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ARTICLE

Dyslipidemia and stroke-related mortality in the United States: a nationwide analysis for 2010-2020

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Abstract

Dyslipidemias are a significant risk factor for stroke. Still, there is limited data on mortality trends where both dyslipidemia and stroke are either contributing or underlying causes of death among adults aged ≥25 years. We aimed to evaluate the demographic, regional, and temporal trends in dyslipidemia and stroke-related mortality among adults from 2010 to 2020. The CDC WONDER mortality data were utilized to identify deaths with both dyslipidemia and stroke as either underlying or contributing causes of death in adults aged ≥25 years. Age-adjusted mortality rates (AAMRs) per 100,000 and annual percent change (APC) were calculated and further categorized by year, sex, race/ethnicity, region, and urban-rural status. Joinpoint regression was used to determine changes in trends over time. Between 2010 and 2020, a total of 106,813 dyslipidemia and stroke-related deaths occurred among adults aged ≥25 years, with the most in medical facilities (35.7%), at home (27.7%), or in nursing/long-term care facilities (26.9%). The AAMR increased from 3.47 in 2010 to 5.47 in 2020, stable through 2018 (APC 1.6 [95% CI, -0.4 to 2.7]) then rising sharply (APC 15.1 [95% CI, 7.5 to 19.5]). Men had higher mortality than women (AAMR: 4.44 *vs* 3.66). The Non-Hispanic (NH) Black or African American population had the highest overall AAMR (4.97), followed by the NH White population (3.99), the NH American Indian or Alaska Native population (3.87), the NH Asian or Pacific Islander population (3.59), and the Hispanic or Latino population (3.25) Vermont (10.15) and Georgia (1.99) had the highest and lowest state-level rates, respectively. Regionally, the West (4.61) exceeded the Northeast (3.43). Nonmetropolitan areas (4.81) had consistently higher mortality than metropolitan areas (3.85). Dyslipidemia and stroke-related mortality increased significantly after a period of stability. The highest AAMRs were observed in men, NH Black individuals, and people living in the Western US and nonmetropolitan areas. Effective policies are required to reduce these mortality rates and improve cardiovascular health.

Key words: heart failure; dyslipidemia; stroke; CDC WONDER; mortality.

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Introduction

Dyslipidemias are defined as higher plasma levels of total cholesterol, LDL cholesterol, or triglycerides, or decreased plasma levels of HDL cholesterol or a combination of these abnormalities, and are a significant risk factor for cardiovascular disease (CVD).[1] Globally, the prevalence of dyslipidemia is more than 50% in adults.[2] In the US, approximately 53% of adults have dyslipidemia.[3] Stroke affects nearly 89 million people and is the leading cause of disability and the second most common cause of mortality worldwide, accounting for almost 5.5 million deaths (9.7% of all deaths) annually.[4,5] In the US, the prevalence of stroke is 3.3% among adults, which increases with advancing age.[6] Nearly 800,000 strokes occur each year, and approximately 140,000 people die from stroke each year in the US.[4,7] Stroke is the fourth leading cause of death, with 1 death occurring every 4 min in the US.[7]

Dyslipidemias are a significant risk factor for stroke. According

to the Global Burden of Disease study in 2019, an estimated 610,000 ischemic stroke deaths (22.4% of the total) were attributable to high LDL cholesterol.[8,9] High LDL cholesterol results in endothelial dysfunction, resulting in atherosclerosis, which increases the risk for stroke. Elevated levels of triglycerides are also associated with higher stroke risk, whereas high HDL cholesterol decreases the risk.[6,10] A large study demonstrated that every 1 mmol/L rise in total cholesterol was associated with 25% higher rates of ischemic stroke.[11]

Although both dyslipidemia and stroke are closely linked, there is limited data analyzing mortality trends where both conditions are simultaneously listed as causes of death. Understanding the different variations in this joint mortality burden is crucial for identifying the most affected populations and addressing healthcare disparities. Therefore, we conducted this study to assess temporal, regional, and demographic trends in dyslipidemia and stroke concomitant mortality among adults in the US from 2010 to 2020.

Methods

Study design

The mortality data were sourced from the CDC WONDER (Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research) database and analyzed for dyslipidemia and stroke-related mortality among adults aged 25 and above between 2010 and 2020 using codes from the International Statistical Classification of Diseases and Related Health Problems-10th Revision (ICD-10). A similar age cut-off for adults has been used in previous studies.[12,13] The Multiple Cause-of-Death Public Use record death certificates were studied to identify records where both dyslipidemia and stroke were mentioned as either a contributing or underlying cause of death. Dyslipidemia patients were identified with ICD-10 code E78.x, and stroke patients were identified with ICD-10 codes I60.x, I61.x, I63.x, I64, I69.0, I69.1, I69.3, I69.4. Similar codes have been used in previous studies.[14,15] The study utilized de-identified data from a government-issued, publicly accessible database, so it did not require institutional review board approval. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed in this study.

Data extraction

The data on deaths due to coexisting dyslipidemia and stroke, including the total population, year, sex, age, race/ethnicity, urban-rural status, region, place of death, and state, were extracted. Race/ethnicity was further subdivided into non-Hispanic (NH) White, NH Black or African American, Hispanic or Latino, NH Asian or Pacific Islander, and NH American Indian or Alaskan Native. The place of death was classified as the decedent's home, medical facilities, nursing homes or long-term care facilities, hospice centers, and others. The census regions were categorized as the Northeast, the Midwest, the South, and the West. The National Center for Health Statistics Urban-Rural Classification Scheme was used to categorize the population as urban (large metropolitan area [population ≥1 million], medium/small metropolitan area [population 50,000-999,999]), and rural (population <50,000) areas.[16]

Statistical analysis

The age-adjusted mortality rates (AAMR) and crude rates per 100,000 population were calculated by year, sex, race/ethnicity, state, and urban-rural status with 95% CIs between 2010 and 2020 to examine national trends in coexisting dyslipidemia and stroke-related mortality. The crude mortality rates were calculated by dividing the number of dyslipidemia and stroke-related deaths by the total US population of that year. The AAMRs were determined by standardizing the number of deaths to the 2000 US population.[17] To examine yearly national trends in mortality where both dyslipidemia and stroke were listed as causes of death, the Joinpoint Regression Program (version 5.2.0.0; National Cancer Institute) was used to estimate the annual percent change (APC) with 95% CI in AAMR.[18] This approach applies log-linear regression models that account for temporal variation to detect significant changes in AAMR over time. APCs were classified as increasing or decreasing using 2-tailed t-testing if the slope showing the change in mortality showed a significant deviation from zero. A p-value <0.05 was considered statistically significant.

Results

There was a total of 106,813 deaths among adults aged ≥25 years, where both dyslipidemia and stroke were either underlying or contributing causes in the US between 2010 and 2020 (*Supplementary Table 1*). Out of these, 35.7% occurred in medical facilities, 27.7% occurred at home, 26.9% occurred in nursing homes/long-term care facilities, and 5.5% occurred in hospices (*Supplementary Table 2*).

Annual trends for dyslipidemia and stroke-related mortality

In 2010, the AAMR for dyslipidemia and stroke-related deaths was 3.47, which increased to 5.47 in 2020. There was a period of stability in the overall AAMR from 2010 to 2018 (APC: 1.6; 95% CI: -0.4 to 2.7), followed by a significant rise from 2018 to 2020 (APC: 15.1; 95% CI: 7.5 to 19.5) (Figure 1; *Supplementary Tables 3 and 4*).

Sex stratification

The overall AAMRs were consistently higher in men compared to women during the study period (overall AAMR Men: 4.44; 95% CI: 4.40 to 4.48; Women: 3.66; 95% CI: 3.63 to 3.69). The overall AAMR for men in 2010 was 3.76 (95% CI: 3.63 to 3.89), which increased to 4.67 in 2018 (APC: 2.2; 95% CI: 0.9 to 3.1), followed by a further rise to 6.11 in 2020 (APC: 15.9; 95% CI: 10.5 to 19.6). For women, there was a period of stability from 2010 to 2018 (APC: 1.2; 95% CI: -1.3 to 2.4), followed by a sig-

nificant rise in AAMR until 2020 (APC: 15.2; 95% CI: 6.6 to 20.3) (Figure 1; *Supplementary Tables 3 and 4*).

Racial stratification

The overall AAMRs were the highest in NH Black or African American individuals (AAMR: 4.97; 95% CI: 4.87 to 5.06), followed by NH White (AAMR: 3.99; 95% CI: 3.96 to 4.02), NH American Indian or Alaska Native (AAMR: 3.87; 95% CI: 3.53 to 4.20), NH Asian or Pacific Islander (AAMR: 3.59; 95% CI: 3.47 to 3.70), and Hispanic or Latino population (AAMR: 3.25; 95% CI: 3.17 to 3.33). The AAMRs for all races, except the NH American Indian or Alaska Native population, remained stable from 2010 to 2018, followed by an exponential increase from 2018 to 2020. For the NH American Indian or Alaska Native population, the AAMRs were stable throughout the whole study duration from 2010 to 2020 (Figure 2; *Supplementary Tables 3 and 5*).

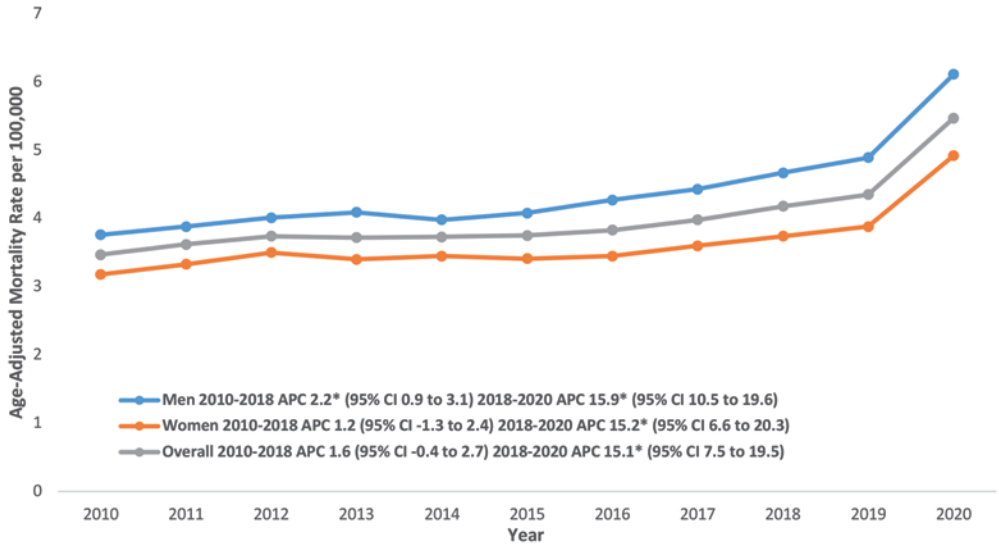

Figure 1. Overall and sex-stratified dyslipidemia and stroke-related AAMRs per 100,000 in adults in the United States, 2010 to 2020. *Indicates that the annual percentage change (APC) is significantly different from zero at α = 0.05. AAMR, age-adjusted mortality rate.

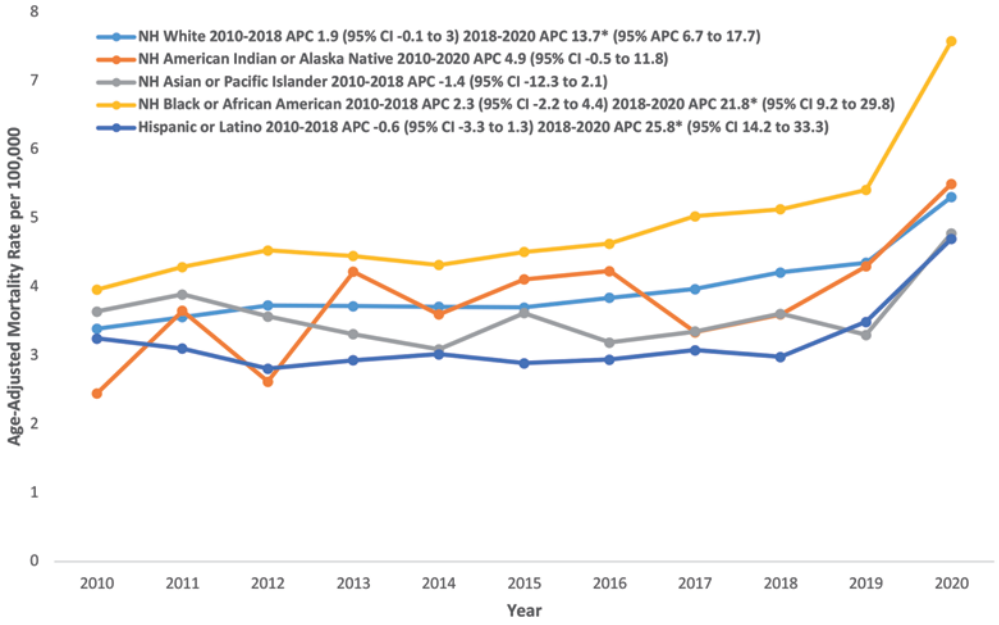

Figure 2. Dyslipidemia and stroke-related AAMRs per 100,000 stratified by race in adults in the United States, 2010 to 2020. *Indicates that the annual percentage change (APC) is significantly different from zero at α = 0.05. AAMR, age-adjusted mortality rate.

Geographic stratification

There were significant variations in AAMRs across different states. Vermont had the highest dyslipidemia and stroke-related mortality trends (AAMR: 10.15; 95% CI: 9.33 to 10.96), while Georgia had the lowest (AAMR: 1.99; 95% CI: 1.89 to 2.1). States with the highest AAMRs in the top 90th percentile were Vermont, Nebraska, Oregon, Minnesota, and Washington. States with the lowest AAMRs in the lower 10th percentile were Georgia, New Mexico, Nevada, Massachusetts, and Connecticut (Figure 3) (*Supplementary Table 6*). For Census regions, the highest mortality rate was observed in the Western region (AAMR: 4.61; 95% CI: 4.55 to 4.66), followed by the Midwestern (AAMR: 4.23; 95% CI: 4.17 to 4.28), Southern (AAMR: 3.84; 95% CI: 3.80 to 3.87), and Northeastern (AAMR: 3.43; 95% CI: 3.38 to 3.48) (*Supplementary Table 7*).
Throughout the study, nonmetropolitan areas (AAMR: 4.81; 95% CI: 4.75 to 4.88) had higher mortality rates than metropolitan areas (AAMR: 3.85; 95% CI: 3.82 to 3.87). The AAMR for nonmetropolitan areas increased from 2010 to 2017 (APC: 2; 95% CI: 0.2 to 3.1), followed by a further rise until 2020 (APC: 11.2; 95% CI: 7.9 to 16.7). For metropolitan areas, there was a period of stability from 2010 to 2018 (APC: 1.4; 95% CI: -0.8 to 2.5), followed by a substantial increase until 2020 (APC: 15.4; 95% CI: 7 to 20.2) (Figure 4; (*Supplementary Tables 3 and 8*).

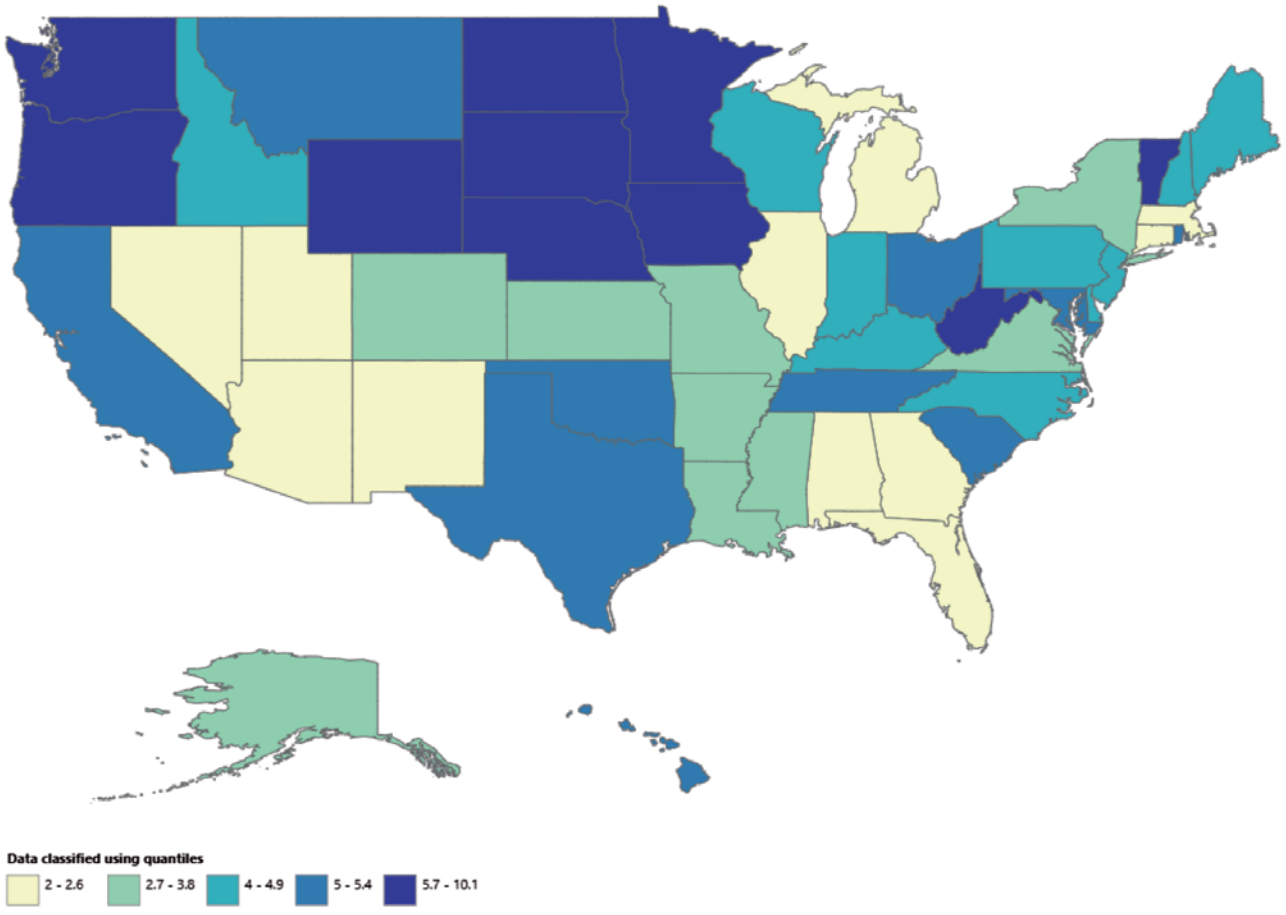

Figure 3. Dyslipidemia and stroke-related AAMRs stratified by state in adults in the United States, 2010 to 2020.

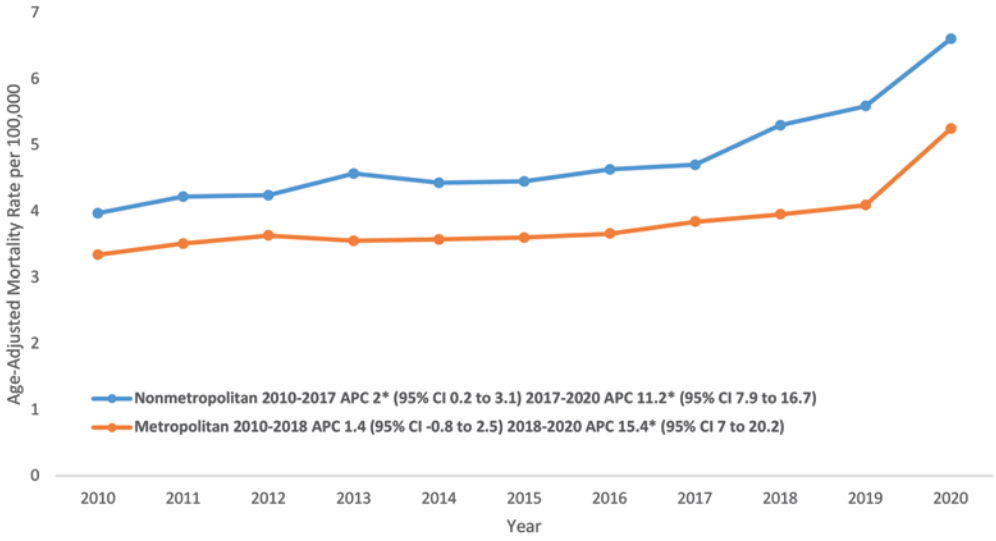

Figure 4. Dyslipidemia and stroke-related AAMRs stratified by urban-rural status in adults in the United States, 2010 to 2020. *Indicates that the annual percentage change (APC) is significantly different from zero at α = 0.05. AAMR, age-adjusted mortality rate.

Discussion

In our analysis of the CDC WONDER database for dyslipidemia and stroke-related mortality among US adults aged 25 and older from 2010 to 2020, we report several key findings. First, the overall AAMR increased during this period, with a period of stability from 2010 to 2018, followed by a distinct surge from 2018 to 2020 in every demographic, racial, and regional group. Second, men had higher AAMRs than women. Third, the NH Black or African American population had the highest AAMRs across all races. Fourth, significant regional disparities were also observed, with nonmetropolitan areas having higher AAMRs than metropolitan areas. Additionally, the Western region had the highest mortality among all census regions. These findings highlight a rising public health burden of coexisting dyslipidemia and stroke mortality, and disparities observed in different subgroups in the US. Recognizing these disparities is essential to formulate long-term strategies and reduce cardiovascular death.

According to data from the US National Health and Nutrition Examination Surveys (NHANES), there was a reduction in total cholesterol from 197 mg/dl in 2007-2008 to 189 mg/dl in 2017-2018 among US adults.[19] Similarly, LDL cholesterol improved from 116 mg/dl to 111 mg/dl, mean triglycerides decreased from 111.4 mg/dl to 91.4 mg/dl, but there was no significant change in lipid control after statin therapy from 2007-2008 to 2017-2018.[19,20] Moreover, the overall prevalence of stroke was stable from 2007-2010 to 2015-2018.[21] These trends are consistent with our finding of a period of relative stability in coexisting dyslipidemia and stroke mortality among adults from 2010 to 2018, despite an increasing aging population. COVID-19 resulted in worsening of dyslipidemia due to a sedentary lifestyle and an imbalanced diet during the lockdown. Additionally, dyslipidemia increased the severity and mortality from COVID-19. The viral-induced inflammation impairs the function of HDL apolipoproteins, resulting in lower HDL and higher LDL and triglyceride levels, which cause further endothelial damage and increase CVD-related complications and mortality from COVID-19.[22] Similarly, COVID-19 was associated with higher stroke risk and mortality.[23,24] People with COVID-19 had a ten times higher stroke risk within the first three days compared to people without the disease.[24] This was attributed to viral-induced inflammation, endothelial dysfunction, respiratory distress causing hypoxemia, and neuronal damage.[23] Moreover, the pandemic was associated with decreased hospital admissions, imaging, and reperfusion interventions for stroke, resulting in higher mortality rates observed during this time.[25] This aligns with our finding of an exponential increase in dyslipidemia and stroke-related mortality from 2018 to 2020 across all subgroups.

We observed that men had higher dyslipidemia and stroke-related mortality rates than women. This is consistent with previous studies.[26,27] Women are more likely to have higher HDL and lower LDL cholesterol levels, which are atheroprotective, whereas men tend to have higher LDL cholesterol and triglyceride levels, which are atherogenic.[28] Moreover, men have higher CVD mortality, comorbidities, and risk factors, including higher tobacco use and alcohol consumption.[29,30] The incidence and mortality from stroke are higher in men compared to women.[31] This could be due to the protective effect of estrogen on cerebral circulation.[27] These factors may have contributed to higher dyslipidemia and stroke-related mortality rates among men. These disparities should be addressed by targeted strategies that focus on reducing tobacco and alcohol use and improving cardiovascular risk screening among men.

Our results showed significant racial variations, with the NH Black or African American population having the highest dyslipidemia and stroke-related mortality, while the Hispanic or Latino population had the lowest. This aligns with previous studies.[26,27] These disparities could be attributed to the highest incidence of stroke in the NH Black population among all eth-

nicities.[32] Additionally, NH Black individuals have a higher prevalence of CVD risk factors.[33] Socioeconomic factors, structural racism, and inequities in healthcare access may have contributed to the observed disparities.[34] The lowest mortality rates in the Hispanic population could be attributed to the Hispanic paradox phenomenon, where Hispanic people have lower CVD mortality rates despite a high prevalence of CVD risk factors and socioeconomic inequities.[35] These disparities should be addressed with targeted interventions to improve healthcare access among these populations.[36]

We also noticed significant geographic disparities. The Western region had the highest mortality rates, while the Northeast region had the lowest. This is in contrast to previous studies, where the Southeastern region has the highest stroke mortality and is considered "The Stroke Belt".[37] However, the mortality trends are different when both dyslipidemia and stroke are considered together. These disparities could be attributed to differences in the prevalence of CVD risk factors, comorbidities, and access to healthcare across different regions. The lowest mortality rates observed in the Northeast region may, in part, be due to better healthcare accessibility, as well as the greater number of medical centers and teaching hospitals compared to other regions.[38] These findings indicate the need for larger population-based studies to better understand the underlying factors responsible for these variations and formulate effective policies to improve healthcare across the US.

We also observed that nonmetropolitan areas had higher mortality rates than metropolitan areas. These could be attributed to the higher prevalence of multiple CVD risk factors in the rural population compared to the urban population.[39] Additionally, the rural population is more likely to experience limited access to healthcare, food security, and decreased income, which may adversely affect their cardiovascular health, resulting in higher mortality rates.[33]

Limitations

There are several limitations in our study. First, the reliance on ICD codes may result in misclassification or omission of dyslipidemia or stroke as causes of death. Second, the analysis lacks important clinical details of the patients, like lipid profile values, presence of other comorbidities, medication use, and subtypes of stroke. Last, data on various socioeconomic factors is missing, which could impact healthcare access and disease management.

Conclusions

In this nationwide analysis of the CDC WONDER database, we noticed that dyslipidemia and stroke-related mortality among adults were relatively stable from 2010 to 2018, followed by an exponential rise from 2018 to 2020. The highest mortality rates were observed in men, NH Black individuals, and people living in the Western US and nonmetropolitan areas. Our findings highlight the need for targeted interventions to improve dyslipidemia and stroke management and outcomes.

Conflict of interest

The authors declare no conflict of interest, and all authors confirm accuracy.

Contributions

MMUR, conceptualization; MMUR, IM, methodology; IM, MSA, formal analysis and investigation; MMUR, MSA, SRS, manuscript original drafting; WD, AK, manuscript review and editing; WD, supervision.

Ethical approval

Not required as this research is based on de-identified data.

Availability of data and material

All data analyzed in this study are publicly available from the CDC WONDER database and can be accessed without restriction.

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Online supplementary material:

Supplementary Table 1. Dyslipidemia and stroke-related deaths, stratified by sex and race.

Supplementary Table 2. Dyslipidemia and stroke-related mortality, stratified by place of death. Supplementary Table 3. Annual percent change (APC) dyslipidemia and stroke-related age-adjusted mortality rates.

Supplementary Table 4. Overall and sex stratified age-adjusted mortality rates.

Supplementary Table 5. Dyslipidemia and stroke-related age-adjusted mortality rates, stratified by race.

Supplementary Table 6. Dyslipidemia and stroke-related age-adjusted mortality rates, stratified by states.

Supplementary Table 7. Dyslipidemia and stroke-related age-adjusted mortality rates, stratified by census regions.

Supplementary Table 8. Dyslipidemia and stroke-related age-adjusted mortality rates, stratified by urban-rural classification.