASMs. Meanwhile, AIAN individuals had 1.30 (95% CI: 1.03–1.64) times the odds, and the relationship was less clear for Asian individuals (aOR: 0.93 [95% CI: 0.82–1.06]) (Table 4, model 2). We also observed that those who were diagnosed with epilepsy later (newly diagnosed in 2013 or 2014), who were female, younger, high utilizers, or who received care from a neurologist had higher odds of being on a newer-generation ASM (Table 4, model 2). Even after adjusting for these inequities in generation, there were persistent racial/ethnic adherence differences in Black, Asian, and Hispanic individuals; all had lower odds of adherence when compared with White individuals (Table 4, model 1).

In a supplemental analysis, we observed that among those on newer ASMs, Black and AIAN individuals had lower odds of being on third-generation ASMs (vs second generation) compared with White individuals (eTable 2, links.lww.com/CPJ/A390). When we restricted to newly diagnosed (incident) cases, the relationships were generally stronger, and the OR for being on a being on newer-generation ASM was similar or slightly lower (eTable 2, links.lww.com/CPJ/A390). Note that this lowering of ORs moved the AIAN estimate closer to the null. Finally, our third supplemental analysis stratified between those who saw a neurologist and those who did not. We observed that although the overall findings were similar, disparities were more common among those who did not see a neurologist (eTable 2, links.lww.com/CPJ/A390). Compared with White individuals, Black and Hispanic individuals had lower odds of being on a newer ASM whether they saw a neurologist or not. Asian and NHOPI had lower odds of being on a newer ASM only when

Figure 1 Antiseizure Medication Generation Stratified by Race/Ethnicity



The displayed percentage represents the column percent for that generation and will sum to 100% within each race/ethnicity.

they did not have a neurologist. We also observed that a substantially lower percent of AIAN, Asian, Hispanic, and NHOPI individuals saw a neurologist than White individuals (eTable 3, links.lww.com/CPJ/A390). Furthermore, a slightly higher percentage of Black individuals saw a neurologist when compared with White individuals (eTable 3, links.lww.com/CPJ/A390).

Discussion

Our work provides several important findings. First, we identified clear racial and ethnic differences in ASM use among people with epilepsy on Medicaid. Specifically, we observed that minoritized populations had lower odds, compared with White individuals, of being on newer-generation ASMs even after adjusting for a wide variety of factors, including receiving care from a neurologist. These differences were seen for Black, Asian, and Hispanic individuals and Native Hawaiian and Other Pacific Islanders. The patterns were less clear for American Indians and Alaskan Natives. The differences we observed most likely reflect inequities in care rather than simple differences or benign disparities. We posit that this is the case given adjustment for a wide array of factors that could explain away these inequities and the consistency of our results across our supplemental analyses. Similarly, although newer ASMs may not be the best choice for all patients, we currently have no medical explanation for these observed racial and ethnic differences in their use. Thus, the mechanisms driving these differences are worthy of further investigation.

We also observed that newer ASM generation was associated with better adherence. Although this pattern was only seen in

those who did not switch generations of ASM, this is potentially due to the switch in ASM generation being caused by poor seizure control or side effects that influenced their adherence. While adding complexity to the interpretation, ASM switching is an inextricable component evaluating population-level ASM use. Those who do not switch ASM generations likely tolerate the ASM generation they are on well. For those who have not yet demonstrated access to responsive clinical care (switchers), we find evidence that the odds of adherence are lower with newer-generation drugs. In addition, we observed that individuals who were diagnosed later in the study period and were treated by a neurologist had greater odds of being on newer-generation ASMs.

These findings are consistent with previous literature that has identified racial and ethnic differences in ASM adherence.^{15-19,34} Although this work and other inequities in epilepsy care and outcomes are well established,^{16,18,19,35-37} the picture of ASM inequities remains incomplete. The prior work examining inequities was limited to a more narrow set of racial and ethnic groups, reducing our understanding of potentially more complex patterns.²¹ Our study builds on these limitations and clarifies that most minoritized populations are less likely to be on newer ASMs.^{38,39}

From the patterns we observed, there is the potential that a sizeable proportion of people with epilepsy may not be on an optimal ASM regimen, and the differences appear to reflect clear racial and ethnic inequities in epilepsy care. This could be due to several factors such as access to neurologists and epileptologists. Indeed, in our supplemental analyses, we saw that some, but not all, of these disparities were eliminated when stratified by those who received care from a neurologist

Table 4 Models 1 and 2, Focusing on Generation of ASM, Adjusted Odds Ratios With 95% CIs

	Adjusted odds ratio (95% CI)	
	Model 1: adherence	Model 2: new-generation ASM
ASM generation		
First generation	Ref	—
Second generation, no switch	1.17 (1.11–1.23)	—
Second generation, switch	0.83 (0.80–0.86)	—
Third generation, no switch	1.50 (0.61–3.67)	—
Third generation, switch	0.86 (0.81–0.91)	—
Race/ethnicity		
White	Ref	Ref
Black	0.62 (0.60–0.65)	0.71 (0.68–0.75)
AIAN	0.87 (0.72–1.06)	1.30 (1.03–1.64)
Asian	0.81 (0.72–0.92)	0.93 (0.82–1.06)
Hispanic	0.78 (0.74–0.82)	0.93 (0.88–0.99)
NHOPI	0.96 (0.85–1.09)	0.77 (0.67–0.88)
Other	0.93 (0.88–0.98)	0.90 (0.84–0.97)
Age, y		
18–24	Ref	Ref
25–34	1.22 (1.17–1.27)	0.72 (0.69–0.76)
35–44	1.35 (1.29–1.42)	0.56 (0.53–0.59)
45–54	1.54 (1.46–1.62)	0.47 (0.44–0.50)
55+	1.66 (1.56–1.77)	0.42 (0.39–0.45)
Sex		
Female	Ref	Ref
Male	1.29 (1.25–1.34)	0.65 (0.63–0.68)
Rurality		
Nonrural	Ref	Ref
Rural	1.03 (0.99–1.08)	0.96 (0.91–1.01)
Missing	0.41 (0.10–1.60)	0.73 (0.18–2.84)
Neurologists per 100,000	1.00 (0.99–1.00)	1.00 (1.00–1.01)
Index year		
2010	Ref	Ref
2011	0.91 (0.87–0.95)	0.82 (0.78–0.86)
2012	1.08 (1.03–1.14)	0.95 (0.90–1.01)
2013	1.53 (1.45–1.62)	1.12 (1.04–1.19)
2014	2.60 (2.39–2.84)	1.29 (1.16–1.42)

Table 4 Models 1 and 2, Focusing on Generation of ASM, Adjusted Odds Ratios With 95% CIs (continued)

	Adjusted odds ratio (95% CI)	
	Model 1: adherence	Model 2: new-generation ASM
Emergency department visits		
Quartiles 1–3	Ref	Ref
Quartile 4	0.54 (0.52–0.57)	1.52 (1.44–1.61)
Neurologist		
No	Ref	Ref
Yes	1.10 (1.06–1.14)	3.26 (3.13–3.41)
Comorbidities		
HIV/AIDS	1.18 (1.02–1.37)	1.62 (1.34–1.97)
Alcohol abuse	0.66 (0.62–0.70)	0.85 (0.79–0.92)
Deficiency anemia	1.07 (1.02–1.11)	1.03 (0.98–1.09)
Arthritis	0.81 (0.75–0.87)	1.91 (1.69–2.15)
Blood loss	0.78 (0.67–0.90)	1.12 (0.92–1.35)
Congestive heart failure	0.98 (0.91–1.07)	1.08 (0.97–1.20)
Chronic lung disease	0.85 (0.82–0.88)	1.08 (1.03–1.13)
Coagulopathy	0.95 (0.88–1.03)	1.07 (0.97–1.18)
Depression	0.93 (0.88–0.98)	1.33 (1.24–1.43)
Diabetes	1.04 (0.99–1.10)	1.10 (1.03–1.17)
Diabetes w/ complications	0.93 (0.86–1.01)	1.48 (1.33–1.65)
Drug abuse	0.72 (0.69–0.76)	1.15 (1.07–1.23)
Hypertension	1.01 (0.98–1.05)	1.00 (0.96–1.05)
Hypothyroidism	1.17 (1.12–1.23)	0.98 (0.92–1.03)
Liver disease	0.85 (0.79–0.91)	1.40 (1.27–1.54)
Lymphoma	0.92 (0.71–1.20)	0.95 (0.69–1.32)
Electrolyte disorder	0.97 (0.93–1.01)	1.31 (1.24–1.38)
Metastatic cancer	0.88 (0.71–1.09)	1.00 (0.75–1.32)
Obesity	1.00 (0.95–1.05)	1.21 (1.13–1.28)
Paralysis	1.10 (1.05–1.14)	0.92 (0.87–0.96)
Peripheral vascular disease	1.07 (0.99–1.16)	1.21 (1.10–1.34)
Psychoses	1.03 (0.99–1.06)	1.15 (1.10–1.20)
Pulmonary circulation disorder	1.10 (0.97–1.23)	0.87 (0.74–1.01)
Renal failure	1.12 (1.02–1.23)	0.99 (0.88–1.11)
Tumor	1.01 (0.93–1.10)	1.29 (1.16–1.44)
Ulcer	0.93 (0.60–1.45)	1.27 (0.70–2.32)
Valvular disease	0.93 (0.85–1.02)	0.93 (0.83–1.04)

Continued

Table 4 Models 1 and 2, Focusing on Generation of ASM, Adjusted Odds Ratios With 95% CIs (*continued*)

	Adjusted odds ratio (95% CI)	
	Model 1: adherence	Model 2: new-generation ASM
Weight loss	0.98 (0.92–1.05)	1.06 (0.97–1.15)
Injuries	0.92 (0.88–0.95)	1.29 (1.23–1.35)
Developmental disabilities	1.80 (1.74–1.87)	0.63 (0.60–0.65)

Abbreviations: AIAN = American Indian or Alaskan Native; ASM = antiseizure medication; CI = confidence interval; NHOPi = Native Hawaiian or Other Pacific Islander. The unadjusted odds ratios can be found in eTable 1, links.lww.com/CPI/A390.

and that there were clear racial/ethnic differences in neurologist use. This suggests that improving access to neurologists, with a focus on racial and ethnic minoritized populations, may continue to reduce these inequities. It is also important to consider the role that systematic racism and implicit bias may play with respect to health care. Although we do not have direct measures of these factors or demonstrate causation in this study, our results raise key hypotheses. How does racism at all levels influence the effectiveness of epilepsy care? Is it driven by racial disparities in health care access, communication, physician perceptions, or instead by pharmacogenetic responses to medication that are highly correlated with the social construction of race? Research is starting to illuminate how implicit bias affects treatment, such as increased medical mistrust leading to decreased adherence.^{40,41} It is also documented that complaints and treatment of pain are taken less seriously for Black patients, and racial concordance between a patient and their care provider influences communication and engenders trust between a patient.^{42,43} In the context of our study and ASM use, these factors may make patients less likely to report side effects or breakthrough seizures and/or make providers more likely to ignore the severity of these complaints. For example, a minoritized patient may initially be put on a first-generation ASM with a high side effect burden resulting in nonadherence and seizures. Subsequently, minoritized patients may be less likely to tell their White care provider of these side effects while the White care provider attributes the seizures to poor adherence and subsequently does not take an active effort to change the ASM regimen. It is estimated that 2.8% of the neurologists in the United States are Black compared with 22.6% of our study population and 13.6% of the US population.^{44,45} In addition to lessening the opportunities for a minoritized patient to have a care provider of the same race/ethnicity, this workforce disparity may have indirect effects on care. For example, greater clinician diversity at a facility may help increase overall trust between minoritized patients and the health care system and improve the focus on equitable practices. Taken together, these observations could lead to the patterns we observed with

minoritized populations being on potentially inferior ASMs. Thus, increasing racial diversity among providers may reduce disparities in ASM prescribing and adherence. These hypotheses should be tested in future research.

Given the results of this study, it is important to consider how to reduce these inequities in ASM use. From a research perspective, future work should continue to unpack the specific mechanisms that cause these observed inequities. Qualitative and mixed methods work may be needed to characterize the potential role that implicit bias and mistrust may play. In addition, and more immediately, individual departments and neurology practices could evaluate their own data, under a health equity quality improvement framework, to understand whether there are inequities in the care they provide.⁴⁶ Furthermore, it is important to note that there were persistent inequities in ASM adherence, even after adjusting for generation. This underscores that factors affecting adherence are complex and vary greatly across patients. For example, factors such as social support, education level, seizure control, and ASM toxicity should be evaluated to further understand the causes of these differences. At the individual patient level, our work highlights that simply evaluating ASM use is not sufficient to understand the motivations behind taking, or not taking, ASMs. Providers who attempt to assess these motivations in their patient encounters may illuminate more immediate intervention possibilities for individual patients. For example, adverse reactions may be more common in some people due to their genetic constitutions and the ability to process specific drugs.^{47–49} Alleles that affect drug metabolism may differ among the racial groups we assessed and hence may affect adherence and the need to switch generations.^{47,48} Importantly, we found that individuals who are seen by a neurologist and those who were newly diagnosed had higher odds of being on a newer-generation ASM. Taken together, these findings indicate leverage points to begin reducing inequities in epilepsy care. This may include increasing referral to neurologists and exploring whether a newer ASM may be equally effective but with fewer side effects, thus increasing overall adherence.

Our study has several strengths. First, as everyone in our study was on Medicaid, we do not face the issue of insurance status or affordability of ASMs—an important predictor of nonadherence.⁵⁰ In addition, with 5 years of data, we were able to capture changes that may have occurred over a longer period of time (rather than a single year or 2). Finally, we had representation of racial and ethnic populations that have been previously understudied in the epilepsy literature. We identified that these inequities persist for these subgroups of the population even among people enrolled in Medicaid, a program designed to be an equalizer within a state. We also acknowledge that not all Medicaid patients are the same. There are likely varying levels of social support that may influence these findings, and we were unable to capture these factors. Future work should investigate whether these

findings are consistent in privately insured populations while considering additional individual-level social factors.

Our study also has several limitations. One of the most noteworthy limitations of this study is that to identify people with epilepsy using claims data, the most reliable algorithms require at least 2 fills of an ASM. Although this increases the sensitivity of the algorithm, we also potentially introduce bias into our study by excluding patients who remain untreated. Although some of these patients may not be prescribed ASMs, others may not fill their prescription. There is work indicating that there are specific subgroups of the population who are less likely to be on ASMs.²² Future work should examine whether there are additional inequities in the prescription and filling of ASMs that would highlight even broader inequities in epilepsy treatment than this study has indicated. Furthermore, we were unable to assess the specific reasons for ASM use or switching. For example, some women in our study may have been pregnant or breastfeeding, necessitating a switch due to toxicity. Future work should examine these trends among more narrow subsets of people with epilepsy. In addition, a new-generation ASM may not be necessary or the best clinical decision for all patients, as evidence indicates not all newer ASMs are truly better⁶⁻⁸; however, it does provide a reasonable measure of quality of care. Similarly, we did not know whether what we identified as an ASM was prescribed for seizure control or another indication. For example, pregabalin may be prescribed for nerve pain and not seizure control. Polypharmacy, or the use of multiple other medications concurrently, would also be an important area of future work to better understand these patterns in ASM use. Our measure of adherence, the PDC, is also prone to underdetecting suboptimal adherence and is based on prescription fills not whether a patient is actively taking a medication. In addition, Medicaid policies and formularies may vary by state (e.g., some states may require trying older agents before approving newer ones). Although we accounted for clustering of patients by state, future work could take a policy-oriented approach to understand how this may contribute to these findings. In a supplemental analysis, we observed slight variation by state in the proportion of patients on new-generation ASMs (eTable 4, links.lww.com/CPJ/A390). Finally, our data end in 2014, and we cannot access more recent years. However, this was the most recently available data at the time of study initiation. It is likely that the use of new-generation ASMs has increased, and it would be crucial to see whether, in newer data, these inequities persisted or were ameliorated.

In conclusion, our study found that newer ASM generation, among those who did not switch generations, was associated with adherence. Meanwhile, racial and ethnic minoritized populations with epilepsy on Medicaid had lower odds of being on newer-generation ASMs. Although these differences in ASM prescribing do not account for all of the racial differences in ASM adherence, they represent modifiable drivers of disparities. Furthermore, we showed that those who are seen by a neurologist and those who were newly

diagnosed had higher odds of being on a newer ASM. Finally, we note that many of the observed disparities were reduced in the subset of patients being treated by a neurologist. Although further study is needed to characterize these differences and probe their mechanisms, our work illuminates previously unknown distinctions in epilepsy care. These critical gaps may represent modifiable asymmetries in quality of care, and they warrant greater attention. To eliminate health inequities among people with epilepsy, we must address these observed inequities in ASM use.

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Disclosure

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TAKE-HOME POINTS

- Those who were only on newer-generation ASMs had greater odds of being adherent.
- Racial and ethnic minoritized populations with epilepsy had lower odds of being on newer ASMs when compared with White individuals.
- These findings represent potential and addressable inequities in health care and health outcomes for people living with epilepsy.

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Guadalupe Fernandez-Baca Vaca, MD	Department of Neurology, University Hospitals Cleveland Medical Center and School of Medicine, Case Western Reserve University, Cleveland, OH	Interpretation of results and drafting and revision of the manuscript

Appendix (continued)

Name	Location	Contribution
Philip M. Alberti, PhD	AAMC Center for Health Justice, Association of American Medical Colleges, Washington, DC	Interpretation of results and drafting and revision of the manuscript
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Martha Sajatovic, MD	Case Western Reserve University, Cleveland, Ohio	Study design, interpretation of results, and drafting and revision of the manuscript
Siran M. Koroukian, PhD	Department of Population and Quantitative Health Sciences, School of Medicine, Case Western Reserve University, Cleveland, OH	Study design, data acquisition, interpretation of results, and drafting and revision of the manuscript

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