ORIGINAL RESEARCH

Demographic and Regional Trends in Stroke-Related Mortality in Young Adults in the United States, 1999 to 2019

Robert W. Ariss, MD; Abdul Mannan Khan Minhas, MD; Jacob Lang, MSc; P. Kasi Ramanathan, MD; Safi U. Khan, MD; Mahwash Kassi, MD; Haider J. Warraich, MD, MPH; Dhaval Kolte, MD, PhD; Mohamad Alkhouli, MD; Salik Nazir, MD

BACKGROUND: Despite improvements in the management and prevention of stroke, increasing hospitalizations for stroke and stagnant mortality rates have been described in young adults. However, there is a paucity of contemporary national mortality estimates in young adults.

METHODS AND RESULTS: Trends in mortality related to stroke in young adults (aged 25–64 years) were assessed using the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research database. Age-adjusted mortality rates per 100,000 people with associated annual percentage change were calculated. Joinpoint regression was used to assess the trends in the overall sample and different demographic (sex, race and ethnicity, and age) and geographical (state, urban-rural, and regional) subgroups. Between 1999 and 2019, a total of 566,916 stroke-related deaths occurred among young adults. After the initial decline in mortality in the overall population, age-adjusted mortality rate increased from 2013 to 2019 with an associated annual percentage change of 1.5 (95% CI, 1.1–2.0). Mortality rates were higher in men versus women and in non-Hispanic Black people versus individuals of other races and ethnicities. Non-Hispanic American Indian or Alaskan Native people had a marked increase in stroke-related mortality (annual percentage change 2010–2019: 3.3). Furthermore, rural (nonmetropolitan) counties experienced the greatest increase in mortality (annual percentage change 2012–2019: 3.1) compared with urban (metropolitan) counties.

CONCLUSIONS: Following the initial decline in stroke-related mortality, young adults have experienced increasing mortality rates from 2013 to 2019, with considerable differences across demographic groups and regions.

Key Words: disparities ■ mortality ■ stroke ■ young adults

Stroke is a leading cause of mortality and morbidity in the United States.1 In young adults, stroke is associated with long-term mortality and morbidity, including functional disability, cognitive impairment, and economic loss.2 Stroke mortality rates have declined over the past 4 decades; however, despite improvements in the management and prevention of stroke, the national stroke mortality rate has stalled from 2003 to 2015, particularly in adults aged 35 to 64 years.3 In addition, recent studies have shown increasing hospitalizations for acute ischemic and hemorrhagic stroke within young adults.4,5 Despite increasing hospitalizations for stroke among young adults, there is a paucity of contemporary national mortality estimates within this population. Moreover, demographic and geographic trends of stroke mortality within young adults are underexplored. Therefore, we used a nationwide database of death certificates to describe the contemporary trends...
CLINICAL PERSPECTIVE

What Is New?
- Following an initial decline, stroke-related mortality in young adults has been increasing from 2013 to 2019.
- Young non-Hispanic Black or African American adults had persistently greater mortality throughout the study period.
- Young adults in rural counties had higher stroke-related mortality compared with those in urban counties.

What Are the Clinical Implications?
- Further studies are needed to understand the underlying mechanism of the recent increase in mortality related to stroke in young adults.
- More strenuous efforts are needed to reduce the evident disparities in stroke mortality in young adults.

Nonstandard Abbreviations and Acronyms

| Abbreviation | Definition |
|--------------|------------|
| AAMR         | age-adjusted mortality rate |
| APC          | annual percentage change |
| CDC          | Centers for Disease Control and Prevention |
| WONDER       | Wide-Ranging Online Data for Epidemiologic Research |

in stroke-related mortality, stratified by demographic and geographic characteristics.

METHODS

Deaths occurring within the United States related to stroke (including ischemic, hemorrhagic, and unspecified) were extracted from the Centers for Disease Control and Prevention (CDC) Wide-Ranging Online Data for Epidemiologic Research (WONDER) database.6 The Multiple Cause-of-Death Public Use record death certificates were studied to select stroke as a contributing or underlying cause of death on nationwide death certificates. The data are available publicly online through the CDC WONDER website. This database has previously been used in several other studies to determine trends in mortality of cardiovascular diseases.7-9 Death certificates with stroke as an underlying or contributing cause of death were identified with International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes I60.x, I61.x, I63.x, I64, I69.0, I69.1, I69.3, and I69.4. Deaths in patients aged 25 to 64 years were selected, as done in a prior study of stroke hospitalizations in young adults.4 This study did not require institutional review board approval because the CDC WONDER is a publicly available database that contains deidentified data.

Stroke-related deaths and population sizes were extracted from 1999 to 2019. We abstracted data on stroke subtypes (ischemic, hemorrhagic, and unspecified), location of death (including medical facilities [outpatient, emergency department, inpatient, death on arrival, or status unknown], home, hospice, and nursing home/long-term care facility), age, sex, race and ethnicity, urban-rural classification, region, and states. Race and ethnicities were defined as non-Hispanic White people, non-Hispanic Black or African American people, Hispanic or Latino people, non-Hispanic American Indian or Alaskan Native people, and non-Hispanic Asian or Pacific Islander people. These race and ethnicity categories rely on data reported on death certificates and have been used within analyses from the CDC WONDER database.3,6 Age groups were defined as 25 to 34, 35 to 44, 45 to 54, and 55 to 64 years. For urban-rural classifications, the National Center for Health Statistics Urban-Rural Classification Scheme was used to divide the population into urban (large metropolitan area [population ≥1 million] or medium/small metropolitan area [population 50,000–999,999]) and rural (nonmetropolitan [population <50,000]) counties per the 2013 US census classification.10 Regions were classified into Northeast, Midwest, South, and West, according to the US Census Bureau definitions.

Statistical Analysis

Stroke-related age-adjusted mortality rates (AAMRs) per 100,000 population were determined. AAMRs were calculated by standardizing the stroke-related deaths to the year 2000 US population, as previously described.11 Crude mortality rates were determined by dividing the number of stroke deaths in a given year by the corresponding population number of that year. The Joinpoint Regression Program (Joinpoint V 4.9.0.0; National Cancer Institute) was used to determine trends in AAMR using annual percentage change (APC).12 This method identifies significant changes in AAMR over time by fitting log-linear regression models where temporal variation occurred. APCs with 95% CIs for the AAMR were calculated at the identified line segments linking joinpoints using the Monte Carlo permutation test. APCs were considered increasing or decreasing if the slope describing the change in mortality was significantly different than 0 using 2-tailed t testing. Statistical significance was set at P<0.05.

RESULTS

Between 1999 and 2019, a total of 566,916 stroke-related deaths occurred in the overall study population.
When stratified by stroke subtype, unspecified stroke had the greatest AAMR throughout the study period, followed by hemorrhagic and ischemic stroke (Figure S1 and Table S2). Ischemic stroke-related AAMR increased from 2012 to 2019 with an associated APC of 14.4 (95% CI, 10.5–18.5). Of 550,081 stroke-related deaths with data available on place of death, 73.2% occurred at medical facilities, 9.5% occurred at nursing homes/long-term care facilities, 3.3% occurred at hospice, and 14.0% occurred at home (Table S3).

Overall, stroke-related AAMR was 18.92 in 1999 and 14.57 in 2019 (Table S4). From 1999 to 2010, the AAMR decreased, with an associated APC of −3.3 (95% CI, −3.4 to −3.1). Following the initial decline, AAMR increased from 2013 to 2019, with an associated APC of 1.5 (95% CI, 1.1–2.0) (Figure 1).

**Demographic Trends**

**Sex**

Men had higher stroke-related AAMR compared with women throughout the study period (Table S4). Following the initial decline, the AAMR in men increased from 2011 to 2019, with an associated APC of 1.5 (95% CI, 1.2–1.9) (Figure 1). Similarly, the AAMR in women increased from 2013 to 2019, with an associated APC of 1.4 (95% CI, 0.8–2.0).

**Race and Ethnicity**

Overall, non-Hispanic Black or African American people had the highest stroke-related AAMR, followed by non-Hispanic American Indian or Alaskan Native people, Hispanic or Latino people, non-Hispanic White people, and non-Hispanic Asian and Pacific Islander people (Table S5). Non-Hispanic Black or African American people had continuous declines in AAMR from 1999 to 2013, followed by stable AAMR from 2013 to 2019, with an associated APC of 0.6 (95% CI, 0–1.3) (Figure 2).

Similar to non-Hispanic Black or African American people, non-Hispanic Asian or Pacific Islander people had decreasing AAMR from 1999 to 2009, followed by stable AAMR from 2009 to 2019, with an associated APC of 0.2 (95% CI, −0.7 to 1.0) (Figure 2).

Conversely, the increasing stroke-related AAMR in the overall population was driven by increases in non-Hispanic American Indian or Alaskan Native people, Hispanic or Latino people, and non-Hispanic White people. Non-Hispanic American Indian or Alaskan

---

*Figure 1.* Trends in overall and sex-stratified, age-adjusted, stroke-related mortality rates among adults aged 25 to 64 years in the United States, 1999 to 2019.

*Indicates that the annual percentage change (APC) is significantly different from 0 at α=0.05.
Native people had a marked increase in stroke-related AAMR from 2010 to 2019, with an associated APC of 3.3 (95% CI, 1.3–5.3) (Figure 2). Hispanic or Latino people AAMR increased from 2012 to 2019, with an associated APC of 1.0 (95% CI, 0.1–1.9). Finally, non-Hispanic White people AAMR increased from 2012 to 2019, with an associated APC of 1.9 (95% CI, 1.5–2.2).

**Age**

When stratified by age groups, people aged 55 to 64 years had the highest crude mortality rates throughout the study period, followed by those aged 44 to 54, 35 to 44, and 25 to 34 years (Table S6).

People aged 25 to 34 and 35 to 44 years had increases in stroke-related crude mortality rate from 2010 or 2011, respectively, to 2019 (Figure 3A and Table S6). In addition, people aged 45 to 54 and 55 to 64 years had increases in stroke-related crude mortality rate from 2012 or 2013, respectively, to 2019 (Figure 3B and Table S6).

**Geographic Trends**

**Urban-Rural**

Overall, nonmetropolitan counties had the greatest AAMR, followed by medium/small metropolitan and large metropolitan counties (Table S7). After the initial decline, nonmetropolitan counties had a pronounced increase in AAMR from 2012 to 2019, with an associated APC of 3.1 (95% CI, 2.3–3.8) (Figure 4). Similarly, medium/small metropolitan counties had an increase in AAMR from 2011 to 2019, and large metropolitan counties had an increase in AAMR from 2014 to 2019.

**Statewide**

The AAMR from 1999 to 2009 varied widely, from 31.34 in District of Columbia to 9.13 in Vermont (Table S8). States in the ≥90th percentile of stroke-related AAMR included District of Columbia, Mississippi, Louisiana, Arkansas, South Carolina, and Alabama. States in the ≤10th percentile of AAMR included Vermont, New Hampshire, Massachusetts,
Figure 3. Trends in crude stroke-related mortality rates among adults aged 25 to 64 years, stratified by age groups in the United States, 1999 to 2019.

A. Crude mortality rates for those aged 25 to 34 and 35 to 44 years. B. Crude mortality rates for those aged 45 to 54 and 55 to 64 years. *Indicates that the annual percentage change (APC) is significantly different from 0 at α=0.05.
Colorado, Connecticut, and Minnesota (Figure 5A and Table S8). From 2010 to 2019, a similar distribution of stroke-related AAMR was seen with high mortality in southern states (Figure 5B and Table S9).

Regional

Stroke-related AAMR was highest in the South region, followed by the Midwest, West, and Northeast (Table S10).

DISCUSSION

In this nationwide study, we report several important findings on stroke-related mortality in young adults using US CDC data from 1999 to 2019. First, after an initial decline, stroke-related mortality in young adults increased from 2013 to 2019. Second, AAMR was higher in men compared with women throughout the study period. Third, the stroke-related mortality in non-Hispanic Black or African American people was substantially higher than all other races and ethnicities. In addition, the increase in mortality nationally from 2013 to 2019 was predominantly attributable to increases in mortality among non-Hispanic American Indian or Alaskan Native people, Hispanic or Latino people, and non-Hispanic White people. Fourth, rural (nonmetropolitan) counties had higher mortality compared with urban (metropolitan) counties. Fifth, stroke-related mortality was highest in the South throughout the study period.

Stroke mortality in the overall population and young adults has previously been reported to be declining from the 1980s to 2010s. However, since the early 2010s, the declines in stroke mortality in the overall and young adult population have stagnated. In addition, county-level mortality data have demonstrated an increasing stroke-related mortality rate in young adults in ≈56% of individual US counties from 2010 to 2016. In our study using contemporary data to 2019, we report a concerning reversal in national trends of stroke-related mortality among young adults, demonstrating increasing mortality from 2013 to 2019. In addition, we report wide variations in mortality rates...
Figure 5. State-level, age-adjusted, stroke-related mortality rates among adults aged 25 to 64 years in the United States from 1999 to 2009 (A) and from 2010 to 2019 (B).
among different demographic and geographic young adult groups.

Stoke-related mortality in young adults increased by ≈1.5% annually from 2013 to 2019, which may be explained by increases in the hospitalizations for stroke secondary to a greater burden of cardiovascular risk factors within this population. Hospitalizations for stroke in young adults have increased from ≈2000 to 2017.4,5,17 In addition, the burden of comorbidities and cardiovascular risk factors has increased among young people hospitalized for stroke.17-19 For example, the prevalence of hypertension, dyslipidemia, and tobacco use has increased in young adults from 2003 to 2012, and the prevalence of atrial fibrillation has increased across all age groups from 2006 to 2018 in the United States.4,20 In addition, national increases in the prevalence of diabetes, obesity, and mean systolic blood pressure reported within the National Health and Nutrition Examination Surveys may contribute to increasing stroke hospitalizations and subsequent deaths for young adults.21-23 Interestingly, when analyzed by stroke type, there was a 14.4% annual increase in ischemic stroke-related mortality in young adults over a similar period. However, the stroke subtype results should be interpreted with caution given that many recorded stroke deaths were attributable to unspecified stroke. In a report from the Clinformatics Data Mart database (Optum Inc), the use of mechanical thrombectomy and intravenous tPA (tissue-type plasminogen activator) increased over this time period within young adults with acute ischemic stroke; however, age-standardized 30-, 60-, and 90-day and 6-month acute ischemic stroke mortality in patients aged 18 to 70 years has not improved over this time period.24 Coupled with increasing ischemic stroke hospitalizations in young adults, in-hospital case fatality has also declined less among young compared with older adults.8 Taken together, the increasing ischemic stroke-related deaths in young adults within this study, despite higher use of mechanical thrombectomy or tPA, may reflect the combination of increasing incidence of acute ischemic stroke without improving case fatality rates.

The increasing stroke-related mortality from 2013 to 2019 was predominantly observed in non-Hispanic American Indian or Alaskan Native people, Hispanic or Latino people, and non-Hispanic White people. Notably, there was a pronounced increase in stroke-related deaths among non-Hispanic American Indian or Alaskan Native people from 2013 to 2019. In a recent study examining nonhemorrhagic stroke risk among race and ethnicity groups, American Indian people were noted to have the highest frequency of stroke risk factors, including diabetes, obesity, and smoking. Furthermore, they were at persistently higher risk of stroke following adjustment for known stroke risk factors compared with other races and ethnicities.25 Unfortunately, vascular risk factors have been reportedly increasing among stroke hospitalizations in Native American people.26 In addition, American Indian people have higher risk of developing atrial fibrillation and experienced greater distances to certified stroke care compared with other races and ethnicities within the United States.27,28 Adverse social determinants of health are prevalent within Native American communities and contribute to worse cardiovascular outcomes.29 For example, American Indian or Alaskan Native people experience lower educational attainment, higher poverty rates, wealth inequities, and underinsurance, which may result in lower access to preventive health care and stroke risk factor control.29 Although non-Hispanic Black or African American young adults did not have increasing mortality throughout the study period, the overall AAMR in non-Hispanic Black or African American young adults was ≈2.8 times greater than non-Hispanic White people and was greater than the remainder of the other race and ethnicity groups. Within the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study cohort, Black people aged 45 to 64 years had higher mortality attributable to stroke compared with White people, attributed primarily to increased incidence of ischemic stroke rather than case fatality.30,31 Non-Hispanic Black or African American people experience inequities in cardiovascular care and a greater burden of cardiovascular risk factors than other race and ethnic groups, and structural racism (eg, redlining) and other sociodemographic factors have also been demonstrated to be associated with higher incidence rates of stroke and likely contribute to this disparity in mortality.21,32-36 For example, among children in the United States, Black or African American children experience a higher prevalence of hypertension compared with White children or Hispanic children (13.8% versus 8.4% and 10.4%, respectively).35,37 This disparity continues throughout adulthood, with higher incidence of hypertension, diabetes, and dyslipidemia among Black or African American people compared with White people aged >45 years.35,38 Furthermore, Black or African American people treated for hypertension have been reported to be less likely to reach blood pressure goals compared with White people, leading to reduced benefit of optimizing this potent stroke risk factor.35,39 Similar disparities exist among other stroke risk factors. For example, within the REGARDS study, Black people with atrial fibrillation were less likely to receive warfarin compared with White people with atrial fibrillation.40 Similarly, the initiation of direct-acting oral anticoagulants for incident atrial fibrillation has been reported to be lower among Black patients compared with White patients within the Veterans Affairs Health System, which is concerning for health provider or system-level bias.41 Next, Black or African American people experience a greater burden of adverse social
determinants of health, including poverty, stress, and neighborhood safety concerns, and racial discrimination. For example, perceived racial discrimination has been associated with hypertension and incident cardiovascular disease. Taken together, racial disparities in the incidence and treatment of stroke risk factors require greater efforts for primordial prevention among Black or African American people and efforts to reduce structural racism and physician bias among health care providers to ensure equitable care, address adverse social determinants of health, and, subsequently, reduce the stroke burden among young Black or African American adults.

When examining urban-rural trends, rural counties demonstrated the highest mortality during the study period, likely predominately explained by higher prevalence of stroke risk factors within rural communities. Within the REGARDS study, people living within small or large rural cities had greater risk of incident stroke. When adjusted for traditional stroke and socioeconomic risk factors, the risk for incident stroke was slightly reduced, suggesting the greater burden of cardiovascular risk and adverse social factors experienced by people living in rural areas may contribute to the higher stroke incidence within these areas. For example, hypertension, diabetes, and smoking are more prevalent within rural areas. In addition, rural residents have been reported to have higher levels of adverse socioeconomic factors, such as lower income, lower access to care, lower access to food security, and others, which may negatively impact cardiovascular health. For system-level factors, lower rates of intravenous thrombolysis, endovascular therapy, access to stroke units, and in-hospital mortality for rural patients hospitalized with stroke may also contribute to the higher stroke burden seen in rural young adults.

In addition, of the 4 US Census regions, the South demonstrated the highest mortality during our study period. This is congruent with the previously reported higher mortality in the Stroke Belt (ie, the southeastern region of the United States) that has persisted for all ages since at least 1940. This region has a higher incidence than all other regions as well as a higher prevalence of stroke risk factors and has been extensively studied.

There are several limitations for this study. First, death certificates may potentially be misclassified within the CDC WONDER database. However, this database has been used in multiple studies of cardiovascular diseases and is a comprehensive source of vital statistics and mortality trends within the United States. Although widely used and a comprehensive source for national trends in mortality, death certificate data are subject to misclassification-related errors in diagnosis or completion of death certificates, race and ethnicity misclassification, or changes in coding practices.

Second, death certificate information reports causes of death alone and does not report important information on the treatments received, time to presentation, predictors of mortality, or others, which may influence mortality rates, especially within certain demographic or regional groups. Third, the database lacks important information on the cause of stroke, important comorbidities, and imaging data. Fourth, most deaths were classified as unspecified stroke. Therefore, we were unable to reliably ascertain if the increase in mortality was driven by ischemic or hemorrhagic stroke subtype. Fourth, the database lacks information on social determinants of health, which may contribute to mortality in the studied demographic groups. Finally, as the state in which a patient’s death occurred is recorded in the database, migration of patients from their original place of living could impact observed geographic trends.

In conclusion, despite an initial decline, we report a concerning increase in age-adjusted stroke mortality rate in young adults from 2013 to 2019, with considerable differences across demographic groups and regions. This increase is particularly prominent in men and non-Hispanic American Indian or Alaskan Native, Hispanic or Latino, and non-Hispanic White young adults. In addition, non-Hispanic Black or African American people and individuals in rural counties experienced markedly higher rates of mortality than other races and ethnicities and urban counties, respectively. Further efforts are necessary to elucidate the causes of the reversal in national stroke-related mortality trends in young adults, and to address the exhibited disparities over the past decade.

ARTICLE INFORMATION
Received March 22, 2022; accepted July 19, 2022.

Affiliations
Division of Cardiovascular Medicine, University of Toledo Medical Center, Toledo, OH (R.W.A., J.L., S.N.); ProMedica Heart and Vascular Institute, ProMedica Toledo Hospital, Toledo, OH (R.W.A., P.K.R., S.N.); Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA (R.W.A.); Department of Medicine, Forrest General Hospital, Hattiesburg, MS (A.M.M.); Department of Cardiology, Houston Methodist DeBakey Heart and Vascular Center, Houston, TX (S.U.K., M.K.); Division of Cardiovascular Medicine, Brigham and Women’s Hospital, Boston, MA (H.J.W.); Cardiology Section, Department of Medicine, VA Boston Healthcare System, Boston, MA (H.J.W.); Cardiology Division, Massachusetts General Hospital and Harvard Medical School, Boston, MA (D.K.); Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN (M.A.); and Section of Cardiology, Baylor College of Medicine, Houston, TX (S.N.).

Sources of Funding
The ProMedica Toledo Hospital Heart and Vascular Institute provided funds for the open access fee for this study.

Disclosures
None.

Supplemental Material
Tables S1–S10
Figure S1
38. Howard G, Safford MM, Moy CS, Howard VJ, Kleindorfer DO, Unverzagt FW, Soliman EZ, Flaherty ML, McClure LA, Lackland DT. Racial differences in the incidence of cardiovascular risk factors in older black and white adults. J Am Geriatr Soc. 2017;65:83–90. doi: 10.1111/jgs.14472
39. Howard G, Primeas R, Moy C, Cushman M, Kellum M, Temple E, Graham A, Howard V. Racial and geographic differences in awareness, treatment, and control of hypertension: the REasons for Geographic and Racial Differences in Stroke study. Stroke. 2006;37:1171–1178. doi: 10.1161/01.STR.0000217222.09978.ce
40. Meschia JF, Merrill P, Soliman EZ, Howard VJ, Barrett KM, Zakai NA, Kleindorfer D, Safford M, Howard G. Racial disparities in awareness and treatment of atrial fibrillation: the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. Stroke. 2010;41:581–587. doi: 10.1161/STROKEAHA.109.573907
41. Essien UR, Kim N, Hausmann LR, Mor MK, Good CB, Magnani JW, Litam TM, Gellad WF, Fine MJ. Disparities in anticoagulant therapy initiation for incident atrial fibrillation by race/ethnicity among patients in the Veterans Health Administration system. JAMA Netw Open. 2021;4:e2114234. doi: 10.1001/jamanetworkopen.2021.14234
42. Dolezsar CM, McGrath JJ, Herzig AJ, Miller SB. Perceived racial discrimination and hypertension: a comprehensive systematic review. Health Psychol. 2014;33:20–34. doi: 10.1037/a0033718
43. Everson-Rose SA, Lutsey PL, Roetker NS, Lewis TT, Kershaw KN, Alonso A, Diez Roux AV. Perceived discrimination and incident cardiovascular events: the Multi-Ethnic Study of Atherosclerosis. Am J Epidemiol. 2010;182:225–234. doi: 10.1093/aje/kwv035
44. Howard G, Kleindorfer DO, Cushman M, Long DL, Jasne A, Judd SE, Higginsbotham JC, Howard VJ. Contributors to the excess stroke mortality in rural areas in the United States. Stroke. 2017;48:1773–1778. doi: 10.1161/STROKEAHA.117.017089
45. Howard G. Rural-urban differences in stroke risk. Prev Med. 2021;152:106661. doi: 10.1016/j.ypmed.2021.106661
46. Harrington RA, Calif R, Balamurugan A, Brown N, Benjamin RM, Braund WE, Hipp J, König M, Sanchez E, Joynt Maddox KE. Call to action: rural health: a presidential advisory from the American Heart Association and American Stroke Association. Circulation. 2020;141:e615–e644. doi: 10.1161/CIR.0000000000000753
47. Dwyer M, Rehman S, Ottavi T, Stankovich J, Gail S, Peterson G, Ford K, Kinsman L. Urban-rural differences in the care and outcomes of acute stroke patients: systematic review. J Neurol Sci. 2019;397:63–74. doi: 10.1016/j.jns.2018.12.021
48. Hammond G, Luke AA, Elson L, Towfighi A, Joynt Maddox KE. Urban-rural inequities in acute stroke care and in-hospital mortality. Stroke. 2020;51:2131–2138. doi: 10.1161/STROKEAHA.120.029318
49. Howard G, Howard VJ. Twenty years of progress toward understanding the stroke belt. Stroke. 2020;51:742–750. doi: 10.1161/STROKEAHA.119.024155
50. Cross SH, Mehra MR, Bhatt DL, Nasir K, O’Donnell CJ, Califf RM, Warrach HJ. Rural-urban differences in cardiovascular mortality in the US, 1999–2017. JAMA. 2020;323:1852–1854. doi: 10.1001/jama.2020.2047
51. Nambiari L, LeWinter MM, VanBuren PC, Dauerman HL. Decade-long temporal trends in US hypertension-related cardiovascular mortality. J Am Coll Cardiol. 2020;75:2644–2646. doi: 10.1016/j.jacc.2020.03.009
SUPPLEMENTAL MATERIAL
Table S1. Absolute number of stroke-related deaths stratified by sex and race and ethnicity in the United States, 1999-2019.

| Year | Overall | Females | Males | NH White People | NH Black or African American People | NH Asian or Pacific Islander People | NH American Indian or Alaskan Native People | Hispanic or Latino People |
|------|---------|---------|-------|-----------------|-------------------------------------|--------------------------------------|---------------------------------------------|--------------------------|
| 1999 | 26933   | 12173   | 14760 | 16611           | 7100                                | 868                                  | 198                                         | 2040                     |
| 2000 | 27405   | 12429   | 14976 | 16842           | 7245                                | 837                                  | 225                                         | 2140                     |
| 2001 | 26824   | 12160   | 14664 | 16232           | 7232                                | 874                                  | 198                                         | 2182                     |
| 2002 | 27019   | 12270   | 14749 | 16375           | 7307                                | 823                                  | 220                                         | 2208                     |
| 2003 | 27135   | 12134   | 15001 | 16153           | 7426                                | 928                                  | 212                                         | 2316                     |
| 2004 | 26831   | 11963   | 14868 | 16155           | 7230                                | 861                                  | 207                                         | 2309                     |
| 2005 | 26844   | 11785   | 15059 | 16117           | 7177                                | 865                                  | 242                                         | 2387                     |
| 2006 | 26785   | 11747   | 15038 | 16039           | 7155                                | 910                                  | 183                                         | 2421                     |
| 2007 | 26512   | 11484   | 15028 | 15726           | 7125                                | 878                                  | 218                                         | 2501                     |
| 2008 | 25641   | 11206   | 14435 | 15245           | 6814                                | 938                                  | 188                                         | 2370                     |
| 2009 | 25702   | 11157   | 14545 | 15353           | 6616                                | 914                                  | 232                                         | 2488                     |
| 2010 | 25511   | 10991   | 14520 | 15239           | 6590                                | 950                                  | 209                                         | 2457                     |
| 2011 | 26170   | 11266   | 14904 | 15586           | 6662                                | 1017                                 | 239                                         | 2598                     |
| 2012 | 25901   | 11084   | 14817 | 15269           | 6664                                | 1038                                 | 212                                         | 2619                     |
| 2013 | 26074   | 10991   | 15170 | 15457           | 6522                                | 1017                                 | 238                                         | 2746                     |
| 2014 | 26691   | 11270   | 15421 | 15802           | 6745                                | 1071                                 | 242                                         | 2743                     |
| 2015 | 27427   | 11573   | 15854 | 16063           | 6929                                | 1083                                 | 255                                         | 2971                     |
| 2016 | 27982   | 11716   | 16266 | 16453           | 6822                                | 1216                                 | 260                                         | 3114                     |
| 2017 | 28632   | 11911   | 16721 | 16501           | 7190                                | 1176                                 | 286                                         | 3368                     |
| 2018 | 28988   | 12054   | 16934 | 16808           | 7213                                | 1244                                 | 294                                         | 3329                     |
| 2019 | 29909   | 12415   | 17494 | 17196           | 7398                                | 1313                                 | 323                                         | 3584                     |
| Total| 566916  | 245692  | 321224| 337222          | 147162                              | 20821                                | 4881                                        | 54891                    |

NH: Non-Hispanic
Table S2. Stroke-related age-adjusted mortality rates per 100,000 among adults aged 25-64 years stratified by stroke subtype in the United States, 1999-2019.

| Year | Unspecified | Hemorrhagic | Ischemic |
|------|-------------|-------------|----------|
| 1999 | 9.3         | 7.9         | 2.0      |
| 2000 | 9.2         | 7.9         | 1.9      |
| 2001 | 9.0         | 7.4         | 1.7      |
| 2002 | 8.7         | 7.2         | 1.7      |
| 2003 | 8.5         | 7.0         | 1.7      |
| 2004 | 8           | 6.9         | 1.6      |
| 2005 | 7.9         | 6.6         | 1.5      |
| 2006 | 7.7         | 6.4         | 1.4      |
| 2007 | 7.5         | 6.2         | 1.3      |
| 2008 | 7.2         | 5.8         | 1.2      |
| 2009 | 7.0         | 5.6         | 1.3      |
| 2010 | 7.0         | 5.4         | 1.2      |
| 2011 | 7.0         | 5.3         | 1.2      |
| 2012 | 6.9         | 5.2         | 1.2      |
| 2013 | 7.0         | 5.1         | 1.2      |
| 2014 | 7.1         | 5.0         | 1.3      |
| 2015 | 7.2         | 5.1         | 1.4      |
| 2016 | 7.0         | 5.3         | 1.6      |
| 2017 | 6.6         | 5.2         | 2.4      |
| 2018 | 6.5         | 5.2         | 2.7      |
| 2019 | 7.0         | 5.3         | 2.4      |
| Total| 7.5         | 6.10        | 1.6      |
Table S3. Absolute number of stroke-related deaths among adults aged 25-64 years stratified by location of death in the United States, 1999-2019.

| Year | Medical Facility | Nursing Home/Long Term Care | Hospice   | Home   |
|------|------------------|-----------------------------|-----------|--------|
| 1999 | 21288            | 2330                        | Missing   | 2848   |
| 2000 | 21641            | 2463                        | Missing   | 2800   |
| 2001 | 21023            | 2396                        | Missing   | 2874   |
| 2002 | 20992            | 2427                        | Missing   | 2996   |
| 2003 | 20759            | 2464                        | 17        | 3106   |
| 2004 | 20303            | 2410                        | 32        | 3225   |
| 2005 | 19989            | 2487                        | 186       | 3334   |
| 2006 | 19788            | 2446                        | 355       | 3380   |
| 2007 | 19364            | 2550                        | 473       | 3380   |
| 2008 | 18094            | 2325                        | 640       | 3343   |
| 2009 | 17658            | 2395                        | 696       | 3266   |
| 2010 | 18073            | 2281                        | 892       | 3542   |
| 2011 | 18174            | 2455                        | 1121      | 3668   |
| 2012 | 17708            | 2347                        | 1282      | 3817   |
| 2013 | 17566            | 2421                        | 1301      | 3858   |
| 2014 | 17696            | 2507                        | 1588      | 4189   |
| 2015 | 18083            | 2612                        | 1739      | 4319   |
| 2016 | 18394            | 2625                        | 1905      | 4412   |
| 2017 | 18654            | 2748                        | 2018      | 4566   |
| 2018 | 18645            | 2811                        | 1994      | 4865   |
| 2019 | 19078            | 2900                        | 2108      | 5076   |
| Total| 402970           | 52400                       | 18347     | 76864  |
Table S4. Overall and sex-stratified stroke-related age-adjusted mortality rates per 100,000 among adults aged 25-64 years in the United States, 1999 to 2019.

| Year | Overall | Male  | Female |
|------|---------|-------|--------|
| 1999 | 18.92   | 21.37 | 16.63  |
| 2000 | 18.89   | 21.24 | 16.67  |
| 2001 | 17.93   | 20.12 | 15.81  |
| 2002 | 17.38   | 19.49 | 15.44  |
| 2003 | 16.92   | 19.23 | 14.81  |
| 2004 | 16.27   | 18.49 | 14.18  |
| 2005 | 15.78   | 18.13 | 13.57  |
| 2006 | 15.31   | 17.61 | 13.14  |
| 2007 | 14.81   | 17.13 | 12.57  |
| 2008 | 14.02   | 16.17 | 12.03  |
| 2009 | 13.75   | 15.9  | 11.7   |
| 2010 | 13.4    | 15.58 | 11.36  |
| 2011 | 13.39   | 15.58 | 11.34  |
| 2012 | 13.21   | 15.44 | 11.11  |
| 2013 | 13.2    | 15.67 | 10.85  |
| 2014 | 13.33   | 15.73 | 11.02  |
| 2015 | 13.56   | 15.99 | 11.26  |
| 2016 | 13.75   | 16.31 | 11.37  |
| 2017 | 13.96   | 16.69 | 11.4   |
| 2018 | 14.08   | 16.77 | 11.53  |
| 2019 | 14.57   | 17.33 | 11.95  |
| Total| 14.87   | 17.21 | 12.62  |
Table S5. Stroke-related age-adjusted mortality rates per 100,000 among adults aged 25-64 years stratified by race and ethnicity in the United States, 1999 to 2019.

| Year | NH White People | NH Black or African American People | NH Asian or Pacific Islander People | NH American Indian or Alaskan Native People | Hispanic or Latino People |
|------|-----------------|-------------------------------------|--------------------------------------|---------------------------------------------|---------------------------|
| 1999 | 15.09           | 47.66                               | 16.98                                | 20.22                                       | 17.82                     |
| 2000 | 15.11           | 47.34                               | 15.51                                | 21.92                                       | 17.89                     |
| 2001 | 14.2            | 45.5                                | 15.09                                | 18.34                                       | 17.02                     |
| 2002 | 13.33           | 44.29                               | 13.33                                | 19.63                                       | 16.25                     |
| 2003 | 13.33           | 43.37                               | 14.19                                | 18.23                                       | 16.18                     |
| 2004 | 13.02           | 40.65                               | 12.45                                | 17.22                                       | 15.17                     |
| 2005 | 12.68           | 38.8                                | 11.79                                | 19.5                                        | 14.82                     |
| 2006 | 12.33           | 37.29                               | 11.77                                | 14.31                                       | 14.22                     |
| 2007 | 11.9            | 35.92                               | 10.81                                | 16.52                                       | 13.94                     |
| 2008 | 11.36           | 33.3                                | 10.99                                | 13.86                                       | 12.44                     |
| 2009 | 11.29           | 31.25                               | 10.27                                | 14.93                                       | 11.84                     |
| 2010 | 11.05           | 30.36                               | 10.33                                | 16.66                                       | 12.45                     |
| 2011 | 11.12           | 29.75                               | 10.55                                | 16.52                                       | 11.85                     |
| 2012 | 10.97           | 29.12                               | 10.4                                 | 14.41                                       | 11.53                     |
| 2013 | 11.06           | 27.98                               | 9.87                                 | 16.17                                       | 11.6                      |
| 2014 | 11.29           | 28.42                               | 9.9                                  | 15.91                                       | 11.08                     |
| 2015 | 11.47           | 28.71                               | 9.66                                 | 17.07                                       | 11.45                     |
| 2016 | 11.79           | 27.92                               | 10.71                                | 17.25                                       | 11.67                     |
| 2017 | 11.88           | 28.82                               | 10.01                                | 18.68                                       | 12.12                     |
| 2018 | 12.1            | 28.81                               | 10.32                                | 18.46                                       | 11.66                     |
| 2019 | 12.49           | 29.39                               | 10.65                                | 20.68                                       | 12.22                     |
| Total| 12.27           | 33.96                               | 11.21                                | 17.21                                       | 12.98                     |

NH: Non-Hispanic
Table S6. Stroke-related crude mortality rates per 100,000 stratified by age groups in the United States, 1999 to 2019.

| Year | Age 25-34 | Age 35-44 | Age 45-54 | Age 55-64 |
|------|-----------|-----------|-----------|-----------|
| 1999 | 2.14      | 7.6       | 21.1      | 62.79     |
| 2000 | 2.11      | 7.49      | 21.37     | 62.33     |
| 2001 | 2.18      | 7.2       | 20.28     | 58.67     |
| 2002 | 2.07      | 7.14      | 20.41     | 55.63     |
| 2003 | 2.13      | 7.12      | 20.03     | 53.47     |
| 2004 | 2.09      | 6.89      | 19.65     | 50.55     |
| 2005 | 1.92      | 6.58      | 19.31     | 49.03     |
| 2006 | 1.87      | 6.45      | 18.94     | 47.17     |
| 2007 | 1.76      | 6.33      | 18.3      | 45.47     |
| 2008 | 1.8       | 5.84      | 17.59     | 42.84     |
| 2009 | 1.72      | 5.68      | 17.31     | 42.02     |
| 2010 | 1.63      | 5.6       | 16.61     | 41.3      |
| 2011 | 1.74      | 5.41      | 16.65     | 41.51     |
| 2012 | 1.71      | 5.38      | 16.3      | 40.89     |
| 2013 | 1.61      | 5.36      | 16.4      | 40.78     |
| 2014 | 1.69      | 5.51      | 16.1      | 41.73     |
| 2015 | 1.81      | 5.57      | 16.37     | 42.3      |
| 2016 | 1.82      | 5.85      | 16.65     | 42.63     |
| 2017 | 1.79      | 5.82      | 16.92     | 43.51     |
| 2018 | 1.91      | 5.61      | 17.01     | 44.28     |
| 2019 | 1.94      | 5.85      | 17.69     | 45.58     |
| Total| 1.87      | 6.23      | 18.07     | 46.24     |
Table S7. Stroke-related age-adjusted mortality rates per 100,000 among adults aged 25-64 years stratified by urban (Medium/Small Metropolitan) and Rural (Nonmetropolitan) classification in the United States, 1999 to 2019.

| Year | Nonmetropolitan | Medium/Small Metropolitan | Large Metropolitan |
|------|----------------|---------------------------|--------------------|
| 1999 | 20.69          | 19.14                     | 18.23              |
| 2000 | 20.63          | 19.08                     | 18.21              |
| 2001 | 19.57          | 17.8                      | 17.47              |
| 2002 | 19.74          | 17.5                      | 16.62              |
| 2003 | 18.78          | 17.34                     | 16.17              |
| 2004 | 18.2           | 16.62                     | 15.49              |
| 2005 | 17.82          | 16.32                     | 14.89              |
| 2006 | 17.48          | 15.89                     | 14.38              |
| 2007 | 17.05          | 15.29                     | 13.89              |
| 2008 | 16.06          | 14.53                     | 13.18              |
| 2009 | 16.04          | 14.5                      | 12.66              |
| 2010 | 16.22          | 13.97                     | 12.31              |
| 2011 | 15.92          | 13.91                     | 12.46              |
| 2012 | 15.43          | 14                        | 12.22              |
| 2013 | 15.59          | 13.98                     | 12.13              |
| 2014 | 16.47          | 14.32                     | 12.01              |
| 2015 | 16.77          | 14.58                     | 12.17              |
| 2016 | 17.45          | 14.89                     | 12.24              |
| 2017 | 17.82          | 15.01                     | 12.42              |
| 2018 | 17.79          | 15.57                     | 12.37              |
| 2019 | 18.95          | 15.72                     | 12.87              |
| Total| 17.54          | 15.53                     | 13.76              |
Table S8. State-level stroke-related age-adjusted mortality rates per 100,000 among adults aged 25-64 years in the United States, 1999 to 2009.

| State          | Rank | Percentile | AAMR |
|----------------|------|------------|------|
| Vermont        | 1    | 0          | 9.13 |
| New Hampshire  | 2    | 2          | 9.32 |
| Massachusetts  | 3    | 4          | 9.68 |
| Colorado       | 4    | 6          | 10.84|
| Connecticut    | 5    | 8          | 11.01|
| Minnesota      | 6    | 10         | 11.21|
| Maine          | 7    | 12         | 11.35|
| Utah           | 8    | 14         | 11.44|
| Idaho          | 9    | 16         | 11.78|
| New York       | 10   | 18         | 11.98|
| Montana        | 11   | 20         | 12.1 |
| Alaska         | 12   | 22         | 12.17|
| Iowa           | 13   | 24         | 12.35|
| Rhode Island   | 14   | 26         | 12.45|
| North Dakota   | 15   | 28         | 12.58|
| Arizona        | 16   | 30         | 12.71|
| Nebraska       | 17   | 32         | 12.81|
| Wisconsin      | 18   | 34         | 12.97|
| Washington     | 19   | 36         | 13.1 |
| Wyoming        | 20   | 38         | 13.21|
| New Mexico     | 21   | 40         | 13.48|
| South Dakota   | 22   | 42         | 13.57|
| New Jersey     | 23   | 44         | 13.86|
| Oregon         | 24   | 46         | 13.88|
| Kansas         | 25   | 48         | 14.29|
| State              | Age | Mortality Rate |
|--------------------|-----|----------------|
| Pennsylvania       | 26  | 14.73          |
| Nevada             | 27  | 15.16          |
| Virginia           | 28  | 15.2           |
| Delaware           | 29  | 15.43          |
| Michigan           | 30  | 15.81          |
| Illinois           | 31  | 15.82          |
| California         | 32  | 16.03          |
| Florida            | 33  | 16.09          |
| Indiana            | 34  | 16.3           |
| Missouri           | 35  | 16.62          |
| Maryland           | 36  | 17.36          |
| Ohio               | 37  | 17.4           |
| Kentucky           | 38  | 17.5           |
| Texas              | 39  | 18.49          |
| Hawaii             | 40  | 18.67          |
| West Virginia      | 41  | 19.09          |
| North Carolina     | 42  | 20.27          |
| Oklahoma           | 43  | 21.01          |
| Georgia            | 44  | 21.52          |
| Tennessee          | 45  | 21.83          |
| Alabama            | 46  | 24.91          |
| South Carolina     | 47  | 24.94          |
| Arkansas           | 48  | 24.98          |
| Louisiana          | 49  | 25.01          |
| Mississippi        | 50  | 30.14          |
| District of Columbia | 51 | 31.34 |

AAMR: Age-adjusted mortality rate
Table S9. State-level stroke-related age-adjusted mortality rates per 100,000 among adults aged 25-64 years in the United States, 2010 to 2019.

| State            | Rank | Percentile | AAMR |
|------------------|------|------------|------|
| New Hampshire    | 1    | 0          | 7.66 |
| Massachusetts    | 2    | 2          | 7.67 |
| Connecticut      | 3    | 4          | 8.25 |
| Vermont          | 4    | 6          | 8.68 |
| New York         | 5    | 8          | 9.51 |
| Colorado         | 6    | 10         | 9.63 |
| Utah             | 7    | 12         | 9.86 |
| Maine            | 8    | 14         | 10.09|
| Minnesota        | 9    | 16         | 10.27|
| Rhode Island     | 10   | 18         | 10.4 |
| Montana          | 11   | 20         | 10.55|
| North Dakota     | 12   | 22         | 10.61|
| Iowa             | 13   | 24         | 10.65|
| New Jersey       | 14   | 26         | 10.75|
| Idaho            | 15   | 28         | 10.8 |
| Nebraska         | 16   | 30         | 11.07|
| Wisconsin        | 17   | 32         | 11.16|
| Wyoming          | 18   | 34         | 11.26|
| Pennsylvania     | 19   | 36         | 11.55|
| Arizona          | 20   | 38         | 11.72|
| New Mexico       | 21   | 40         | 11.93|
| South Dakota     | 22   | 42         | 11.98|
| Oregon           | 23   | 44         | 11.99|
| Alaska           | 24   | 46         | 12.07|
| Washington       | 25   | 48         | 12.17|
| State              | Rank | Life expectancy | AAMR  |
|-------------------|------|-----------------|-------|
| Virginia          | 26   | 50              | 12.27 |
| Illinois          | 27   | 52              | 12.28 |
| Kansas            | 28   | 54              | 12.82 |
| California        | 29   | 56              | 12.99 |
| Michigan          | 30   | 58              | 13    |
| Nevada            | 31   | 60              | 13.07 |
| Florida           | 32   | 62              | 13.49 |
| Maryland          | 33   | 64              | 13.66 |
| Delaware          | 34   | 66              | 14.14 |
| Missouri          | 35   | 68              | 14.21 |
| Ohio              | 36   | 70              | 14.7  |
| Indiana           | 37   | 72              | 15.66 |
| North Carolina    | 38   | 74              | 15.83 |
| Texas             | 39   | 76              | 16.32 |
| Georgia           | 40   | 78              | 16.59 |
| Kentucky          | 41   | 80              | 17.52 |
| Hawaii            | 42   | 82              | 17.94 |
| West Virginia     | 43   | 84              | 18.96 |
| Alabama           | 44   | 86              | 19.81 |
| Tennessee         | 45   | 88              | 19.93 |
| Louisiana         | 46   | 90              | 20.42 |
| Oklahoma          | 47   | 92              | 20.9  |
| South Carolina    | 48   | 94              | 21.09 |
| Arkansas          | 49   | 96              | 21.51 |
| District of Columbia | 50  | 98              | 21.8  |
| Mississippi       | 51   | 100             | 28.01 |

AAMR: Age-adjusted mortality rate
Table S10. Stroke-related age-adjusted mortality rates per 100,000 among adults aged 25-64 years stratified by census region in the United States, 1999-2019.

| Census Region | Year | AAMR |
|---------------|------|------|
| Northeast     | 1999 | 14.9 |
| Northeast     | 2000 | 14.92|
| Northeast     | 2001 | 14.12|
| Northeast     | 2002 | 13.52|
| Northeast     | 2003 | 13.1 |
| Northeast     | 2004 | 12.38|
| Northeast     | 2005 | 11.76|
| Northeast     | 2006 | 11.83|
| Northeast     | 2007 | 10.94|
| Northeast     | 2008 | 10.63|
| Northeast     | 2009 | 10.3 |
| Northeast     | 2010 | 10.06|
| Northeast     | 2011 | 9.92 |
| Northeast     | 2012 | 9.64 |
| Northeast     | 2013 | 9.9  |
| Northeast     | 2014 | 9.84 |
| Northeast     | 2015 | 9.72 |
| Northeast     | 2016 | 9.65 |
| Northeast     | 2017 | 9.79 |
| Northeast     | 2018 | 9.77 |
| Northeast     | 2019 | 10.21|
| Northeast     | Total| 11.16|
| Midwest       | 1999 | 17.55|
| Midwest       | 2000 | 17.86|
| Region | Year | Value |
|--------|------|-------|
| Midwest | 2001 | 16.65 |
| Midwest | 2002 | 16.55 |
| Midwest | 2003 | 15.86 |
| Midwest | 2004 | 15.05 |
| Midwest | 2005 | 14.95 |
| Midwest | 2006 | 14.38 |
| Midwest | 2007 | 14.17 |
| Midwest | 2008 | 13.41 |
| Midwest | 2009 | 12.92 |
| Midwest | 2010 | 12.59 |
| Midwest | 2011 | 12.83 |
| Midwest | 2012 | 12.47 |
| Midwest | 2013 | 12.51 |
| Midwest | 2014 | 12.7 |
| Midwest | 2015 | 12.74 |
| Midwest | 2016 | 12.86 |
| Midwest | 2017 | 13.3 |
| Midwest | 2018 | 13.69 |
| Midwest | 2019 | 13.66 |
| Midwest | Total | 14.06 |
| South  | 1999 | 22.81 |
| South  | 2000 | 22.7 |
| South  | 2001 | 21.97 |
| South  | 2002 | 21.26 |
| South  | 2003 | 20.6 |
| South  | 2004 | 19.99 |
| South  | 2005 | 19.46 |
| South  | 2006 | 18.68 |
| South  | 2007 | 18.12 |
| Year | South   |    | West   |    |
|------|---------|----|--------|----|
| 2008 | 17.16   |    |        |    |
| 2009 | 16.95   |    |        |    |
| 2010 | 16.5    |    |        |    |
| 2011 | 16.34   |    |        |    |
| 2012 | 16.16   |    |        |    |
| 2013 | 16      |    |        |    |
| 2014 | 16.32   |    |        |    |
| 2015 | 16.77   |    |        |    |
| 2016 | 16.81   |    |        |    |
| 2017 | 17.33   |    |        |    |
| 2018 | 17.08   |    |        |    |
| 2019 | 17.86   |    |        |    |
| Total| 18.18   |    |        |    |
| 1999 | 17.63   |    |        |    |
| 2000 | 17.23   |    |        |    |
| 2001 | 15.94   |    |        |    |
| 2002 | 15.37   |    |        |    |
| 2003 | 15.44   |    |        |    |
| 2004 | 14.77   |    |        |    |
| 2005 | 14.07   |    |        |    |
| 2006 | 13.73   |    |        |    |
| 2007 | 13.31   |    |        |    |
| 2008 | 12.42   |    |        |    |
| 2009 | 12.26   |    |        |    |
| 2010 | 11.87   |    |        |    |
| 2011 | 12.13   |    |        |    |
| 2012 | 12.04   |    |        |    |
| 2013 | 11.87   |    |        |    |
| 2014 | 11.91   |    |        |    |
|        |     |     |
|--------|-----|-----|
| West   | 2015| 12.17|
| West   | 2016| 12.89|
| West   | 2017| 12.43|
| West   | 2018| 12.9 |
| West   | 2019| 13.31|
| West   | Total| 13.39|
| Total  | Total| 14.87|

AAMR: Age-adjusted mortality rate
Figure S1. Trends in age-adjusted stroke-related mortality rates among adults aged 25-64 years stratified by stroke subtype in the United States, 1999 to 2019.

*Indicates that the annual percentage change (APC) is significantly different from zero at α=0.05.