

# Race-Ethnic Disparities in Rates of Declination of Thrombolysis for Stroke

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## Abstract

### Background and Objectives

Prior regional or single-center studies have noted that 4% to 7% of eligible patients with acute ischemic stroke (AIS) decline IV tissue plasminogen activator (tPA). We sought to determine the prevalence of tPA declination in a nationwide registry of patients with AIS and to investigate differences in declination by race/ethnicity.

### Methods

We used the Get With The Guidelines–Stroke registry to identify patients with AIS eligible for tPA and admitted to participating hospitals between January 1, 2016, and March 28, 2019. We compared patient demographics and admitting hospital characteristics between tPA-eligible patients who received and those who declined tPA. Using multivariable logistic regression, we determined patient and hospital factors associated with tPA declination.

### Results

Among 177,115 tPA-eligible patients with AIS at 1,976 sites, 6,545 patients (3.7%) had tPA declination as the sole documented reason for not receiving tPA. Patients declining treatment were slightly older, were more likely to be female, arrived more often at off-hours and earlier after symptom onset, and were more likely to present to Primary Stroke Centers. Compared with non-Hispanic White, non-Hispanic Black race/ethnicity was independently associated with increased (adjusted odds ratio [aOR] 1.21, 95% CI 1.11–1.31), Asian race/ethnicity with decreased (aOR 0.72, 95% CI 0.58–0.88), and Hispanic ethnicity (any race) with similar odds of tPA declination (OR 0.98, 95% CI 0.86–1.13) in multivariable analysis.

### Discussion

Although the overall prevalence of tPA declination is low, eligible non-Hispanic Black patients are more likely and Asian patients less likely to decline tPA than non-Hispanic White patients. Reducing rates of tPA declinations among non-Hispanic Black patients may be an opportunity to address disparities in stroke care.

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## Glossary

**AIS** = acute ischemic stroke; **aOR** = adjusted odds ratio; **GWTG-Stroke** = Get With The Guidelines–Stroke; **NIHSS** = NIH Stroke Scale; **tPA** = tissue plasminogen activator.

The development of hospital-based quality improvement initiatives such as the American Heart Association's Get With The Guidelines–Stroke (GWTG-Stroke) Program and Target: Stroke campaign has led to the nationwide improvement in appropriate and timely administration of IV tissue plasminogen activator (tPA) in eligible patients with acute ischemic stroke (AIS).<sup>1</sup> Despite these efforts, tPA treatment rates for patients with AIS remain suboptimal, ranging from 3% to 7%,<sup>2,3</sup> with lower rates among Black patients.<sup>4</sup>

Racial and ethnic disparities have been observed in many aspects of stroke care, including prehospital care, acute treatment with tPA, and poststroke outcomes.<sup>5</sup> For example, non-Hispanic Black patients are 20% less likely to arrive by emergency medical services and are less likely to achieve door-to-needle times of  $\leq 60$  minutes.<sup>6,7</sup> Non-Hispanic Black patients are more likely to be disabled after stroke and half as likely to receive tPA compared to non-Hispanic White patients.<sup>8,9</sup> These racial disparities in tPA treatment rates persist regardless of the stroke certification status of the receiving hospital.<sup>4</sup>

Our prior work found that among tPA-eligible patients with AIS at stroke centers in Chicago,  $>7\%$  of patients or their proxies declined tPA treatment.<sup>10</sup> Declining tPA was more common in non-Hispanic Black patients compared to non-Black patients and accounted for lower tPA treatment rates among all non-Hispanic Black patients. Building on these findings, we sought to determine the prevalence of tPA treatment declination in a nationwide registry of patients with AIS and to investigate differences in tPA declination by race/ethnicity.

## Methods

### Data Source

The GWTG-Stroke registry is a quality improvement program for stroke care in the United States that collects clinical outcomes data via a web-based Patient Management Tool.<sup>11</sup> IQVIA (Parsippany, NJ) serves as the data collection and coordination center, and the Duke Clinical Research Institute (Durham, NC) serves as the data analysis center.

### Standard Protocol Approvals, Registrations, and Patient Consents

Data analysis was done by the Duke Clinical Research Institute with local institutional review board approval. Under the common rule, sites are granted a waiver of informed consent because the data are collected from medical records for local quality improvement purposes.

### Data Collection and Study Population

We identified patients with diagnosis of AIS in the GWTG-Stroke registry between January 1, 2016, and March 28 2019, who were not enrolled in a clinical trial, not admitted for elective carotid interventions, or not from a hospital with  $>25\%$  of missing medical history data. Excluded patients (Figure 1) included those who (1) had an in-hospital stroke, (2) were transferred from another hospital, (3) had a documented onset to arrival time  $>4.5$  hours or no documented arrival time, (4) had missing data regarding tPA administration, or (5) had any documented medical contraindication to tPA, except for patient/family declining therapy, within the 0- to 3-hour or 3- to 4.5-hour treatment windows.

### Patient and Hospital Characteristics

Demographic covariates of interest included patient age, sex, self-reported race/ethnicity, insurance status, arrival via ambulance (yes/no), arrival to the emergency room during off-hours (7 PM–6 AM) (yes/no), NIH Stroke Scale (NIHSS) score, time from symptom onset to hospital arrival, and medical history. Race/ethnicity was extracted from the electronic health record and entered into the registry. Medical history included the presence of atrial fibrillation/flutter, previous stroke or TIA, coronary artery disease or prior myocardial infarction, carotid stenosis, diabetes (treated or not treated with insulin), peripheral vascular disease, hypertension, dyslipidemia, smoking, heart failure, and renal insufficiency. Hospital characteristics included region, hospital type (teaching/nonteaching), percent Black patients treated, number of beds, annual ischemic stroke volume (0–150, 151–200, 251–350,  $\geq 351$ ), annual case volume of IV tPA administration, rural location, and stroke center status (primary or comprehensive). Percent Black patients treated was calculated as the percent treated over the study period, and missing race was counted as not Black.

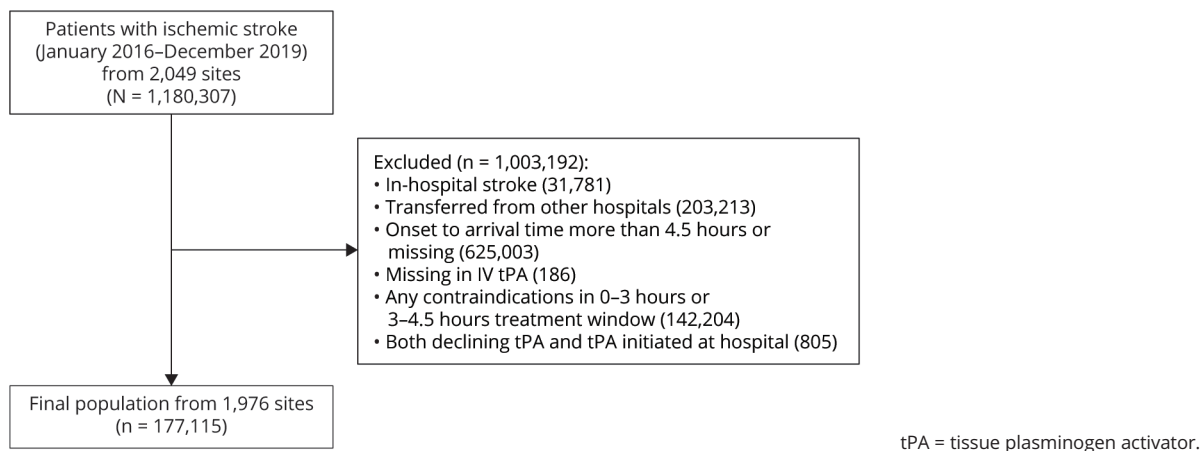
### Outcomes

The GWTG-Stroke coding instructions and Patient Management Tool provide a discrete patient/family refusal variable to be entered as a relative exclusion criterion for tPA within either the 0- to 3-hour or the 3- to 4.5-hour treatment windows (eTable 1, [links.ahajournals.org/doi/10.1161/STROKEAHA.119.02857](https://www.ahajournals.org/doi/10.1161/STROKEAHA.119.02857)). We defined patient/family refusal as an indication of tPA declination, the primary outcome of this study.

### Statistical Analysis

All statistical analyses were performed with SAS (SAS Institute Inc, Cary, NC). Demographic and clinical characteristics for populations declining and receiving tPA were presented as counts and percentages for categorical/binary variables and mean, SD, and interquartile range for continuous variables. Pearson  $\chi^2$  tests were used to compare differences in categorical variables, and

**Figure 1** Population Chart of Final Study Cohort



Wilcoxon rank-sum tests were used to compare continuous variables across the 2 groups. For statistical significance, we used the standard  $\alpha$  level of 0.05. However, given the large sample size, we present standardized differences wherein standardized differences  $>10$  indicate a significant difference between groups. Given the large sample sizes, many significant differences were expected on the basis of  $p$  values. To lessen the effect of sample size, we also report standardized differences. A standardized difference  $>10\%$  can indicate a meaningful difference.

Multivariable logistic regression models were performed to identify factors associated with tPA declination. The generalized estimating equation method was applied to account for the clustering of patients within each hospital. Covariates in the model included all patient and hospital characteristic variables described above. For interpretability, linear splines were applied to age, NIHSS admission score, onset-to-arrival time, and percent Black patients treated by site, with knots at age 65 years, NIHSS score of 15, 90-minute arrival time, and at 15% Black patients treated. In this cohort, the missing data rate was  $<5\%$  for all variables (eTable 2, [links.lww.com/WNL/B857](https://links.lww.com/WNL/B857)). Missing hospital characteristic variables were not imputed. Missing NIHSS scores were not imputed because these data were likely not missing at random. For other medical history covariates, missing data were all imputed as “no”. Prior studies have demonstrated disparities in tPA use by race and gender, so an interaction between race and gender was included as an additional sensitivity analysis.

Data not provided in the article because of space limitations may be shared (anonymized) at the request of any qualified investigator for purposes of replicating procedures and results.

## Results

Among the 1,180,307 patients with AIS from 2,049 sites in the GWTG-Stroke registry during the study period, 177,115 patients from 1,976 sites met the inclusion criteria (Figure 1).

Overall, 6,545 (3.7%) of tPA-eligible patients with AIS had declination as the sole documented reason for not receiving tPA. Baseline characteristics of patients declining and not declining tPA are described in Table 1. Absolute rates of declination were 3.8% in non-Hispanic White, 3.7% in non-Hispanic Black, 2.5% in Asian, and 3.2% in Hispanic patients. Patients who declined tPA were older; were more often female; arrived more often during off-hours; arrived on average slightly earlier after last known well; had milder deficits; more often had atrial fibrillation, coronary artery disease, prior stroke or TIA, and hypertension; and less often were current smokers. Compared to patients who did not decline tPA, patients who declined tPA were more often cared for at Primary Stroke Centers, nonteaching hospitals, smaller hospitals (bed size), and hospitals with lower annual tPA administration and stroke patient admission volumes.

In multivariable analyses to identify factors associated with tPA declination (Table 2), non-Hispanic Black compared with non-Hispanic White race/ethnicity was associated with higher odds of tPA declination (adjusted odds ratio [aOR] 1.21, 95% CI 1.11–1.31), while non-Hispanic Asian race/ethnicity was associated with lower odds (aOR 0.72, 95% CI 0.58–0.88) and Hispanic ethnicity (any race) with similar odds (OR 0.98, 95% CI 0.86–1.13) of tPA declination. Other patient characteristics associated with higher risk of declining tPA included being female, age when the patient is  $>65$  years of age, not arriving by ambulance, arriving during off-hours, arriving within 90 minutes of symptom onset, being insured by Medicaid, history of stroke, and absence of dyslipidemia. Hospital characteristics associated with higher odds of tPA declination included being a nonteaching hospital, having a large annual AIS patient volume, having fewer beds, and treating fewer patients with tPA annually.

To determine the relationship between NIHSS score and tPA declination, a sensitivity analysis of the subpopulation of patients with a documented NIHSS score ( $n = 169,201$ ) found a nonlinear U-shaped relationship with tPA

**Table 1** Patient Characteristics and Comparison of Demographic, Medical, and Clinical Data Between Those Who Declined and Those Who did Not Decline tPA<sup>a</sup>

Characteristics	Total (N = 177,115)	Declined tPA no (n = 170,570)	Declined tPA yes (n = 6,545)	p Value	Abs std diff
Age mean (SD), y	70.6 (15.0)	70.4 (14.9)	75.7 (15.7)	<0.0001	34.13
Female, n (%)	89,525 (50.5)	85,677 (50.2)	3,848 (58.8)	<0.0001	17.26
Race/ethnicity, n (%)				<0.0001	9.48
Non-Hispanic White	121,991 (68.9)	117,285 (68.8)	4,706 (71.9)		
Non-Hispanic Black	29,121 (16.4)	28,058 (16.5)	1,063 (16.2)		
Hispanic (any race)	13,673 (7.7)	13,236 (7.8)	437 (6.7)		
Asian	5,217 (2.9)	5,085 (3.0)	132 (2.0)		
Other (includes UTD)	7,054 (4.0)	6,849 (4.0)	205 (3.1)		
Arrival by EMS, n (%)	129,048 (73.0)	124,338 (73.0)	4,710 (72.2)	0.13	1.88
Off-hour arrival, n (%)	94,025 (53.1)	90,225 (52.9)	3,800 (58.1)	<0.0001	10.40
Onset-to-arrival time, min	77.0 (45.0, 142.0)	77.0 (45.0, 143.0)	74.0 (46.0, 122.0)	<0.0001	16.79
Insurance, n (%)				<0.0001	10.92
Private/VA/Champus/other	65,274 (36.9)	63,055 (37.0)	2,219 (33.9)		
Medicaid	16,618 (9.4)	16,037 (9.4)	581 (8.9)		
Medicare	55,915 (31.6)	53,631 (31.4)	2,284 (34.9)		
Self-pay/no insurance	6,437 (3.6)	6,273 (3.7)	164 (2.5)		
Not documented	32,871 (18.6)	31,574 (18.5)	1,297 (19.8)		
NIHSS score, median (IQR)	6.0 (3.0, 12.0)	6.0 (3.0, 12.0)	5.0 (2.0, 11.0)	0.0002	4.87
Atrial fibrillation/flutter, n (%)	33,171 (18.8%)	31,662 (18.6%)	1,509 (23.1%)	<0.0001	11.10
Previous stroke, n (%)	42,436 (24.0%)	40,546 (23.8%)	1,890 (29.0%)	<0.0001	11.63
Previous TIA, n (%)	16,653 (9.4%)	15,915 (9.4%)	738 (11.3%)	<0.0001	6.41
CAD/prior MI, n (%)	40,616 (23.0)	39,007 (22.9)	1,609 (24.7)	0.0012	4.03
Carotid stenosis, n (%)	5,301 (3.0)	5,098 (3.0)	203 (3.1)	0.60	0.65
Diabetes, n (%)	55,419 (31.4)	53,449 (31.4)	1,970 (30.2)	0.03	2.70
PVD, n (%)	6,535 (3.7)	6,290 (3.7)	245 (3.8)	0.81	0.29
Hypertension, n (%)	131,398 (74.4)	126,363 (74.3)	5,035 (77.2)	<0.0001	6.63
Dyslipidemia, n (%)	81,135 (46.0)	78,188 (46.0)	2,947 (45.2)	0.19	1.65
Smoking, n (%)	29,431 (16.7)	28,557 (16.8)	874 (13.4)	<0.0001	9.51
Heart failure, n (%)	17,199 (9.7)	16,433 (9.7)	766 (11.7)	<0.0001	6.71
Renal insufficiency, chronic, n (%)	14,591 (8.3)	13,995 (8.2)	596 (9.1)	<0.01	3.21
Hospital region, n (%)				<0.0001	6.21
Northeast	34,829 (19.7)	33,635 (19.7)	1,194 (18.2)		
Midwest	33,484 (18.9)	32,104 (18.8)	1,380 (21.1)		
South	72,301 (40.8)	69,649 (40.8)	2,652 (40.5)		
West	36,501 (20.6)	35,182 (20.6)	1,319 (20.2)		
Hospital location, rural, n (%)	6,910 (3.9)	6,601 (3.9)	309 (4.7)	0.0005	4.20
Primary Stroke Center, n (%)	95,519 (53.9)	91,917 (53.9)	3,602 (55.0)	<0.0001	21.11

Continued

**Table 1** Patient Characteristics and Comparison of Demographic, Medical, and Clinical Data Between Those Who Declined and Those Who did Not Decline tPA<sup>a</sup> (continued)

Characteristics	Total (N = 177,115)	Declined tPA no (n = 170,570)	Declined tPA yes (n = 6,545)	p Value	Abs std diff
Teaching hospital, n (%)	129,885 (74.4)	125,548 (74.7)	4,337 (67.5)	<0.0001	15.93
Annual IV tPA volume, mean (SD), median (IQR)	31.5 (21.3) 27.1 (16.3, 40.4)	31.7 (21.4) 27.3 (16.6, 40.7)	26.7 (18.6) 22.1 (13.6, 34.9)	<0.0001	24.84
No. of beds, median (IQR)	360.0 (235.0, 540.0)	362.0 (235.0, 545.0)	310.0 (203.0, 473.0)	<0.0001	20.21
AIS volume, median (IQR)	244.8 (171.1, 368.1)	245.9 (171.3, 370.3)	226.3 (158.4, 321.0)	<0.0001	19.10
Percent Black patients treated	10.3 (3.6, 22.2)	10.3 (3.6, 22.2)	9.6 (3.1, 20.4)	0.0002	4.74

Volume is measured in number of patients treated annually at the hospital level.

Abbreviations: Abs std diff = absolute standardized difference; AIS = annual ischemic stroke; CAD = coronary artery disease; EMS = emergency medical services; IQR = interquartile range; MI = myocardial infarction; NIHSS = NIH Stroke Scale; PVD = peripheral vascular disease; tPA = tissue plasminogen activator; VA = Veterans Affairs.

<sup>a</sup> Given the large sample size, the absolute standardized difference is shown for comparison.

declination (eFigure 1, [links.lww.com/WNL/B857](https://links.lww.com/WNL/B857)). Among patients with an NIHSS score  $\leq 15$ , higher NIHSS scores were associated with lower odds of tPA declination (aOR 0.94, 95% CI 0.94–0.95;  $p < 0.0001$  per 1-point increase in NIHSS score), while among patients with NIHSS score  $> 15$ , higher NIHSS scores were associated with higher odds of tPA declination (aOR 1.11, 95% CI 1.09–1.12;  $p < 0.0001$ , per 1-point increase in NIHSS score). Yet, non-Hispanic Black race/ethnicity still remained independently associated with higher odds of tPA declination (aOR 1.25, 95% CI 1.15–1.35;  $p = 0.005$ ) and Asian race with lower odds of tPA declination (aOR 0.75, 95% CI 0.61–0.92) compared to non-Hispanic White patients after adjustment for baseline NIHSS score (eTable 3).

In sensitivity analyses to assess for interaction, there was no interaction between race (Black vs other) and gender after adjustment for relevant covariates in the overall cohort ( $p = 0.0595$ ) and in the subgroup with documented NIHSS score ( $p = 0.0707$ ).

## Discussion

In this nationwide analysis of hospitalized patients with AIS eligible for thrombolysis, we found that 3.7% of otherwise eligible patients declined tPA. While absolute rates of declining tPA were similar for non-Hispanic Black, non-Hispanic White, and Hispanic patients, after adjustment for possible confounders, non-Hispanic Black patients were 21% more likely to decline tPA than non-Hispanic White patients. Despite the absolute rates, this represents a significant opportunity to optimize delivery of a proven therapy that is currently given to only  $< 10\%$  of patients with ischemic stroke. Improving the consent process for tPA among non-Hispanic Black patients with AIS might be a target for future efforts to reduce disparities in stroke care.

Racial and ethnic disparities in acute treatment, rehabilitation, and prevention of stroke have been documented,<sup>12</sup> and racism

has been identified as a clear contributor to health disparities.<sup>13</sup> The current study did not measure provider-level factors such as prejudice, unconscious bias, cultural competency, or concordance between provider and patient race, all of which may have contributed to the differences observed in declining care. These unmeasured provider-level factors may have resulted in providers discussing treatments differently according to the patient's race or ethnicity and ultimately affecting informed consent. In addition, structural racism, a known driver of health disparities,<sup>14</sup> may have contributed to the differences observed in acute stroke thrombolysis declination. Further research could look at both provider- and system-level factors that contribute to declining tPA for AIS.

The observed prevalence of tPA declination in this national cohort is less than previously reported in single-center or regional studies (4.2%–7.5% declined tPA).<sup>10,15,16</sup> This may be due to an overestimation of treatment declination in smaller sample cohorts, the impact of national efforts to improve tPA use among GWTG-Stroke participating hospitals, or underlying regional variation in declining tPA across the country.<sup>10</sup> Despite the lower overall prevalence of tPA declination, the current study provides further evidence in support of previous observations that non-Hispanic Black patients with AIS are more likely to decline tPA than non-Black patients.<sup>10</sup>

Besides racial/ethnic differences, we also found that women were more likely than men to decline tPA treatment. These data support prior observations that women may be less likely to accept treatment for AIS.<sup>17</sup> Factors driving this difference may include differences in presentation, education, and risk tolerance between genders and gender bias among clinicians. In addition, in patients presenting with an NIHSS score  $< 15$ , lower NIHSS score was associated with a greater risk of tPA declination, consistent with other published reports.<sup>10,15</sup> Patients with minor deficits may perceive risks of disability differently from patients with more debilitating deficits, and this



**Table 2** aORs and 95% CIs for Factors Contributing to tPA Declination in Multivariable Analysis

Characteristics	aOR (95% CI)	Adjusted p Value
Female vs male	1.17 (1.11–1.23)	<0.0001
<b>Race/ethnicity (vs non-Hispanic White)</b>		
Non-Hispanic Black	1.21 (1.11–1.31)	<0.0001
Hispanic (any race)	0.98 (0.86–1.13)	0.82
Asian	0.72 (0.58–0.88)	0.001
Other (includes UTD)	0.86 (0.74–1.00)	0.04
EMS arrival (vs no)	0.77 (0.72–0.82)	<0.0001
Off-hour arrival (vs no)	1.29 (1.22–1.36)	<0.0001
<b>Insurance (vs private//VA/Champus/other)</b>		
Medicaid	1.12 (1.01–1.25)	0.03
Medicare	1.00 (0.93–1.08)	0.99
Self-pay/no insurance	0.98 (0.83–1.17)	0.85
Not documented	1.07 (0.96–1.19)	0.22
Atrial fibrillation/flutter (vs no)	0.99 (0.93–1.05)	0.66
Previous stroke (vs no)	1.29 (1.22–1.36)	<0.0001
Previous TIA (vs no)	1.06 (0.98–1.15)	0.17
CAD/prior MI (vs no)	1.03 (0.97–1.10)	0.35
Carotid stenosis (vs no)	0.95 (0.82–1.11)	0.53
Diabetes (vs no)	1.03 (0.97–1.09)	0.39
PVD (vs no)	0.93 (0.81–1.05)	0.23
Hypertension (vs no)	1.04 (0.98–1.12)	0.22
Dyslipidemia (vs no)	0.89 (0.84–0.94)	<0.0001
Smoking (vs no)	1.09 (1.00–1.18)	0.06
Heart failure (vs no)	1.06 (0.97–1.15)	0.18
Renal insufficiency, chronic (vs no)	0.98 (0.90–1.08)	0.73
<b>Hospital region (vs West)</b>		
Northeast	0.97 (0.83–1.13)	0.65
Midwest	1.15 (0.97–1.34)	0.10
South	1.13 (0.99–1.30)	0.08
Hospital location, rural (vs no)	0.87 (0.70–1.09)	0.23
Primary Stroke Center (vs no)	0.98 (0.89–1.08)	0.70
Teaching hospital (vs no)	0.84 (0.75–0.94)	0.002
<b>AIS volume (vs 0–150), n</b>		
151–250	1.12 (0.99–1.27)	0.08
251–350	1.20 (0.99–1.46)	0.07
≥351	1.30 (1.02–1.66)	0.04
Age ≤65 y (per 5-y unit increase) <sup>a</sup>	0.97 (0.94–0.99)	0.003
Age >65 y (per 5-y unit increase) <sup>a</sup>	1.29 (1.25–1.34)	<0.0001

Continued

**Table 2** aORs and 95% CIs for Factors Contributing to tPA Declination in Multivariable Analysis (continued)

Characteristics	aOR (95% CI)	Adjusted p Value
Onset-to-arrival time $\leq 90$ min (per 15-min unit increase) <sup>b</sup>	1.11 (1.09–1.13)	<0.0001
Onset-to-arrival time $> 90$ min (per 15-min unit increase) <sup>b</sup>	0.81 (0.79–0.83)	<0.0001
Annual IV tPA volume (per 10-case unit increase)	0.89 (0.85–0.93)	<0.0001
No. of beds (per 100-case unit increase)	0.96 (0.93–0.99)	0.009
Percent Black patients treated $\leq 15\%$ (per 5% increase)	0.98 (0.93–1.03)	0.36
Percent Black patients treated $> 15\%$ (per 5% increase)	1.02 (0.96–1.09)	0.47

Volume is measured in number of patients treated annually at the hospital level.

Abbreviations: AIS = annual ischemic stroke; aOR = adjusted odds ratio; CAD = coronary artery disease; EMS = emergency medical services; MI = myocardial infarction; PVD = peripheral vascular disease; tPA = tissue plasminogen activator; VA = Veterans Affairs.

<sup>a</sup> The multivariable logistic regression has difference estimation on ORs for age  $\leq 65$  and  $> 65$  years.

<sup>b</sup> The multivariable logistic regression has difference estimation on odds ratio for onset-to-arrival time  $\leq 90$  and  $> 90$  minutes.

perception may affect decision-making about treatment with tPA. Declining care was also more likely in patients with very severe stroke (NIHSS score  $> 15$ ). Physicians obtaining consent for tPA may conduct the informed consent process for tPA differently with patients presenting with either minor or severe symptoms by minimizing potential benefits or highlighting risks, respectively.

Time from last known well to arrival was associated with tPA declination, with patients arriving  $< 90$  minutes from symptom onset more likely to decline tPA. Conversely, patients arriving  $> 90$  minutes after symptom onset were less likely to decline. For the late-arriving group, patients and physicians may experience increased urgency as the tPA treatment time window begins to expire. This may translate into a more expedited consent process. There may be an effect of a shorter time for consent on decreasing the chance of treatment declination, although psychological studies of nonmedical decision-making may be informative. For example, when given advice too early in the decision-making process, people may make poor choices.<sup>18</sup> As pressure increases and less time is available to learn about treatment options or outcomes, clinicians may emphasize different aspects of the treatment. Future work should explore the time-dependent association with treatment declination.

Several hospital-level factors were associated with tPA declination in the adjusted model. Patients arriving at the hospital during off-hours were more likely to decline tPA. A potential explanation may be that fewer personnel are available to facilitate explaining and obtaining informed consent. Patients arriving at hospitals with larger annual AIS volumes ( $> 350$  cases) were also more likely to decline tPA, but an increasing annual number of tPA treated cases was associated with a lower odds of declining when adjusted for hospital bed size. This suggests that personnel at hospitals that deliver tPA more frequently may be more comfortable and adept at discussing treatment options and obtaining informed consent.

This finding mirrors the relationship between lower door-to-needle times with higher number of tPA-treated cases.<sup>6</sup>

There are several limitations to this study. As a retrospective analysis of quality data, the study relies on physician documentation of patient/proxy declining tPA. However, it is possible that physicians may document differently by race/ethnicity. Race/ethnicity was also based on self-report, and the study relied on abstraction of the medical record to determine race/ethnicity; therefore, this covariate was not subject to independent verification. Residual measured and unmeasured confounding may account for some of the findings of the study, and there may be factors beyond race/ethnicity that influenced the observed differences. We cannot exclude the possibility of missing cases or bias in documentation at some participating hospitals. There is also a potential for sampling bias in that the GWTG-Stroke database may overrepresent patients from teaching and higher-performing hospitals. Thus, these data may underestimate the true prevalence of tPA declination given that both high tPA volume and teaching hospital status were associated with lower odds of tPA declination.

In a large national registry of patients with AIS, we found that 3.7% of otherwise tPA-eligible patients did not receive tPA because the patient/family declined treatment. Although the overall rate of tPA declination is low, eligible non-Hispanic Black patients have greater risk-adjusted odds and Asian patients have lower risk-adjusted odds of tPA declination compared to non-Hispanic White patients. Reducing rates of tPA declination among non-Hispanic Black patients may be an opportunity to address disparities in stroke care.

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<b>Roland Matsouaka, PhD</b>	Duke Clinical Research Institute, Durham, NC	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data
<b>Ying Xian, PhD</b>	Duke Clinical Research Institute, Durham, NC	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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## Appendix (continued)

Name	Location	Contribution
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