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Trends and Racial-Geographic Disparities in Stroke-Related Mortality Among U.S. Older Adults with Diabetes Mellitus, 1999–2020

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- Multiple Cause of Death, 1999-2020, https://wonder.cdc.gov/mcd-icd10.html

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ABSTRACT:

Background: The combination of stroke and diabetes significantly increases mortality in older adults. Despite past progress, U.S. death rates are stalling and demographic gaps persist, yet long-term national research on this specific group remains scarce. ***Methods:*** We conducted a population-based mortality study using the CDC WONDER Multiple Causes of Death database from 1999 to 2020. Adults aged ≥65 years with stroke as the underlying cause of death (ICD-10 codes I60–I64, I69) and DM as a contributing cause (ICD-10 codes E10–E14) were included. Crude and age-adjusted mortality rates (AAMRs) per 100,000 population were calculated using the 2000 U.S. standard population. Temporal trends were analyzed using Joinpoint regression to estimate annual percent change (APC) and average annual percent change (AAPC). Stratified analyses were performed by age, sex, race/ethnicity, urban–rural status, and region. ***Results:*** A total of 201,269 deaths met inclusion criteria. Overall AAMRs declined from 32.50 in 1999 to 19.27 in 2020 (AAPC: −2.77; $p<0.001$), with significant reductions until 2014 followed by stabilization. Mortality rates were higher among males and highest among non-Hispanic Black individuals. Adults aged ≥85 years had the greatest mortality burden. Rural areas consistently showed higher mortality than urban areas, with notable regional variation. ***Conclusions***: Stroke-related mortality among U.S. adults aged ≥65 years with DM declined substantially from 1999 to 2020. However, recent trend stabilization and persistent disparities highlight the need for targeted prevention strategies and equitable access to care to sustain progress in this high-risk population.

Keyword: Stroke; Diabetes Mellitus; Epidemiology; Mortality; Public Health

1. INTRODUCTION:

Stroke and Diabetes mellitus (DM) are major global public health problems that affect socioeconomic situations and put a heavy burden on healthcare systems (1).In 2019, stroke was the second most common cause of death globally, accounting for 6.55 million deaths(2).Similarly, diabetes mellitus and its complications continue to contribute prominently to U.S. mortality, with studies showing substantial increases in type 2 diabetes–related death rates over recent decades, particularly among certain racial/ethnic groups and in particular geographic regions (3). After adjusting for age, data indicates that the risk of stroke is roughly doubled for those with diabetes compared to those without the disease (4).

The combination of diabetes and stroke creates a particularly dangerous situation, since diabetes not only raises the risk of cerebrovascular incidents but also leads to poorer results, such as enduring disability and increased mortality(5).Additionally, microvascular dysfunction is prevalent in diabetics, which increases their vulnerability to ischemic and haemorrhagic cerebrovascular accidents (6).The age-adjusted mortality rate (AAMR) for combined stroke and

diabetes mellitus-related mortality in U.S. adults decreased from 20.08 per 100,000 to 16.04 per 100,000 between 1999 and 2020, according to a national epidemiological study by Ahmed F et al. However, there were notable demographic and regional disparities that persisted across sex and geographic location, suggesting that even though overall mortality decreased, the combined burden of diabetes and stroke remains significant, especially in Southern and rural populations(7). It has been demonstrated that hyperglycemia deteriorates prognosis and hinders recovery following a stroke (8). As a result, stroke and diabetes together constitute a "high-risk combination," and the intricate reciprocal relationships between the two diseases highlight the critical need for closer observation and coordinated care in this susceptible group.

Although previous research has looked at the mortality rates associated with stroke and diabetes mellitus alone, there are still few age-specific evaluations of the long-term mortality trends associated with both conditions combined. The unique feature of this age-stratified technique is that it highlights unique mortality trends within adult age groups that are frequently hidden in aggregate analysis. Therefore, in order to identify age groups with disproportionate changes in mortality and to inform targeted prevention and public health strategies, this study uses national CDC WONDER mortality data from 1999–2020 to examine demographic and temporal trends in stroke and diabetes mellitus–related mortality in the U.S. population.

2. METHODS:

2.1 Study designs

In this study, we extracted death certificates from the CDC WONDER (Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research) database. We examined them from 1999 to 2020 for stroke and diabetes mellitus (DM) related mortality in adults aged 65 years or older at the time of their death. Adults aged 65 years and older were included because stroke and DM disproportionately affect older adults, with higher incidence and mortality rates, and this age threshold aligns with standard definitions of the elderly in epidemiological studies. The codes used were from the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), including I60–I64 and I69 for stroke, and E10–E14 for DM and extensively used in previously published studies (9, 10). This data includes cause of death from death certificates for the 50 states and the District of Columbia. The Cause-of-Death Public Use record death certificates were studied to select stroke-related deaths as the underlying cause of death (UCD), and DM as a multiple cause of death (MCD). The research was considered exempt from needing approval from the institutional review board, since the data is de-identified, obtained from government sources, and accessible to the public. This research complies with the reporting criteria established by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (11).

2.2 Data extraction

The data was extracted by age groups, race or ethnicity, gender, place of death, urban vs non-urban settings, census regions and states. The place of death was categorized into medical

facilities, the decedent's home, nursing homes or long-term care facilities, hospice centres, and others. Race or ethnicity was classified as Hispanic or Latino, Non-Hispanic (NH) Asian Pacific islander, NH American Indian or Alaska Native, NH Black or African American, and NH White (12). Age group was divided into 10 year intervals from 65 to 85+ years. The National Center for Health Statistics Urban-Rural Classification Scheme was used to assess the population by metropolitan (large central, large fringe, medium, and small metropolitan) and non-metropolitan areas (13). Census regions were classified into Northeast, Midwest, South, and West according to the U.S. Census Bureau definitions (14).

2.3 Statistical analysis:

Crude mortality rates (CMRs) and age-adjusted mortality rates (AAMRs) were calculated to analyze trends at the national level. CMRs were obtained by dividing the number of disease-related deaths by the corresponding U.S. population for each year. AAMRs were determined by adjusting the mortality figures to the year 2000 U.S. standard population (15). Both crude and age-adjusted mortality rate trends were evaluated using the Joinpoint Regression Program (Version 4.9.0.0, National Cancer Institute), which applies log-linear regression models made up of successive linear segments joined by points where significant temporal shifts occur (16). Autocorrelation was checked by the Joinpoint Regression Program, and default permutation tests were used to determine the number of joinpoints. Annual percentage changes (APCs) were calculated for each time segment between joinpoints and show the rate of change per year in that specific period with 95% confidence intervals (CIs). To classify APCs as increasing or decreasing, we used a two-tailed t-test to determine if each APC was significantly different from zero. A p-value of less than 0.05 indicated a significantly increasing or decreasing trend.

3. RESULTS:

Stroke and DM-related mortality contributed to 201,269 deaths in the United States between 1999 and 2020. Among them, 42.98% were males with 86505 deaths, and rest, 57.02%, were females with 114764 deaths (Supplemental Table 1). By location of death, the majority were in medical facilities (n=87,029; 43.25%), then in nursing homes/long-term care (n=68,452; 34.01%), followed by the decedent's home (n=29,702; 14.76%) and hospice facility (n=9,286; 4.61%). A reduced percentage of death was reported in other locations (n=6,267; 3.11%), and place of death unknown (n=533; 0.26%). (Supplemental Table 2, Figure 1)

Overall:

The total age-adjusted mortality rate (AAMR) of stroke patients with DM exhibited a decline from [AAMR: 32.50 (95% CI: 31.89 to 33.10)] in 1999 to [AAMR: 19.27 (95% CI: 18.89 to 19.65)] in 2020 (Supplemental Table 4), with an [AAPC: -2.77 (95% CI: -3.28 to -2.26). P-value: <0.000001]. Between 1999 and 2014, there was a statistically significant negative trend [APC: -

4.18 (95% CI: -4.57 to -3.79). P-value: <0.000001], followed by an increase between 2014 and 2020 [APC: 0.84 (95% CI: -0.83 to 2.55). P-value: 0.31] (Supplemental Table 3,4 Figure 2).

Demographic Differences:

Sex Stratified:

The AAMR among both females and males declined between 1999 and 2020. In females, the AAMR declined from [30.89 (95% CI: 30.14 to 31.63)] in 1999 to [17.44 (95% CI: 16.97 to 17.91)] in 2020. Consistently, in males, the AAMR declined from [35.08 (95% CI: 34.04 to 36.12)] in 1999 to [21.67 (95% CI: 21.05 to 22.28)] in 2020.
In females, there was a significant decline in AAMR between 1999 and 2015 [APC: -4.20 (95% CI: -4.54 to -3.86). P-value: < 0.000001], followed by an increase between 2015 and 2020 [APC: 0.96 (95% CI: -1.22 to 3.19). P-value: 0.37]. Overall trends showed a continued significant decline [AAPC: -3.00 (95% CI: -3.52 to -2.47). P-value: < 0.000001].
Likewise, the AAMR among males decreased significantly between 1999 and 2014 [APC: -4.08 (95% CI: -4.51 to -3.64). P-value: < 0.000001], with an increase between 2014 and 2020 [APC: 1.68 (95% CI: -0.13 to 3.51). P-value: 0.07], the overall period showed a significant decrease [AAPC: -2.47 (95% CI: -3.02 to -1.92). P-value: < 0.000001] (Supplemental Table 3,4; Figure 2).

Race Stratified:

Between 1999 and 2020, the AAMR declined in all racial/ethnic groups: Non-Hispanic American Indian or Alaska Natives [AAMR: 39.55 (95% CI: 28.95 to 52.75)] to [AAMR: 20.15 (95% CI: 15.98 to 25.08)]; Non-Hispanic Asian or Pacific Islanders [AAMR: 40.73 (95% CI: 35.78 to 45.68)] to [AAMR: 22.97 (95% CI: 21.12 to 24.82)]; Non-Hispanic Black or African Americans [AAMR: 56.16 (95% CI: 53.34 to 58.98)] to [AAMR: 31.76 (95% CI: 30.16 to 33.36)]; Non-Hispanic White [AAMR: 30.21 (95% CI: 29.60 to 30.82)] to [AAMR: 17.68 (95% CI: 17.29 to 18.07)] and Hispanic or Latinos [AAMR: 38.13 (95% CI: 34.91 to 41.36)] to [AAMR: 25.25 (95% CI: 23.76 to 26.74)].
Among Non-Hispanic American Indian or Alaska Native individuals, joinpoint identified a consistent downward trajectory across the entire study period [AAPC: -3.03 (95% CI: -3.95 to -2.09). P-value: 0.000002], reflecting a statistically significant decline in mortality over time.
For Non-Hispanic Asian or Pacific Islander individuals, AAMR represented a significant initial decline between 1999 and 2017 [APC: -4.62 (95% CI: -5.11 to -4.13). P-value: < 0.000001], which was subsequently followed by a statistically significant increase between 2017 and 2020 [APC: 7.07 (95% CI: 0.57 to 13.98). P-value: 0.03], and an overall significant decline [AAPC: -3.03 (95% CI: -3.93 to -2.13). P-value: < 0.000001].
Among Non-Hispanic Black or African American individuals, mortality showed an initial significant decrease from 1999 to 2016 [APC: -4.54 (95% CI: -5.08 to -4.01). P-value: < 0.000001], followed by a slight increase from 2016 to 2020 [APC: 2.31 (95% CI: -2.60 to 7.47). P-value: 0.34], with the overall rates suggesting a significant downward trend [AAPC: -3.27

(95% CI: -4.20 to -2.33). P-value: < 0.000001].
Among Non-Hispanic White individuals, the AAMR represented a significant initial decline from 1999 to 2014 [APC: -4.17 (95% CI: -4.56 to -3.77). P-value: < 0.000001], followed by an increasing trend between 2014 and 2020 [APC: 0.93 (95% CI: -0.80 to 2.68). P-value: 0.27], and an overall significant downward trend [AAPC: -2.74 (95% CI: -3.25 to -2.22). P-value: < 0.000001].
For Hispanic or Latino individuals, mortality showed a significant downward trend from 1999 to 2015 [APC: -3.47 (95% CI: -4.06 to -2.87). P-value: < 0.000001], followed by an increase from 2015 to 2020 [APC: 1.23 (95% CI: -1.77 to 4.32). P-value: 0.40], with an overall significant downward trajectory [AAPC: -2.37 (95% CI: -3.15 to -1.59). P-value: < 0.000001] (Supplemental Table 3,5; Figure 3).

Age Stratified:

During the entire study period, significant variations in crude mortality rates (CMRs) were noted for each age group. Between 1999 and 2020, CMRs exhibited an overall decreasing pattern among adults aged 65–74 years, 75–84 years, and 85 years and older. This suggests that the burden of stroke and DM-related mortality has decreased over time for all older age groups. The AAMR for adults aged 65–74 years decreased from [14.75 (95% CI: 14.19 to 15.30)] in 1999 to [8.84 (95% CI: 8.51 to 9.16)] in 2020. The CMR among adults aged 75–84 years declined from [41.24 (95% CI: 40.10 to 42.37)] in 1999 to [23.26 (95% CI: 22.52 to 23.99)] in 2020. Similarly, AAMR decreased among adults aged 85 years and older from [83.08 (95% CI: 80.30 to 85.85)] in 1999 to [52.19 (95% CI: 50.45 to 53.92)] in 2020.
From 1999 to 2020, trend analysis displayed varying temporal patterns across age categories. Among adults aged 65–74 years [AAPC: -2.53 (95% CI: -3.09 to -1.96). P-value: <0.000001], the CMR showed a significant initial decline from 1999 to 2015 [APC: -4.24 (95% CI: -4.64 to -3.84). P-value: <0.000001], followed by a significant increase from 2015 to 2020 [APC: 3.14 (95% CI: 0.84 to 5.50). P-value: 0.01].
Among adults aged 75–84 years [AAPC: -2.95 (95% CI: -3.55 to -2.34). P-value: <0.000001], the CMR exhibited a significant decrease from 1999 to 2014 [APC: -4.21 (95% CI: -4.66 to -3.76). P-value: <0.000001], followed by an increasing trend from 2014 to 2020 [APC: 0.27 (95% CI: -1.75 to 2.33). P-value: 0.78].
In contrast, adults aged 85 years and older [AAPC: -2.53 (95% CI: -3.07 to -1.98). P-value: <0.000001] showed a significant decline in CMR from 1999 to 2015 [APC: -3.87 (95% CI: -4.23 to -3.50). P-value: <0.000001], followed by an increasing trend from 2015 to 2020 [APC: 1.89 (95% CI: -0.34 to 4.17). P-value: 0.09] (Supplemental Table 3,6; Figure 4).

Regional variation:

Stratified by Urbanization:

The AAMR decreased in both urban and rural areas from 1999 to 2020. In urban areas, the AAMR decreased from [AAMR: 31.48 (95% CI: 30.82 to 32.14)] in 1999 to [AAMR: 18.27 (95% CI: 17.86 to 18.67)] in 2020, while in non-urban areas it decreased from [AAMR: 36.93

(95% CI: 35.47 to 38.39)] in 1999 to [AAMR: 24.24 (95% CI: 23.21 to 25.27)] in 2020.
For urban areas [AAPC: -2.82 (95% CI: -3.32 to -2.31). P-value: <0.000001], the AAMR trend decreased from 1999 to 2014 [APC: -4.31 (95% CI: -4.70 to -3.92). P-value: <0.000001], followed by an increasing trend from 2014 to 2020 [APC: 1.02 (95% CI: -0.67 to 2.74). P-value: 0.22].
For non-urban areas [AAPC: -2.06 (95% CI: -3.06 to -1.04). P-value: 0.00008], the AAMR trend decreased from 1999 to 2018 [APC: -3.20 (95% CI: -3.52 to -2.89). P-value: <0.000001], followed by an increasing trend from 2018 to 2020 [APC: 9.53 (95% CI: -2.12 to 22.57). P-value: 0.11] (Supplemental Table 3,8; Figure 6).

Stratified by Census:

The AAMR decreased across all U.S. census regions from 1999 to 2020. In the Northeast, the AAMR decreased from [AAMR: 12.67 (95% CI: 12.02 to 13.33)] in 1999 to [AAMR: 6.19 (95% CI: 5.79 to 6.59)] in 2020; in the Midwest, from [AAMR: 17.33 (95% CI: 16.61 to 18.05)] to [AAMR: 9.45 (95% CI: 8.99 to 9.91)]; in the South, from [AAMR: 15.54 (95% CI: 14.98 to 16.09)] to [AAMR: 10.76 (95% CI: 10.40 to 11.12)]; and in the West, from [AAMR: 18.85 (95% CI: 18.03 to 19.67)] to [AAMR: 11.03 (95% CI: 10.55 to 11.51)].
The Northeast region showed a significant decline from 1999 to 2009 [APC: -5.88 (95% CI: -6.56 to -5.20). P-value: < 0.000001] followed by a statistically significant decline until 2020 [APC: -1.82 (95% CI: -2.53 to -1.10). P-value: 0.000054] with an overall AAPC [-3.78 (95% CI: -4.23 to -3.32). P-value: < 0.000001]. The Midwest region exhibited an initial significant decrease between 1999 and 2016 [APC: -4.29 (95% CI: -4.68 to -3.89). P-value: < 0.000001], followed by an increase from 2016 to 2020 [APC: 3.18 (95% CI: -0.73 to 7.25). P-value: 0.11], with an overall AAPC [-2.91 (95% CI: -3.63 to -2.17). P-value: < 0.000001]. In the South region, an initial significant decrease was observed from 1999 to 2014 [APC: -3.58 (95% CI: -4.04 to -3.12). P-value: < 0.000001] and an increase from 2014 to 2020 [APC: 1.65 (95% CI: -0.23 to 3.57). P-value: 0.08] with an overall AAPC [-2.11 (95% CI: -2.69 to -1.54). P-value: < 0.000001]. The AAMR for the West region experienced a decrease from 1999 to 2003 [APC: -1.77 (95% CI: -5.94 to 2.58). P-value: 0.39], subsequently followed by a significant decline from 2003 to 2009 [APC: -7.23 (95% CI: -10.24 to -4.11). P-value: 0.00024]. This was followed by a decrease from 2009 to 2020 [APC: -0.80 (95% CI: -1.79 to 0.21). P-value: 0.11] with an overall AAPC [-2.86 (95% CI: -4.06 to -1.65). P-value: <0.001] (Supplemental Table 3,7; Figure 5).

Stratified by State:

Variations in AAMRs were observed among different states, with AAMRs ranging from as low as [AAMR: 9.80 (95% CI: 9.04 to 10.56)] in Nevada to as high as [AAMR: 33.31 (95% CI: 32.29 to 34.34)] in Oregon. States falling within the top 90th percentile included Oregon [AAMR: 33.31 (95% CI: 32.29 to 34.34)], Mississippi [AAMR: 32.19 (95% CI: 30.97 to 33.41)], Oklahoma [AAMR: 31.89 (95% CI: 30.84 to 32.94)], California [AAMR: 31.01 (95% CI: 30.66 to 31.36)], Vermont [AAMR: 29.42 (95% CI: 27.07 to 31.77)], and Texas [AAMR: 28.87 (95% CI: 28.42 to 29.31)], which had more than twice as high AAMRs compared to states in the lower 10th percentile, which included Massachusetts [AAMR: 14.21 (95% CI: 13.71 to 14.71)], New Jersey [AAMR: 14.12 (95% CI: 13.68 to 14.57)], Louisiana [AAMR: 13.94 (95% CI: 13.28 to 14.59)],

Arizona [AAMR: 11.30 (95% CI: 10.83 to 11.77)], Florida [AAMR: 10.47 (95% CI: 10.24 to 10.70)], and Nevada [AAMR: 9.80 (95% CI: 9.04 to 10.56)] (Supplemental Table 9; Figure 7)

4. DISCUSSIONS:

This study offers crucial insights concerning stroke and diabetes mellitus-related mortality among United States U.S. adults aged ≥65 from 1999 to 2020 using the CDC WONDER database. A total of 201,269 deaths were recorded, with males consistently showing higher mortality than females. By race and ethnicity, NH Black or African American adults had the highest mortality, followed by Hispanic or Latino, NH Asian or Pacific Islander, NH American Indian or Alaska Native, and NH White adults, although all groups experienced overall declines. Geographic differences were also notable: rural areas had consistently higher mortality than urban areas. Among census regions, the West had the highest AAMRs, followed by the South, Midwest, and Northeast. Age-specific analyses indicated reductions in mortality among older adults, though some age categories showed recent increases. Most deaths occurred in medical facilities, followed by nursing homes or long-term care facilities, the decedent's home, and hospice settings, highlighting persistent structural and regional disparities in outcomes. Finally, state-level variation was pronounced, with the highest-mortality states having more than double the AAMRs of the lowest-mortality states. (Figure 8).

Overall, age-adjusted mortality rates for diabetes mellitus-related stroke initially declined from 1999 to 2014 but showed a slight increase afterwards. This pattern reflects a combination of biological, clinical, and reporting factors. The decline likely reflects advancements in early detection, better cardiovascular risk control, and guideline-directed diabetes management, as emphasized in the ADA 2010 Standards of Care (17). During the late 1990s and early 2000s, increased awareness of diabetes and stroke risk factors, including hypertension and dyslipidemia, was associated with more aggressive management and improved control of major cardiovascular risk factors [18]. At the same time, improvements in statin therapy in individuals with diabetes have been demonstrated to significantly reduce the risk of ischemic stroke and other cardiovascular events compared with non-users (19). Also, improved blood pressure control in people with diabetes significantly reduces stroke risk and major cardiovascular outcomes (20). Additionally, certain glucose-lowering agents, such as SGLT2 inhibitors, have been shown to lower composite cardiovascular outcomes, with neutral to mild effects on stroke risk (21). For instance, as part of the composite endpoint, the EMPA-REG OUTCOME study showed that the SGLT2 inhibitor empagliflozin significantly decreased severe adverse cardiovascular events, such as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke, in patients with diabetes (22).

Rising diabetes prevalence, brought on by obesity and sedentary lifestyles, increased the population at risk for stroke, which may have contributed to slowing the decline after 2014 (23). Systemic barriers, such as limited access to care, poor adherence to therapies, and delayed adoption of updated guidelines, further limited reductions in mortality (24). Similarly, the LEADER trial found that liraglutide improved cardiovascular outcomes in high-risk diabetic patients, indirectly impacting stroke risk (25). Despite updated ADA Standards of Care in 2018

and 2020 emphasizing individualized glycemic targets, blood pressure control, and lipid management, real-world implementation lagged, which may explain the slight increase in mortality after 2014 (26, 27, 28). This trend was probably exacerbated by racial/ethnic discrepancies in healthcare access, urban-rural differences, and socioeconomic disparities (29). Taken together, the observed trends reflect a period of substantial improvements in diabetes and cardiovascular management leading to initial declines, followed by a plateau and slight increase due to rising diabetes prevalence, delayed guideline implementation, and persistent disparities in care (17–29).

Sex-stratified analysis showed persistently elevated fatality rates in males contrast to females, despite significant declines in both sexes from 1999 to the mid-2010s. Prior studies, including Kautzky-Willer et al., also demonstrated a higher incidence of cardiovascular and cerebrovascular diseases, such as stroke, in men with DM compared to women, largely explained by sex disparities in socio- behavioral, metabolic and environmental factors (30, 31, 33). Additionally, stroke and DM have been identified to be influenced by sex disparities in healthcare access and disease control across different populations (32). Behavioral factors, such as higher smoking prevalence and poorer long-term risk-factor control in men, further increases stroke risk and mortality in diabetic populations (30, 31, 33). On the other hand, women may benefit from premenopausal estrogen-mediated vascular protection. This enhances endothelial function, down regulates inflammation, and delays atherosclerotic plaque formation, contributing to lower stroke mortality (30, 34). Nevertheless, several studies from the United States indicated that women with DM were less prone to attain cardiovascular risk factor targets despite higher healthcare utilization (35). The plateau and subsequent rise in AAMR post 2014–2015 in both sexes likely indicate worsening glycemic control, rising obesity prevalence, and delayed implementation of secondary prevention strategies, particularly among older women who lose hormonal protection post-menopause (30, 36).

NH Blacks or African Americans had the highest AAMR while NH Whites had the lowest AAMR. This finding is consistent with prior literature showing the higher mortality rates from cardiovascular diseases and diabetes-related complications faced by African Americans compared to their White counterparts (37, 38). One of the major causes of these disparities is the unequal distribution of opportunities and resources that promote health. Marginalized racial and ethnic groups are disproportionately affected by factors that exacerbate their health outcomes such as socioeconomic struggles, environmental injustices, and limited access to high-quality healthcare (39, 40). Key social determinants such as unstable employment, barriers to health care, and limited educational opportunities also generate chronic stress, which has been associated with higher morbidity and mortality (40, 41). Additionally, NH Black Americans carry a higher burden of diabetes and exhibit elevated risk of cardiovascular diseases, such as stroke (42). Moreover, NH Blacks receive their diagnoses earlier in life, which increases their lifetime risk of hyperglycemia and cardiovascular problems, such as stroke (43).

Our study also demonstrates that mortality rates fell overall in both urban and rural areas, with faster declines initially, followed by a recent non-significant upward trend in both urban (post-2014) and non-urban (post-2018) areas. The mortality rates were higher in rural areas than urban areas for the entire period. The sharper decline in urban areas may partly reflect better access to

healthcare specialists, more developed health infrastructure, and broader preventive efforts (44). On the other hand, there are typically fewer healthcare facilities in rural areas, which limits access to early detection and timely intervention (44). The management of chronic diseases is further hampered in these areas by socioeconomic disadvantages, such as lower income, limited education, and transportation barriers (45). According to Basu et al., density of primary care physicians decreased overall between 2005 and 2015, with disproportionately larger decreases observed in rural areas compared with urban areas (46). Furthermore, it can be more challenging to combat these diseases in rural areas due to several lifestyle-related risk factors like higher prevalence of smoking, poor dietary habits, and lack of physical activity to address these risk factors (47).

Furthermore, we also observed significant geographic variations in stroke-related mortality in patients with DM across U.S. census regions from 1999 to 2020. Although all regions experienced a significant overall decline in age-adjusted mortality rates, the Western region demonstrated the highest mortality burden in recent years, while the Northeast consistently exhibited the lowest rates and the greatest average annual percentage decline. These disparities may be attributed to the uneven distribution of risk factors across regions.

The more pronounced improvements observed in the Northeast may be the result of adequate medical facilities and quicker emergency response, as prior studies state that the majority of the states in this region had less than 60 minutes' time to reach level 1 or 2 trauma centers contributing to better outcomes (48). In contrast, the relatively higher burden observed in the West and the slower pace of decline in the South may be due to regional differences in population demographics, healthcare delivery, and access to timely care (49). Notably, several regions, such as the Midwest and the South, showed a slowing or non-significant reversal of declining trends in recent years, indicating emerging challenges such as socioeconomic factors, including lower income and education levels, in sustaining earlier public health gains (49).

Age-stratified analysis revealed an overall decline in stroke and diabetes mellitus–related mortality across all older age groups from 1999 to the mid-2010s, followed by stabilization or modest increases by 2020. Adults aged 85 years and older consistently experienced the highest mortality burden despite a notable long-term reduction, likely due to the cumulative effects of multimorbidity, frailty, and heightened susceptibility to acute cerebrovascular events in advanced age. This sustained decline may be attributed to improvements in cardiovascular risk-factor control, particularly enhanced management of blood pressure and lipid levels, which have been shown to significantly reduce stroke mortality among older adults with diabetes (51). The use of antihypertensive medications and statin therapy has also been associated with reduced stroke-related mortality in elderly diabetic populations (50).

Among adults aged 75–84 years, mortality declined steadily for most of the study period before reaching a plateau, a pattern that may reflect advances in chronic disease management, earlier identification of diabetes and vascular risk factors, and increased adherence to thrombolytic therapy (53). Broader population-level improvements, including reduced smoking prevalence and improved control of blood pressure and cholesterol, have also contributed to declining cardiovascular and stroke mortality in high-risk older adults (51,52). However, the later

stabilization may be influenced by increasing obesity prevalence, longer duration of diabetes, and improved survival among individuals with multiple comorbid conditions (54, 55).

In adults aged 65–74 years, mortality rates remained the lowest across age groups and demonstrated a pronounced decline followed by a recent slight increase. The earlier reduction likely reflects the benefits of improved cardiometabolic risk management, particularly intensive control of blood pressure and lipid levels, which are strongly linked to lower stroke and cardiovascular mortality in younger older adults (51, 52). The more recent upward trend may be associated with rising metabolic risk factors, including increasing prevalence of obesity and diabetes, along with evolving population health profiles and delayed risk-factor control in more recent cohorts (54, 55).

Place of death patterns provide further insight into healthcare delivery. Over two-fifths of the deaths (42.8%) occurred in inpatient medical facilities. This predominance may be due to the acute and severe complications associated with stroke and diabetes mellitus, which often require intensive medical management. Notably, nursing homes and long-term care facilities accounted for 34.4% (56). This substantial proportion likely reflects the chronic nature of these conditions , advanced age, frailty, multi-morbidity, and functional dependence of residents among elderly residents(57, 58). Furthermore, 14.9% of deaths occurred at the decedent's home, indicating patient preference, sudden clinical deterioration, or barriers to timely hospital access (59). Also, hospice facilities accounted for 4.61% of deaths, reflecting under utilization of palliative services, limited awareness, or late-stage referral patterns in this population (60). The smallest proportion of deaths occurred in other settings (3.2%), suggesting that most deaths took place within structured healthcare environments due to monitoring needs and disease complexity (59).

State-level analysis demonstrated pronounced geographic variation in stroke and diabetes mellitus–related mortality across the United States, highlighting significant regional differences in population health outcomes. Higher mortality burdens observed in Oregon, Mississippi, Oklahoma, California, Vermont, and Texas likely reflect a greater prevalence of cardiometabolic risk factors—particularly obesity, diabetes, and hypertension—which are well-established contributors to stroke incidence and mortality and remain unevenly distributed across U.S. populations (63). These disparities may also be influenced by differences in healthcare access and quality, including the availability of stroke centers, utilization of preventive services, and timeliness of acute treatment, all of which play a critical role in survival following cerebrovascular events (61). Furthermore, socioeconomic factors such as poverty and rural residence may exacerbate these patterns by limiting access to early diagnosis, effective chronic disease management, and specialized care (62, 63). In contrast, comparatively lower mortality observed in Nevada, Florida, Arizona, New Jersey, and Massachusetts may reflect more favorable cardiovascular risk-factor control, broader access to preventive healthcare, and more developed healthcare infrastructure that supports early detection, timely treatment, and improved survival outcomes (64).

Despite the decreasing overall stroke mortality trend in diabetic patients, there is a slight recent spike in the AAMR, presenting a threat of performing a pivotal role in amplifying the burden of death statistics. This further exposes the states already living below the poverty line to

disproportionate vulnerability. Further research is needed to clarify the recent plateau and rise in stroke mortality among diabetic patients, particularly the contributions of rising obesity, longer diabetes duration, multimorbidity, and healthcare access disparities. Current data are limited on how socioeconomic and regional factors interact with biological risks. Longitudinal and multilevel studies are required to identify high-risk groups and guide targeted interventions. Expanding access to certified stroke centers, tele-stroke services, and aggressive diabetes and cardiovascular risk management can reduce mortality, especially in underserved and high-risk regions. Strong evidence shows that inadequate glycemic control, delayed recognition of stroke symptoms, and limited access to timely acute care are major contributors to mortality in diabetic stroke patients, highlighting modifiable targets for intervention. Healthcare providers, policymakers, and public health stakeholders must collaborate to implement prevention, improve access to care, and ensure equitable management of diabetes and stroke to reduce mortality.

5. LIMITATIONS AND STRENGTH:

This research has several shortcomings. Firstly, the dependence on ICD-10 codes and death certificates may result in the misclassification or omission of stroke as a cause of death, potentially impacting the precision of mortality trends. Secondly, our examination is restricted to aggregate data, which limits our ability to evaluate individual-level risk factors, such as comorbidities, socioeconomic status, and access to healthcare. Thirdly, fluctuations in diagnostic criteria and reporting practices over time could have affected the trends observed. Fourthly, we did not investigate stroke incidence data, limiting our capability to determine whether the mortality trends indicate changes in stroke occurrence versus case fatality. Lastly, we did not directly assess regional variations in healthcare quality and access, which could influence stroke outcomes. Additionally, the authors did not receive any financial support for the research, authorship, and publication of this article.

6. CONCLUSION:

Stroke mortality rates declined from 1968 through the 1990s but have increased again over the past decade. Despite these temporal changes, disparities in stroke outcomes have remained largely unchanged across demographic groups. Males, Black individuals, and older adults consistently exhibited the highest age-adjusted mortality rates, while geographically, the Southern United States continued to report persistently elevated mortality. These findings underscore the

need for targeted public health strategies to reduce stroke-related disparities and address the deeply rooted inequities that continue to shape stroke outcomes

FIGURES:

Figure 1: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by place of death

Figure 2: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Year and Gender

Figure 3: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Race and Ethnicity

Figure 4: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Age group

Figure 5: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Census region

Figure 6: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Urbanization

Figure 7: Stroke and Diabetes Mellitus- related Age Adjusted Mortality Rate in U.S. population, 1999-2020, stratified by state

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FIGURES:

Figure 1: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by place of death

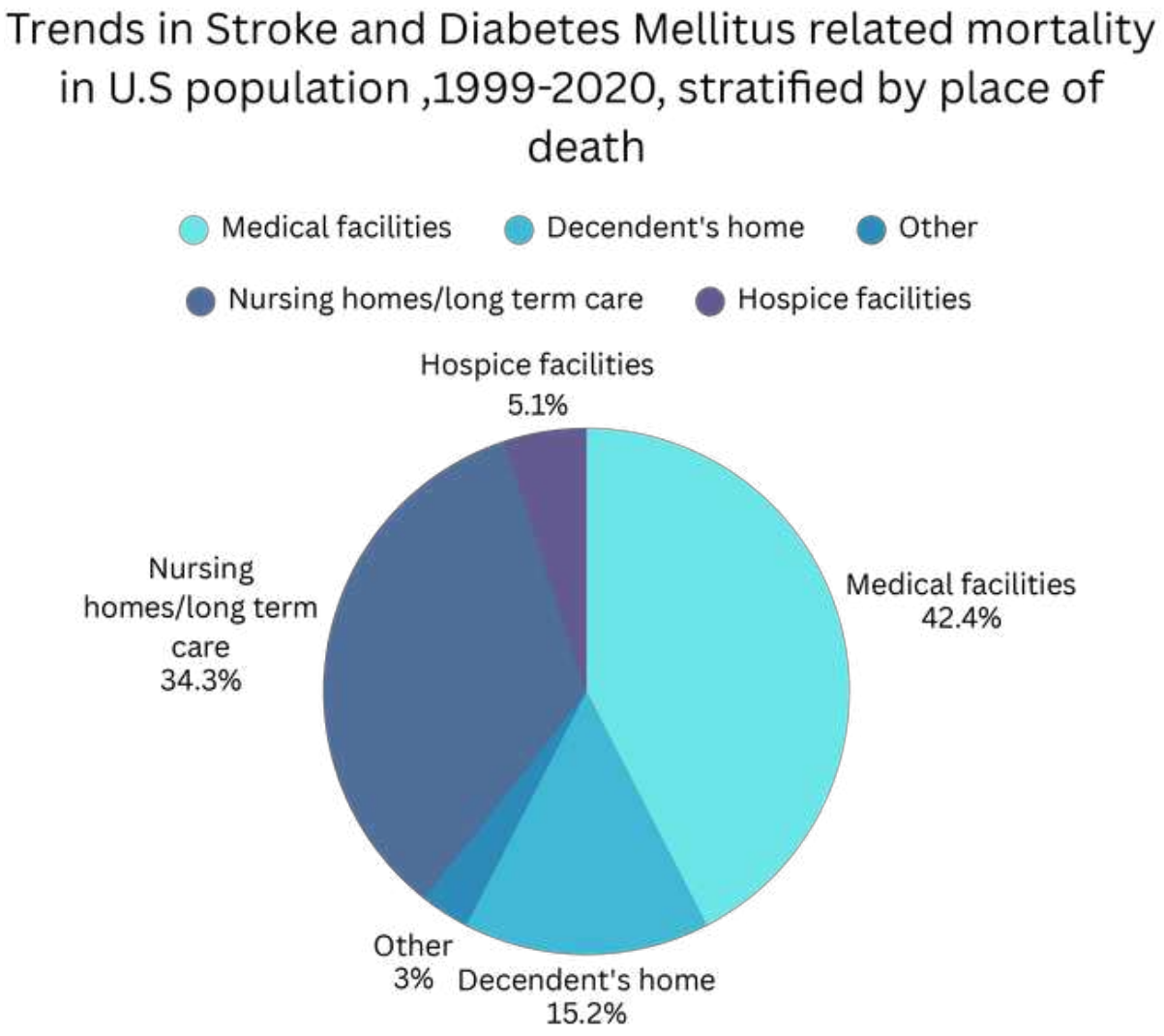


Figure 2: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Year and Gender

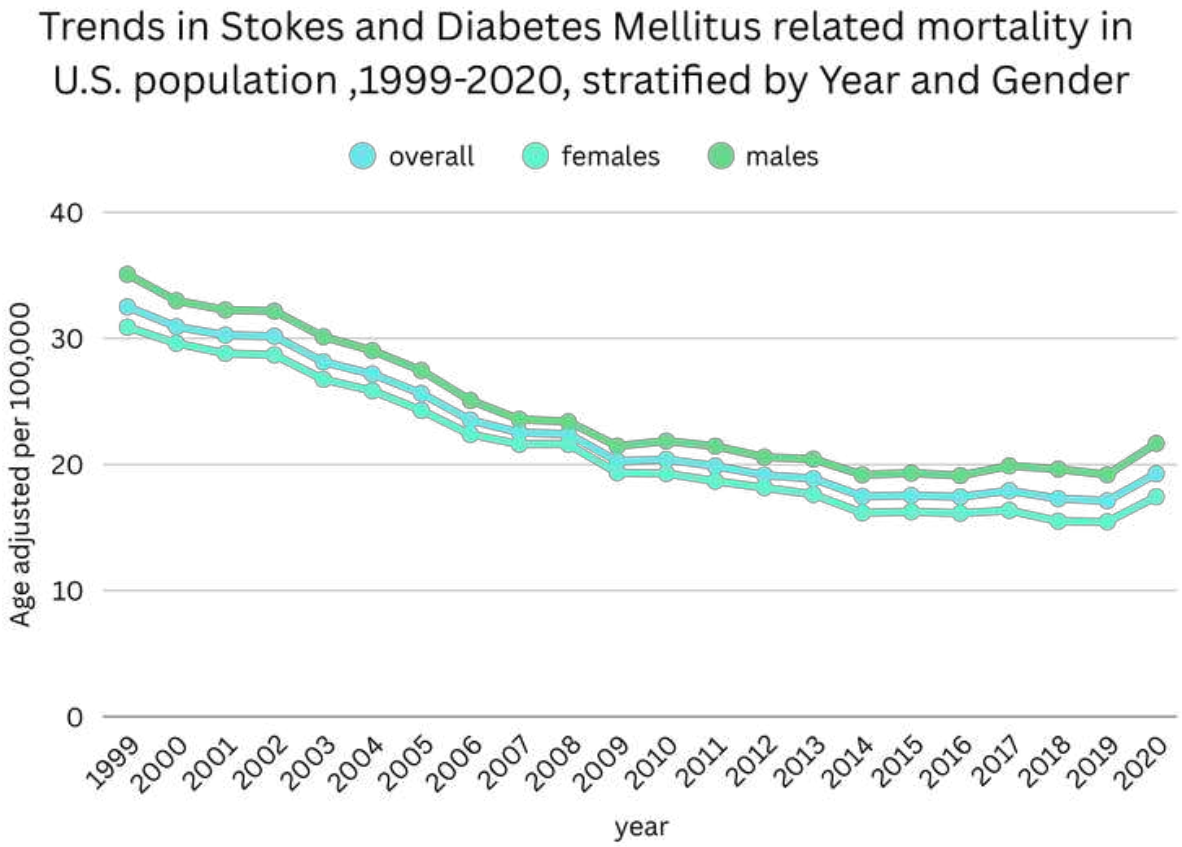


Figure 3: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Race and Ethnicity

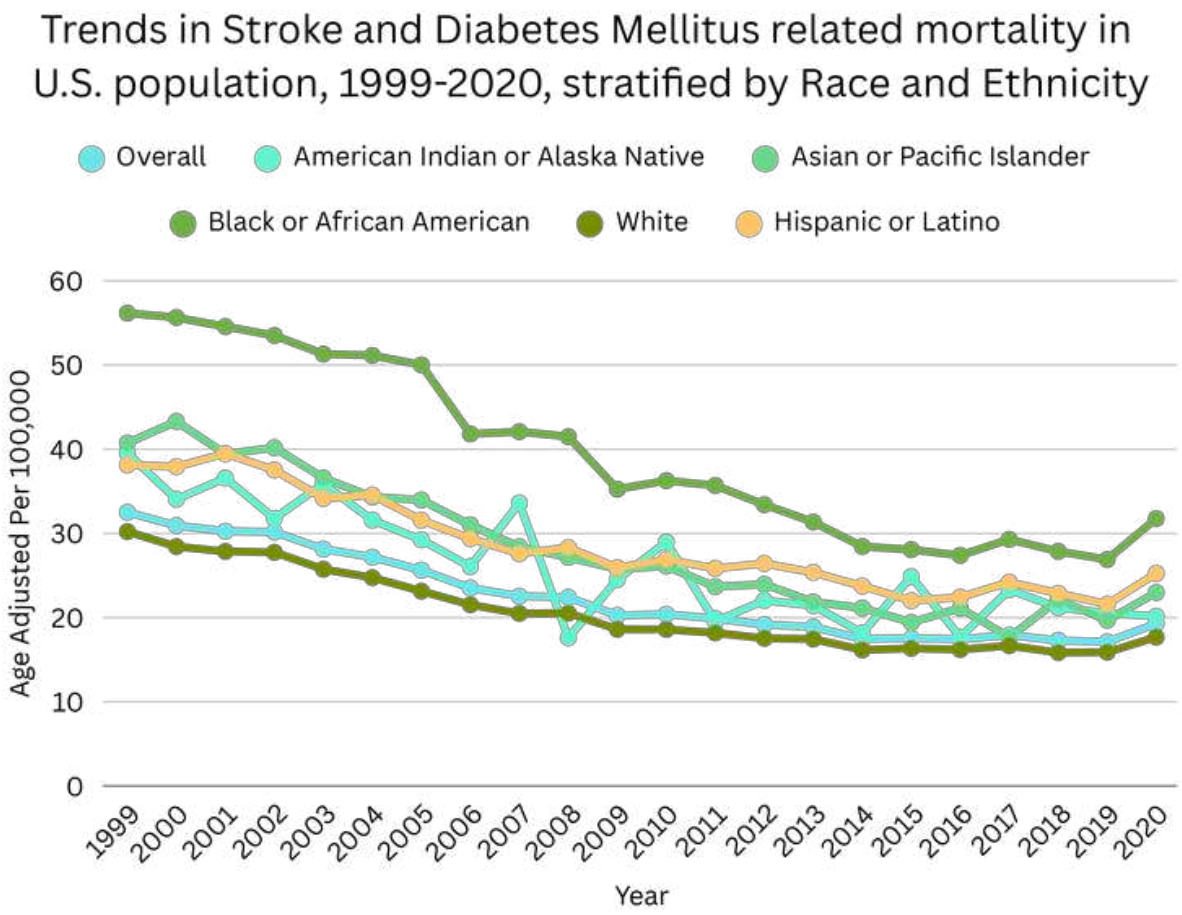


Figure 4: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Age group

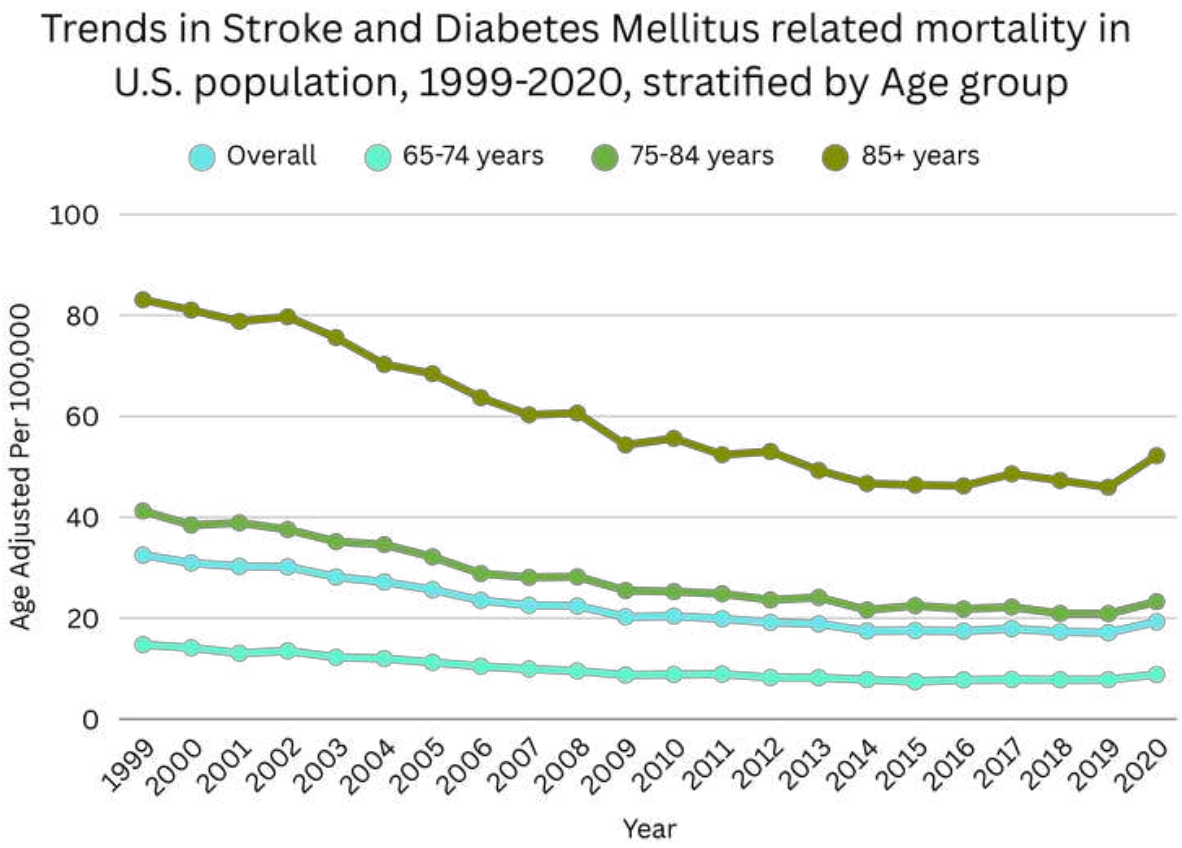


Figure 5: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Census region

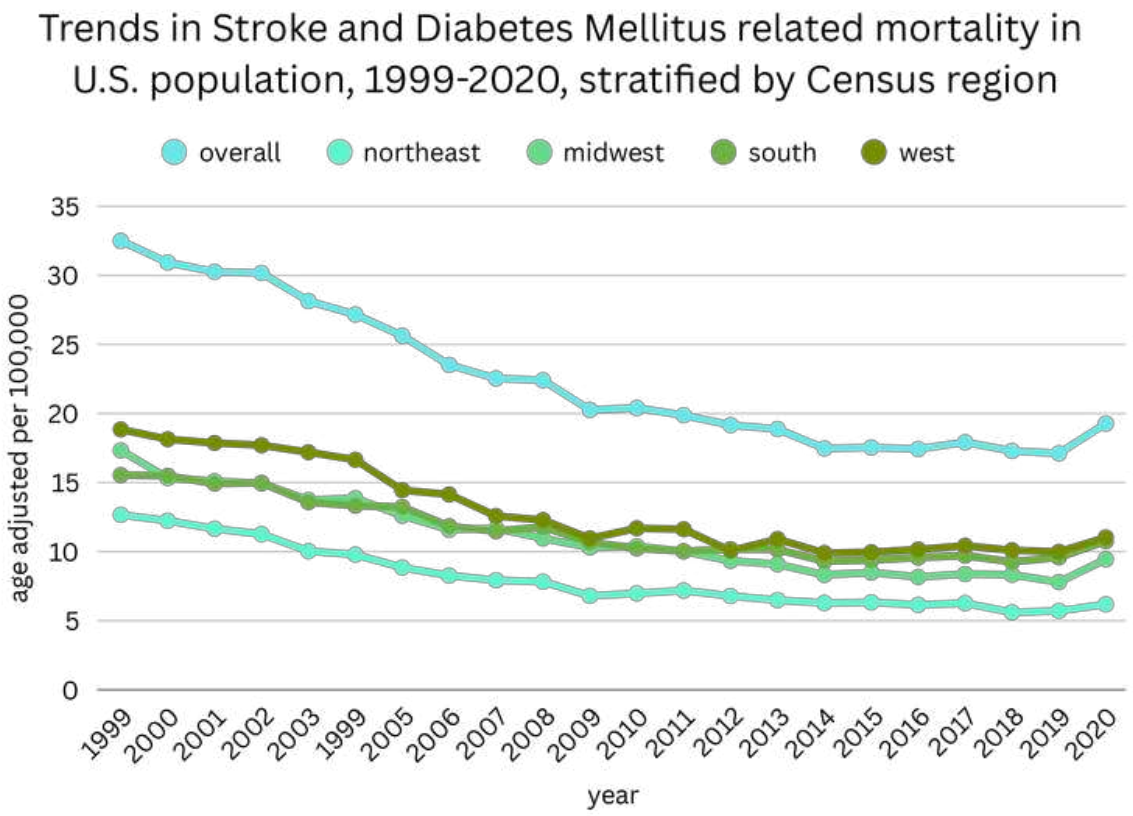


Figure 6: Trends in Stroke and Diabetes Mellitus related mortality in U.S. population, 1999-2020, stratified by Urbanization

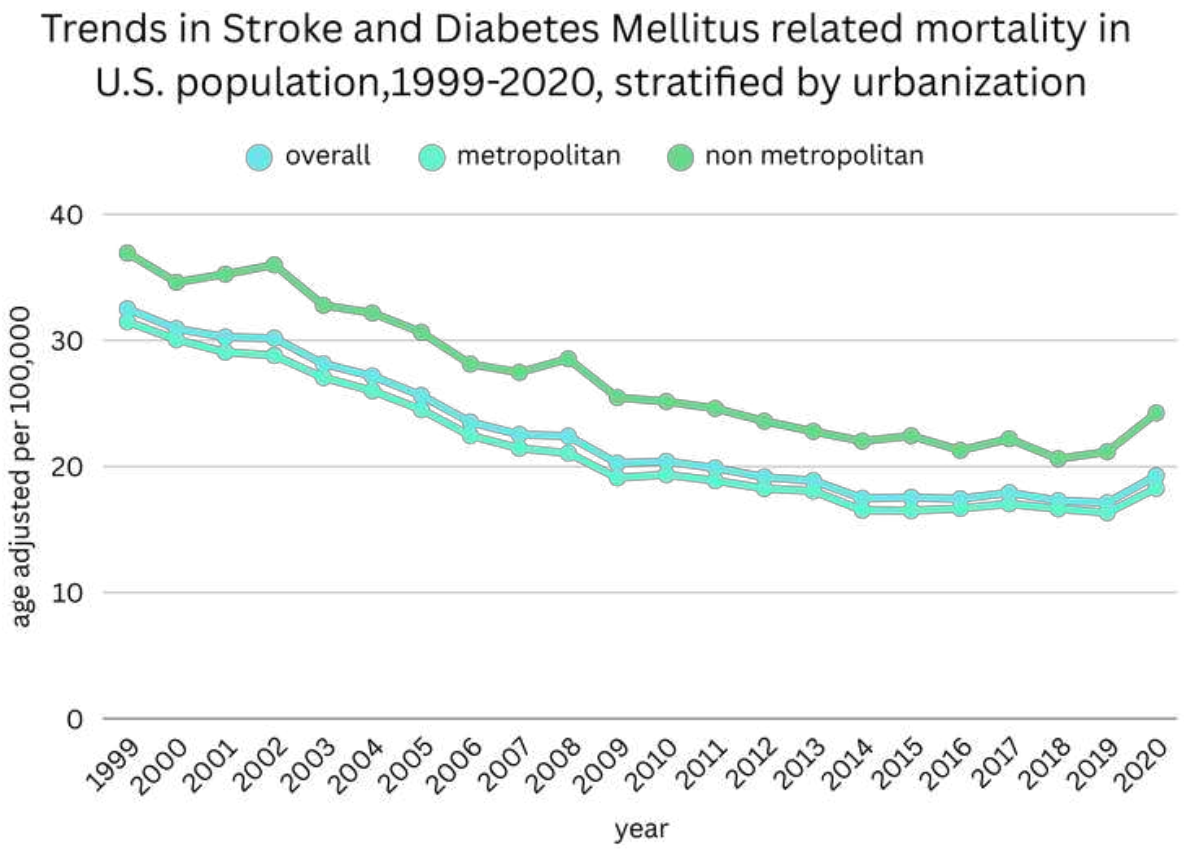


Figure 7: Stroke and Diabetes Mellitus- related Age Adjusted Mortality Rate in U.S. population, 1999-2020

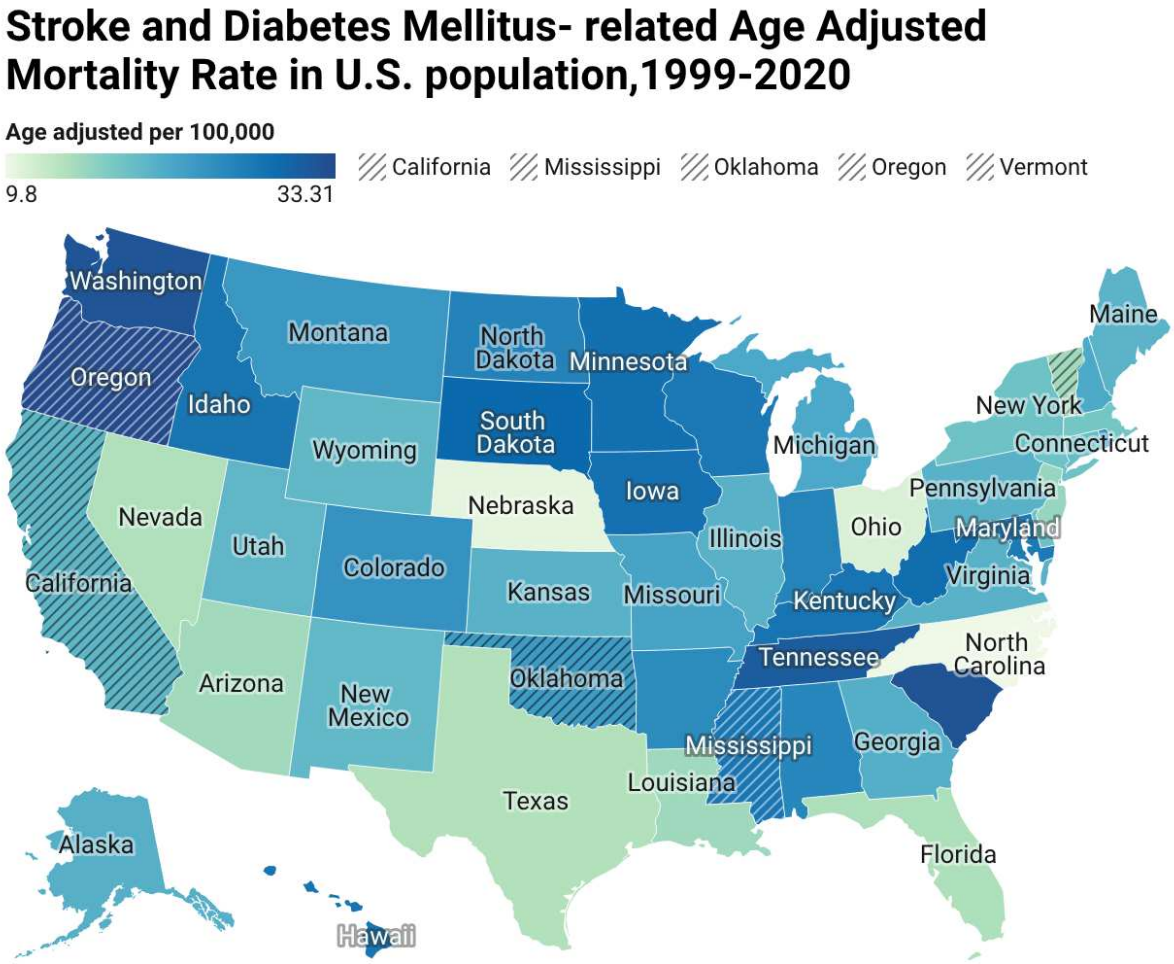


Figure 8: Central Illustration

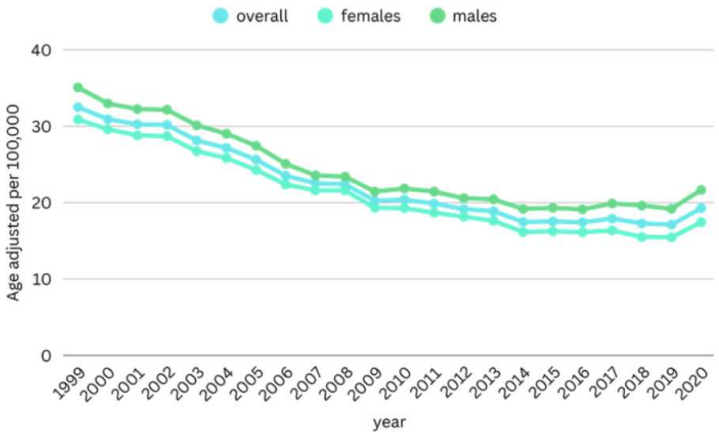
CENTRAL ILLUSTRATION Trends in stroke and DM-related mortality in U.S. Adults, 1999-2020

201,269 Stroke and DM -related deaths among adults aged aged ≥65 years between 1999 and 2020

MEN
35.08 in 1999
21.67 in 2020

WOMEN
30.89 in 1999
17.44 in 2020

Annual Trends



The overall **AAMR** for **Stroke and DM** among adults aged ≥65 years decreased from **32.5** in **1999** to **20.4** in **2010**, followed by a sustained trend of **17.12** till **2019** and then by a slight increase to **19.27** in **2020**

Racial disparities

37.74
Black or African American

>

27.07
Hispanic

>

25.44
Asian or Pacific Islander

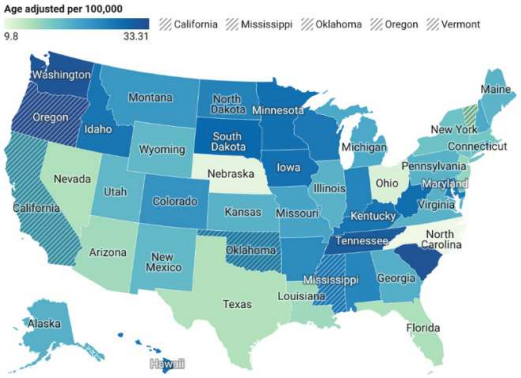
>

24.52
American Indian or Alaska Native

>

20.29
White

Geographic disparities



West **(12.59)**
South **(11.33)**
MidWest **(10.98)**
NorthEast **(7.92)**

Mon-metropolitan **(26.82)**
Metropolitan **(20.91)**

The 90th percentile in Stroke and DM-related AAMR was achieved by the Oregon, Mississippi, Oklahoma, California, Vermont, Texas.

AAMR = Age Adjusted Mortality Rate; DM = Diabetes Mellitus;

SUPPLEMENTAL TABLES:

Supplemental Table 1: Demographics Table for Stroke and Diabetes mellitus (DM)-related mortality in U.S. Population, 1999-2020

NUMBER OF DEATHS DUE TO STROKE AND DM												
Year	**Overall**	**Females**	**Males**	**65-74 years**	**75-84 years**	**85+ years**	**Black or African American**	**American Indian or Alaska Native**	**Asian or Pacific Islander**	**White**	**Hispanic or Latino**	**Population**
1999	11208	6663	4545	2716	5041	3451	1538	48	276	9346	561	34797841
2000	10785	6466	4319	2598	4751	3436	1534	48	315	8888	585	34991753
2001	10692	6367	4325	2397	4896	3399	1533	55	301	8803	640	35290291
2002	10761	6380	4381	2484	4795	3482	1515	49	339	8858	645	35522207
2003	10176	6017	4159	2265	4535	3376	1465	58	333	8320	620	35863529
2004	9925	5834	4091	2239	4491	3195	1481	54	327	8063	652	36203319
2005	9535	5585	3950	2121	4202	3212	1487	52	348	7648	632	36649798
2006	8883	5200	3683	2009	3776	3098	1271	47	337	7228	619	37164107
2007	8667	5112	3555	1955	3674	3038	1307	60	325	6975	612	37825711
2008	8795	5187	3608	1957	3688	3150	1317	34	328	7116	653	38777621
2009	8084	4698	3386	1850	3318	2916	1154	50	329	6551	631	39623175
2010	8273	4757	3516	1917	3301	3055	1215	63	352	6643	677	40267984
2011	8279	4693	3586	2002	3272	3005	1240	47	347	6645	707	41394141
2012	8229	4674	3555	1974	3134	3121	1202	56	373	6598	760	43145356
2013	8283	4612	3671	2067	3240	2976	1181	61	370	6671	779	44704074
2014	7896	4334	3562	2061	2959	2876	1119	52	380	6345	776	46243211
2015	8090	4414	3676	2046	3128	2916	1133	76	378	6503	757	47760852
2016	8272	4516	3756	2218	3106	2948	1152	58	440	6622	827	49244195
2017	8737	4706	4031	2329	3265	3143	1312	80	391	6954	935	50858679
2018	8693	4563	4130	2379	3220	3094	1281	79	518	6815	921	52431193
2019	8829	4641	4188	2459	3336	3034	1290	80	487	6972	922	54058263
2020	10177	5345	4832	2876	3826	3475	1575	84	603	7915	1125	55659365
TOTALS	201269	114764	86505	48919	82954	69396	29302	1291	8197	162479	16036	928476665

Supplemental Table 2: Stroke and Diabetes mellitus (DM)-related mortality in U.S. Population, 1999-2020, stratified by Place of Death (POD)

Place Of Death	No. Of Deaths	Percentage of Deaths
Medical Facilities	87029	43.25%
Decedent's home	29702	14.76%
Hospice Facility	9286	4.61%
Nursing home/long term care	68452	34.01%
Other	6267	3.11%
Place of death unknown	533	0.26%
Total	201269	1 00%

Supplemental Table 3: Annual Percentage Change (APC) for Stroke and Diabetes mellitus (DM)-related mortality in U.S. Population, 1999-2020

Annual and Average Annual Percentage Change (AAPC) + 95% Confidence Intervals (CI)						
Variable	**Lower Endpoint**	**Upper Endpoint**	**APC**	**Lower CI**	**Upper CI**	**P Value**
Overall and Gender						
Female	1999	2015	-4.2016*	-4.5433	-3.8587	< 0.000001
Female	2015	2020	0.9623	-1.2184	3.1912	0.367721
Male	1999	2014	-4.0780*	-4.5138	-3.6402	< 0.000001
Male	2014	2020	1.675	-0.1267	3.5092	0.066577
Overall	1999	2014	-4.1810*	-4.5713	-3.7891	< 0.000001
Overall	2014	2020	0.8427	-0.833	2.5467	0.305476
Female		Full Range	-2.9966*	-3.524	-2.4663	< 0.000001
Male		Full Range	-2.4683*	-3.0155	-1.9181	< 0.000001
Overall		Full Range	-2.7717*	-3.2767	-2.2641	< 0.000001
Age-group						
65-74 years	1999	2015	-4.2364*	-4.6354	-3.8358	< 0.000001
65-74 years	2015	2020	3.1437*	0.8384	5.5017	0.010196
75-84 years	1999	2014	-4.2082*	-4.6564	-3.7578	< 0.000001
75-84 years	2014	2020	0.2716	-1.7453	2.3299	0.78163
85+ years	1999	2015	-3.8675*	-4.23	-3.5035	< 0.000001
85+ years	2015	2020	1.8904	-0.339	4.1697	0.091956
65-74 years		Full Range	-2.5286*	-3.0931	-1.9609	< 0.000001
75-84 years		Full Range	-2.9491*	-3.5515	-2.3429	< 0.000001
85+ years		Full Range	-2.5268*	-3.0688	-1.9817	< 0.000001
Census						
Northeast	1999	2009	-5.8826*	-6.5637	-5.1965	< 0.000001
Northeast	2009	2020	-1.8198*	-2.5298	-1.1046	0.000054
Midwest	1999	2016	-4.2859*	-4.6792	-3.8909	< 0.000001
Midwest	2016	2020	3.1828	-0.7297	7.2495	0.10544

South	1999	2014	-3.5804*	-4.041	-3.1176	< 0.000001
South	2014	2020	1.6475	-0.2345	3.565	0.082565
West	1999	2003	-1.7692	-5.9355	2.5817	0.391952
West	2003	2009	-7.2280*	-10.2403	-4.1147	0.000246
West	2009	2020	-0.7977	-1.794	0.2086	0.110861
Northeast		Full Range	-3.7759*	-4.2342	-3.3153	< 0.000001
Midwest		Full Range	-2.9062*	-3.6325	-2.1745	< 0.000001
South		Full Range	-2.1148*	-2.6897	-1.5365	< 0.000001
West		Full Range	-2.8614*	-4.0614	-1.6463	0.000005
Urbanization						
Urban	1999	2014	-4.3093*	-4.6984	-3.9185	< 0.000001
Urban	2014	2020	1.0201	-0.6671	2.736	0.220704
Non-Urban	1999	2018	-3.2023*	-3.5182	-2.8853	< 0.000001
Non-Urban	2018	2020	9.5281	-2.1221	22.5651	0.105943
Urban		Full Range	-2.8159*	-3.3224	-2.3069	< 0.000001
Non-Urban		Full Range	-2.0565*	-3.0623	-1.0402	0.00008
Race						
American Indian or Alaska Native	1999	2020	-3.0281*	-3.9538	-2.0934	0.000002
Asian or Pacific Islander	1999	2017	-4.6194*	-5.1095	-4.1268	< 0.000001
Asian or Pacific Islander	2017	2020	7.0669*	0.5689	13.9847	0.034321
Black or African American	1999	2016	-4.5432*	-5.0776	-4.0058	< 0.000001
Black or African American	2016	2020	2.3126	-2.5974	7.4701	0.340445
White	1999	2014	-4.1655*	-4.562	-3.7673	< 0.000001
White	2014	2020	0.9251	-0.7954	2.6754	0.274208
Hispanic or Latino	1999	2015	-3.4684*	-4.0641	-2.8691	< 0.000001
Hispanic or Latino	2015	2020	1.226	-1.7733	4.3169	0.40457
American Indian or Alaska Native		Full range	-3.0281*	-3.9538	-2.0934	0.000002
Asian or Pacific Islander		Full range	-3.0315*	-3.9259	-2.1288	< 0.000001
Black or African American		Full range	-3.2737*	-4.2048	-2.3336	< 0.000001

White		Full range	-2.7378*	-3.2547	-2.2181	< 0.000001
Hispanic or Latino		Full range	-2.3708*	-3.1454	-1.59	< 0.000001

Supplemental Table 4: Stroke and Diabetes mellitus (DM)-related Age-Adjusted Mortality Rate (AAMR) in U.S. Population, 1999-2020, stratified by Year and Gender

Year	Overall	Females	Males
1999	32.5 (31.89 to 33.1)	30.89 (30.14 to 31.63)	35.08 (34.04 to 36.12)
2000	30.93 (30.35 to 31.51)	29.61 (28.88 to 30.33)	32.99 (31.99 to 33.99)
2001	30.26 (29.69 to 30.84)	28.81 (28.1 to 29.52)	32.25 (31.28 to 33.23)
2002	30.17 (29.6 to 30.74)	28.69 (27.98 to 29.39)	32.16 (31.2 to 33.13)
2003	28.14 (27.59 to 28.69)	26.75 (26.07 to 27.43)	30.13 (29.2 to 31.06)
2004	27.17 (26.64 to 27.71)	25.84 (25.18 to 26.51)	29.03 (28.13 to 29.93)
2005	25.63 (25.12 to 26.15)	24.29 (23.65 to 24.93)	27.45 (26.58 to 28.31)
2006	23.52 (23.03 to 24.01)	22.38 (21.76 to 22.99)	25.08 (24.26 to 25.89)
2007	22.54 (22.07 to 23.02)	21.61 (21.01 to 22.21)	23.58 (22.8 to 24.36)
2008	22.41 (21.94 to 22.87)	21.6 (21.01 to 22.19)	23.4 (22.64 to 24.17)
2009	20.26 (19.81 to 20.7)	19.34 (18.78 to 19.9)	21.46 (20.73 to 22.18)
2010	20.4 (19.96 to 20.84)	19.28 (18.72 to 19.83)	21.86 (21.13 to 22.58)
2011	19.88 (19.45 to 20.31)	18.68 (18.13 to 19.22)	21.45 (20.74 to 22.16)
2012	19.16 (18.74 to 19.58)	18.16 (17.63 to 18.69)	20.58 (19.9 to 21.26)
2013	18.88 (18.47 to 19.29)	17.62 (17.1 to 18.13)	20.43 (19.76 to 21.1)
2014	17.47 (17.08 to 17.86)	16.16 (15.67 to 16.65)	19.18 (18.54 to 19.82)
2015	17.54 (17.16 to 17.93)	16.25 (15.76 to 16.74)	19.32 (18.69 to 19.95)
2016	17.43 (17.05 to 17.81)	16.13 (15.66 to 16.61)	19.12 (18.5 to 19.74)
2017	17.92 (17.54 to 18.29)	16.36 (15.89 to 16.84)	19.89 (19.27 to 20.51)
2018	17.29 (16.93 to 17.66)	15.5 (15.04 to 15.95)	19.63 (19.02 to 20.23)
2019	17.12 (16.76 to 17.48)	15.46 (15.01 to 15.9)	19.19 (18.6 to 19.78)
2020	19.27 (18.89 to 19.65)	17.44 (16.97 to 17.91)	21.67 (21.05 to 22.28)

Supplemental Table 5: Stroke and Diabetes mellitus (DM)-related Age-Adjusted Mortality Rate (AAMR) in U.S. Population, 1999-2020, stratified by Race and Ethnicity

Year	American Indian or Alaska Native	Asian or Pacific Islander	Black or African American	White	Hispanic or Latino
1999	39.55 (28.95 to 52.75)	40.73 (35.78 to 45.68)	56.16 (53.34 to 58.98)	30.21 (29.6 to 30.82)	38.13 (34.91 to 41.36)

2000	34.05 (24.93 to 45.42)	43.29 (38.38 to 48.19)	55.64 (52.85 to 58.44)	28.43 (27.84 to 29.02)	37.92 (34.78 to 41.05)
2001	36.57 (27.39 to 47.83)	39.44 (34.89 to 43.99)	54.56 (51.82 to 57.3)	27.86 (27.28 to 28.45)	39.49 (36.38 to 42.6)
2002	31.78 (23.35 to 42.25)	40.18 (35.81 to 44.55)	53.5 (50.79 to 56.21)	27.75 (27.18 to 28.33)	37.53 (34.58 to 40.48)
2003	35.9 (27.12 to 46.62)	36.57 (32.56 to 40.58)	51.3 (48.66 to 53.94)	25.74 (25.18 to 26.29)	34.16 (31.42 to 36.89)
2004	31.57 (23.5 to 41.5)	34.33 (30.55 to 38.11)	51.14 (48.52 to 53.76)	24.74 (24.2 to 25.28)	34.54 (31.84 to 37.24)
2005	29.24 (21.63 to 38.65)	33.97 (30.35 to 37.59)	50.01 (47.46 to 52.57)	23.14 (22.62 to 23.66)	31.56 (29.07 to 34.06)
2006	26.06 (18.94 to 34.99)	31.01 (27.66 to 34.37)	41.81 (39.5 to 44.12)	21.52 (21.02 to 22.02)	29.38 (27.03 to 31.73)
2007	33.6 (25.51 to 43.43)	28.4 (25.28 to 31.52)	42.08 (39.78 to 44.37)	20.49 (20.01 to 20.97)	27.6 (25.39 to 29.81)
2008	17.6 (12.04 to 24.85)	27.15 (24.18 to 30.11)	41.49 (39.24 to 43.75)	20.52 (20.04 to 20.99)	28.31 (26.12 to 30.5)
2009	24.53 (18.09 to 32.52)	25.77 (22.96 to 28.58)	35.25 (33.21 to 37.3)	18.61 (18.16 to 19.06)	25.91 (23.87 to 27.94)
2010	28.97 (22.1 to 37.29)	26.11 (23.36 to 28.87)	36.26 (34.21 to 38.31)	18.59 (18.14 to 19.04)	26.9 (24.85 to 28.94)
2011	19.54 (14.25 to 26.15)	23.67 (21.16 to 26.18)	35.69 (33.69 to 37.69)	18.18 (17.74 to 18.62)	25.84 (23.92 to 27.76)
2012	22.04 (16.51 to 28.83)	23.95 (21.5 to 26.4)	33.41 (31.51 to 35.32)	17.53 (17.1 to 17.95)	26.42 (24.53 to 28.32)
2013	21.42 (16.22 to 27.75)	21.86 (19.61 to 24.1)	31.35 (29.54 to 33.15)	17.45 (17.02 to 17.87)	25.36 (23.56 to 27.15)
2014	18.17 (13.44 to 24.02)	21.13 (18.99 to 23.27)	28.44 (26.76 to 30.13)	16.16 (15.76 to 16.57)	23.74 (22.05 to 25.42)
2015	24.86 (19.45 to 31.31)	19.43 (17.46 to 21.41)	28.07 (26.42 to 29.73)	16.33 (15.93 to 16.73)	22.01 (20.43 to 23.59)
2016	17.67 (13.31 to 23)	21.12 (19.13 to 23.12)	27.39 (25.78 to 29)	16.2 (15.8 to 16.59)	22.41 (20.86 to 23.95)
2017	23.31 (18.36 to 29.17)	17.66 (15.9 to 19.43)	29.29 (27.68 to 30.9)	16.66 (16.26 to 17.06)	24.21 (22.64 to 25.77)
2018	21.17 (16.65 to 26.53)	22.1 (20.18 to 24.02)	27.86 (26.31 to 29.41)	15.84 (15.46 to 16.22)	22.88 (21.38 to 24.37)
2019	20.55 (16.19 to 25.72)	19.69 (17.92 to 21.45)	26.9 (25.4 to 28.39)	15.88 (15.5 to 16.25)	21.59 (20.18 to 23)
2020	20.15 (15.98 to 25.08)	22.97 (21.12 to 24.82)	31.76 (30.16 to 33.36)	17.68 (17.29 to 18.07)	25.25 (23.76 to 26.74)

Supplemental Table 6: Stroke and Diabetes mellitus (DM)-related Crude Rates in U.S. Population, 1999-2020, stratified by Age Group

Year	**65-74 years**	**75-84 years**	**85+ years**
1999	14.75 (14.19 to 15.3)	41.24 (40.1 to 42.37)	83.08 (80.3 to 85.85)
2000	14.13 (13.58 to 14.67)	38.43 (37.34 to 39.53)	81.05 (78.34 to 83.76)
2001	13.04 (12.52 to 13.56)	38.88 (37.79 to 39.97)	78.82 (76.17 to 81.47)

Year	65-74 years	75-84 years	85+ years
1999	14.75 (14.19 to 15.3)	41.24 (40.1 to 42.37)	83.08 (80.3 to 85.85)
2002	13.51 (12.98 to 14.04)	37.56 (36.5 to 38.63)	79.7 (77.05 to 82.35)
2003	12.24 (11.74 to 12.75)	35.16 (34.14 to 36.19)	75.59 (73.04 to 78.14)
2004	11.99 (11.5 to 12.49)	34.57 (33.56 to 35.58)	70.28 (67.85 to 72.72)
2005	11.23 (10.76 to 11.71)	32.14 (31.17 to 33.11)	68.44 (66.07 to 70.8)
2006	10.46 (10 to 10.92)	28.84 (27.92 to 29.75)	63.67 (61.43 to 65.91)
2007	9.92 (9.48 to 10.36)	28.07 (27.16 to 28.98)	60.28 (58.14 to 62.43)
2008	9.54 (9.12 to 9.97)	28.2 (27.29 to 29.11)	60.63 (58.51 to 62.74)
2009	8.71 (8.32 to 9.11)	25.48 (24.61 to 26.35)	54.33 (52.36 to 56.3)
2010	8.83 (8.43 to 9.22)	25.27 (24.41 to 26.14)	55.61 (53.64 to 57.58)
2011	8.91 (8.51 to 9.3)	24.83 (23.98 to 25.69)	52.38 (50.5 to 54.25)
2012	8.23 (7.87 to 8.59)	23.61 (22.79 to 24.44)	53.01 (51.15 to 54.87)
2013	8.2 (7.84 to 8.55)	24.1 (23.27 to 24.93)	49.27 (47.5 to 51.04)
2014	7.81 (7.47 to 8.14)	21.63 (20.85 to 22.41)	46.67 (44.97 to 48.38)
2015	7.43 (7.1 to 7.75)	22.47 (21.68 to 23.25)	46.38 (44.7 to 48.06)
2016	7.75 (7.42 to 8.07)	21.82 (21.05 to 22.59)	46.2 (44.54 to 47.87)
2017	7.85 (7.53 to 8.16)	22.2 (21.44 to 22.96)	48.59 (46.89 to 50.29)
2018	7.8 (7.49 to 8.12)	20.92 (20.19 to 21.64)	47.28 (45.61 to 48.94)
2019	7.81 (7.5 to 8.12)	20.89 (20.18 to 21.6)	45.94 (44.3 to 47.57)
2020	8.84 (8.51 to 9.16)	23.26 (22.52 to 23.99)	52.19 (50.45 to 53.92)

Supplemental Table 7: Stroke and Diabetes mellitus (DM)-related Age-Adjusted Mortality Rate (AAMR) in U.S. Population, 1999-2020, stratified by Census Region

Year	Northeast	Midwest	South	West
1999	12.67 (12.02 to 13.33)	17.33 (16.61 to 18.05)	15.54 (14.98 to 16.09)	18.85 (18.03 to 19.67)
2000	12.24 (11.61 to 12.88)	15.33 (14.66 to 16.01)	15.49 (14.94 to 16.04)	18.14 (17.34 to 18.94)
2001	11.66 (11.04 to 12.28)	15.1 (14.43 to 15.77)	14.93 (14.4 to 15.47)	17.87 (17.09 to 18.66)
2002	11.27 (10.66 to 11.88)	14.94 (14.28 to 15.6)	14.98 (14.44 to 15.51)	17.7 (16.93 to 18.47)
2003	10.04 (9.47 to 10.61)	13.74 (13.11 to 14.37)	13.59 (13.08 to 14.09)	17.2 (16.45 to 17.95)
2004	9.79 (9.23 to 10.36)	13.86 (13.22 to 14.49)	13.33 (12.83 to 13.82)	16.65 (15.91 to 17.38)
2005	8.85 (8.31 to 9.39)	12.61 (12.01 to 13.21)	13.23 (12.74 to 13.72)	14.45 (13.77 to 15.13)
2006	8.27 (7.75 to 8.79)	11.59 (11.02 to 12.17)	11.84 (11.39 to 12.3)	14.14 (13.47 to 14.81)
2007	7.93 (7.43 to 8.44)	11.69 (11.11 to 12.26)	11.48 (11.03 to 11.92)	12.58 (11.95 to 13.2)
2008	7.83 (7.33 to 8.34)	10.96 (10.41 to 11.52)	11.79 (11.34 to 12.24)	12.29 (11.68 to 12.9)
2009	6.8 (6.34 to 7.27)	10.31 (9.78 to 10.85)	10.68 (10.26 to 11.1)	10.96 (10.39 to 11.53)
2010	6.98 (6.5 to 7.45)	10.39 (9.86 to 10.93)	10.24 (9.83 to 10.65)	11.69 (11.11 to 12.28)
2011	7.19 (6.71 to 7.67)	10.02 (9.5 to 10.55)	10.03 (9.63 to 10.43)	11.62 (11.04 to 12.19)
2012	6.79 (6.33 to 7.25)	9.34 (8.84 to 9.85)	10.18 (9.78 to 10.58)	10.06 (9.54 to 10.59)
2013	6.49 (6.04 to 6.93)	9.09 (8.6 to 9.58)	10.16 (9.76 to 10.55)	10.91 (10.36 to 11.45)
2014	6.29 (5.86 to 6.73)	8.32 (7.85 to 8.78)	9.31 (8.94 to 9.68)	9.9 (9.4 to 10.41)
2015	6.33 (5.89 to 6.77)	8.49 (8.02 to 8.95)	9.39 (9.02 to 9.76)	9.96 (9.46 to 10.46)
2016	6.15 (5.72 to 6.57)	8.17 (7.71 to 8.62)	9.57 (9.2 to 9.93)	10.16 (9.66 to 10.66)
2017	6.27 (5.85 to 6.7)	8.38 (7.93 to 8.84)	9.71 (9.35 to 10.07)	10.43 (9.93 to 10.92)
2018	5.61 (5.21 to 6)	8.33 (7.89 to 8.77)	9.26 (8.92 to 9.61)	10.1 (9.63 to 10.58)
2019	5.71 (5.32 to 6.1)	7.8 (7.38 to 8.23)	9.59 (9.24 to 9.93)	9.99 (9.52 to 10.45)
2020	6.19 (5.79 to 6.59)	9.45 (8.99 to 9.91)	10.76 (10.4 to 11.12)	11.03 (10.55 to 11.51)

Supplemental Table 8: Stroke and Diabetes mellitus (DM)-related Age-Adjusted Mortality Rate (AAMR) in U.S. Population, 1999-2020, stratified by Urbanization

Year	Urban	Non-urban
1999	31.48 (30.82 to 32.14)	36.93 (35.47 to 38.39)
2000	30.06 (29.42 to 30.7)	34.61 (33.21 to 36.02)
2001	29.07 (28.44 to 29.69)	35.25 (33.83 to 36.66)
2002	28.8 (28.18 to 29.42)	35.99 (34.56 to 37.41)
2003	27.05 (26.46 to 27.65)	32.78 (31.43 to 34.14)
2004	26 (25.42 to 26.58)	32.17 (30.83 to 33.52)
2005	24.51 (23.95 to 25.07)	30.64 (29.34 to 31.94)
2006	22.45 (21.92 to 22.98)	28.12 (26.88 to 29.36)
2007	21.44 (20.93 to 21.95)	27.46 (26.24 to 28.67)
2008	21.06 (20.56 to 21.57)	28.54 (27.31 to 29.78)
2009	19.1 (18.63 to 19.58)	25.47 (24.3 to 26.63)
2010	19.35 (18.87 to 19.82)	25.15 (24 to 26.3)
2011	18.88 (18.42 to 19.35)	24.6 (23.47 to 25.73)
2012	18.25 (17.8 to 18.7)	23.59 (22.49 to 24.68)
2013	18.05 (17.61 to 18.49)	22.78 (21.72 to 23.85)
2014	16.53 (16.11 to 16.94)	22.01 (20.97 to 23.05)
2015	16.5 (16.09 to 16.91)	22.43 (21.39 to 23.47)
2016	16.67 (16.26 to 17.08)	21.28 (20.28 to 22.29)
2017	17.04 (16.63 to 17.44)	22.19 (21.17 to 23.2)
2018	16.64 (16.24 to 17.03)	20.61 (19.64 to 21.58)
2019	16.34 (15.95 to 16.72)	21.17 (20.2 to 22.14)
2020	18.27 (17.86 to 18.67)	24.24 (23.21 to 25.27)

Supplemental Table 9: Stroke and Diabetes mellitus (DM)-related Age-Adjusted Mortality Rate (AAMR) in U.S. Population, 1999-2020, stratified by State

State	AAMR
Oregon	33.31 (32.29 to 34.34)
Mississippi	32.19 (30.97 to 33.41)
Oklahoma	31.89 (30.84 to 32.94)
California	31.01 (30.66 to 31.36)
Vermont	29.42 (27.07 to 31.77)
Texas	28.87 (28.42 to 29.31)
Ohio	28.51 (27.96 to 29.05)
Nebraska	28.46 (27.09 to 29.83)
North Carolina	28.11 (27.48 to 28.75)

South Carolina	28.08 (27.18 to 28.98)
Washington	27.81 (27.05 to 28.57)
Tennessee	27.77 (27 to 28.53)
South Dakota	27.43 (25.5 to 29.36)
West Virginia	27.19 (25.92 to 28.46)
Minnesota	26.23 (25.43 to 27.02)
Iowa	26.1 (25.14 to 27.06)
Kentucky	25.73 (24.84 to 26.62)
Hawaii	25.13 (23.67 to 26.59)
Idaho	24.16 (22.68 to 25.64)
Wisconsin	23.99 (23.28 to 24.7)
Maryland	23.94 (23.18 to 24.7)
North Dakota	23.55 (21.6 to 25.5)
Indiana	23.07 (22.39 to 23.76)
Alabama	22.08 (21.31 to 22.86)
Arkansas	21.4 (20.45 to 22.34)
Colorado	21.31 (20.48 to 22.13)
District of Columbia	20.66 (18.42 to 22.89)
Rhode Island	20.52 (19.05 to 21.98)
Montana	20.35 (18.8 to 21.9)
Missouri	20.32 (19.68 to 20.96)
Michigan	20.31 (19.8 to 20.81)
New Hampshire	20.29 (18.9 to 21.69)
Georgia	20.01 (19.42 to 20.61)
Alaska	19.86 (17.1 to 22.62)
Pennsylvania	19.66 (19.25 to 20.06)
Virginia	19.54 (18.94 to 20.13)
Illinois	19.44 (18.99 to 19.89)
Kansas	18.98 (18.08 to 19.89)
Maine	18.28 (17.06 to 19.49)
Utah	18.25 (17.11 to 19.39)
Wyoming	17.71 (15.6 to 19.82)
New Mexico	15.58 (14.57 to 16.59)
Connecticut	15.09 (14.39 to 15.78)
Delaware	14.96 (13.53 to 16.38)
New York	14.92 (14.61 to 15.22)
Massachusetts	14.21 (13.71 to 14.71)
New Jersey	14.12 (13.68 to 14.57)
Louisiana	13.94 (13.28 to 14.59)
Arizona	11.3 (10.83 to 11.77)
Florida	10.47 (10.24 to 10.7)
Nevada	9.8 (9.04 to 10.56)