OPEN

Sex Differences in Stroke Hospitalization Incidence, 30-Day Mortality, and Readmission in a Regional Medical Center in the Southwestern United States

Jeff A. Dennis, PhD, Yan Zhang, PhD, Fangyuan Zhang, PhD, Noah De La Cruz, MPH, Greg Hannabas, MD, MPH, MPA, and Nan Mi, MA

Objectives: This study explores sex differences in ischemic stroke hospitalization incidence, 30-day mortality, and 30-day readmission in a southwestern US medical center.

Methods: Ischemic stroke admissions in a regional medical center in the southwestern United States were obtained for a 6.5-year time frame (N = 1968). Logistic regression models examine the adjusted effects of sex on 30-day mortality and 30-day readmission outcomes among individuals hospitalized for ischemic stroke.

Results: Findings confirm that although women experience higher mortality than men (9.1% vs 6.7%), the sex disparity in mortality is explained by the age distribution of strokes. Women experience far more strokes and deaths because of stroke at older ages. No differences in principal procedure or 30-day readmission emerged.

Conclusions: Men experienced higher stroke hospitalization incidence, although women exhibited higher 30-day mortality. Age composition explained sex differences in mortality, but higher male stroke hospitalization incidence represents a larger public health issue that suggests the need for behavioral change at the population level. No meaningful sex differences emerged in treatment, mortality, or readmission.

Key Words: 30-day mortality, age composition, sex differences, ischemic stroke

From the Department of Public Health and Department of Family and Community Medicine, Texas Tech University Health Sciences Center, Lubbock, Department of Mathematics, Texas Tech University, Lubbock, Harris College of Nursing and Health Sciences, Texas Christian University, Ft Worth, and the Department of Mathematics, Western Michigan University, Kalamazoo.

Correspondence to Dr Jeff A. Dennis, Department of Public Health, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9430, Lubbock, TX 79430. E-mail: jeff.dennis@ttuhsc.edu.

The datasets generated and/or analyzed during this study are not publicly available because they are derived hospital billing records, but they are available from the corresponding author on reasonable request and approval by the Texas Tech University Health Sciences Center institutional review board.

The study was funded by a grant from the Laura W. Bush Institute for Women's Health at Texas Tech University Health Sciences Center.

The authors did not report any other financial relationships or conflicts of interest.

Accepted October 15, 2020.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (http://sma.org/smj).

0038-4348/0–2000/114-174

DOI: 10.14423/SMJ.0000000000001221

Ongoing health research identifies that health disparities persist by sex in the United States, some driven by biological and others by social or behavioral explanations.[1] In the study of specific health conditions, it is important to identify gender gaps and understand explanatory factors relating to treatment.

Stroke is one of the leading causes of death and disability among American adults in the United States. Based on National Health and Nutrition Examination Survey 2013–2016 data, an estimated 7.0 million American adults (20 years and older) self-reported having had a stroke.[2] Data from the 2016 Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System showed that the sex prevalence of prior stroke is similar among American adults (2.9% of men and 2.8% of women 18 years of age and older).[2] The patterns of stroke incidence and mortality are complex relating to sex and age. It is well known that the severity of stroke increases with age. Since women live longer than men, their risk of having a stroke is higher, which in turn will have a more negative impact on their lives.[3] Census estimates by sex indicate that the population of women at ages 85 years and older is >2 times the population size of men at those ages.[4] Age-specific stroke incidence in the United States tends to be higher for men, except among older

Key Points

- Female mortality for ischemic stroke is higher than male mortality.
- The age composition of stroke incidence explains sex differences in stroke mortality.
- Analysis of principal procedure reveals no meaningful sex differences in stroke treatment.

age groups.[5–7] Males typically have higher age-specific stroke prevalence, although given that stroke risk increases substantially with age and women make up a larger proportion of individuals aged 80 and older, the absolute number of strokes in the United States is higher for women compared with men.[8]

Stroke may have a greater impact on women than men because women have a greater number of stroke events at older ages from which they are less likely to recover.[3,5,9,10] Although several reports have found that women are less likely to receive some in-hospital interventions, most differences disappear after accounting for age and comorbidities.[6] Women who experience a stroke may receive different treatments and have more unfavorable functional outcomes compared with men.[3] Sex disparities also were found in the use of thrombolytic treatment and lipid testing.[3] Sex differences in outcomes for stroke treatment remain controversial.[5,11,12] Whereas some argue there is no sex difference in stroke rehabilitation functional outcomes, other studies have found poorer functional outcomes and quality of life after stroke in women.[3,6,13] Sohrabji and colleagues' analysis suggested that the Food and Drug Administration–approved stroke therapy (tissue plasminogen activator for acute ischemic stroke) produced more robust favorable stroke outcomes among women compared with men.[14] A recent study on patients treated with endovascular stroke thrombectomy also showed that women experienced comparable functional outcomes and greater years of optimal life after intervention compared with men.[15] This inconsistency warrants the need for the further assessment of sex differences in stroke outcomes. Understanding these disparities is essential to help improve the quality of care for women with stroke.

Hospitals typically track two common stroke outcome metrics: 30-day mortality and 30-day readmission. Previous studies have estimated that overall, 30-day stroke mortality is approximately 7% and 30-day stroke readmission is approximately 21%.[16] Patient characteristics identified as significant risk factors of readmission include older age (75 years and older), living in a facility, or living at home without a spouse, as well as comorbidities.[17,18] Whether sex is a risk factor remains understudied.

The present study explores sex differences in stroke hospitalization incidence, 30-day mortality, and readmission to understand whether disparities exist that would necessitate the meaningful examination of differences in stroke awareness by sex or treatment of stroke. The study describes sex and age differences in the incidence of hospitalization for stroke and 30-day mortality and readmission for stroke in a large hospital sample.

Methods

This study uses data from all hospital admissions for ischemic stroke at a large county-owned regional medical center in the southwestern United States that serves both an urban area and surrounding rural communities. Six and one-half years of data, from January 2013 to June 2019, were analyzed to maximize the study population size. Ischemic stroke diagnoses represented approximately 61.5% of all stroke hospitalizations during this period (N = 1968). This time span included a shift from *International Classification of Diseases, Ninth Revision* to *International Classification of Diseases, Tenth Revision* classification in October 2015, and as such, diagnosis and procedure codes are matched accordingly. The study was approved for exempt review by the Texas Tech University Health Sciences Center institutional review board. Following approval, the hospital provided deidentified patient data for all hospital admissions for ischemic stroke during the approved time period. Confidential patient information such as patient identification, medical record number, date of birth, and ZIP code were not included.

Independent variables included sociodemographics (age, sex, race/ethnicity, and insurance status) and clinical factors related to outcome (admission date, discharge date, principal diagnosis, discharge status, standard payer, principal procedure, and length of stay). Principal diagnosis was not used for analysis, as >63% of all ischemic strokes were coded as "cerebral infarction, unspecified," with a similar proportion of men and women

Table 1. Sample characteristics of individuals hospitalized for ischemic stroke, by sex

	Male, Mean (SD)	Female, Mean (SD)	*t*	*P*
N (%)	1064 (54.0)	904 (46.0)		
Age, y (hospitalized)	64.0 (13.7)	68.1 (16.2)	6.06	<0.001
Age, y (deceased)	69.7 (13.2)	74.6 (15.9)	2.03	0.044
LOS	6.4 (5.9)	6.1 (5.7)	−1.14	0.26
	Median	**Median**	*z*	*P*
Median age (hospitalized)	64	70	−6.87	<0.001
Median age, y (deceased)	72	78	−2.65	0.008
	N (%)	**N (%)**	χ^2	*P*
30-d mortality				
Living	992 (93.3)	822 (90.9)	3.90	0.048
Deceased	71 (6.7)	82 (9.1)		
30-d readmission				
No	982 (92.4)	834 (92.3)	0.01	0.918
Yes	81 (7.6)	70 (7.7)		
Race/ethnicity				
White	729 (74.4)	791 (80.6)	14.06	0.003
Black	69 (9.4)	100 (7.6)		
Hispanic	52 (9.7)	103 (5.8)		
Other/unknown	54 (6.5)	69 (6.0)		
Insurance				
Private	153 (14.4)	115 (12.7)	48.65	<0.001
Medicare	579 (54.5)	605 (66.9)		
Medicaid	88 (8.3)	79 (8.7)		
Uninsured/self-pay	123 (11.6)	54 (6.0)		
Other	120 (11.3)	51 (5.6)		

LOS, length of stay; SD, standard diviation.

receiving this code. Principal procedure was grouped into eight categories based on frequencies and matched across *International Classification of Diseases, Ninth Revision* and *International Classification of Diseases, Tenth Revision*, including none specified, ultrasound or other imaging, thrombolytic agent, extirpation of blood vessel, feeding tube, respiratory assistance, arterial dilation, and other. The most common principal procedure listed was none specified, suggesting that medications may have been given but no billable procedure was performed.

Outcome variables included 30-day mortality for patients hospitalized for stroke as well as readmission rates, in alignment with the Hospital Readmission Reduction Program requirements federally mandated by Centers for Medicare & Medicaid Services. The 30-day mortality and readmission were dichotomized as living versus deceased and readmitted versus not readmitted, respectively.

Statistical Analysis

Bivariate tests compared mean differences using *t* tests, median differences using Mann-Whitney-Wilcoxon tests, and group proportions using χ^2 tests.[19] Multivariate logistic regression was used to analyze the two binary outcomes of 30-day mortality and 30-day readmission. Analysis for the study was performed using STATA 15.1. (StataCorp, College Station, TX), and statistical significance was set at $\alpha < 0.05$.

Results

Table 1 provides a description of the study population. Men hospitalized for ischemic stroke were, on average, approximately 4 years younger than women. Among those who died in the hospital, men were approximately 5 years younger than women. Men were more often uninsured or used self-pay, whereas women were more often covered under Medicare. Thirty-day mortality for women (9.1%) was significantly higher than for men (6.7%, $P = 0.048$), but no differences were observed by sex for 30-day readmission rates or length of stay following hospitalization for stroke. Further analyses focus primarily on the incidence of hospitalization for stroke and 30-day mortality because of the lack of sex differences in readmission and length of stay. Age patterns in hospitalization for stroke and stroke mortality provide important insights into understanding sex differences for this condition.

Figure 1 shows the incidence of hospitalization for ischemic stroke by sex and age during the 6.5-year period. Stroke incidence is higher for men at younger ages, with the largest gender gap from ages 55 to 69. Incidence roughly evens out by sex at approximately age 75, followed by a substantially higher female stroke incidence after age 85.

Figure 2 highlights the primary driver in stroke mortality between men and women, which is that the greatest gender gap in 30-day mortality falls in the 85 and older age group. In this oldest age group, approximately 15.3% of female stroke patients died (23/150) compared with approximately 11.8% of male stroke patients (8/68). Although the relative risk of death is approximately 1.3 times higher for women compared with men, it is not statistically significant ($P = 0.48$). Nonetheless, the fact that more than twice as many females aged 85 and older were hospitalized for ischemic stroke is a meaningful contributor to the observed sex disparity in mortality.

Figure 3 provides some insight into another potential mortality gap. Between ages 55 and 74, men have substantially more stroke hospitalizations than women, yet more women die of stroke in those age groups. Approximately 8.7% of female stroke

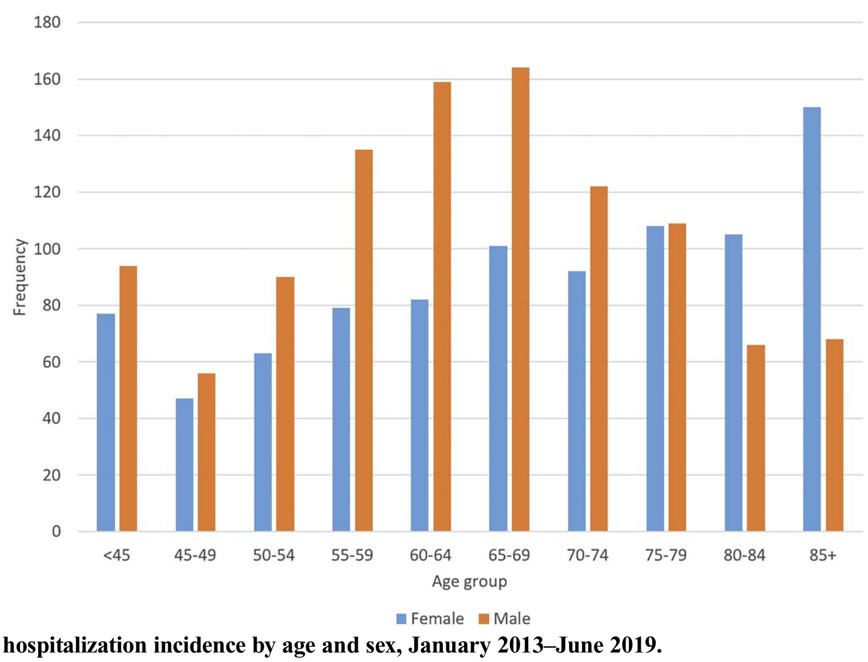

Fig. 1. **Ischemic stroke hospitalization incidence by age and sex, January 2013–June 2019.**

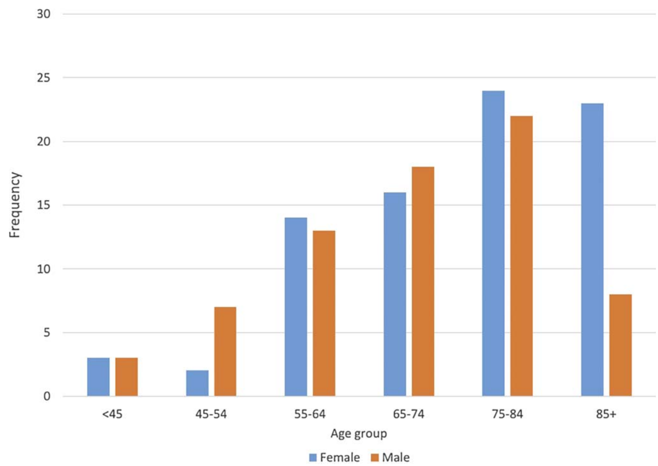

Fig. 2. **Frequency of 30-d mortality among individuals hospitalized for ischemic stroke, by age and sex, January 2013–June 2019.**

patients between the ages of 55 and 74 died compared with 5.6% of males, but this comparison does not meet statistical significance for a 2-tailed *t* test ($P = 0.08$).

Table 2 shows no meaningful difference in procedures by sex, but highly different mortality rates by procedure. More than 50% of individuals requiring a ventilator or other respiratory assistance died, compared with approximately 5% of those receiving no principal procedure. Procedure in many cases appears to stand as a proxy for severity of stroke, and does not appear to be biased by sex. For example, although a seemingly larger percentage of females receiving thrombolytic agents died (10.2% female, 4.4% male), this difference is not statistically significant (data not shown).

Table 3 logistic regression odds ratios suggest that the significant sex difference in 30-day mortality found in Table 1 is statistically accounted for by age. Race/ethnicity and insurance status did not significantly predict mortality in the adjusted model, and due to multicollinearity between Medicare and age, insurance was dropped from the final model. The Supplemental

Table 2. **Principal procedures among individuals hospitalized and for ischemic stroke, by sex and mortality**

Principal procedure	Male	Female	Total
None	404 (38.0)	357 (39.5)	761 (38.7)
Ultrasound	282 (26.5)	227 (25.1)	509 (25.9)
Thrombolytic agent	91 (8.6)	98 (10.8)	189 (9.6)
Extirpation of vessel	70 (6.6)	61 (6.7)	131 (6.7)
Feeding tube	38 (3.6)	33 (3.7)	71 (3.6)
Respiratory assistance	52 (4.9)	42 (4.6)	94 (4.8)
Arterial dilation	19 (1.8)	8 (0.9)	27 (1.4)
Other	107 (10.1)	78 (8.6)	185 (9.4)
χ^2	7.36		
P	0.392		
Principal procedure	**Not deceased**	**Deceased**	**Total**
None	720 (39.7)	41 (26.8)	761 (38.7)
Ultrasound	501 (27.6)	8 (5.2)	509 (25.9)
Thrombolytic agent	175 (9.6)	14 (9.2)	189 (9.6)
Extirpation of vessel	110 (6.1)	21 (13.7)	131 (6.7)
Feeding tube	71 (3.9)	0 (0.0)	71 (3.6)
Respiratory assistance	46 (2.5)	48 (31.4)	94 (4.8)
Arterial dilation	26 (1.4)	1 (0.7)	27 (1.4)
Other	165 (9.1)	20 (13.1)	185 (9.4)
χ^2	300.38		
P	<0.001		

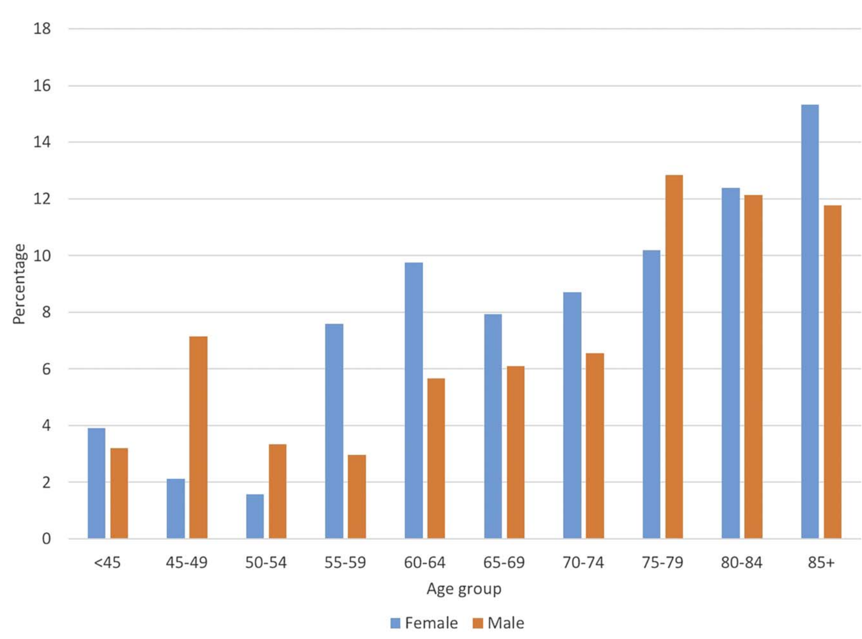

Fig. 3. **Age-specific mortality percentages among individuals hospitalized for ischemic stroke, by sex, January 2013–June 2019.**

Table 3. Multivariate logistic regression odds ratios predicting 30-d ischemic stroke mortality (N = 1967)

	Unadjusted			Adjusted		
	OR	95% CI	*P*	OR	95% CI	*P*
Female	1.39	1.00–1.94	0.049	1.21	0.86–1.70	0.281
Age				1.03	1.02–1.05	<0.001
Race/ethnicity (ref = non-Hispanic White)						
Non-Hispanic Black				1.02	0.52–2.02	0.953
Hispanic				1.39	0.77–2.51	0.271
Other				1.28	0.65–2.53	0.479
r^2			0.004			0.033

CI, confidence interval; OR, odds ratio.

Digital Content table (http://links.lww.com/SMJ/A215) shows a similar model predicting 30-day readmission for stroke, although the overall predictive power of the model is poor. Insurance status predicted readmission slightly better than age, and as such age was dropped from the final model because of multicollinearity. Adjusted models demonstrate no meaningful sex differences in 30-day mortality or 30-day readmission for ischemic stroke. Procedures were not included in regression models because they did not have a substantial effect on sex disparities in survival, and proved highly variable in their association with 30-day mortality.

Discussion

Data from a single county hospital over 6.5 years provide a number of insights into ischemic stroke incidence and mortality, some of which may obscure larger issues. For example, bivariate observation suggests that female mortality is higher for stroke, male stroke hospitalization incidence is higher before age 70, and female stroke hospitalization incidence is higher after age 80. Nuanced observation of specific age groups suggests that although male stroke hospitalization is higher before age 80, female ischemic stroke mortality between ages 55 and 74 may be slightly higher.

This study focuses on a single hospital site. As a county hospital, the site has a patient demographic that may trend toward lower socioeconomic status relative to a similar private hospital in the area. Although socioeconomic status is widely understood to shape health disparities, we have no reason to believe that sex differences in strokes or stroke outcomes should be appreciably different in this hospital compared with others. Identifying principal procedures based on billing data limits the consistency of reporting somewhat, as risk factors such as patient obesity, smoking status, hypertension, or other comorbidities are not available. That is, the severity of the patient's condition can only be inferred based on the type of procedure, and the complexity of hospital treatments or treatment decisions cannot be fully captured in such a retrospective study. Institutional review board restrictions did not permit patient ZIP code to be collected, which prevented an analysis of the differences between urban and rural areas served by the hospital.

Conclusions

National data suggest a larger absolute number of strokes among women, with similar gender-specific incidence when adjusted for population size.[8] Our study population shows higher overall stroke hospitalization incidence for men, suggesting that risk factors such as smoking, hypertension, and obesity in the hospital service region may put men disproportionately at risk for stroke relative to the national population. Because they are included in a hospital-based study, however, our data are not set up to explore lifestyle factors in the hospital service region to examine that phenomenon. Our study found no meaningful sex disparities among ischemic stroke hospitalizations that would necessitate policy changes in stroke management by sex.

Principal procedures were evenly distributed by sex, and higher female stroke mortality was explained almost entirely by age differences in incidence. Notably, nearly 40% of all ischemic stroke hospitalizations included no principal procedure, suggesting that a large number of included treatment did not involve a billable procedure. Although not statistically significant, future work should revisit our findings suggesting that female stroke mortality rates may be higher at ages 55 to 74 despite lower female incidence of stroke hospitalization at these ages.

Whereas simple bivariate analysis suggests higher ischemic stroke mortality rates among women, the difference is explained almost entirely by the fact that women live longer, and therefore live more years in high stroke-risk age groups. This study highlights the importance of understanding age and sex composition in understanding populations with common health conditions, and not only provides insight into hospital treatment practices, but also useful information relating to sex differences in the population served by the hospital. Public health practitioners can use data of this nature and partner with clinical providers to better understand at-risk populations and collaborate to reduce stroke hospitalizations through prevention.[20,21] Understanding the risk profile of those most likely to be hospitalized for ischemic stroke can be a valuable tool toward the development of health education programs to reduce stroke prevalence in the population.

Acknowledgment

The authors acknowledge the contribution of the Texas Tech University Health Sciences Center Clinical Research Institute for assistance with this research.

References

1. National Academies of Sciences, Engineering, and Medicine. *Communities in Action: Pathways to Health Equity.* Washington, DC: The National Academies Press; 2017.
2. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation* 2019;139:e56–e528.

3. Reeves MJ, Bushnell CD, Howard G, et al. Sex differences in stroke: epidemiology, clinical presentation, medical care, and outcomes. *Lancet Neurol* 2008;7:915–926.
4. Howden LM, Meyer JA. Age and sex composition, 2010. https://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf. Accessed January 9, 2021.
5. Christensen H, Bentsen L, Christensen L. Update on specificities of stroke in women. *Presse Med* 2016;45:e409–e418.
6. Guzman RP, Weighell W, Guzman C, et al. Female sex does not influence 30-day stroke and mortality rates after carotid endarterectomy. *Ann Vasc Surg* 2014;28:245–252.
7. Katsiki N, Ntaios G, Vemmos K. Stroke, obesity and gender: a review of the literature. *Maturitas* 2011;69:239–243.
8. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *Circulation* 2016;133:e38–e360.
9. Girijala RL, Sohrabji F, Bush RL. Sex differences in stroke: review of current knowledge and evidence. *Vasc Med* 2017;22:135–145.
10. Appelros P, Stegmayr B, Terént A. Sex differences in stroke epidemiology: a systematic review. *Stroke* 2009;40:1082–1090.
11. Chalos V, de Ridder IR, Lingsma HF, et al. Does sex modify the effect of endovascular treatment for ischemic stroke? A subgroup analysis of 7 randomized trials. *Stroke* 2019;50:2413–2419.
12. Hiraga A. Gender differences and stroke outcomes. *Neuroepidemiology* 2017;48:61–62.
13. Mizrahi EH, Waitzman A, Arad M, et al. Gender and the functional outcome of elderly ischemic stroke patients. *Arch Gerontol Geriat* 2012; 55:438–441.
14. Sohrabji F, Park MJ, Mahnke AH. Sex differences in stroke therapies. *J Neurosci Res* 2017;95:681–691.
15. Sheth SA, Lee S, Warach SJ, et al. Sex differences in outcome after endovascular stroke therapy for acute ischemic stroke. *Stroke* 2019;50: 2420–2427.
16. Fehnel CR, Lee Y, Wendell LC, et al. Post-acute care data for predicting readmission after ischemic stroke: a nationwide cohort analysis using the minimum data set. *J Am Heart Assoc* 2015;4:e002145.
17. Nouh AM, McCormick L, Modak J, et al. High mortality among 30-day readmission after stroke: predictors and etiologies of readmission. *Front Neurol* 2017;8:632.
18. Rao A, Barrow E, Vuik S, et al. Systematic review of hospital readmissions in stroke patients. *Stroke Res Treat* 2016;2016:1–11.
19. Conroy RM. What hypotheses do "nonparametric" two-group tests actually test? *Stata J* 2012;12:182–190.
20. Felipe RA, Plescia M, Peterman E, et al. A public health framework to improve population health through health care and community clinical linkages: the ASTHO/CDC Heart Disease and Stroke Prevention Learning Collaborative. *Prev Chronic Dis* 2019;16:E124.
21. Salinas J, Schwamm LH. Behavioral interventions for stroke prevention: the need for a new conceptual model. *Stroke* 2017;48:1706–1714.