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Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Longitudinal outcomes following stroke

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Summary for Social Media If Published

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Current Knowledge: Mexican American persons have worse neurologic, functional, cognitive, and quality of life outcomes three months after stroke than non-Hispanic white persons.

Study Question: To investigate functional, cognitive, neurologic, and quality of life outcomes measured at three, six and 12 months following first-ever ischemic stroke overall and by ethnicity in a population-based longitudinal stroke study.

New Knowledge: In both ethnic groups, stroke outcomes were at their worst at three months, improved significantly between three and six months and then stabilized thereafter. Worse outcomes in Mexican American persons compared with non-Hispanic white persons were evident at three months post-stroke and remained unchanged over time.

Potential Impact: Results suggest continued assessment for rehabilitation or other services in the chronic phase of stroke, including screening for functional, neurologic and cognitive deficits, may be beneficial. Greater detail regarding recommendations for ongoing assessments in the chronic phase of stroke should be considered in future stroke-specific guidelines.

Abstract

Objective: To investigate stroke outcomes at three, six and 12 months post-stroke overall and by ethnicity in a population-based, longitudinal study.

Methods: First-ever ischemic strokes (2014-2019, n=1,332) among Mexican American (MA) persons (n=807) and non-Hispanic white (NHW) persons (n=525) were identified from the Brain Attack Surveillance in Corpus Christi Project. Data were collected from patient or proxy interviews (baseline, 3, 6 and 12 months post-stroke) and medical records, including functional (activities of daily living (ADL)/instrumental activities of daily living (IADL) score), neurologic (National Institutes of Health Stroke Scale (NIHSS)), cognitive (Modified Mini-Mental State Examination (3MSE)) and quality of life (QOL) outcomes (Stroke-specific QOL-12). Outcome trajectories were analyzed using multivariable adjusted linear models, with generalized estimating equations to account for within-subject correlations; interactions between ethnicity and time were included to investigate ethnic differences in trajectories.

Results: Median age was 67 years (IQR: 58,78), 48.5% were women, and 60.6% were MA. For all outcomes, significant improvement was seen between three and six months ($p<0.05$ for all), with stability between six and 12 months. MA persons had significantly worse outcomes compared with NHW persons at all time points (three, six, and 12 months) with the exception of NIHSS which did not differ by ethnicity at six and 12 months, and average change in outcomes did not vary significantly by ethnicity.

Interpretation: Outcomes were at their worst at three months post-stroke, and ethnic disparities were already present suggesting the need for early assessment and strategies to improve outcomes and possibly reduce disparities.

Introduction

Given the growing number of stroke survivors worldwide,[1] contemporary population-level estimates of longitudinal outcomes, including functional, cognitive and neurologic outcomes and quality of life, are critical. These data have multiple uses including providing patients and families with information and prognostic data about recovery, identifying subgroups of patients to target for health equity initiatives, and informing needed clinical and patient resources spanning the acute to post-acute stroke period.

Some registry and population-based studies have considered longitudinal stroke outcomes although contemporary data from the last decade are limited and therefore, existing estimates of recovery may not reflect outcomes in the current era of improved stroke detection and acute care.[1-3] Further, there are few studies with longitudinal outcomes in racially-ethnically diverse populations who are disproportionately impacted by stroke. We have previously reported worse neurologic, functional, cognitive, and quality of life outcomes three months after stroke in Mexican Americans (MA) persons compared with non-Hispanic whites (NHW) persons.[4, 5] It is unclear whether MA persons have a different trajectory of recovery following stroke and whether disparities in outcomes persist after three months. The objective of this study was to investigate functional, cognitive, neurologic, and quality of life outcomes measured at three, six and 12 months following first-ever ischemic stroke overall and by ethnicity in a population-based longitudinal stroke study.

Methods

This paper results from a pre-specified primary aim of the Brain Attack Surveillance in Corpus Christi (BASIC) Project. BASIC is conducted in Nueces County, Texas. Nueces County is located in south Texas and includes a primarily bi-ethnic population. The county is roughly 65% MA.[6] There is little out migration of County residents in this community facilitating the long-term

follow-up of these individuals for stroke outcomes. Furthermore, MA persons in Nueces County are almost exclusively non-immigrant, a foreshadowing of the future U.S. population.

In BASIC, strokes have been ascertained via active and passive surveillance methods using a consistent approach and stroke definition.[7] Briefly, active surveillances entails reviewing hospital admission logs for stroke screening terms. Hospital units are also monitored for possible in-hospital strokes. Passive surveillance involves reviewing hospital and emergency department discharge diagnosis codes for stroke. Possible strokes undergo validation by a stroke fellowship-trained physician blinded to ethnicity using source documentation from the medical record. For the current study, only first-ever ischemic strokes defined as an acute onset of focal neurologic symptoms lasting greater than 24 hours were included. History of stroke was ascertained from the medical record. For the time period under study (2014-2019), there were no changes in stroke ascertainment methods.

Shortly after stroke, patients were asked to participate in a baseline interview, as well as outcome interviews collected at three, six and 12 months following stroke. Interviews are conducted in English or Spanish depending on the patient preference. Participation in the baseline interview was 74.8% during the study period, with higher participation for MA persons (78.8% vs. 69.4% for NHWs, chi-squared test p-value < 0.001). Baseline interviews were completed by patients (75.4%) or proxies (24.6%) if the patient was unable to answer questions for themselves, with no difference in proxy use by ethnicity (MA persons: 24.3%, NHW persons: 25.1%). Information collected in the baseline interview includes race-ethnicity, pre-stroke functional disability (modified Rankin scale), pre-stroke cognitive function assessed by an informant (Informant Questionnaire of Cognitive Decline in the Elderly (IQCODE)) and categorized using established cutpoints to represent normal cognition, cognitive impairment not demented, and dementia,[8] pre-stroke depression status (self-reported physician diagnosis and

use of antidepressant medications), educational attainment, marital status, and insurance status. In addition to the interview, participants' charts undergo a medical record abstraction to collect additional data on demographics (age, sex), documented history of stroke risk factors and comorbidities (hypertension, diabetes, heart disease/myocardial infarction, atrial fibrillation, high cholesterol, cancer, Parkinson disease, Alzheimer disease/dementia, COPD, congestive heart failure, epilepsy, end stage renal disease, and body mass index (BMI)), initial stroke severity measured by the National Institutes of Health Stroke Scale (NIHSS), and stroke treatment with intravenous tissue plasminogen activator (IV tPA). Endovascular treatment was not available in the study community for the study time period. Data on all-cause mortality were ascertained from the Texas Department of State Health Services.

All attempts were made to follow-up with the participants to ascertain outcomes. Outcomes were collected in-person at three, six and 12 months post-stroke (plus/minus two weeks) whenever possible including in nursing homes. Outcomes included functional outcome, neurologic outcome, quality of life and cognitive outcome as previously described.[4, 5] Functional outcome was assessed based on patient or proxy self-report of difficulty with 15 Activities of Daily Living (ADL) and 7 Instrumental Activities of Daily Living (IADL). Response options included: 1 (no difficulty with activity), 2 (some difficulty with activity), 3 (a lot of difficulty with activity) and 4 (can only do with help). ADLs and IADLs were averaged and the resulting score ranged from 1 to 4. Neurologic outcome was assessed by study coordinators using the NIHSS (0-42, higher scores worse). Quality of life was assessed by patient or proxy self-report using the short-form Stroke-specific Quality of Life (SS-QOL) scale which has been validated in our study population (1-5, higher scores better).[9] Cognitive outcomes were assessed by the modified mini mental status examination (3MSE, scores range from 0 to 100 with higher scores representing better cognitive function). Cognitive outcomes were limited to patient interviews only. Use of proxies to assess functional and quality of life outcomes was stable over time and

did not differ by ethnicity at any time point (three months MA persons 14.9%, NHW persons 12.9%; p-value=0.40; six months MA persons 14.6%, NHW persons 12.2%; p-value=0.35; 12 months MA persons 13.0%, NHW persons 12.0%; p-value=0.69).

Study participants

The initial analysis sample included 1,952 baseline-eligible patients who had ischemic stroke between January 2014 and December 2019. We sequentially excluded patients who were not NHW or MA (n=142), those with missing data on variables used for constructing inverse probability weights (n=30), and patients who did not complete baseline interview (n=448) which resulted in a final sample of 1,332 participants (Figure 1), including 807 MA persons and 525 NHW persons. Sample sizes for each outcome at each time point are included in Figure 2.

Statistical analysis

We examined missing data patterns for all variables and compared characteristics based on baseline participation. In order to account for differential baseline attrition, we modeled the probability of participating at baseline using a logistic regression model (n=1,780) to generate inverse probability weights (IPW). Variables included in the model were age (modeled quadratically), sex, race/ethnicity, initial NIHSS, comorbidity index (calculated as the sum of the aforementioned risk factors and comorbidities from the medical record), and IV tPA. We stabilized the weights by multiplying each weight by the average probability of participating in the baseline interview. Among baseline participants, the weights ranged from 0.46 to 2.44, with a mean of 1.07. Additionally, to account for differential mortality, weights for mortality prior to three, six, and 12 months were constructed using logistic regression and the same variables as the baseline IPW.

The baseline covariate with the highest percentage of missing data was pre-stroke cognitive function as measured by the IQCODE (19.1%), followed by pre-stroke functional disability as measured by the mRS (2.6%). Missing data for other variables, including education attainment, marital status and health insurance status, were less than 1%. We assumed missing at random (MAR) and used multiple imputation with chained equations (MICE) for all variables and the "Just Another Variable" approach for longitudinal data to generate 30 imputed datasets.[10] After we confirmed similar distributions comparing the fully imputed longitudinal outcomes without IPW for mortality and the partially missing outcomes with IPW for mortality, imputed observations at post-mortality time points were dropped.

We calculated descriptive statistics and compared baseline sample characteristics between NHW and MA persons using chi-squared tests for categorical variables and Kruskal–Wallis tests for continuous variables. We examined the trajectories of stroke outcomes using linear models; NIHSS score was log-transformed to stabilize the variance for this outcome. Generalized estimating equations (GEE) with unstructured working covariance were used to account for within-subject correlations for each continuous outcome variable. Because outcomes were assessed at time points with unbalanced time intervals, we treated time as a categorical variable with the three-month time point as the reference category. Covariates included age, sex, educational attainment, marital status, health insurance status, initial stroke severity (log-transformed NIHSS scores), comorbidity index (measured as a sum of 15 risk factors measured from the medical record), pre-stroke functional disability as measured by modified Rankin Scale (mRS), and pre-stroke cognitive function as measured by IQCODE. Note we did not adjust for individual risk factors, including hypertension, diabetes, atrial fibrillation, and coronary artery disease, which are included in the comorbidity index, as we have previously not found them to be associated with the current outcomes.[4] Functional forms of continuous covariates were determined by the significance of their quadratic term. Test statistics from the imputed datasets

were pooled using Rubin's rules.[11] We investigated ethnic differences in the change in the outcomes by introducing interactions between time and ethnicity into the models. Combined tests of all interactions (f-tests with 2 degrees of freedom) from the multiply imputed datasets were estimated using a multivariate extension of Rubin's rules.[12] To visualize the results, we computed estimates for the conditional expected outcomes for each ethnicity at each time point, also using the multivariate extension of Rubin's rules to compute the standard errors for the linear combinations of coefficients. The covariate reference levels used for conditioning were mean initial log-transformed NIHSS (1.44, roughly 3.3 on original scale) and age (68.1 years), male sex, high school education, no tPA administered, unmarried, uninsured, moderate pre-stroke disability (mRS 2-3), and no pre-stroke cognitive impairment (IQCODE 0-3). These conditional expected outcomes were then plotted with their associated 95% confidence intervals. Finally, to assess the stability of outcomes overtime, we implemented mixed models with restricted maximum likelihood on complete case data and using the same covariates as for the primary analysis to quantify inter- and intrapersonal variability of the four primary outcomes; these were summarized by the intraclass correlation coefficient (ICC) and its complement, respectively. Statistical analyses were completed using SAS version 9.4 (SAS Institute Inc.)

Sensitivity Analyses

We conducted a series of sensitivity analyses to inform the robustness of our primary findings. To confirm that the longitudinal changes in outcome were not influenced by recurrent stroke, we performed a sensitivity analysis, which included, in the primary models, a variable indicating time points that occurred after a recurrent stroke. Because there was variability in the timing of the outcome assessments (plus/minus two weeks around each time period), we conducted a sensitivity analysis modeling time (in days) as a continuous covariate (calculated as the difference between the date of the outcome

assessment and the date of stroke). Models used the same approach as the primary analysis with the exception that time was modeled with linear and quadratic terms to account for the non-linear associations and limited to those with complete outcome data. To inform the possibility of ceiling effects in recovery, we conducted an analysis additionally including interaction terms between initial stroke severity (mild NIHSS 1-5, moderate >5) and time in the models and calculated effect estimates stratified by initial NIHSS stroke status.Written informed consent was signed by all participants. The BASIC study was approved by the Institutional Review Boards at the University of Michigan and local hospitals.

Results

Median age of the study populations was 67 years (IQR: 58, 78), 48.5% were women, and 60.6% were MA. The majority had some pre-stroke functional disability and among those with information on pre-stroke cognitive function, roughly half had mild to moderate pre-stroke cognitive impairment. Initial stroke severity, on average, was mild. MA persons were younger on average, had lower educational attainment, and were more likely to be uninsured than NHW persons (Table 1). Median and average levels of the unadjusted outcomes for the three time points are included in Table 2. On average at three months, the stroke cases experienced some (value of 2 on ADL/IADL score) to a lot of difficulty (value of 3 on ADL/IADL score) with ADLs/IADLs, low NIHSS, and some cognitive deficits, and required a little to some help on the SS-QOL scale items. The strongest correlation among outcomes was noted between functional outcome and quality of life (r=-0.82) and neurologic outcomes (r=0.64)), while correlations were lowest between cognitive outcome and neurologic (r=-0.35) and quality of life outcomes (r=0.38, Supplementary Figure). Unadjusted all-cause mortality was slightly lower in MA persons than NHW persons throughout the observation period (overall Kaplan-Meier log-rank p-value=0.03):

at three months (MA 10.9%, NHW 15.4%; p-value=0.02), six months (MA 13.4%, NHW 17.7; p-value=0.03) and 12 months (MA 16.5%, NHW 21.0%; p-value=0.04). Unadjusted risk of recurrence was higher in MA persons than NHW persons at three (MA 3.0 %, NHW 0.3%; p=0.01), six (MA 4.4%, NHW 1.1%; p-value=0.01), and 12 months (MA 7.2%, NHW 3.95%; p-value=0.09) although absolute differences were small.

Table 3 includes the results from the multivariable models and Figure 2 displays the expected outcomes by race-ethnicity from these models. For all outcomes, improvement was seen between three and six months with stability in the outcomes between six and 12 months. Descriptive statistics, including measures of within- and between-person variability, suggest that while the majority of variation in outcomes is driven by interpersonal factors (ICC ranging from 0.57 for neurologic outcome to 0.81 for functional outcome), changes in individuals' scores over time still contribute to some variation.

MA persons had significantly worse outcomes compared with NHW persons at all outcome time points (Table 2), with the exception of NIHSS which did not differ significantly by ethnicity at six and 12 months, and average change in the outcomes did not vary significantly by ethnicity for any of the outcomes (Figure 2, p-value for interaction between ethnicity and time for all outcomes > 0.05 for all).

The inclusion of a time-varying covariate for stroke recurrence during the one-year follow-up period did not alter the main results (Table 3). Similarly, results were consistent when time was modeled continuously (data not shown). While no significant interactions were noted between time and initial stroke severity (Supplementary table), results of the sensitivity analyses do suggest, at least qualitatively, that those with greater initial NIHSS had greater improvements

between three and six months in stroke severity (both ethnic groups) and in functional outcome in MA persons.

Discussion

This population-based, longitudinal stroke study describes the average change in multiple stroke outcomes in the year following stroke. The results show that following an acute ischemic stroke, functional, neurologic, cognitive and quality of life outcomes improve significantly between three and six months and stabilize thereafter. While significant improvements were demonstrated between three and six months, improvements were small on the absolute scale across all outcomes and, on average, some functional, neurologic and cognitive deficits remain in the year after stroke, with significant variability in the patterns of recovery between and within individuals.

Although care aimed at maximizing outcomes begins in the hospital, the majority of stroke survivors in this community and nationally are discharged home or after short stays in inpatient rehabilitation settings.[13, 14] Our results detail the persistence of functional, cognitive and neurologic deficits in the year following stroke. Stroke rehabilitation guidelines state that it is "reasonable" that individuals with stroke who return home receive follow-up on their functional and communication abilities within 30 days of discharge.[15] Because patients' specific needs can change over time and beyond 30 days, continued assessment for rehabilitation or other services in the chronic phase of stroke, including screening for functional, neurologic and cognitive deficits, may be beneficial. A recently published American Heart Association/American Stroke Association scientific statement covers the critical role of primary care in improving population-level health for stroke survivors and highlights that even in the subacute and chronic phase of stroke many patients would benefit from continued rehabilitation, which our results support.[16]

Greater detail regarding recommendations for ongoing assessments in the chronic phase of stroke should be considered in future stroke-specific guidelines.

Our results demonstrate that ethnic differences in outcomes emerge early after stroke, persist in the year following stroke, and are not explained by ethnic differences in pre-stroke functional disability and cognition or in initial stroke severity. Existing data point to some possible factors that may explain the emergence of ethnic differences soon after stroke. Despite overall utilization of inpatient rehabilitation that is similar to national estimates, we have shown that MA persons in this community are less likely to be discharged to inpatient rehabilitation, the post-acute care setting with the greatest intensity of rehabilitation, even after accounting for Medicare eligibility.[13, 14] Ethnic differences in inpatient rehabilitation are potentially important as a randomized trial has shown that more intense rehabilitation settings reduce disability compared to less intense rehabilitation.[17] We do not have data on utilization of rehabilitation in the current study population to assess its impact on ethnic differences in outcome, although we are prospectively collecting this information to directly test this hypothesis in the future. . MA persons with stroke are also more likely to have post-stroke sleep-disordered breathing, which often goes unrecognized and untreated, and sleep-disordered breathing confers a greater risk of worse stroke outcomes in MA persons.[18] An ongoing clinical trial is testing whether treatment with continuous positive airway pressure improves stroke outcomes, so sleep-disordered breathing may represent a possible intervention target to reduce ethnic outcome disparities.[19] Finally, while tPA use was accounted for in the current analysis, trend data from BASIC suggest that disparities in tPA treatment may be emerging such that MA persons are less likely to receive tPA than NHW persons.[20] More recent acute interventions, including endovascular therapy and alternate thrombolytics, which are still uncommon in this community, should be prospectively monitored for possible ethnic differences. These factors represent some possible points of intervention at the patient and provider levels to improve outcomes, although other

factors, such as lifestyle modifications and screening and treatment of post-stroke depression, should also be the subject of future research.

The strengths of this study include the population-based design, diverse study population, high rate of outcome follow-up, adjustment for pre-stroke functional disability and cognitive status, as well as initial stroke severity, and use of methods to minimize possible selection bias due to study participation, which varied by ethnicity. Limitations include missing data for some covariates, most notably pre-stroke cognitive status, although imputation methods were employed to minimize potential bias, and lack of data on cognitive outcomes for those requiring a proxy respondent. While the imputation methods used assume data are missing at random, which may not be accurate, our previous research has shown that ethnic differences in the outcomes remain statistically significant across various strengths of the association between the missing values for outcomes and the likelihood of missing values.[4] The study participants are from a single community in Texas and predominantly represent strokes of mild initial severity. Therefore, our findings of minimal improvement after six months may be due to biologic reasons resulting in ceiling effects as suggested by our sensitivity analysis, and the results may not be generalizable to other populations, such as those at academic medical centers, although the study population is likely representative of the broader stroke population.

Summary

In both ethnic groups, stroke outcomes were at their worst at three months, improved significantly between three and six months and then stabilized thereafter. These findings, in combination with the observation that worse outcomes in MA persons compared with NHW persons emerged early after stroke and remained unchanged over time, suggest the need for early assessment and maximizing post-acute care to improve outcomes and possibly reduce disparities.

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Author contributions

LDL and LBM contributed to the conception and design of the study.

LDL, DLB, LD, DZ, MK, EC, MAS, JFC, XS, MC and LBM contributed to the acquisition and analysis of data.

LDL, LD, MK and XS contributed to drafting the text or preparing the figures.

Potential conflicts of interest: None

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Figure Legend

Figure 1. Study population and derivation of study sample.

Figure 2. Expected functional, neurologic, cognitive and quality of life outcomes by ethnicity from multivariable models. Adjusted for sex (results shown for males), age (centered at mean age of68.1), IQCODE (results shown for 0-3), pre-stroke mRS (0-1), education (high school graduate) insurance status (insured), marital status (unmarried), initial log-transformed NIHSS (centered at average of 1.45) , number of comorbidities, and no tPA administered.

Table 1. Baseline characteristics by ethnicity

	MA persons (n=807)		NHW persons (n=525)		
Variable	N missing	Median (IQR) or n (%)	N missing	Median (IQR) or n (%)	P-value
Age	0	65 (57-76)	0	70 (61-80)	<0.0001
Sex (% female)	0	395 (49.0)	0	251 (47.8)	0.6849
Education	7		1		<0.0001
< high school		338 (42.3)		44 (8.4)	
high school degree completed		229 (28.6)		162 (30.9)	
> high school		233 (29.13)		318 (60.7)	
Uninsured	8	49 (9.4)	2	136 (17.0)	<0.0001
Married	1	375 (46.5)	0	250 (47.6)	0.6962
Initial stroke severity	0	3 (1-7)	0	3 (1-7)	0.6983
Pre-stroke functional disability	25		9		0.3031
mRS 0-1		336 (43.0)		244 (47.3)	
mRS 2-3		353 (45.1)		217 (42.1)	
mRS 4-5		93 (11.9)		55 (10.7)	
Pre-stroke cognitive function	149		105		0.7417
IQCODE 0-3		380 (57.8)		240 (57.1)	
IQCODE 3-3.44		179 (27.2)		122 (29.1)	
IQCODE > 3.44		99 (15.1)		58 (13.8)	
Pre-stroke depression	188		133		0.2001
None		386 (62.4)		259 (66.1)	
History of depression		109 (17.6)		72 (18.4)	
Current use of antidepressants		124 (20.0)		61 (15.6)	
IV-tPA	0	118 (14.6)	0	96 (18.3)	0.0752
Comorbidity index	0	3 (2-4)	0	3 (1-4)	0.2327

*Percentages are calculated for among non-missing values for all categorical variables

MA = Mexican American, NHW = non-Hispanic white, mRS = modified Rankin score, IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly, IV-tPA = intravenous tissue plasminogen activator

Table 2. Mean of outcomes by follow-up time period and ethnicity and adjusted ethnic differences in stroke outcomes by follow-up time period

	Functional outcome (ADL/IADL)			Neurologic outcome (NIHSS)		
	MA persons	NHW persons		MA persons	NHW persons	
	mean (SD)	mean (SD)	Adjusted difference (95% CI)	mean (SD)	mean (SD)	Adjusted difference (95% CI)
3 month	2.27 (0.94)	2.04 (0.95)	0.20 (0.09, 0.30)	3.01 (4.10)	2.37 (3.87)	0.43 (0.09, 0.77)
6 month	2.16 (0.92)	1.91 (0.87)	0.20 (0.09, 0.31)	2.14 (3.07)	1.74 (2.78)	0.23 (-0.05, 0.52)
12 month	2.17 (0.92)	1.95 (0.92)	0.21 (0.09, 0.32)	2.11 (3.10)	1.92 (4.09)	0.28 (-0.07, 0.63)
	Quality of Life (SSQOL)			Cognitive outcome (3MSE)		
	MA persons	NHW persons		MA persons	NHW persons	
	mean (SD)	mean (SD)	Adjusted difference (95% CI)	mean (SD)	mean (SD)	Adjusted difference (95% CI)
3 month	3.28 (1.07)	3.58 (1.06)	-0.13 (-0.28, -0.00)	83.3 (13.0)	88.3 (11.3)	-3.7 (-5.5, -2.0)
6 month	3.32 (1.08)	3.71 (1.03)	-0.19 (-0.32, -0.05)	84.2 (12.8)	89.6 (10.6)	-3.3 (-5.1, -1.6)
12 month	3.33 (1.12)	3.68 (1.02)	-0.20 (-0.35, -0.05)	84.1 (14.4)	89.6 (11.5)	-3.5 (-5.4, -1.5)

MA = Mexican American, NHW = non-Hispanic white, ADL/IADL = activities of daily living/instrumental activities of daily living, NIHSS = National Institutes of Health Stroke Scale, SS-QOL = Stroke Specific Quality of Life Scale, 3MSE = Modified Mini-mental State Exam.

Models adjusted for sex, age, IQCODE, pre-stroke mRS, education, insurance status, marital status, initial NIHSS, IV-tPA use, and comorbidity index.

Table 3. Results from the multivariable models of temporal associations with stroke outcomes by ethnicity with and without accounting for recurrent stroke. Reported estimates are estimates at the reference levels of average age, male sex, high school education, no IV-tPA administered, pre-stroke mRS 2-3, IQCODE < 3, average log-transformed initial NIHSS, insured, no comorbidities, and unmarried marital status. Estimates of change in NIHSS were transformed back to original scale.

	Functional outcome (ADL/IADL score)		Stroke Severity (NIHSS)		Quality of Life (SS-QOL)		Cognitive outcome (3MSE)	
	MA persons	NHW persons	MA persons	NHW persons	MA persons	NHW persons	MA persons	NHW persons
Estimated 3 month outcome	2.25 (2.10, 2.40)	2.05 (1.90, 2.20)	2.14 (1.71, 2.64)	1.71 (1.34, 2.15)	3.28 (3.10, 3.45)	3.41 (3.22, 3.60)	79.7 (77.2, 82.3)	83.5 (81.1, 85.9)
6 vs 3 months	-0.11 (-0.15, -0.07)	-0.11 (-0.16, -0.07)	-0.50 (-0.69, -0.32)	-0.30 (-0.48, -0.12)	0.06 (0.00, 0.11)	0.11 (0.03, 0.18)	1.3 (0.4, 2.3)	0.9 (-0.0, 1.9)
12 vs 6 months	0.04 (-0.00, 0.08)	0.03 (-0.01, 0.08)	0.02 (-0.14, 0.18)	-0.02 (-0.20, 0.16)	-0.03 (-0.10, 0.03)	-0.02 (-0.09, 0.04)	-0.4 (-1.4, 0.6)	-0.3 (-1.3, 0.8)
	After accounting for recurrent stroke							
	MA persons	NHW persons	MA persons	NHW persons	MA persons	NHW persons	MA persons	NHW persons
Estimated 3 month outcome	2.23 (2.08, 2.37)	2.05 (1.90, 2.20)	2.09 (1.70, 2.54)	1.68 (1.32, 2.09)	3.29 (3.12, 3.46)	3.4 (3.22, 3.59)	80.2 (77.7, 82.7)	83.8 (81.1, 86.5)
6 vs 3 months	-0.12 (-0.16, -0.08)	-0.12 (-0.17, -0.06)	-0.53 (-0.77, -0.35)	-0.29 (-0.47, -0.12)	0.06 (0.01, 0.12)	0.12 (0.04, 0.19)	1.3 (0.5, 2.2)	0.9 (-0.0, 1.9)
12 vs 6 months	0.02 (-0.02, 0.06)	0.01 (-0.04, 0.07)	0.01 (-0.14, 0.16)	-0.07 (-0.24, 0.09)	-0.01 (-0.07, 0.05)	-0.00 (-0.08, 0.07)	-0.1 (-1.1, 0.8)	-0.2 (-1.4, 1.0)

MA = Mexican American, NHW = non-Hispanic white, ADL/IADL = activities of daily living/instrumental activities of daily living, NIHSS = National Institutes of Health Stroke Scale, SS-QOL = Stroke Specific Quality of Life Scale, 3MSE = Modified Mini-mental State Exam.

Models adjusted for sex, age, IQCODE, pre-stroke mRS, education, insurance status, marital status, initial NIHSS, IV-tPA use, and comorbidity index.

ICMJE DISCLOSURE FORM

Date: 8/4/2022

Your Name: Morgan S Campbell III

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The author's relationships/activities/interests should be defined broadly. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

In item #1 below, report all support for the work reported in this manuscript without time limit. For all other items, the time frame for disclosure is the past 36 months.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	**Specifications/Comments (e.g., if payments were made to you or to your institution)**
Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☐ **None**	
		Local Primary Investigator, BASIC	Annual administrative fee for project oversight
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

Please place an "X" next to the following statement to indicate your agreement:

☒ I certify that I have answered every question and have not altered the wording of any of the questions on this form.

ICMJE DISCLOSURE FORM

Date: 7/29/2022

Your Name: Devin Brown

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Time frame: Since the initial planning of the work			
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		NIH	
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
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ICMJE DISCLOSURE FORM

Date: 7/29/2022

Your Name: Lynda Lisabeth

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☐ **None**	
		NIH grant funding	Payment to institution
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
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12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 7/29/2022

Your Name: Lewis Morgenstern

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

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		NIH grant funding	
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

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12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 7/29/2022

Your Name: Madeline Kwicklis

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

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		Time frame: Since the initial planning of the work	
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☐ None	
			Click the tab key to add additional rows.
		Time frame: past 36 months	
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

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4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
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12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 8/26/2021

Your Name: Melinda Cox

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

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Time frame: Since the initial planning of the work			
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		NIH NINDS	Institution
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

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12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 8/1/2022

Your Name: Xu Shi

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☒ None	
			Click the tab key to add additional rows.
		Time frame: past 36 months	
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

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13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 7/29/2022

Your Name: Darin Zahuranec

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

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		]	
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☐ **None**	
		NIH Grants R01AG069148, R01NS091112]	To my institution for research in the same community
3	Royalties or licenses	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
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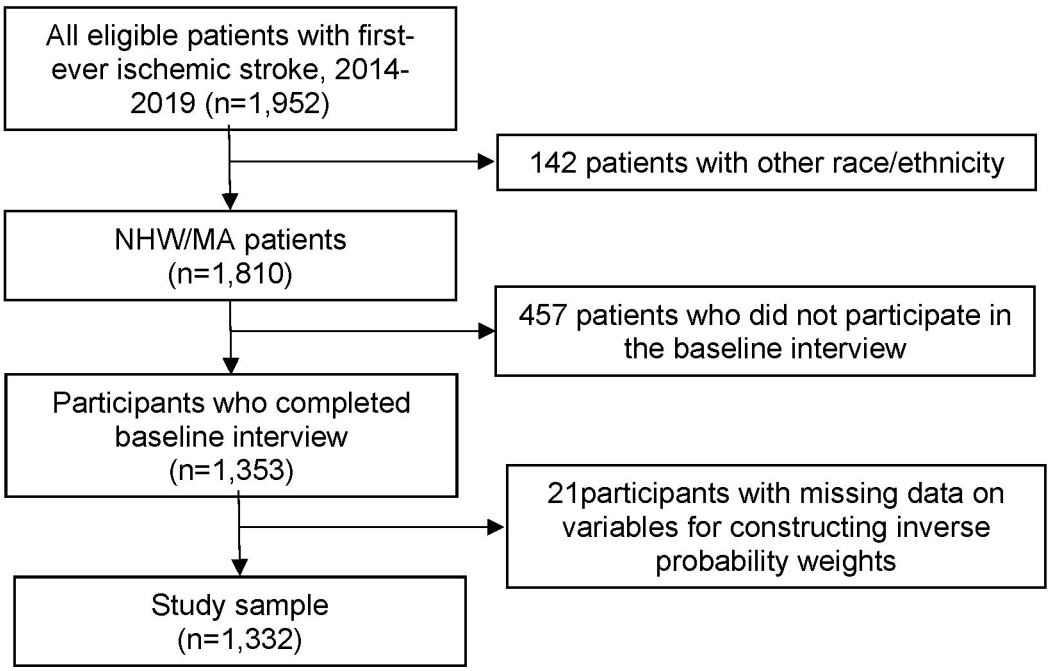

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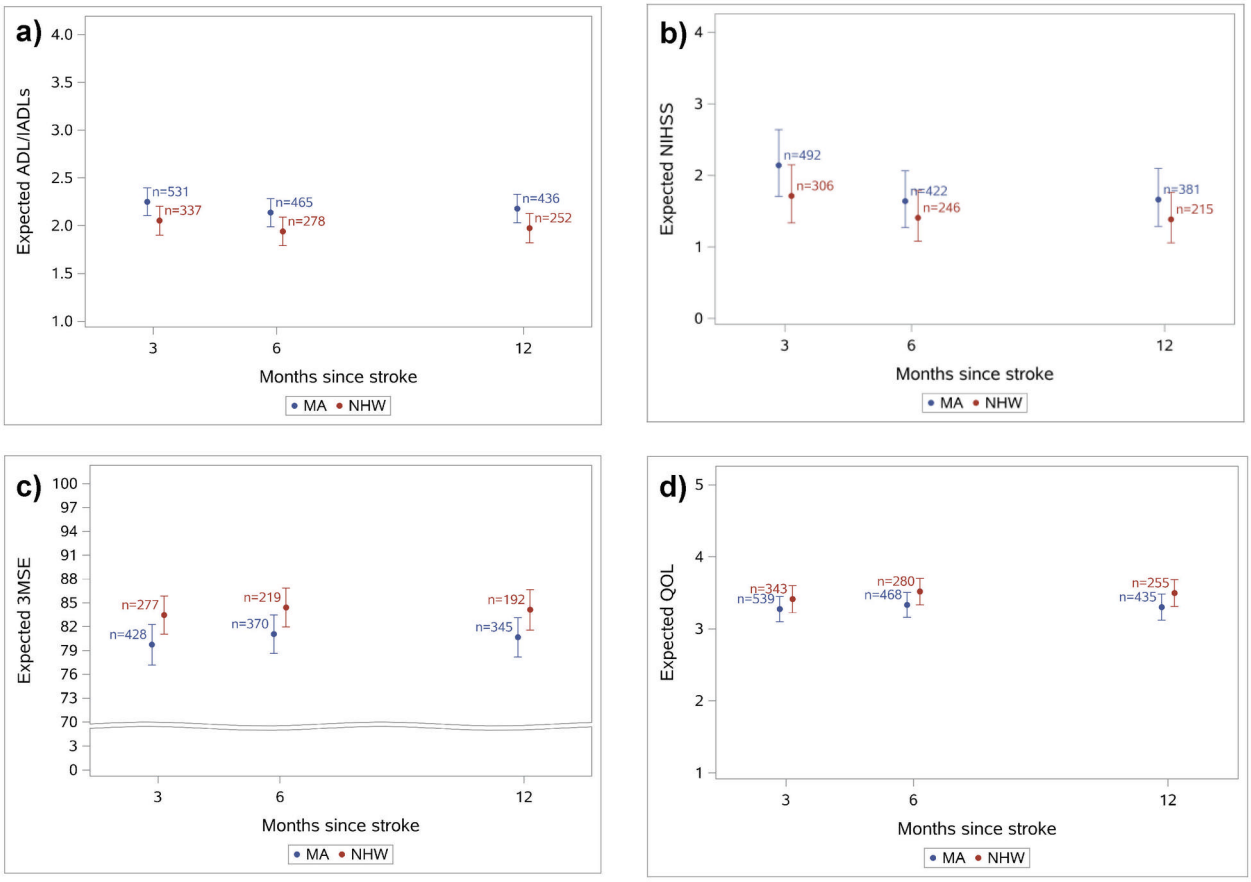

ANA_26513_Figure 2.tiff

ICMJE DISCLOSURE FORM

Date: 7/29/2022

Your Name: Erin Case

Manuscript Title: Outcomes in the year after first-ever ischemic stroke in a bi-ethnic population

Manuscript Number (if known): ANA-22-0526

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			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☐ **None**	
		NIH	Position is funded by NIH grant
3	Royalties or licenses	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

Please place an "X" next to the following statement to indicate your agreement:

☒ I certify that I have answered every question and have not altered the wording of any of the questions on this form.