RESEARCH ARTICLE

Acute Ischemic Stroke Interventions in the United States and Racial, Socioeconomic, and Geographic Disparities

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Abstract

Background and Objectives

In patients with ischemic stroke (IS), IV alteplase (tissue plasminogen activator [tPA]) and endovascular thrombectomy (EVT) reduce long-term disability, but their utilization has not been fully optimized. Prior research has also demonstrated disparities in the use of tPA and EVT specific to sex, race/ethnicity, socioeconomic status, and geographic location. We sought to determine the utilization of tPA and EVT in the United States from 2016–2018 and if disparities in utilization persist.

Methods

This is a retrospective, longitudinal analysis of the 2016–2018 National Inpatient Sample. We included adult patients who had a primary discharge diagnosis of IS. The primary study outcomes were the proportions who received tPA or EVT. We fit a multivariate logistic regression model to our outcomes in the full cohort and also in the subset of patients who had an available baseline National Institutes of Health Stroke Scale (NIHSS) score.

Results

The full cohort after weighting included 1,439,295 patients with IS. The proportion who received tPA increased from 8.8% in 2016 to 10.2% in 2018 ($p < 0.001$) and who had EVT from 2.8% in 2016 to 4.9% in 2018 ($p < 0.001$). Comparing Black to White patients, the odds ratio (OR) of receiving tPA was 0.82 (95% confidence interval [CI] 0.79–0.86) and for having EVT was 0.75 (95% CI 0.70–0.81). Comparing patients with a median income in their zip code of ≤$37,999 to >$64,000, the OR of receiving tPA was 0.81 (95% CI 0.78–0.85) and for having EVT was 0.84 (95% CI 0.77–0.91). Comparing patients living in a rural area to a large metro area, the OR of receiving tPA was 0.48 (95% CI 0.44–0.52) and for having EVT was 0.92 (95% CI 0.81–1.05). These associations were largely maintained after adjustment for NIHSS, although the effect size changed for many of them. Contrary to prior reports with older datasets, sex was not consistently associated with tPA or EVT.

Discussion

Utilization of tPA and EVT for IS in the United States increased from 2016 to 2018. There are racial, socioeconomic, and geographic disparities in the accessibility of tPA and EVT for patients with IS, with important public health implications that require further study.

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Glossary

AUC = area under the receiver operating characteristic curve; **CI** = confidence interval; **EVT** = thrombectomy; ***ICD-10*-CM** = International Classification of Diseases, 10th revision, Clinical Modification; **IS** = ischemic stroke; **NIHSS** = National Institutes of Health Stroke Scale; **NIS** = National Inpatient Sample; **OR** = odds ratio; **tPA** = tissue plasminogen activator; **VIF** = variance inflation factor.

Acute ischemic stroke (IS) affects almost 700,000 Americans a year and remains the leading cause of long-term disability.[1,2] In eligible patients with IS, IV alteplase (tissue plasminogen activator [tPA]) and endovascular thrombectomy (EVT) are proven to reduce the likelihood of long-term disability from IS, but their availability and utilization has not yet been fully optimized,[3-5] despite consensus guidelines advocating their use.[6] Prior research has also demonstrated patient-level disparities in the use of tPA and EVT specific to sex, race/ethnicity, socioeconomic status, and geographic location.[7-16]

In October 2016, the Centers for Medicare & Medicaid Services released *ICD-10*-CM codes for the admission National Institutes of Health Stroke Scale (NIHSS) score, to be used in conjunction with the IS coding category (I63.x).[17] Baseline stroke severity (NIHSS) is important for accurate modeling of IS outcomes[18-20] and for evaluating the utilization of IS interventions, which vary by stroke severity.[6] As of this writing, the National Inpatient Sample (NIS) provides 3 years of data (2016–2018) with the potential for NIHSS documentation.[21] We explored the changes in the utilization of tPA and EVT in NIS and whether there were persistent disparities in access to IS interventions after adjusting for stroke severity (NIHSS).

Methods

Study Design

This is a retrospective, longitudinal analysis of the 2016–2018 NIS data, which corresponds to the release of the *ICD-10*-CM update. NIS is the largest all-payer inpatient claims-based database in the United States and is designed as a stratified sample of hospitals participating in the Healthcare Cost and Utilization Project.[22] We included nonelective admissions of adult patients (≥18 years) who had a primary discharge diagnosis of IS defined by *ICD-10*-CM (code I63).[23] We excluded patients with missing data on demographic variables (<1% of patients). Patients could be represented more than one time if they were discharged with IS from a hospital more than once during the study period.

There were 2 study cohorts: the full cohort with all available patients and the NIHSS cohort with patients who had an NIHSS recorded in their claims data. According to Centers for Medicare & Medicaid Services instructions, the NIHSS (*ICD-10*-CM R29.7x) is meant to be the initial or admission NIHSS.[17] The primary study outcomes were the proportions of patients with IS who received tPA (ICD-10-PCS 3E03317)[24] or had EVT (ICD codes in eTable 1, links.lww.com/WNL/B615). The secondary outcome was whether NIHSS was documented in 2017–2018. We conformed to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cohort studies.

Starndard Protocol Approvals, Registrations, and Patient Consents

Our study used de-identified publicly available data and was thus exempt from University of Utah institutional review board approval. Informed consent is not obtained by the Centers for Medicare & Medicaid Services for the NIS because the dataset does not contain identifiable information.

Demographic and Hospital Variables

We classified sex as male or female; race/ethnicity as non-Hispanic White, non-Hispanic Black, Hispanic (any race), Asian or Pacific Islander, Native American (NIS designation for American Indian/Alaskan Native), and other; and age as <55, 55–64, 65–74, and ≥75 years. Other patient-level variables included median income in the patient's zip code by quartiles, patient urban–rural location (county-based urban–rural classification with 6 categories developed by the National Center for Health Statistics for use in health care research),[25] the Elixhauser Comorbidity Index,[26] and the medical comorbidities of diabetes, hypertension, obesity, congestive heart failure, and intubation. Hospital-level variables included United States Census region, bed size using region-specific NIS criteria (small/medium/large),[27] and teaching status (nonteaching vs teaching).

Statistical Analysis

Statistical analysis was performed using STATA version 16.1 (Stata Corp) and the SVY suite of commands to account for the NIS survey design. We obtained national estimates by using the yearly sampling weights provided in the NIS.[21] In order to estimate the standard error in single sampling units, which only occur in 0.4% of strata in the full cohort, we used the single-unit (centered) approach, which centers them at the overall population mean. Alternative approaches to single sampling units would be to exclude them or use a scaling factor derived from the average of the variances from strata with multiple sampling units. For the current analysis, we chose the centered approach because excluding strata or using a scaled approach would inherently introduce more bias, which is consistent with how prior researchers have approached the NIS.[28] For subpopulation estimations, we used the subpop() option of SVY for accurate estimation. We report the weighted descriptive statistics for the demographic and hospital variables and plotted a smoothed graph of the weighted monthly proportion of

Table 1 Weighted Patient Demographics, Acute Stroke Interventions, and Hospital Characteristics for the Full Cohort and NIHSS Cohort

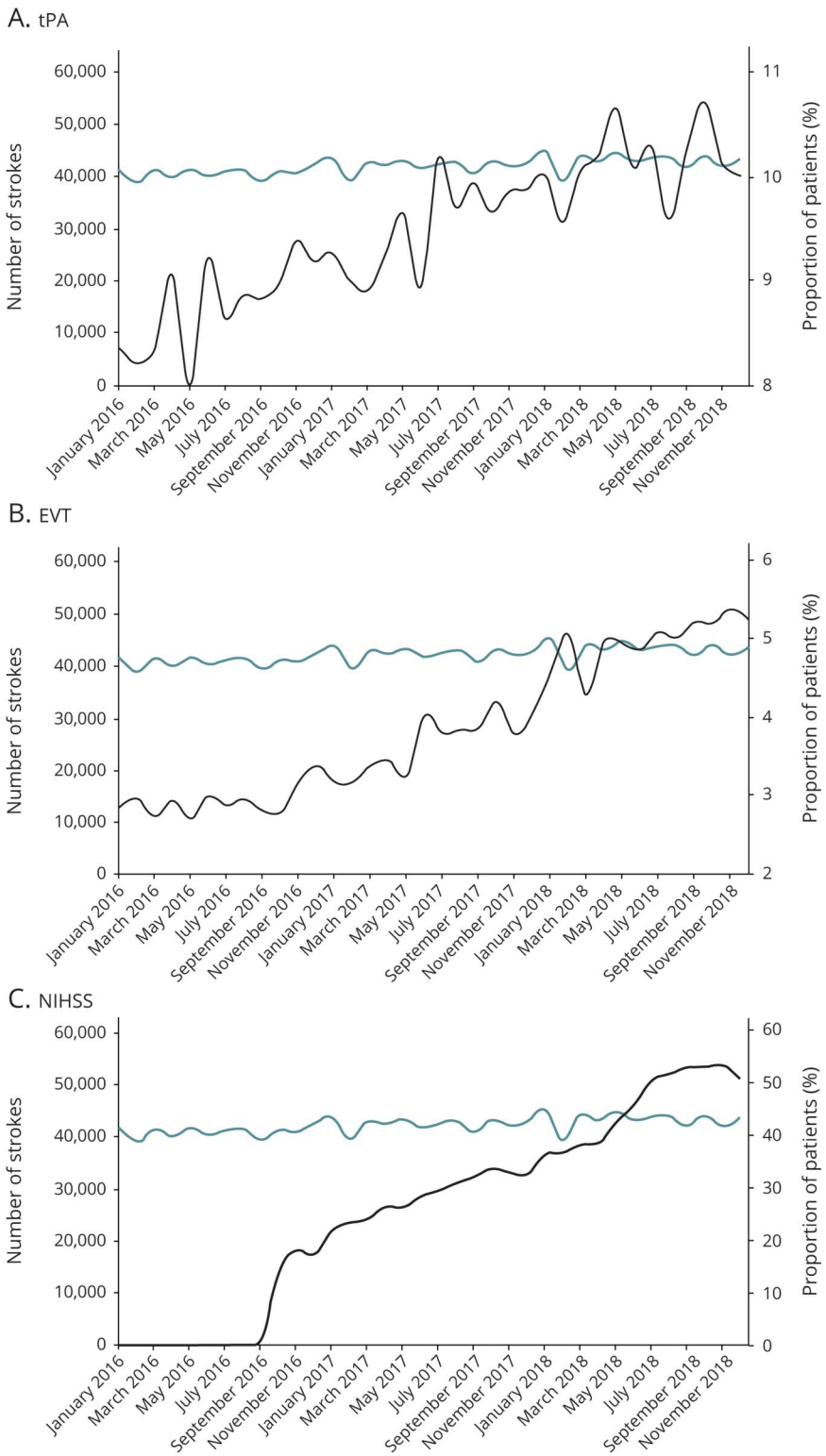
Variable	Full cohort (n = 1,439,295)	NIHSS cohort (n = 384,700)
Age, y	70.2 (13.9)	69.7 (14.0)
Age categories, y		
<55	13.9	14.5
55–64	19.5	20.1
65–74	24.3	24.9
≥75	42.3	40.5
Female sex	50.2	49.3
Race/ethnicity		
White	68.5	68.8
Black	17.2	17.2
Hispanic	8.3	8.1
Asian or Pacific Islander	3.1	3.0
Native American	0.4	0.4
Other	2.5	2.6
Median household income in patient's zip code		
≥$64,000	19.3	20.0
$48,000–$63,999	23.7	24.3
$38,000–$47,999	26.2	26.2
≤$37,999	30.8	29.5
Patient location		
Large metro with ≥1 million	28.6	30.7
Suburb of large metro	24.3	24.3
Metro with 250,000–999,000	21.3	21.7
Metro with 50,000–249,000	9.6	8.5
Micropolitan	9.2	8.5
Rural	7.0	6.3
Hypertension	84.8	85.1
Diabetes	38.9	37.1
Obesity	13.6	14.7
Cardiac arrhythmia	33.1	34.0
Congestive heart failure	18.1	17.6
Admission NIHSS score	—	6.95 (7.35)
Elixhauser comorbidity score	4.10 (2.00)	4.17 (1.95)
APR-DRG severity of illness	2.48 (0.79)	2.55 (0.80)
Intubation	3.5	3.8
IV alteplase	9.5	15.1
Endovascular thrombectomy	3.8	7.3
Hospital length of stay, d	4.9 (6.2)	4.8 (5.7)
Hospital Census region		
Northeast	18.1	18.6
Midwest	21.0	24.2
South	42.5	41.8
West	18.4	15.5
Hospital bed size		
Small	16.3	13.2
Medium	29.4	26.4
Large	54.3	60.4
Teaching hospital	70.5	79.1
Number of unique hospitals	4,723	3,575
Expected primary payer		
Medicare	65.8	64.6
Medicaid	9.2	9.0
Private insurance	18.7	19.7
Self-pay	3.9	4.3
No charge	0.3	0.3
Other	2.1	2.1

Abbreviations: APR-DRG = All Patients Refined Diagnosis-Related Groups; NIHSS = National Institutes of Health Stroke Scale.
Continuous variables shown as mean (SD) and other values as %. White and Black race categories are non-Hispanic. NIHSS and Elixhauser comorbidity score treated as a continuous variable. For hospital bed size, the National Inpatient Sample has a sliding scale for the ordinal categories based on Census region, which can be found at hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp.

patients who had primary outcomes. We also report proportions of tPA, EVT, and NIHSS after stratification by patient- and hospital-level variables and tested for intergroup differences with a design-based χ^2 test.

We fit multivariable logistic regression models to derive odds ratios (ORs) for our primary outcomes, which a priori included the covariates of patient age, sex, and race/ethnicity. We also included hospital Census region, hospital teaching status, hospital bed size, patient location, and median income in the patient's zip code to provide point estimates of additional geographic and socioeconomic factors that could affect the likelihood of receiving tPA or EVT,[29-33] and to account for those disparities when providing point estimates for age, sex, and race/ethnicity.

Figure 1 Monthly Trends for the Full Cohort in Usage of IV Alteplase (tPA), EVT, and NIHSS



(A) IV alteplase (tissue plasminogen activator [tPA]). (B) Endovascular thrombectomy (EVT). (C) National Institutes of Health Stroke Scale (NIHSS).

In the NIHSS cohort, we also adjusted for NIHSS, which was modeled as an interval variable with possible values of 0–42. As a sensitivity analysis, we also modeled NIHSS in quartiles and as a nonlinear restricted cubic spline with 5 knots. Because future research that adjusts for NIHSS as a measure of stroke severity, and not the exposure of interest, is likely to use NIHSS as an interval variable, we treated it as such in our main models. After logistic regression, we used marginal

Table 2 Proportions in Key Demographics of the Full Cohort Who Received IV Alteplase (tPA) or had EVT

Variable	Percentage who received tPA	*p* Value	Percentage who received EVT	*p* Value
Age, y		<0.001		<0.001
<55	11.9		4.4	
55–64	9.5		3.8	
65–74	9.2		3.8	
≥75	8.9		3.6	
Race/ethnicity		<0.001		<0.001
White	9.5		3.9	
Black	8.9		3.3	
Hispanic	10.7		3.8	
Asian or Pacific Islander	10.0		4.2	
Native American	6.7		2.9	
Other	10.1		5.0	
Sex		0.290		0.153
Male	9.6		3.8	
Female	9.5		3.9	
Median income in the patient's zip code		<0.001		<0.001
≥$64,000	11.2		4.3	
$48,000–$63,999	10.3		3.9	
$38,000–$47,999	8.8		3.7	
≤$37,999	8.5		3.5	
Patient location		<0.001		<0001
Large metro with ≥1 million	11.3		4.4	
Suburb of large metro	9.8		3.9	
Metro with 250,000–999,000	10.4		3.8	
Metro with 50,000–249,000	9.0		3.0	
Micropolitan	5.0		3.0	
Rural	5.3		3.2	
Hospital Census region		<0.001		0.023
Northeast	8.7		3.7	
Midwest	8.7		3.6	
South	9.5		3.7	
West	11.2		4.4	
Hospital bed size[a]		<0.001		<0.001
Small	7.3		1.2	
Medium	9.8		2.5	
Large	10.1		5.3	

Continued

Table 2 Proportions in Key Demographics of the Full Cohort Who Received IV Alteplase (tPA) or had EVT *(continued)*

Variable	Percentage who received tPA	*p* Value	Percentage who received EVT	*p* Value
Hospital teaching status		<0.001		<0.001
Nonteaching	7.8		1.2	
Teaching	10.2		4.9	

Abbreviations: EVT = endovascular therapy; tPA = tissue plasminogen activator.
[a] For hospital bed size, the National Inpatient Sample has a sliding scale for the ordinal categories based on Census region, which can be found at hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp.

effects to calculate the predicted probability of our outcomes for the change of specific variables while holding the other variables at their average predicted value.[34]

We calculated the variance inflation factor for each variable by fitting a regression model to the individual variable with all other covariates as predictors and manually calculated the variance inflation factor by the formula VIF = $1/(1 - R^2)$.[35] An acceptable VIF was defined as a mean value <10. To explore whether the addition of NIHSS improved discrimination of our logistic regression models, we report the area under the receiver operating characteristic curve (AUC) with and without NIHSS as a covariate.

Data Availability

The data used in this analysis are publicly available from the Centers for Medicare & Medicaid Services at distributor.hcup-us.ahrq.gov.

Results

The full cohort included 1,439,295 patients with IS, of which 32.1% were from 2016, 33.5% from 2017, and 34.4% from 2018, consistent with a small increase in patients with IS in the NIS during this time period. Within the full cohort, 384,700 (26.7%) had a documented admission NIHSS. The demographics for the full cohort are shown in Table 1; 50.2% of patients were female, 68.5% were White, and the mean age was 70 years. Vascular risk factors such as hypertension, diabetes, and obesity were common in patients with IS, affecting 84.8%, 38.9%, and 13.6%, respectively. Overall, 9.5% of patients with IS received tPA and 3.8% had EVT during the study's time period.

Throughout the study period, there was a consistent increase in the proportion of patients with IS who received tPA or EVT (Figure 1, A and B). The proportion of patients with IS who received tPA was 8.8% in 2016, 9.6% in 2017, and 10.2% in 2018 ($p < 0.001$) and who had EVT was 2.8% in 2016, 3.6% in 2017, and 4.9% in 2018 ($p < 0.001$). Beginning in late 2016, the proportion of patients with IS with a documented admission NIHSS increased consistently, and stayed above 50% after June 2018 (Figure 1C).

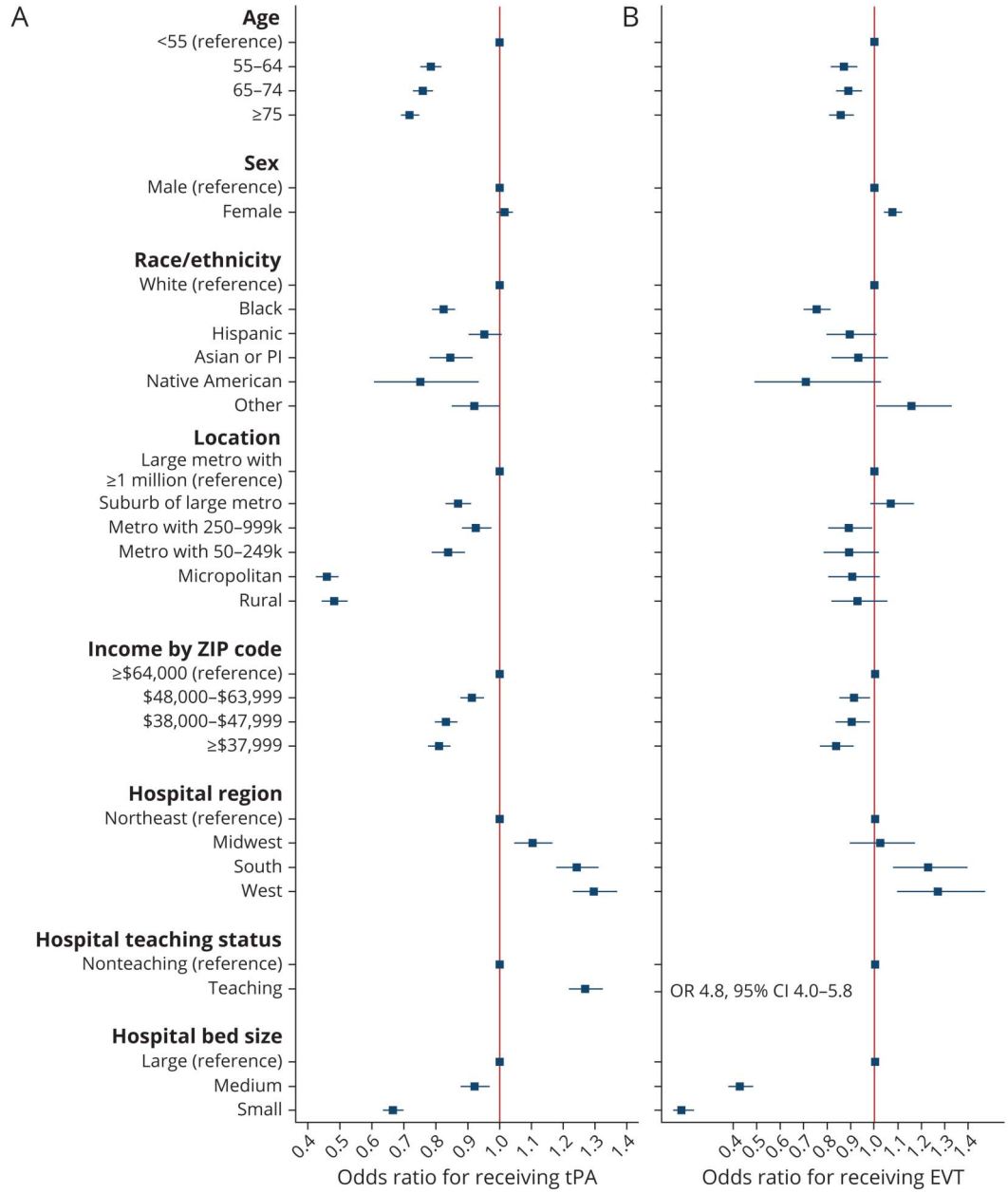
After stratification by key demographic and hospital variables, the proportion of patients who received tPA or EVT is shown in Table 2 for the full cohort. Black and Native American patients had the lowest proportion for both tPA and EVT. Compared to White patients, of whom 9.5% and 3.9% received tPA and EVT, respectively, only 6.7% and 2.9% of Native American patients did and 8.9% and 3.3% of Black patients. Other variables that predicted low rates of tPA and EVT included age ≥75 years, with a median income in the patient's zip code ≤$37,999, in more rural locations, at nonteaching hospitals, and in small bed size hospitals.

The results of our multivariable models fit to tPA and EVT in the full cohort are shown in Figure 2. The mean VIF of the models was <2, indicating acceptable collinearity. Comparing Black to White patients, the OR of receiving tPA was 0.82 (95% confidence interval [CI] 0.79–0.86) and for having EVT was 0.75 (95% CI 0.70–0.81). Comparing patients with a median income in their zip code of ≤$37,999 to >$64,000, the OR of receiving tPA was 0.81 (95% CI 0.78–0.85) and for having EVT was 0.84 (95% CI 0.77–0.91). Comparing patients living in a rural area to a large metro area, the OR of receiving tPA was 0.48 (95% CI 0.44–0.52) and for having EVT was 0.92 (95% CI 0.81–1.05). These findings are shown in relation to the difference in predicted probability in Table 3.

In the NIHSS cohort, our multivariable logistic regression models demonstrated a significant increase in the ability of the models to predict receipt of IV tPA or EVT when NIHSS was included as a covariate. The AUC of the model fit to tPA increased from 0.584 (95% CI 0.579–0.589) to 0.649 (95% CI 0.643–0.655) with the addition of NIHSS and the AUC of the model fit to EVT increased from 0.707 (95% CI 0.695–0.718) to 0.854 (95% CI 0.847–0.860). While modeling NIHSS in quartiles or as a restricted cubic spline further increased the AUCs of these models, the increase was marginal (eTable 2, links.lww.com/WNL/B615).

The associations seen in the full cohort were largely maintained in the NIHSS cohort, although the effect size changed for many of them (Figure 3). For example, without adjusting for NIHSS, the OR for receiving tPA in patients ≥75 was 0.79 (95% CI 0.74–0.84), while after adjustment for NIHSS, it was

Figure 2 Adjusted Odds of Receiving IV Alteplase (tPA) Shown for Demographic, Hospital, and Socioeconomic Categories in the Full Cohort and for Those Receiving EVT



Adjusted odds of receiving IV alteplase (tissue plasminogen activator [tPA]) shown for demographic, hospital, and socioeconomic categories in the full cohort (A) and for those receiving endovascular therapy (EVT) (B). Model adjusted for patient age, sex, race/ethnicity, hospital Census region, hospital teaching status, hospital bed size, patient location, and median household income by patient zip code. Model in patients with an National Institutes of Health Stroke Scale (NIHSS) is also adjusted for NIHSS. CI = confidence interval; OR = odds ratio.

0.68 (95% CI 0.64–0.72). Without adjusting for NIHSS, Asian or Pacific Islander patients had a nonsignificant lower odds of receiving EVT than White patients (hazard ratio 0.93, 95% CI 0.78–1.10), but after adjusting for NIHSS, the association became significant (hazard ratio 0.78, 95% CI 0.65–0.95). Without adjusting for NIHSS, women appeared more likely to have EVT than men (OR 1.12, 95% CI 1.06–1.18); after adjustment for NIHSS, the association was no longer significant (OR 0.99, 95% CI 0.93–1.05). To further illustrate this point, eFigure 1 (links.lww.com/WNL/B615) shows how the probability of receiving tPA or EVT by different race/ethnicity can change in adjusted vs unadjusted models and how adjusting for NIHSS affects the point estimates.

We also fit a multivariable logistic regression model to the secondary outcome of documentation of an NIHSS in 2017–18 (n = 977,695). We restricted this analysis to 2017–2018 because ICD documentation of an NIHSS only became available in late

Table 3 Predicted Probabilities for IV Alteplase (tPA) or EVT After Multivariable Logistic Regression

Demographic	Difference in predicted probability of tPA, %[a]	95% CI	*p* Value	Difference in predicted probability of EVT, %[a]	95% CI	*p* Value
Age, y						
<55	Ref	—	—	Ref	—	—
55–64	−2.3	−2.6, −1.9	<0.001	−0.5	−0.8, −0.3	<0.001
65–74	−2.6	−3.0, −2.2	<0.001	−0.4	−0.7, −0.2	<0.001
≥75	−3.0	−3.4, −2.6	<0.001	−0.6	−0.8, −0.3	<0.001
Race/ethnicity						
White	Ref	—	—	Ref	—	—
Black	−1.6	−1.9, −1.2	<0.001	−0.9	−1.1, −0.7	<0.001
Hispanic	−0.4	−0.9, 0.1	0.081	−0.4	−0.8, 0.0	0.060
Asian or Pacific Islander	−1.4	−2.0, −0.8	<0.001	−0.3	−0.7, 0.2	0.271
Native American	−2.3	−3.8, −0.7	0.004	−1.1	−2.2, −0.1	0.035
Other	−0.7	−1.4, −0.0	0.037	0.6	0.00, 1.2	0.052
Sex						
Male	Ref	—	—	Ref	—	—
Female	0.1	−0.1, 0.4	0.232	0.3	0.1, 0.4	<0.001
Median income in the patient's zip code						
≥$64,000	Ref	—	—	Ref	—	—
$48,000–$63,999	−0.8	−1.2, −0.5	<0.001	−0.3	−0.6, −0.1	0.016
$38,000–$47,999	−1.6	−2.0, −1.2	<0.001	−0.4	−0.7, −0.1	0.017
≤$37,999	−1.8	−2.2, −1.4	<0.001	−0.6	−1.0, −0.3	<0.001
Patient location						
Large metro with ≥1 million	Ref	—	—	Ref	—	—
Suburb of large metro	−1.3	−1.7, −0.9	<0.001	0.3	−0.1, 0.6	0.126
Metro with 250,000–999,000	−0.8	−1.2, −0.2	0.003	−0.4	−0.8, 0.0	0.034
Metro with 50,000–249,000	−1.6	−2.2, −1.1	<0.001	−0.4	−0.8, 0.1	0.087
Micropolitan	−5.6	−6.1, −5.1	<0.001	−0.3	−0.9, 0.1	0.108
Rural	−5.4	−5.9, −4.8	<0.001	−0.3	−0.7, 0.2	0.256
Hospital Census region						
Northeast	Ref	—	—	Ref	—	—
Midwest	0.8	3.5, 1.2	<0.001	0.1	−0.4, 0.5	0.717
South	1.8	1.3, 2.2	<0.001	0.7	0.3, 1.2	0.002
West	2.2	1.7, 2.6	<0.001	0.9	0.3, 1.4	0.002
Hospital bed size[b]						
Large	Ref	—	—	Ref	—	—
Medium	−0.7	−1.1, −0.3	0.001	−3.1	−3.4, −2.7	<0.001
Small	−3.2	−3.5, −2.8	<0.001	−4.5	−4.8, −4.1	<0.001

Continued

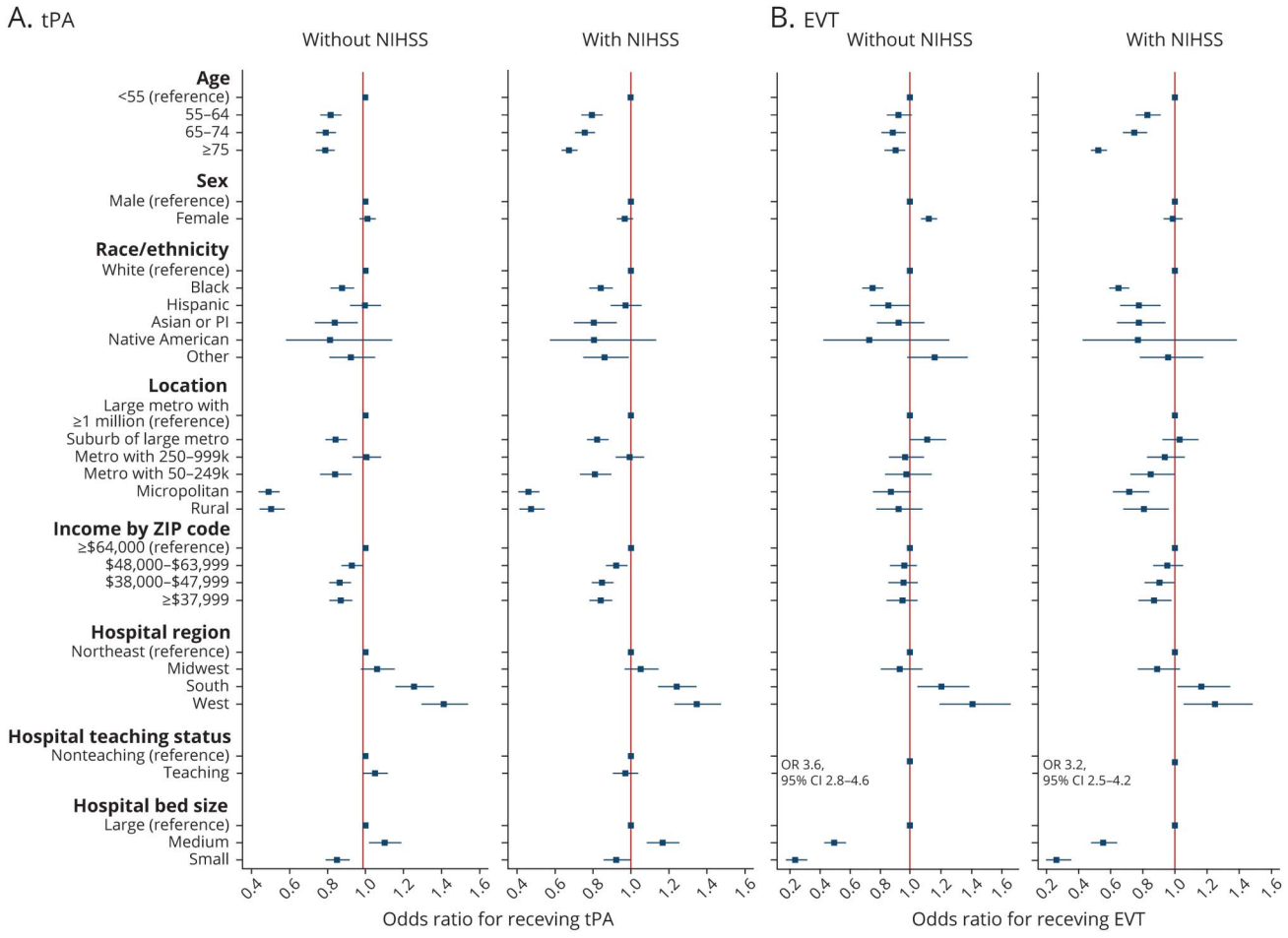
Table 3 Predicted Probabilities for IV Alteplase (tPA) or EVT After Multivariable Logistic Regression *(continued)*

Demographic	Difference in predicted probability of tPA, %[a]	95% CI	*p* Value	Difference in predicted probability of EVT, %[a]	95% CI	*p* Value
Hospital teaching status						
Nonteaching	Ref	—	—	Ref	—	—
Teaching	1.9	1.6, 2.3	<0.001	4.0	3.6, 4.3	<0.001

Abbreviations: CI = confidence interval; EVT = endovascular therapy; tPA = tissue plasminogen activator.
[a] Predicted probabilities derived from marginal output after logistic regression model adjusted for age, sex, race/ethnicity, hospital Census region, hospital teaching status, hospital bed size, patient location, and median household income by patient zip code.
[b] For hospital bed size, the National Inpatient Sample has a sliding scale for the ordinal categories based on Census region, which can be found at hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp.

2016.[17] The results of this analysis are shown in Table 4. Patient-level variables that were associated with lower odds of NIHSS documentation included older age (≥75 years), Black race, lower median income by patient zip code, and female sex. However, hospital level and treatment variables were more predictive. The ORs for NIHSS documentation were 0.64 (95% CI 0.57–0.71) in smaller bed size hospitals, 1.77 (95% CI 1.60–1.95) for teaching hospitals, 2.05 (95% CI 1.98–2.13) for patients who received tPA, and 2.32 (95% CI 2.16–2.49) for patients who received EVT.

Figure 3 Adjusted Odds of Receiving IV Alteplase (tPA) or EVT in Patients With a National Institutes of Health Stroke Scale (NIHSS) Score (n = 384,700), Shown for Models Without and With Adjustment for the NIHSS Score



(A) IV alteplase (tissue plasminogen activator [tPA]). (B) endovascular thrombectomy (EVT). Model adjusted for patient age, sex, race/ethnicity, hospital Census region, hospital teaching status, hospital bed size, patient location, and median household income by patient zip code. Model in patients with an NIHSS is also adjusted for NIHSS.

Table 4 Multivariable Logistic Regression Model Fit to the Secondary Outcome of Having an NIH Stroke Scale Score Recorded

Variable	Odds ratio	95% CI	*p* Value
Age, y		—	
<55	Ref	0.99, 1.05	—
55–64	1.02	0.99, 1.05	0.300
65–74	1.02	0.92, 0.98	0.260
≥75	0.95		0.002
Race/ethnicity		—	
White	Ref	0.87, 0.98	—
Black	0.92	0.91, 1.08	0.005
Hispanic	0.99	0.92, 1.11	0.922
Asian or Pacific Islander	1.01	0.74, 1.16	0.771
Native American	0.93	0.84, 1.03	0.517
Other	0.93		0.182
Sex		—	
Male	Ref	0.95, 0.98	—
Female	0.97		<0.001
Median income in the patient's zip code		—	
≥$64,000	Ref	0.92, 1.03	—
$48,000–$63,999	0.98	0.91, 1.03	0.351
$38,000–$47,999	0.97	0.82, 0.95	0.324
≤$37,999	0.88		0.001
Patient location		—	
Large metro with ≥1 million	Ref	0.85, 1.00	—
Suburb of large metro	0.92	0.84, 1.04	0.041
Metro with 250,000–999,000	0.93	0.74, 0.94	0.226
Metro with 50,000–249,000	0.83	0.83, 1.03	0.003
Micropolitan	0.92	0.78, 1.01	0.153
Rural	0.89		0.075
Hospital Census region		—	
Northeast	Ref	1.05, 1.42	—
Midwest	1.22	0.90, 1.18	0.009
South	1.03	0.65, 0.87	0.679
West	0.75		<0.001
Hospital bed size[a]		—	
Large	Ref	0.67, 0.82	—
Medium	0.74	0.57, 0.71	<0.001
Small	0.64		<0.001
Teaching hospital	1.77	1.60, 1.95	<0.001
Intravenous alteplase	2.05	1.98, 2.13	<0.001
Endovascular thrombectomy	2.32	2.16, 2.49	<0.001

Abbreviation: CI = confidence interval.
[a] For hospital bed size, the National Inpatient Sample has a sliding scale for the ordinal categories based on Census region, which can be found at hcup.us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp.

Discussion

Using NIS data from 2016–2018, we show that in the United States there has been an increase in the utilization of tPA and EVT for IS and administrative coding of the NIHSS. The rise in tPA and EVT use in patients with IS may reflect improved availability and acceptance of these interventions, more widespread teleneurology, better stroke systems of care, and ongoing efforts by the American Heart Association and others to educate patients about seeking timely medical care for IS symptoms.[6,36-42] While these developments are favorable, the persistence of previously demonstrated[7-16] racial, socioeconomic, and geographic disparities in the accessibility of tPA and EVT for patients with IS has important public health implications. We also demonstrated these disparities are present after adjusting for stroke severity with the NIHSS, which is an important confounder that was not previously available in administrative datasets like the NIS. Furthermore, many of the same racial, socioeconomic, and geographic disparities that are associated with tPA or EVT utilization are also associated with documentation of the NIHSS, which has not previously been demonstrated with an administrative dataset.

Our results are consistent with research predating the current study period that showed race/ethnicity, socioeconomic status, and geographic location are determinants of the likelihood that patients with IS will receive interventions.[8,13-16,43-45] The factors that account for disparities in IS interventions remain uncertain, but awareness of stroke symptoms, cultural and language barriers, access to health care facilities, and insurance status and income may all play a role.[46] Although difficult to capture, implicit bias, or potentially explicit bias, may also play a role.[47]

Contrary to prior research and meta-analyses,[7,10,12] we did not find that sex was associated with the likelihood of receiving tPA. The reason for this discrepancy could be

explained by a progressive narrowing of the gap in tPA utilization between male and female patients from 2008 onwards that was shown in a meta-analysis published in 2020.[10] In that study, the most recent year of data was 2015 and our analysis focuses exclusively on 2016–2018 and thus may reflect that a gap is no longer present in the United States. Women did have higher odds of EVT in our full cohort, but it was no longer significant after adjusting for NIHSS, implying that prior research that used administrative datasets may not have accurately measured this association.[12]

We also show that administrative coding of the NIHSS has progressively increased in patients with IS and that the addition of NIHSS as a covariate significantly improves the modeling of IS interventions. The increasing documentation of admission NIHSS will help researchers and hospital quality officers leverage administrative datasets to provide more reliable analyses and investigations.

Our study has several important limitations. The most important is that we lack data on additional patient-specific factors that may influence IS interventions, such as time from stroke onset to initial medical care, contraindications to IS treatments, or neuroimaging data. As with all administrative datasets, misclassification bias is a limitation, although our use of the *ICD-10*-CM code I63 in the primary discharge diagnosis position limits that bias for the identification of patients with IS. It is more likely that we undercaptured cases of tPA or EVT interventions, although that would probably occur in a random fashion and should not have a major effect on our analysis of disparities.

Because the NIS does not have unique patient identifiers, we are unable to account for the possibility that some patients could have had recurrent IS hospital admissions within a short time frame and thus potentially be ineligible for interventions. We also left interhospital transfers (10.7% of the patients) in the analysis, who could therefore appear twice in the dataset. We considered this appropriate because the identification of tPA and EVT was based on procedural codes that would be applicable to only one hospital and excluding these patients would bias the geographic analyses. For example, if a patient is transferred from a rural location or small hospital to a tertiary hospital for an intervention, removing transfers from the dataset would exclude this patient from our analysis.

Similar to prior research that used the NIS to examine disparities in acute stroke care, we cannot exclude unmeasured confounding or explain the root cause of our findings. We also lack granularity in many of our variables due to the administrative nature of NIS. For example, we are not able to examine ethnicity independent of race, or gender independent of sex, because of how information is collected in NIS. However, this study has unique strengths, including its large and nationally representative sample of all-payer claims, up-to-date data, and the ability to conduct subgroup analyses that are adjusted for admission stroke severity.

In a nationally representative sample of patients with IS in the United States from 2016 to 2018, we show an increase in the utilization of tPA and EVT. These advances are not shared equally and we find racial, socioeconomic, and geographic disparities in the accessibility of tPA and EVT, which warrant additional research to determine the most effective methods of closing these gaps.

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Kevin Sheth, MD	Yale University, New Haven, CT	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data
Karen C. Johnston, MD, MSc	University of Virginia, Charlottesville	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Alen Delic, MS	University of Utah, Salt Lake City	Study concept or design; analysis or interpretation of data
Eric Stulberg, MD, MPH	University of Utah, Salt Lake City	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data

Appendix *(continued)*

Name	Location	Contribution
Jennifer Majersik, MD, MS	University of Utah, Salt Lake City	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design
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Shadi Yaghi, MD	Brown University, Providence, RI	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design
David Tirschwell, MD, MS	University of Washington, Seattle	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design
John Ney, MD, MPH	Boston University, MA	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data

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