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Differences in Patterns of Outpatient Epilepsy-Specific Medication Initiation Post-Acute Ischemic Stroke in the Medicare Population

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Abstract

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AUTHOR CONTRIBUTIONS

M.A.D. drafted, edited, and revised the manuscript for intellectual content. J.D.B. completed the data analysis, drafted the methods and results sections, and revised the manuscript for intellectual content. J.H., M.P., D.B. L.S., M.B.W., and S.H. were involved in the study conceptualization and revision for intellectual content. J.P.N. facilitated data access and revising the manuscript for intellectual content. L.M.V.R.M. was involved in study design and conceptualization, obtaining data access, and supervising the study development and manuscript drafting for intellectual content.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Objective: Acute ischemic stroke (AIS) is a leading hospitalization cause and significantly contributes to seizures among older adults. We examined outpatient epilepsy-specific medications (ESM) initiation patterns post-AIS discharge in adults 65 years and older, trends over time (by stratifying the analysis from 2013–2021), and racial/ethnic differences.

Methods: We analyzed nationwide administrative claims data for a 20% sample of U.S. Medicare beneficiaries (enrolled in Traditional Medicare Parts A, B, and D for at least 12 months before admission) aged 65 years and hospitalized for AIS between 2013–2021. We estimated the cumulative incidence of ESM initiation within 90 days post-AIS discharge, with mortality as a competing risk and censoring person time if individuals experienced an inpatient re-admission. We described drug type and stratified our analysis by race, ethnicity, US geographic region, hospital region and year of discharge.

Results: Of 128,174 community-dwelling beneficiaries post-AIS discharge, 2,435 (1.9% [95% CI= 1.8%–2.0%]) initiated ESM within the 90-day follow-up period and Levetiracetam was the most common medication across all years (81%). Mean age was 79 (range 65–110), 56% female, 81% Non-Hispanic White, 10% Black/African American, 5% Hispanic, and 3% Asian. The cumulative incidence of ESM initiation at 90 days in the overall sample was 1.4% (95% CI=1.3–1.4%); 1.8% (95% CI=1.6–2.1%) for Black/African American, 1.9% (95% CI=1.6–2.3%) for Hispanic and 1.2% (95% CI=1.2–1.3%) for Non-Hispanic White beneficiaries. The 90-day cumulative incidence also varied by U.S. census division, from 1.0% (95% CI=0.8–1.3) [West North Central] to 1.5% (95% CI=1.3–1.8%) [East South Central]. We observed an increase in ESM 90-day initiation over time, from 1.2% (95% CI=1.0–1.5%) in 2013 to 1.7% (95% CI=1.5–1.9%) in 2021. ESM initiation was 1.6% (95% CI=1.4–1.8%) in the 65–70 age group and decreased in older age groups.

Significance: Black/African American and Hispanic beneficiaries had a higher 90-day incidence of post-AIS ESM initiation than non-Hispanic Whites. ESM initiation decreased in older age groups.

Keywords

Acute ischemic stroke; Initiation patterns; Antiseizure medication; Older adults

INTRODUCTION

Acute ischemic stroke (AIS) is a leading cause of hospitalizations among older adults. AIS can significantly contribute to post-stroke seizures, with estimates of 2 to 23% of stroke survivors having a seizure during the first few days after stroke and 3 to 67% experiencing late post-stroke seizures (one to two weeks to several years after stroke).¹ The risk of developing post-stroke epilepsy increases with time² and certain risk factors, including preexisting dementia.¹ Post-stroke seizures lead to more extended hospital stays, increased healthcare costs, reduced quality of life, and higher mortality rates in older adults.³ Currently, treatment options for post-stroke seizures include anti-seizure medications (ASMs). However, prophylactic administration of ASM is not recommended for patients with stroke.¹ When prescribing a new ASM, the significant risk of side effects must be weighed against the benefits.

In recent decades, the Food and Drug Administration (FDA) has approved a second and third generation of epilepsy-specific medications (ESMs; i.e., ASMs specifically to manage epilepsy and seizure disorders), such as levetiracetam, lamotrigine, and lacosamide, which are considered safer for older adults due to fewer side effects and drug-drug interactions.⁴ However, ESMs can negatively affect the stroke recovery period and cause serious adverse events in older adults, including drowsiness, dizziness, and cognitive impairment, which increase adverse outcomes like falls and fall-related injuries.^{5,6} According to the American Heart Association Guidelines, no data are available to guide prophylactic ASM initiation post-stroke, and some data suggest that prophylactic ASM use may be associated with poorer outcomes; therefore, administration of ASMs to prevent a seizure (i.e., seizure prophylaxis) is not recommended for patients with stroke¹ and “prophylactic administration of ASMs to patients with stroke but who have not had seizures is not recommended (Class III, Level of Evidence C)”.⁷ There is no consensus on drug choice for seizure prophylaxis in patients 65 years and older post-AIS.^{4,8,9}

Furthermore, stroke incidence is higher in vulnerable populations, particularly among Black/African American and Hispanic individuals, compared to non-Hispanic Whites.¹⁰ Stroke disproportionately affects these populations, with incidence, prevalence, care, and outcomes strongly associated with social determinants of health (SDOH), such as economic stability, social and community context, education access and quality, healthcare access and quality, neighborhood, and built environment (which includes housing quality, transportation access, environmental conditions, access to healthy foods and physical activity opportunities), and individual-level SDOH, such as race, ethnicity, sex, sexual orientation, immigration status, gender identity, acculturation, income, employment, digital literacy, and educational attainment.^{11,12} However, limited data exist on the quality of seizure prophylaxis in AIS survivors and its distribution among vulnerable populations, making it crucial to identify opportunities for healthcare improvement.

Vulnerable populations include those who are racial or ethnic minorities, children, elderly, socioeconomically disadvantaged, underinsured, pregnant women, chronically ill individuals, economically disadvantaged groups, and rural residents with limited access to healthcare, who often have health conditions that are exacerbated by inadequate healthcare.^{13,14} The term “vulnerable population” emphasizes health risks and susceptibility to negative outcomes.^{13,14} Since this study focuses primarily on health outcomes and SDOH rather than sociopolitical disadvantage or power imbalance, we will use “vulnerable populations” rather than “minorities” or “marginalized” hereafter.

We analyzed a national US Medicare dataset to address this gap and assess outpatient ESM initiation patterns following AIS discharge in older adults. We also explored differences in initiation based on race, ethnicity, and US geographic region.

METHODS

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)¹⁵ reporting guidelines and was approved by the Mass General Brigham Institutional Review Board. Because we conducted a secondary analysis of data

collected for routine billing purposes, the requirement for informed consent was waived. The data supporting this study's findings are collected routinely by The Centers for Medicare & Medicaid Services (CMS) for billing purposes and were made available by CMS with no direct identifiers. All results were aggregated following CMS Cell Suppression Policies. Restrictions apply to the availability of these data, which were used under license for this study. Medicare data are available through CMS with their permission. The code that produced the findings is available from the corresponding author upon reasonable request from any qualified investigator.

Study Design

Using national administrative claims data, we analyzed a 20% sample of U.S. Medicare health insurance beneficiaries aged 65 and older hospitalized for AIS between April 1, 2013, and September 30, 2021. We focused on individuals over 65 years old, who are more vulnerable to adverse outcomes due to multiple comorbidities.¹⁶ We selected hospitalizations from the Medicare Provider Analysis and Review (MedPAR) database based on principal diagnosis codes for AIS. We used International Classification of Diseases, 9th Revision (ICD-9) codes 433, 434, 436, and ICD-10 codes I63.x,¹⁷ a validated strategy to capture acute stroke in administrative databases.¹⁸ We included the first stroke hospitalization in the dataset for individuals, using a one-year lookback period to exclude individuals with prior stroke.

We included beneficiaries who were enrolled in traditional Medicare, Parts A (hospital insurance; covers inpatient hospital stays, care in a skilled nursing facility, hospice care, and some home health care), B (medical insurance; covers doctors' services, outpatient care, medical supplies, and preventive services), and Part D (prescription drug coverage) continuously for 12 months before their stroke admission. Traditional Medicare is a Fee-for-service health insurance model. Medicare Advantage (Part C) is an alternative to traditional Medicare coverage, but data was unavailable for this study. Medicare Advantage is a managed care model and may offer more affordable access to healthcare for lower-income beneficiaries.¹⁹ Medicare Advantage enrollees continue to increase over time, and studies have reported that vulnerable groups are more likely to enroll in Medicare Advantage than traditional fee-for-service Medicare.²⁰

We excluded beneficiaries who had been prescribed ESM within 120 days before hospitalization and those who met Medicare's Chronic Condition Warehouse (CCW) definition of epilepsy in the year before hospitalization to eliminate those with prior epilepsy.²¹ We chose a 120-day look-back period to ensure we captured patients currently receiving ASM prescriptions, accounting for patients with 90-day supply prescriptions with a 30-day grace period to account for medication stockpiling from early refills. We excluded those who died during the index hospitalization, left the hospital against medical advice, or were discharged directly to a skilled nursing facility from their first AIS hospitalization. Our sampling approach is shown in Figure 1, and further details of our study design and sensitivity analyses are described in Supplementary Material (sampling criteria in Table S1).

We captured demographic characteristics for each beneficiary from the Master Beneficiary Summary (MBSF) File. In addition, we obtained clinical characteristics from the MedPAR

file, including baseline stroke severity [National Institutes of Health Stroke Scale (NIHSS)], length of hospitalization in days, ICU stay, seizure diagnosis code during hospitalization, seizure present on admission and respiratory tract infection during hospitalization. We calculated the seizure risk score using a claims-based risk score, PSEiCARE.²² We evaluated the presence of baseline conditions using Medicare's CCW algorithms.²³ We also identified baseline dementia for a subset of beneficiaries admitted on January 1, 2018, or later, using a validated ICD-10 definition of dementia.²⁴ Demographic and baseline clinical characteristics for the study sample are presented in Table 1.

Primary Endpoints

The primary endpoint was ESM initiation in the 90 days post-stroke hospitalization discharge. The ESM initiation group was defined as beneficiaries with an ESM prescription claim within 90 days, beginning at the index acute hospitalization discharge date. ESM prescription drug claims in the Part D data were identified using generic and brand names in Table S2. We included ESM, used primarily for the treatment of seizures and epilepsy; we did not include other medications (i.e., benzodiazepines, gabapentinoids, topiramate, and primidone) used for the treatment of pain or other conditions.

Statistical Analysis

We reported the percent completeness for each variable in Table 1. For variables with less than 95% completeness, we showed counts of completed records stratified by initiation status. In subsequent analysis, we did not present results for unknown or missing race and ethnicity or US Region and Census division, as it is unknown who these individuals represent.

We used descriptive statistics mean and standard deviation for continuous variables and counts and percentages for categorical variables for the overall sample. We calculated the percentage of ESM initiators by covariates in Table 1 and calculated 95% confidence intervals using binomial exact intervals. We calculated the number of initiators by medication name, brand or generic medication dispensed, and provider specialty using the first prescription claim as a supplemental analysis. We used the Aalen-Johansen method to estimate the cumulative incidence function of ESM prescriptions in the 90 days post-stroke discharge, with mortality as a competing risk. We censored person time if individuals experienced an inpatient re-admission. If an individual is admitted to a hospital, initiation status is unknown as medications administered in an inpatient setting are not available in Part D prescription claims. We repeated our analysis, which was stratified by demographic factors and year of discharge. We calculated 95% confidence intervals for our incidence measures.

RESULTS

Sample Characteristics

Our final sample included 128,174 AIS survivors, and within 90 days of discharge, 2,435 beneficiaries (1.9% [95% CI = 1.8, 2.0]) were initiated on ESMs. Our study sample had a mean age of 79 (SD 8), was 56% female, 81% Non-Hispanic White, 10% Black or African

American, 5% Hispanic, and 3% Asian. Sample characteristics stratified by initiation status were shown in Table 1, and sensitivity analysis for sample inclusion in Table S3.

ESM Initiation

The cumulative incidence of new ESM initiation at 90 days was 1.4% (95% CI=1.3–1.4%) for the overall sample. During the 90 days after index stroke hospitalization, 1,536 individuals experienced the event of interest (ESM initiation), 11,418 individuals died, 36,016 were re-admitted to an inpatient (hospital, rehabilitation, or SNF) setting, and 79,204 individuals did not experience any event at the end of follow up. Among ESM initiators, 70% initiated within 30 days of discharge, 18% within 30 to 60 days, and 13% within 60 to 90 days. ESM initiation by year is shown in Supplemental Figure S2, Table S3, and S4 (sensitivity analysis for sample inclusion and cumulative incidence method, respectively).

Initiation Patterns by Demographic, Hospital, and Clinical Characteristics

As shown in Figure 2, the 90-day cumulative incidence of ESM initiation by race and ethnicity was higher for Black [1.8% (95% CI=1.6–2.1%)] and Hispanic [1.9% (95% CI=1.6–2.3%)] individuals compared to Non-Hispanic White [1.2% (95% CI=1.2–1.3%)], and Asian [1.2% (95% CI: 0.9, 1.6%)] individuals. ESM initiation was less common for older patients, the cumulative incidence was [1.6% (95% CI: 1.4, 1.8%)] for the 65–69 age category, and it decreased by each 5-year age category, shown in Figure 2 and Supplemental Table S4.

The cumulative incidence of 90-day ESM initiation was lowest in West North Central (Includes Iowa, Kansas, Minnesota, Missouri, Nebraska, North, and South Dakota) [1.0% (95% CI=0.8–1.3)] and highest in East South Central (Includes Alabama, Kentucky, Mississippi, and Tennessee) [1.5% (95% CI=1.3–1.8%)].

In Figure S1, we reported ESM initiation by determining whether the individual had an intensive care unit revenue center claim code during the index stroke hospitalization. We reported the distribution of ESM initiators by first medication choice, brand or generic medication dispensed, and prescriber specialty in Table S5 and Table S6. Our analysis showed that Levetiracetam was the most frequently prescribed ESM, 81% of patients received it as their first post-stroke medication. The use of brand-name medications was uncommon when generic equivalents were available. Of the 69 patients who received brand-name ESMs, most were prescribed Lacosamide, which lacked a generic alternative until March 21, 2022 (after this study timeline).

DISCUSSION

This is the first study to examine patterns of ESM initiation post-AIS using national US administrative claims data in patients 65 years and older. We uncovered differences in stroke care that may help explain the drivers of post-stroke outcomes. Notably, we observed differences in race and ethnicity, age, and US region, which might suggest that some groups are more likely to receive ESMs than others. Specifically, African American/Black and Hispanic Medicare beneficiaries, as well as those in the East-South-Central region of the US, are more likely to be initiated on ESMs after an AIS. We observed that ESM initiation

is not standardized across different patient populations and healthcare settings, leading to differences in care that must be further examined.

Our study focused on stroke survivors discharged home, who may have a lower ESM initiation rate compared to those with more severe strokes discharged directly to other skilled nursing facilities,²⁵ inpatient rehabilitation facilities,²⁶ long-term care hospitals, or home health agencies.²⁷ We found that 1.4% of stroke survivors discharged home initiate outpatient ESM, which was lower compared to a previous study examining inpatient and outpatient ESM initiation at a single academic medical center, which reported that 4.8% of AIS patients initiated ESM after admission.²⁸ This higher initiation rate may be explained by their inclusion of patients with more severe strokes (i.e., those admitted to an inpatient service and who are initiated on ESMs more acutely). We recommend that future studies consider stratifying ESM initiation by stroke severity at discharge, as stroke severity is a predictor of risk of late seizure.²⁹ One other small-scale study in a high-severity setting provided an upper-bound utilization estimate, reaching up to 33.7%.³⁰ Patients included in this study likely had higher ESM initiation for several reasons: they were seen in post-stroke clinic, had continuous electroencephalogram (cEEG) monitoring in the intensive care unit, had clinical concern for post-stroke seizures, and were on average 17 years younger than the current study population.³¹ We found that ESM initiation decreased as age advanced, which aligns with ESM treatment and frailty guidelines and may explain lower initiation rates.^{1,7,9} By comparing ESM prescription rates across different settings and time points, we can better understand current practices and practice variations, assess adherence to guidelines, understand decision-making processes, determine potential overuse, assess the continuity of care, evaluate outcomes, identify areas for improvement, identify potential differences in post-AIS care.

Currently, no other studies examine differences in seizure prophylaxis or ESM initiation among vulnerable populations of Medicare beneficiaries. However, a retrospective study investigating Medicaid claims determined that vulnerable populations had lower odds of receiving second-generation ESMs, with fewer drug-drug interactions (which were better tolerated; i.e., levetiracetam and lamotrigine) and side effects than White individuals.³² We observed that Black and Hispanic patients were most likely to be treated with ESMs. Adverse effects and worse outcomes were more common among Black and Hispanic patients. We understand these are due to many factors, such as comorbidities, underlying conditions, lack of access to specialized care or basic healthcare, and cultural, educational, and religious barriers. There is a higher prevalence of comorbidities (i.e., hypertension, diabetes, and obesity) among these vulnerable groups³³ and inadequate access to continued care among vulnerable populations, which can interfere with drug metabolism and ESM management.^{4,32}

Moreover, a study observed insurance-dependent racial and ethnic disparities and regional variations, where uninsured Hispanic patients and Hispanic Medicare/Medicaid beneficiaries had lower odds of being discharged to a post-acute care facility (e.g., a skilled nursing facility or hospice) and were more often discharged home.³⁴ A systemic review examining the racial or ethnic disparities in outcomes after stroke rehabilitation concluded that Black stroke survivors experience poorer functional outcomes than their White counterparts.³⁵

Intersectionality can be used to better explain the complexity of the problem as a framework developed to assess how a health issue is affected by more than one health inequality.³⁶ The intersectionality of more than three SDOH (e.g., healthcare access and quality, which includes risk for chronic health conditions, long distance to health centers, insurance coverage, etc.) has been associated with higher incident stroke risk in adults aged <75.³⁷ The differences in ESM initiation in Black and Hispanic patients observed in this study may be a driver of disproportionate outcomes and should be an area of further research.

Proper monitoring for side effects is necessary for this vulnerable population, along with depression and anxiety screenings. It's of special importance for primary care physicians, emergency department physicians, general neurologists, and specialists to adequately weigh the risks and benefits of ESMs on a case-by-case basis. Of equal importance is being able to determine if side effects originate from the medication or stroke complications. For example, for a patient with a long-standing history of depression, lamotrigine would be more favorable than levetiracetam.³⁸ Even though few side effects have been observed, levetiracetam has been associated with cognitive impairment, increased anxiety, and depression.^{38,39} Now, for a patient with underlying heart disease, lacosamide would not be the preferred ESM, as it may increase the risk of cardiac arrhythmia.⁴⁰ As another example, if a patient has an electrolyte imbalance and is initiated on carbamazepine, they must be monitored for hyponatremia.⁴¹

Older patients are more often initiated on generic than brand-name medications due to lower costs, increased adherence, and bioequivalence in formulations.⁴² Our analysis demonstrated that levetiracetam was the most frequently initiated ESM among Medicare beneficiaries post-AIS, which aligns with the current literature.^{38,39} Lamotrigine was only available as a brand name through March 21, 2022, and before that time, step therapy may have been required to obtain authorization. In addition, regimen complexity should be considered for medication adherence, as trouble remembering to take medication is a common reason patients reported not adhering to their ESM.⁴³ Several ESMs (lamotrigine and carbamazepine) require titration schedules and follow-up monitoring. The observed ESM initiation patterns in this study suggest that possible formulary or other medication access issues should be considered, and medical providers would benefit from more robust tools to assess seizure risk post-AIS and need clearer guidelines to promote more judicious use of seizure prophylaxis.

Our contribution to the literature offers insights into outpatient ESM initiation in older adults after stroke, a population for which seizure prophylaxis is not recommended. We focus on a nationally representative cohort of post-AIS beneficiaries discharged directly home after a short hospital stay who are in the lowest clinical suspicion and risk categories. Even a low rate of ESM initiation in low-risk patients is concerning because it suggests that vulnerable older adults may be exposed to potential side effects of ESMs without clear evidence of benefit.

Although the analysis presented in this study is descriptive and not intended to analyze causal effects, it lays the foundation for future studies examining differences in care (and potential disparities), comparative effectiveness studies, and interventional studies using

the intersectionality framework (i.e., tailored interventions that can improve access to healthcare).³⁶

Limitations

This study has provided a unique insight into patient profiles of adults aged 65 years and older diagnosed with an AIS. We analyzed information for older adults covered by traditional Medicare. Therefore, the findings of our study may not generalize to other populations, including other age groups,⁴⁴ Medicare Advantage (“Part C”); enrollees, and/or those without Part D prescription drug coverage. In addition, we were limited to information documented in administrative claims. For example, when Current Procedural Terminology (CPT) codes are not the basis for payment, the fields are empty (i.e., data is missing), as was the case with CPT codes for electroencephalograms.⁴⁵

Medicare administrative data does not include separate variables for race, ethnicity, gender identity, or language preference. This limits our ability to uncover specific or additional healthcare differences, which is of importance as stroke has been described as a disease of disparities.⁴⁶ The evidence points to various social and institutional factors contributing to a disproportion in stroke outcomes.^{10,46,47} To name a few of these factors, race and ethnicity (which include a biological component as well as a cultural and social one, with religion and customs), structural racism (e.g., a tendency to overlook symptoms in vulnerable populations),⁴⁷ discrimination, and SDOH (e.g., education and access to healthcare/insurance, transportation, a healthy diet, medication, technology, etc.). Additionally, there might be a clustering effect or an ethnic density effect. This has been previously described across various regions, and it is most pronounced in the Southern and Western US, rural areas, high-poverty regions, and areas with limited access to neurology specialists, where there are lower odds of PWEs being prescribed newer ESMs or higher odds of non-adherence.^{32,48}

A limitation of this study was missing data on NIHSS stroke severity. NIHSS scores in claims are only available for years where ICD-10 coding was used (2016–2021). Additionally, reporting varies wildly; smaller, rural, and non-academic hospitals were associated with nonreporting of NIHSS.⁴⁹ To account for this, we included other factors related to stroke severity like the length of hospitalization, ICU stay, seizure diagnosis code during stroke hospitalization, seizure diagnosis code present on stroke admission, respiratory tract infection present during stroke admission, baseline characteristics or comorbidities (e.g., 12-month anxiety, depression, seizures, dementia, etc.) and seizure risk category.

Lastly, the Medicare prescription drug event data did not include treatment indications. To address this, we focused on ASMs primarily used for seizure prophylaxis, such as levetiracetam, lamotrigine, and lacosamide, to analyze epilepsy-specific prophylaxis initiation patterns.⁵⁰ Although some ASMs, like lamotrigine, have additional indications (e.g., mood disorders), the selected medications are first-line treatments for seizures. This approach excluded ASMs primarily prescribed for pain (e.g., gabapentin or benzodiazepines), as done in previous studies.²⁸ Consequently, the actual outpatient initiation pattern is likely slightly higher than our estimate, as some individuals may have been started on these less specific drugs for seizure prophylaxis.³¹ We did not

report medication dose or total daily dose results, as these may not have been adequately captured and would also vary widely across individuals (e.g., diverse medical comorbidities, tolerance, scheduled titration, etc.).

The observed differences in care may be attributed to unadjusted baseline stroke severity (due to missing data on NIHSS scores), in-hospital and post-discharge care differences, and other factors that require further investigation. Thus, future research should aim to understand the drivers behind the observed differences in care and uncover potential disparities. There is a need for randomized controlled trials (or their equivalent) to establish seizure prophylaxis efficacy among different patient populations and evaluate ESM outcomes. Lastly, risk stratification tools for post-AIS seizure prophylaxis must be developed and validated to aid clinicians and promote adherence to guidelines.

CONCLUSION

Black/African American and Hispanic beneficiaries showed a higher 90-day incidence of post-AIS ESM initiation compared to non-Hispanic Whites. In addition, ESM initiation decreased with advancing age groups. This study emphasizes the importance of considering potential harms associated with ESM initiation and the need for careful risk-benefit assessment in individual patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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CONFLICT OF INTEREST

Maria A. Donahue, Julianne D. Brooks, Mary Price, Lee H. Schwamm, and Sebastien Hanuese have no conflict of interest to disclose.

John Hsu receives support from the National Institute of Health, Agency for Healthcare Research and Quality, Brandies University, Altmed, Cambridge Health Alliance, Columbia University, Invitrx, and the University of South Carolina and reports no conflict of interest.

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Joseph P. Newhouse is the National Committee for Quality Assurance director and reports no conflict of interest.

M. Brandon Westover is a co-founder, scientific advisor, and consultant to Beacon Biosignals and has a personal equity interest in the company.

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DATA AVAILABILITY

We had a Data Use Agreement approved by the Center for Medicare & Medicaid Services (DUA RSCH-2022-58182). Interested researchers may replicate the study by obtaining the

data from CMS. Reproducing this study requires 20% MedPAR, Outpatient, Carrier, and Part D standard analytical files.

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KEY POINTS

- We examined differences in ESM initiation patterns among Traditional Medicare beneficiaries post-AIS discharge (i.e., healthiest possible cohort: AIS survivors discharged home).
- Levetiracetam was the ESM most initiated post-AIS.
- Black/African American and Hispanic beneficiaries had a higher 90-day incidence of post-AIS ESM initiation than non-Hispanic Whites.
- ESM initiation decreased in older age groups
- Differences may arise from unadjusted baseline severity, in-hospital or post-discharge care differences, and other factors requiring further investigation.

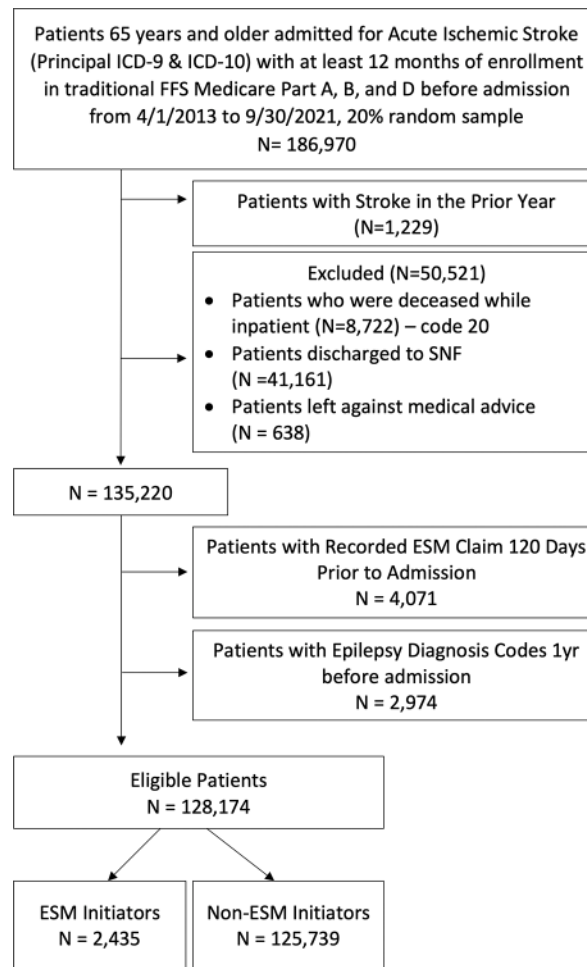


Figure 1. PRISM Diagram Acute Ischemic Stroke Cohort Flow Diagram, 20% Medicare Data Medicare data files used: MedPAR (Inpatient data), MBSF (Summary data); Part D (Drug formulary data); Diagnosed for Acute Ischemic Stroke based on- ICD 9 codes (433, 434, 436) and ICD 10 codes (I63 and I63.9); Part A: Hospital Insurance, Part B: Medical Insurance; Part D: Drug coverage. AIS, Acute Ischemic Stroke; ESM, epilepsy-specific medication; ICD, International Classification of Diseases; MBSF, Medicare's Master Beneficiary Summary; SNF, skilled nursing facility.

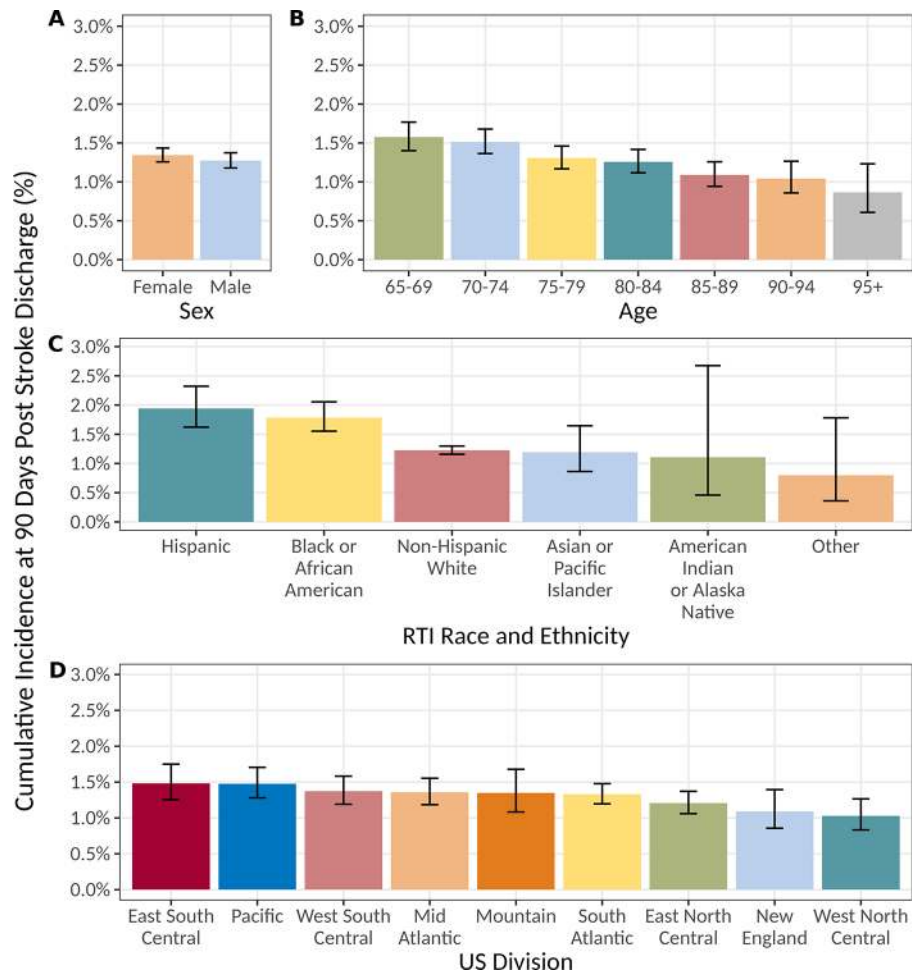


Figure 2. Cumulative Incidence of ESM Initiation at 90 Days Post-Stroke Discharge
 Cumulative Incidence Curves using the Aalen-Johansen estimation were shown in percent for A) reported sex, B) age category, C) Research Triangle Institute Race and Ethnicity, and D) U.S. Census Division. The upper and lower bars show 95% confidence intervals. ESM, epilepsy-specific medication; RTI, Research Triangle Institute.

Table 1.

Sample Characteristics

	Overall	Epilepsy-Specific Medication Initiator	Epilepsy-Specific Medication Non-Initiator	Percent Initiator (95% Confidence Interval)
All	128,174	2,435	125,739	1.9 (1.8, 2.0)
Age Mean (SD)	78.75 (8.25)	77.42 (7.96)	78.78 (8.25)	N/A
Age Category (100% Complete)				
65–69	19,665	459	19,206	2.3 (2.1, 2.6)
70–74	25,427	538	24,889	2.1 (1.9, 2.3)
75–79	25,746	504	25,242	2.0 (1.8, 2.1)
80–84	23,517	433	23,084	1.8 (1.7, 2.0)
85–89	18,952	300	18,652	1.6 (1.4, 1.8)
90–94	10,965	153	10,812	1.4 (1.2, 1.6)
95+	3,902	48	3,854	1.2 (0.9, 1.6)
Sex (100% Complete)				
Male	55,935	1,063	54,872	1.9 (1.8, 2.0)
Female	72,239	1,372	70,867	1.9 (1.8, 2.0)
Race (99.1% Complete)				
White	107,501	1,945	105,556	1.8 (1.7, 1.9)
Black	12,249	308	11,941	2.5 (2.2, 2.8)
Other	1,736	36	1,700	2.1 (1.5, 2.9)
Asian	2,624	42	2,582	1.6 (1.2, 2.2)
Hispanic	2,352	69	2,283	2.9 (2.3, 3.7)
North American Native	***	***	***	1.1 (0.4, 2.5)
Unknown	***	***	***	2.5 (1.6, 3.5)
RTI Race[†](99.2% Complete)				
Non-Hispanic White	30,543	545	29,998	1.8 (1.7, 1.9)
Black/African American	23,923	450	23,473	2.5 (2.3, 2.8)
Asian or Pacific Islander	37,984	751	37,233	1.7 (1.3, 2.2)
Hispanic	15,497	291	15,206	2.7 (2.3, 3.1)
American Indian/Alaska Native	***	***	***	1.1 (0.4, 2.5)
Other	***	***	***	1.8 (1.0, 3.0)
Unknown	930	19	930	2.0 (1.2, 3.2)
U.S. Region (99.8% Complete)				
Midwest	30,543	545	30,543	1.8 (1.6, 1.9)
Northeast	23,923	450	23,923	1.9 (1.7, 2.1)
Southeast	37,984	751	37,984	2.0 (1.8, 2.1)
Southwest	15,497	291	15,497	1.9 (1.7, 2.1)
West	20,027	397	20,027	2.0 (1.8, 2.2)
U.S. Census Division (99.8% Complete)				

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	Overall	Epilepsy-Specific Medication Initiator	Epilepsy-Specific Medication Non-Initiator	Percent Initiator (95% Confidence Interval)
East North Central	21,268	387	20,881	1.8 (1.6, 2.0)
East South Central	10,259	221	10,038	2.2 (1.9, 2.5)
Mid Atlantic	17,393	344	17,049	2.0 (1.8, 2.2)
Mountain	6,481	115	6,366	1.8 (1.5, 2.1)
New England	6,530	106	6,424	1.6 (1.3, 2.0)
Pacific	13,546	282	13,264	2.1 (1.8, 2.3)
South Atlantic	27,725	530	27,195	1.9 (1.8, 2.1)
West North Central	9,275	158	9,117	1.7 (1.5, 2.0)
West South Central	15,497	291	15,206	1.9 (1.7, 2.1)
Dual Eligible[‡](100% Complete)				
No	98,416	1,760	96,656	1.8 (1.7, 1.9)
Yes	29,758	675	29,083	2.3 (2.1, 2.4)
Original Medicare Entitlement (100% Complete)				
Disability or End-Stage Renal Failure	16,603	401	16,202	2.4 (2.2, 2.7)
Old-Age & Survivors Insurance	111,571	2034	109,537	1.8 (1.7, 1.9)
NIHSS Score (27% Complete)				
N Complete	34,591	683	33,908	N/A
Median [IQR]	3 [1, 8]	4 [2, 10]	3 [1, 8]	N/A
Minor (1–4)	20,709	357	20,352	1.7 (1.6, 1.9)
Moderate (5–15)	9,997	223	9,774	2.2 (2.0, 2.5)
Moderate to Severe (16–20)	1,801	60	1,741	3.3 (2.6, 4.3)
Severe (21–42)	2,084	43	2,041	2.1 (1.5, 2.8)
Length of Hospital Stay (days) (100% Complete)				
> 2 weeks	126,068	2,372	123,696	1.9 (1.8, 2)
2 weeks	2,106	63	2,043	3 (2.3, 3.8)
ICU Revenue Center Code During Stroke Hospitalization (100% Complete)				
Any ICU	57,446	1,282	56,164	2.2 (2.1, 2.4)
General or Other	54,666	1,219	53,447	2.2 (2.1, 2.4)
Surgical or Trauma	2,780	63	2,717	2.3 (1.7, 2.9)
None	70,728	1,153	69,575	1.6 (1.5, 1.7)
Seizure Diagnosis Code During Stroke Hospitalization (100% Complete)				
Yes	1,588	600	988	37.8 (35.4, 40.2)
No	126,586	1,835	124,751	1.4 (1.4, 1.5)
Seizure Diagnosis Code Present on Stroke Hospitalization Admission (100% Complete)				

	Overall	Epilepsy-Specific Medication Initiator	Epilepsy-Specific Medication Non-Initiator	Percent Initiator (95% Confidence Interval)
Yes	1320	498	822	37.7 (35.1, 40.4)
No	126,854	1,937	124,917	1.5 (1.5, 1.6)
Respiratory Tract Infection (Pneumonia) Present on Stroke Hospitalization Admission (100% Complete)				
Yes	1,405	29	1,376	2.1 (1.4, 3)
No	126,769	2406	124,363	1.9 (1.8, 2)
Baseline Characteristics (100% Complete)				
12-month Anxiety [§]	15,308	382	14,926	2.5 (2.3, 2.8)
12-month Depression [§]	23,290	551	22,739	2.4 (2.2, 2.6)
12-month Dementia Diagnosis based on Validated Claim-Base Definition *	5,210	96	5,114	1.8 (1.5, 2.2)
Acute Myocardial Infarction	12,195	241	11,954	2 (1.7, 2.2)
Anemia	83,264	1696	81,568	2 (1.9, 2.1)
Asthma	20,760	406	20,354	2 (1.8, 2.2)
Atrial Fibrillation	38,131	722	37,409	1.9 (1.8, 2)
Benign Prostatic Hyperplasia	28,776	526	28,250	1.8 (1.7, 2)
Cancer, Breast	8,056	179	7,877	2.2 (1.9, 2.6)
Cancer, Colorectal	4,645	99	4,546	2.1 (1.7, 2.6)
Cancer, Endometrial	1,470	32	1,438	2.2 (1.5, 3.1)
Cancer, Lung	3,059	100	2,959	3.3 (2.7, 4)
Cancer, Prostate	8,496	160	8,336	1.9 (1.6, 2.2)
Cataract	9,4367	1706	92,661	1.8 (1.7, 1.9)
Chronic Kidney Disease	61,431	1322	60,109	2.2 (2, 2.3)
Chronic Obstructive Pulmonary Disease COPD	44,774	858	43,916	1.9 (1.8, 2)
Cognitive Impairment (Dementia or Alzheimer's)	30,471	654	29,817	2.2 (2, 2.4)
Congestive Heart Failure (CHF)	54,362	1090	53,272	2.2 (2, 2.4)
Diabetes	64,466	1339	63,127	2.1 (2, 2.2)
Glaucoma	34,281	637	33,644	1.9 (1.7, 2)
Hip/Pelvic Fracture	6,819	118	6,701	1.7 (1.4, 2.1)
Hyperlipidemia	113,249	2157	111,092	1.9 (1.8, 2)
Hypertension	120,311	2294	118,017	1.9 (1.8, 2)
Hypothyroidism	41,130	793	40,337	1.9 (1.8, 2.1)
Ischemic Heart Disease	85,439	1680	83,759	2 (1.9, 2.1)
Osteoporosis	32,029	553	31,476	1.7 (1.6, 1.9)
Rheumatoid Arthritis/Osteoarthritis	84,913	1590	83,323	1.9 (1.8, 2)
Seizure Risk Category				
Low (0)	26,944	363	26,581	1.3 (1.2, 1.5)

	Overall	Epilepsy-Specific Medication Initiator	Epilepsy-Specific Medication Non-Initiator	Percent Initiator (95% Confidence Interval)
Medium (1–5)	84,200	1,312	82,888	1.6 (1.5, 1.6)
High (6–10)	16,626	624	16,002	3.8 (3.5, 4.1)
Very High (11)	404	136	268	33.7 (29.1, 38.5)

N/A, not applicable.

Small counts are censored according to Center for Medicare (CMS) cell suppression guidelines

†

RTI (Research Triangle Institute) Algorithm is an algorithm developed to better assign race and ethnicity for Asian and Hispanic individuals

‡

Dual Eligible beneficiaries are eligible for Medicaid and Medicare insurance coverage

§

Diagnosis codes present within the 12 months before stroke admission

*

Dementia admissions from 2018 to 2021 only (N = 51,978)

ESM, epilepsy-specific medication; ICU, Intensive Care Unit; RTI, Research Triangle Institute; SD, Standard Deviation