

Temporal Trends and Demographic Disparities in Mortality Involving Pulmonary Embolism and Diabetes Mellitus Among U.S. Adults Aged ≥ 25 Years, 1999–2024: A CDC WONDER Analysis

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Abstract

Background

Pulmonary embolism (PE) and diabetes mellitus (DM) contribute substantially to cardiovascular mortality, yet national data describing deaths involving both conditions remain limited. This study evaluated temporal trends and demographic disparities in PE and DM-related mortality among U.S. adults aged ≥ 25 years from 1999 to 2024.

Methods

The CDC WONDER Multiple Cause-of-Death database was analyzed for death certificates listing PE (ICD-10 code I26) and DM (ICD-10 codes E10–E14) as underlying or contributing causes of death. Age-adjusted mortality rates (AAMRs) per 100,000 population were calculated using the 2000 U.S. standard population. Joinpoint regression estimated annual percent change (APC) and average annual percent change (AAPC) with 95% confidence intervals (CIs), stratified by sex, age, race/ethnicity, census region, urbanization, state, and place of death.

Results

From 1999 to 2024, 82,180 deaths involving both PE and DM were recorded. The overall AAMR increased from 1.08 in 1999 to 1.88 in 2024, with a significant AAPC of 1.98% (95% CI: 1.10–2.87; $p < 0.001$). Mortality increased modestly from 1999 to 2018, accelerated sharply from 2018 to 2021, and declined significantly from 2021 to 2024. Males had higher and faster-rising AAMRs than females. Black or African American individuals had the highest AAMRs, while adults aged ≥ 65 years carried the greatest absolute burden. The South had the highest regional AAMR by 2024, and non-metropolitan areas had higher rates than metropolitan areas through 2020.

Conclusion

Pulmonary embolism and Diabetes mellitus-related mortality showed an overall increase among U.S. adults aged ≥ 25 years from 1999 to 2024, with substantial sex, racial, age, regional, and urban-rural disparities. Targeted prevention, timely recognition of PE, optimized diabetes management, and equitable access to healthcare are needed to reduce these disparities and the overall mortality burden.

1. Introduction

Pulmonary embolism (PE) represents one of the major cardiac emergencies and the leading cause of death among hospitalized patients (1). It occurs through the obstruction of the pulmonary arterial system due to thrombus migration that typically stems from deep vein thrombosis in the lower

extremities (2). Such a vascular blockage causes inadequate pulmonary perfusion and ventilation, elevated right ventricular pressure overload, and, possibly, hemodynamic complications (2). In spite of progress in diagnostic imaging and anticoagulation therapy of PE, this condition remains an important cause of premature mortality in the United States (U.S.) (3–5). Every year, many Americans suffer from this complication, causing considerable mortality risk for especially those who are elderly and have several concomitant diseases (1). Recently, using the CDC WONDER database, it was established that the overall trends in PE-associated deaths show a decrease or non-linearity during the last two decades, depending on various temporal periods as well as differences by age, gender, race/ethnicity, and geographic area (6).

Diabetes mellitus (DM), a public health problem that is currently gaining rapid momentum within the U.S. (7), is characterized by chronic inflammatory states, endothelial dysfunctions, platelet activation, and a prothrombotic status, all of which have been shown to potentially predispose such individuals to venous thromboembolisms, such as PE (8–10). Individuals suffering from diabetes tend to be afflicted with numerous comorbidities that may complicate the process of PE and raise the risk of mortality (11). Additionally, various vascular complications caused by diabetes may play a role in affecting the prognosis of the patient post-thromboembolism (12). The burden of diabetes-related mortality in the U.S. remains substantial, with notable demographic and regional disparities reported in national mortality datasets (7).

Although several CDC WONDER studies have evaluated temporal trends in mortality related to PE or DM separately (6, 7), limited nationwide data exist examining the combined mortality burden involving both PE and DM. Prior studies have largely focused on PE mortality in specific subgroups, such as patients with cancer or hypertension (13, 14), leaving an important gap regarding the intersection of PE and diabetes-related mortality trends. Understanding long-term mortality patterns is essential for identifying vulnerable populations, guiding preventive strategies, and informing healthcare policy. Therefore, this study aimed to evaluate temporal trends in mortality involving PE and DM in the U.S. using the CDC WONDER database.

2. Methods

2.1. Study Design and Data Source

A retrospective analysis was conducted using national mortality data to evaluate temporal trends in deaths related to PE and DM among adults aged 25 years and older in the U.S. between 1999 and 2024. Data were obtained from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) Multiple Cause-of-Death database (15). PE-related mortality was identified using the International Classification of Diseases, Tenth Revision (ICD-10) code I26, while DM-related mortality was identified using ICD-10 codes E10–E14, encompassing type 1 diabetes, type 2 diabetes, malnutrition-related diabetes, other specified diabetes, and unspecified DM, that align with similar epidemiological studies (16, 17). Decedents were included if both PE (I26) and DM (E10–E14)

appeared anywhere on the death certificate as either underlying or contributing causes of death. Because the database contains publicly available, de-identified records, institutional review board approval and informed consent were not required. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines (18).

2.2. Data Extraction

Variables extracted for analysis included year of death, age at death, sex, race/ethnicity, place of death, geographic region, state of residence, and urbanization status. Age was categorized into three groups: 25–44 years, 45–64 years, and ≥ 65 years. Sex was classified as male or female based on death certificate records. Race/ethnicity analyses were restricted to non-Hispanic (NH) White, NH Black or African American, and Hispanic populations. NH American Indian or Alaska Native and NH Asian or Pacific Islander groups were excluded because mortality estimates for these populations were considered unreliable due to small death counts and statistical instability. Place of death was categorized as medical facility inpatient, medical facility outpatient or emergency department, decedent's home, hospice facility, nursing home/long-term care facility, and other locations. Geographic distribution was evaluated across the four U.S. Census regions (Northeast, Midwest, South, and West), with additional state-level analyses performed where appropriate. Urbanization status was classified according to the National Center for Health Statistics (NCHS) Urban–Rural Classification Scheme and grouped as metropolitan and non-metropolitan areas (19). Urbanization analyses were restricted to 1999–2020 because county-level urbanization classifications were not available in the CDC WONDER dataset for subsequent years at the time of analysis.

2.3. Statistical Analysis

Age-adjusted mortality rates (AAMRs) per 100,000 population were calculated to assess trends in PE and DM-related mortality and were standardized to the 2000 U.S. standard population to facilitate comparisons across time periods and demographic subgroups (20). Temporal trends were analyzed using Joinpoint regression software (version 5.4.0, National Cancer Institute), which identifies statistically significant changes in mortality trends over time (21). The Monte Carlo permutation method was used to determine the optimal number of joinpoints and to test the statistical significance of changes in trend. A maximum of four joinpoints was allowed in the models, reflecting the length of the 1999–2024 study period. For each identified time segment, the Annual Percent Change (APC) in AAMRs was estimated with corresponding 95% confidence intervals, and the Average Annual Percent Change (AAPC) was calculated to summarize the overall trend across the entire study period. Statistical significance was defined as a two-sided p-value < 0.05 .

3. Results

3.1. Overall

A total of 82,180 deaths were recorded, with overall AAMR increasing from 1.08 in 1999 to 1.88 in 2024. Between 1999 and 2024, overall AAMRs increased significantly, with an AAPC of 1.98% (95% CI: 1.10 to 2.87; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 0.74% (95% CI: 0.50 to 0.99; $p < 0.001$), followed by a further increase between 2018 and 2021, with an APC of 23.07% (95% CI: 15.02 to 31.68; $p < 0.001$). From 2021 to 2024, mortality rates showed a significant decline, with an APC of -8.69% (95% CI: -11.78 to -5.49; $p < 0.001$) (Fig. 1, **Supplementary Tables 1 and 8**).

3.2. Stratified by Sex

Among females, AAMRs increased from 1.05 in 1999 to 1.63 in 2024. Overall mortality rates increased significantly between 1999 and 2024, with an AAPC of 1.46% (95% CI: 0.18 to 2.76; $p = 0.025$). From 1999 to 2018, mortality rates showed a non-significant increase (APC: 0.15%; 95% CI: -0.20 to 0.49; $p = 0.389$). However, an increase was observed from 2018 to 2021, with an APC of 21.82% (95% CI: 9.91 to 35.01; $p < 0.001$), followed by a significant decrease between 2021 and 2024 (APC: -8.19%; 95% CI: -12.05 to -4.16; $p < 0.001$).

In males, AAMRs increased from 1.11 in 1999 to 2.19 in 2024. Mortality rates increased significantly overall, with an AAPC of 2.45% (95% CI: 1.45 to 3.46; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 1.27% (95% CI: 0.93 to 1.60; $p < 0.001$), followed by a further increase between 2018 and 2021, by 24.68% (95% CI: 15.39 to 34.71; $p < 0.001$). Thereafter, rates significantly declined from 2021 to 2024, with an APC of -9.41% (95% CI: -12.49 to -6.21; $p < 0.001$) (Fig. 1, **Supplementary Tables 1 and 8**).

3.3. Stratified by Race/Ethnicity

Among Hispanic or Latino individuals, AAMRs increased from 1.15 in 1999 to 1.59 in 2024. Between 1999 and 2024, overall mortality trends showed a non-significant increase, with an AAPC of 1.03% (95% CI: -1.39 to 3.51; $p = 0.407$). From 1999 to 2018, mortality rates showed a non-significant decrease (APC: -0.39%; 95% CI: -1.30 to 0.52; $p = 0.375$). However, a significant increase was observed between 2018 and 2021, with an APC of 33.43% (95% CI: 10.10 to 61.70; $p = 0.006$). Mortality rates significantly decreased from 2021 to 2024, with an APC of -16.30% (95% CI: -22.84 to -9.20; $p < 0.001$).

Among Black or African American individuals, AAMRs increased from 2.78 in 1999 to 4.01 in 2024. Between 1999 and 2024, mortality rates showed a non-significant overall increase, with an AAPC of 1.30% (95% CI: -0.09 to 2.71; $p = 0.067$). From 1999 to 2018, mortality rates showed a non-significant decrease (APC: -0.39%; 95% CI: -0.83 to 0.04; $p = 0.075$), followed by a significant increase between 2018 and 2021, with an APC of 25.03% (95% CI: 12.01 to 39.57; $p < 0.001$). Thereafter, mortality rates significantly declined from 2021 to 2024, with an APC of -8.69% (95% CI: -13.04 to -4.13; $p = 0.001$).

Among White individuals, AAMRs increased from 0.89 in 1999 to 1.73 in 2024. Between 1999 and 2024, overall mortality rates increased significantly, with an AAPC of 2.34% (95% CI: 1.14 to 3.56; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 1.16% (95% CI: 0.79 to 1.53; $p <$

0.001). An increase was observed between 2018 and 2021, with an APC of 21.41% (95% CI: 10.32 to 33.62; $p < 0.001$). mortality rates significantly decreased between 2021 and 2024, with an APC of – 7.11% (95% CI: –10.57 to – 3.52; $p < 0.001$) (Fig. 2, **Supplementary Tables 2 and 8**).

3.4. Stratified by Census Region

In the Northeast region, AAMRs increased from 0.88 in 1999 to 1.53 in 2024. Between 1999 and 2024, mortality rates increased significantly, with an AAPC of 1.75% (95% CI: 0.28 to 3.25; $p = 0.020$). From 1999 to 2018, mortality rates showed a non-significant increase (APC: 0.40%; 95% CI: –0.04 to 0.84; $p = 0.073$). A significant increase was observed between 2018 and 2021, with an APC of 20.70% (95% CI: 7.57 to 35.44; $p = 0.003$). Mortality rates significantly declined from 2021 to 2024, with an APC of – 6.62% (95% CI: –11.62 to – 1.33; $p = 0.018$).

In the Midwest region, AAMRs increased from 1.24 in 1999 to 1.92 in 2024. Between 1999 and 2024, overall mortality rates increased significantly, with an AAPC of 1.60% (95% CI: 0.26 to 2.96; $p = 0.019$). From 1999 to 2018, mortality rates increased significantly (APC: 0.52%; 95% CI: 0.14 to 0.90; $p = 0.010$). An increase was observed between 2018 and 2021, with an APC of 21.31% (95% CI: 9.12 to 34.87; $p = 0.001$). Thereafter, mortality rates significantly declined from 2021 to 2024, with an APC of – 8.92% (95% CI: –13.22 to – 4.40; $p < 0.001$).

In the South region, AAMRs increased from 1.18 in 1999 to 2.11 in 2024. Between 1999 and 2024, overall mortality rates increased significantly, with an AAPC of 2.09% (95% CI: 0.95 to 3.24; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 0.49% (95% CI: 0.15 to 0.84; $p = 0.007$). An increase was observed between 2018 and 2021, during which mortality rates increased by 25.44% (95% CI: 14.59 to 37.32; $p < 0.001$). Subsequently, mortality rates significantly declined between 2021 and 2024, with an APC of – 8.21% (95% CI: –11.48 to – 4.81; $p < 0.001$).

In the West region, AAMRs increased from 0.86 in 1999 to 1.80 in 2024. Between 1999 and 2024, mortality rates demonstrated the largest overall increase among all census regions, with an AAPC of 2.48% (95% CI: 1.00 to 3.98; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 1.72% (95% CI: 1.25 to 2.20; $p < 0.001$). An increase was observed between 2018 and 2021, with an APC of 23.79% (95% CI: 10.13 to 39.14; $p = 0.001$). Thereafter, mortality rates significantly declined from 2021 to 2024, with an APC of – 11.08% (95% CI: –15.27 to – 6.67; $p < 0.001$) (Fig. 3, **Supplementary Tables 3 and 8**).

3.5. Stratified by Age

Among individuals aged 25–44 years, AAMRs increased from 0.15 in 1999 to 0.21 in 2024. Between 1999 and 2024, mortality rates showed a non-significant overall increase, with an AAPC of 1.28% (95% CI: –3.60 to 6.41; $p = 0.614$). From 1999 to 2018, mortality rates increased significantly at an APC of 1.81% (95% CI: 0.67 to 2.96; $p = 0.004$). Between 2018 and 2021, mortality rates showed a non-significant increase (APC: 25.09%; 95% CI: –14.83 to 83.73; $p = 0.237$). Subsequently, mortality rates

significantly declined between 2021 and 2024, with an APC of -20.66% (95% CI: -35.35 to -2.62 ; $p = 0.029$).

Among individuals aged 45–64 years, AAMRs increased from 0.81 in 1999 to 1.41 in 2024. Between 1999 and 2024, overall mortality rates increased significantly, with an AAPC of 1.94% (95% CI: 0.38 to 3.53 ; $p = 0.015$). From 1999 to 2018, mortality rates increased significantly at an APC of 0.97% (95% CI: 0.51 to 1.44 ; $p < 0.001$). A further increase was observed between 2018 and 2021, with an APC of 25.37% (95% CI: 10.68 to 42.02 ; $p = 0.001$). Thereafter, mortality rates significantly declined from 2021 to 2024, with an APC of -11.94% (95% CI: -16.43 to -7.20 ; $p < 0.001$).

Among individuals aged 65 years and older, AAMRs increased from 3.71 in 1999 to 6.64 in 2024. Between 1999 and 2024, mortality rates increased significantly, with an AAPC of 2.07% (95% CI: 1.09 to 3.07 ; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 0.56% (95% CI: 0.26 to 0.86 ; $p < 0.001$). A further increase was observed between 2018 and 2021, with an APC of 22.37% (95% CI: 13.22 to 32.26 ; $p < 0.001$). Subsequently, mortality rates significantly declined between 2021 and 2024, with an APC of -6.43% (95% CI: -9.51 to -3.25 ; $p < 0.001$) (Fig. 4, **Supplementary Tables 4 and 8**).

3.6. Stratified by Urbanization

In metropolitan areas, AAMRs increased from 1.04 in 1999 to 1.85 in 2020. Between 1999 and 2020, mortality rates increased significantly, with an AAPC of 2.34% (95% CI: 1.98 to 2.70 ; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 0.64% (95% CI: 0.48 to 0.80 ; $p < 0.001$). A further increase was observed between 2018 and 2020, with an APC of 20.05% (95% CI: 15.68 to 24.58 ; $p < 0.001$).

In non-metropolitan areas, AAMRs increased from 1.30 in 1999 to 2.70 in 2020. Between 1999 and 2020, overall mortality rates increased significantly, with an AAPC of 3.32% (95% CI: 2.28 to 4.37 ; $p < 0.001$). From 1999 to 2018, mortality rates increased significantly at an APC of 1.10% (95% CI: 0.70 to 1.51 ; $p < 0.001$), followed by a further increase between 2018 and 2020, with an APC of 26.96% (95% CI: 13.96 to 41.44 ; $p < 0.001$) (Fig. 5, **Supplementary Tables 5 and 8**).

3.7. Stratified by Place of Deaths

Most deaths occurred in inpatient medical facilities ($n = 38,572$), followed by deaths at home ($n = 17,237$) and outpatient/emergency room settings ($n = 11,269$). Nursing homes or long-term care facilities accounted for 9,357 deaths, while hospice facilities contributed 2,851 deaths. Smaller proportions of deaths occurred in other locations ($n = 2,190$), were classified as dead on arrival ($n = 518$), had an unknown place of death ($n = 141$), or occurred in medical facilities with status unknown ($n = 43$) (Fig. 6, **Supplementary Table 6**).

3.8. Stratified by States

Considerable geographic variation in AAMRs was observed across U.S. states during both study periods. Between 1999 and 2020, the highest AAMRs were reported in the District of Columbia (2.36), Mississippi (2.08), Kentucky and Maryland (1.78 each), whereas Hawaii (0.62), Nevada (0.64), and Maine (0.71) reported the lowest rates (Fig. 7, **Supplementary Table 7**).

During 2021–2024, AAMRs were higher than in 1999–2020 across most states. The District of Columbia continued to report the highest AAMR (4.29), followed by Mississippi (4.11), Maryland (3.81), South Carolina (3.77), and Wyoming (3.63). In contrast, Maine (0.36), Alaska (0.86), and Connecticut (1.03) demonstrated the lowest mortality rates during this period (Fig. 8, **Supplementary Table 7**).

Central Illustration. Overview of temporal trends, demographic and geographic disparities in mortality involving pulmonary embolism and diabetes mellitus among U.S. adults aged ≥ 25 years in the United States, 1999–2024

4. Discussion

In this retrospective CDC WONDER multiple-cause-of-death analysis, we examined PE-related mortality among U.S. adults aged ≥ 25 years with DM from 1999 to 2024. A total of 82,180 deaths were recorded, and the overall AAMR increased significantly from 1.08 to 1.88 per 100,000. Mortality rose modestly from 1999 to 2018, accelerated sharply from 2018 to 2021, and declined significantly from 2021 to 2024. Stratified analyses showed higher and faster-rising AAMRs among males than females, persistently highest AAMRs among Black or African American individuals, the greatest absolute burden among adults aged ≥ 65 years, and higher rates in non-metropolitan than metropolitan areas through 2020. Regionally, the South had the highest AAMR by 2024, while the West showed the largest relative increase. State-level mortality was highest in the District of Columbia and Mississippi across both periods, with additional high-burden states including Kentucky, Maryland, South Carolina, and Wyoming. These findings indicate a rising but heterogeneous PE- and DM-related mortality burden (**Central illustration**).

PE remains a major cardiovascular emergency in the U.S. Approximately 900,000 people are thought to be affected by PE each year (22), and reported occurrence increased from 0.20% in 2016 to 0.35% in 2021 (23). Acute pulmonary hypertension secondary to PE can rapidly lead to right-sided heart failure, cardiogenic shock, respiratory failure, and death (24). PE is therefore among the most clinically important cardiovascular conditions, with many deaths occurring within the first few hours of symptom onset (24). The co-occurrence of PE or venous thromboembolism (VTE) with diabetes is increasingly relevant, consistent with rising cardiovascular mortality among young adults with comorbid diabetes (25). Diabetes has also been associated with higher PE mortality, particularly among females, suggesting that DM may both increase thrombotic risk and worsen outcomes after PE (11). Diabetic ketoacidosis has additionally been identified as an underlying and contributing factor (26).

Several mechanisms may contextualize these findings. PE pathogenesis reflects Virchow's triad venous stasis, hypercoagulability, and endothelial injury, and most emboli arise from thrombi originating in deep

veins of the lower extremities (27). Obesity, which is closely associated with DM, is an important risk factor for VTE (28). Hyperglycemia is linked with increased procoagulant factors and promotes advanced glycation end-products, receptor for advanced glycation end-products activation, oxidative stress, inflammation, NETosis, and a hypercoagulable state (28). Hyperglycemia has also been associated with worse PE outcomes, including recurrence or death, potentially through platelet activation (29), and type 2 DM is associated with higher plasminogen-activator inhibitor 1 levels, impairing fibrinolysis (30). Sex-related risk patterns may also contribute. Taller stature has emerged as a VTE risk factor in both sexes, with middle-aged men showing greater risk before adjustment for body height (31). The MEGA case-control study similarly reported an association between increasing height and VTE risk, particularly among men (32). In our analysis, males had higher AAMRs and greater overall increases than females; however, this ecological finding should not be attributed to body height alone. The post-2021 decline may reflect changes in risk exposure, reporting, and clinical management. Updated diabetes guidelines emphasizing cardiovascular risk reduction and self-management may have contributed to improved glycemic control and lower thrombotic risk (33). Advanced imaging and artificial intelligence-based assessment of markers such as RV/LV ratio may support earlier PE detection (34). Advances in PE management, including suction thrombectomy (35), and preventive strategies such as statin use (36), may also have improved outcomes, although these mechanisms cannot be confirmed in CDC WONDER data.

The sharp increase from 2018 to 2021 coincided with the COVID-19 era and was consistent across most subgroups. A nationwide analysis reported a 15.5% rise in diabetes-related age-adjusted cardiovascular mortality during the first pandemic year, particularly among individuals aged < 55 years and Hispanic populations (37). SARS-CoV-2 infection is strongly linked to thrombosis, with affected patients demonstrating increased fibrin degradation products and D-dimer levels and reduced antithrombin levels (38). PE has been described as the most common thrombotic manifestation among patients with COVID-19 pneumonia (39). ICU care, hospitalizations, central venous catheterization, healthcare disruption, and immobilization during severe illness may have further increased thrombotic risk. COVID-19 also produces systemic inflammation with elevated mediators such as IL-6, which can promote thrombosis and increase VTE risk (40). These pathways may explain the pronounced mortality acceleration during 2018–2021, while the subsequent decline may reflect reduced pandemic-related disruption and improved acute care delivery.

Marked racial and ethnic disparities were observed. NH Black or African American individuals consistently had the highest AAMRs, whereas NH White individuals had the lowest baseline rates but experienced significant long-term increases; Hispanic and NH Black individuals showed non-significant overall AAPCs despite substantial increases during 2018–2021. Higher diabetes prevalence among NH Black and Hispanic populations than NH White populations may partly explain these differences (41). Social determinants of health, including poverty, lower income, lower educational attainment, and lack of insurance coverage, may contribute to poorer outcomes and higher diabetes-related complications and mortality (41). Racial inequities in healthcare access and quality are also important, as racial and ethnic minority groups are less likely to receive guideline-concordant diabetes care (42). In PE specifically, a

multicenter cohort study reported higher odds of in-hospital mortality among NH Black and Hispanic patients and lower use of advanced therapies, including catheter-directed thrombolysis, among racial and ethnic minority groups, particularly women, compared with NH White men (43). These findings support equitable PE recognition, treatment, and diabetes care.

Age-stratified findings showed that adults aged ≥ 65 years had the highest absolute AAMRs throughout the study period, although significant long-term increases were also observed among adults aged 45–64 years. Among adults aged 25–44 years, the overall increase was not statistically significant, despite a significant rise from 1999 to 2018 and a decline after 2021. Prior studies have reported high rates of provoked and unprovoked PE in elderly populations, with DM among commonly reported comorbidities and substantial one-year mortality after thrombotic events (44). This burden may reflect the high prevalence of diabetes in older adults (45), along with age-related endothelial dysfunction, venous insufficiency, hospitalization, immobilization, disability, and multimorbidity (46). Aging has also been independently associated with VTE recurrence (47), and prolonged hospitalization and transient immobilization are recognized contributors to venous thrombosis in older adults (48).

Geographic heterogeneity was substantial. All census regions had significant overall increases, with the South showing the highest AAMR by 2024 and the West showing the largest relative increase. The 2018–2021 spike overlapped with the broad impact of COVID-19, during which U.S. COVID-19-related mortality between 2020 and 2021 was approximately 270 per 100,000 population and was highest in the Northeast (49). Our findings are consistent with prior work reporting higher PE and obesity-associated AAMRs in the South than in the West and Northeast (50). That study also identified the District of Columbia among the highest-burden areas and Maine among the lowest (50), paralleling our state-level findings. Regional differences may reflect variation in cardiovascular risk factors, physical inactivity, and body mass index, although diabetes prevalence has remained relatively stable across regions (51). Higher Southern mortality may also relate to greater uninsurance and medical financial burden despite the Affordable Care Act (52). Urban-rural differences were also evident. Existing literature reports higher PE-related deaths in urban areas but higher overall mortality in non-urban areas (53), consistent with our finding that non-metropolitan areas had higher AAMRs by 2020. Non-metropolitan hospitals may have lower use of thrombolytic therapies, while most PE admissions occur in urban hospitals (54). Higher comorbidity burden, limited healthcare access, poor mental healthcare availability, and constrained resources may further increase PE-related mortality in rural diabetic patients (55, 56). Diabetes mortality has improved less in noncore areas, particularly in the South, than in urban areas (57). Limited primary care access, lower income, and transportation barriers, including longer travel distances for medical care (58, 59), likely further contribute to these disparities.

Strengths and Limitations

This study used a large, nationally representative CDC WONDER dataset and assessed mortality over more than two decades across demographic and geographic strata. AAMRs and Joinpoint regression enabled standardized temporal assessment. However, death certificate data depend on ICD coding and

may be affected by misclassification, incomplete reporting, or under recognition of chronic conditions. The analysis cannot determine causality, PE severity, diabetes type or duration, glycemic control, body mass index, treatment strategies, or individual-level risk factors. Race/ethnicity analysis was limited to NH White, NH Black or African American, and Hispanic populations because other groups were suppressed in CDC WONDER due to small cell counts. Urbanization data were available only through 2020. As a multiple-cause-of-death analysis, these findings reflect co-documented PE and DM rather than confirmed clinical incidence.

Conclusion

our nationwide analysis of CDC WONDER data from 1999–2024 demonstrates an rise in age-adjusted mortality related to pulmonary embolism and diabetes mellitus, despite multiple periods of fluctuation. Marked disparities were observed across demographics, with the highest burden among males, adults aged ≥ 65 years, Black or African American individuals, and residents of the South. Temporal spikes during the COVID-19 era underscore the vulnerability of this population to external public health crises. These findings highlight the growing cardiovascular disease burden in diabetes and the urgent need for targeted preventive strategies, improved clinical management, and equitable healthcare access.

Declarations

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The authors report no relationships that could be construed as a conflict of interest

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Study Participants:

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The research is based on de-identified data and does not require the consent of the participants or ethics approval.

Availability of data and materials:

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS: **SM:** conceptualization, supervision, formal analysis, validation, visualization, writing–original draft, writing–review and editing; **GL:** conceptualization, project administration, software and formal analysis, visualization, writing–original draft, writing–review and editing; **KI:** methodology, investigation, validation, writing–original draft, writing–review and editing; **PK:** data curation, software analysis, methodology, visualization; **GL, JHJA:** data curation, resources, writing–original draft; **SH:** data curation, resources, writing–original draft; **FH:** investigation, methodology, resources; **VD:** editing, review, supervision **MH:** writing–review, supervision and editing, critical revision

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Figures

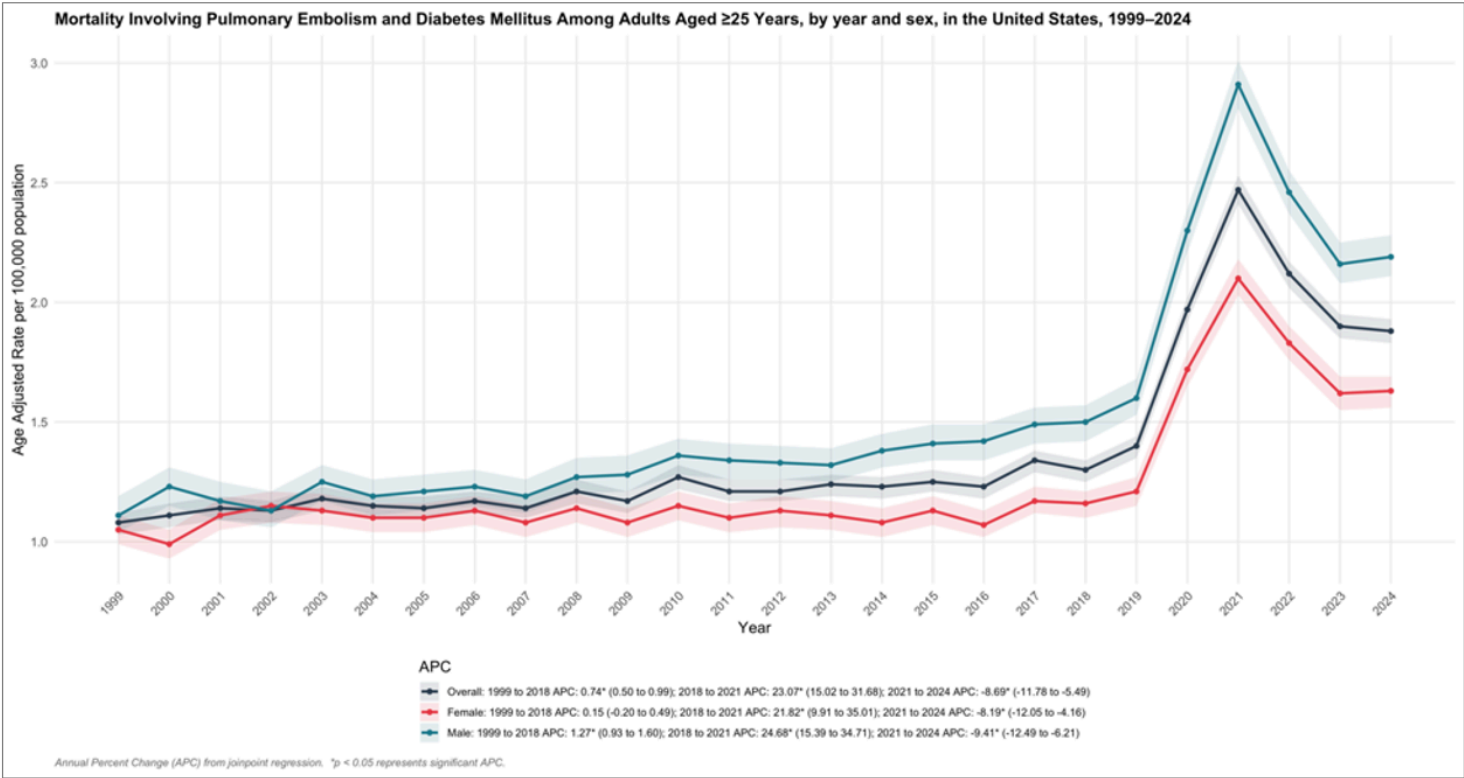


Figure 1

Overall and Sex-Stratified Age-Adjusted Mortality Rates (per 100,000 Population) for Mortality Involving Pulmonary Embolism and Diabetes Mellitus Among U.S. Adults Aged ≥25 Years, United States, 1999–2024.

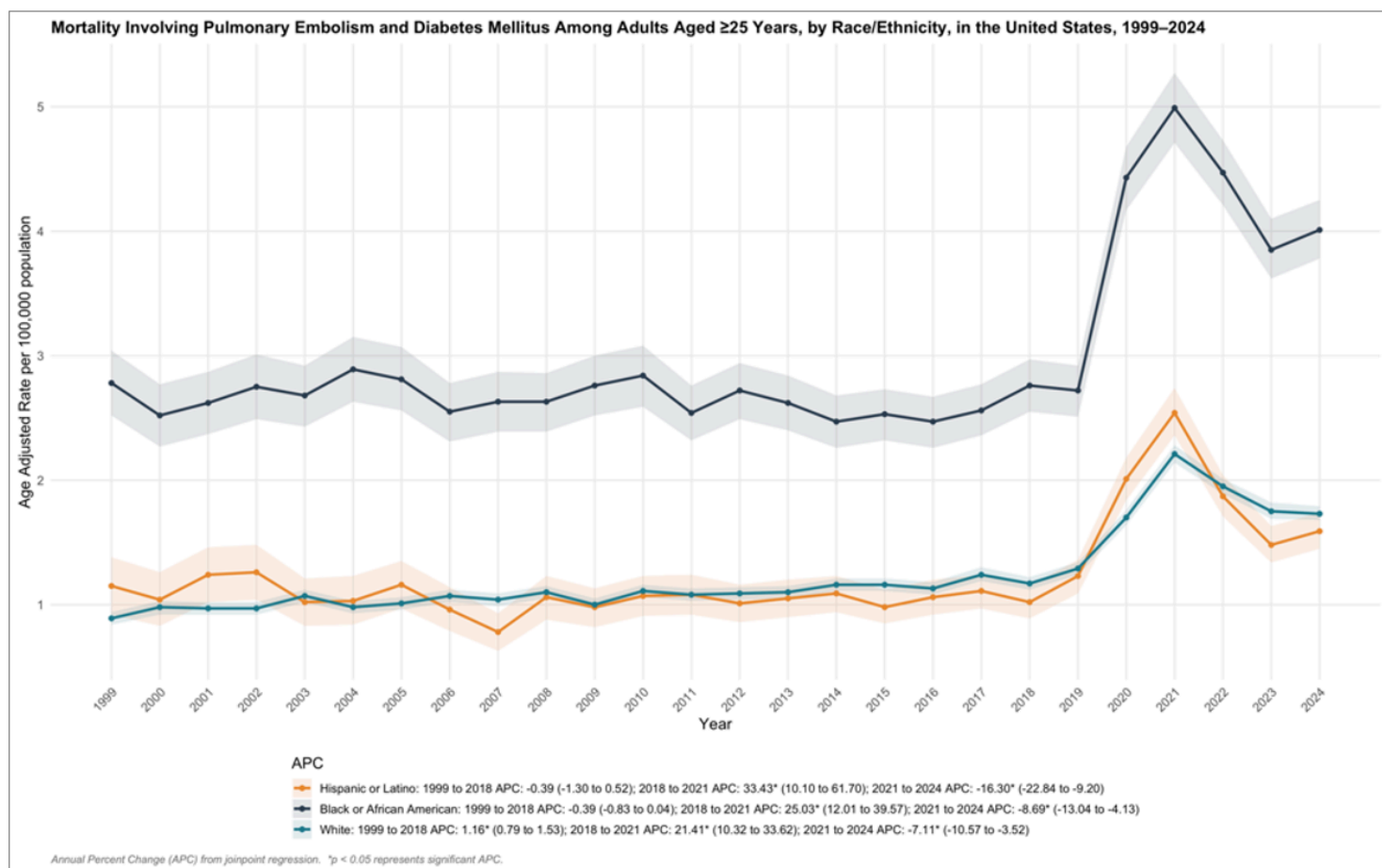


Figure 2

Race-Stratified Age-Adjusted Mortality Rates (per 100,000 Population) for Mortality Involving Pulmonary Embolism and Diabetes Mellitus Among U.S. Adults Aged ≥ 25 Years, United States, 1999–2024.

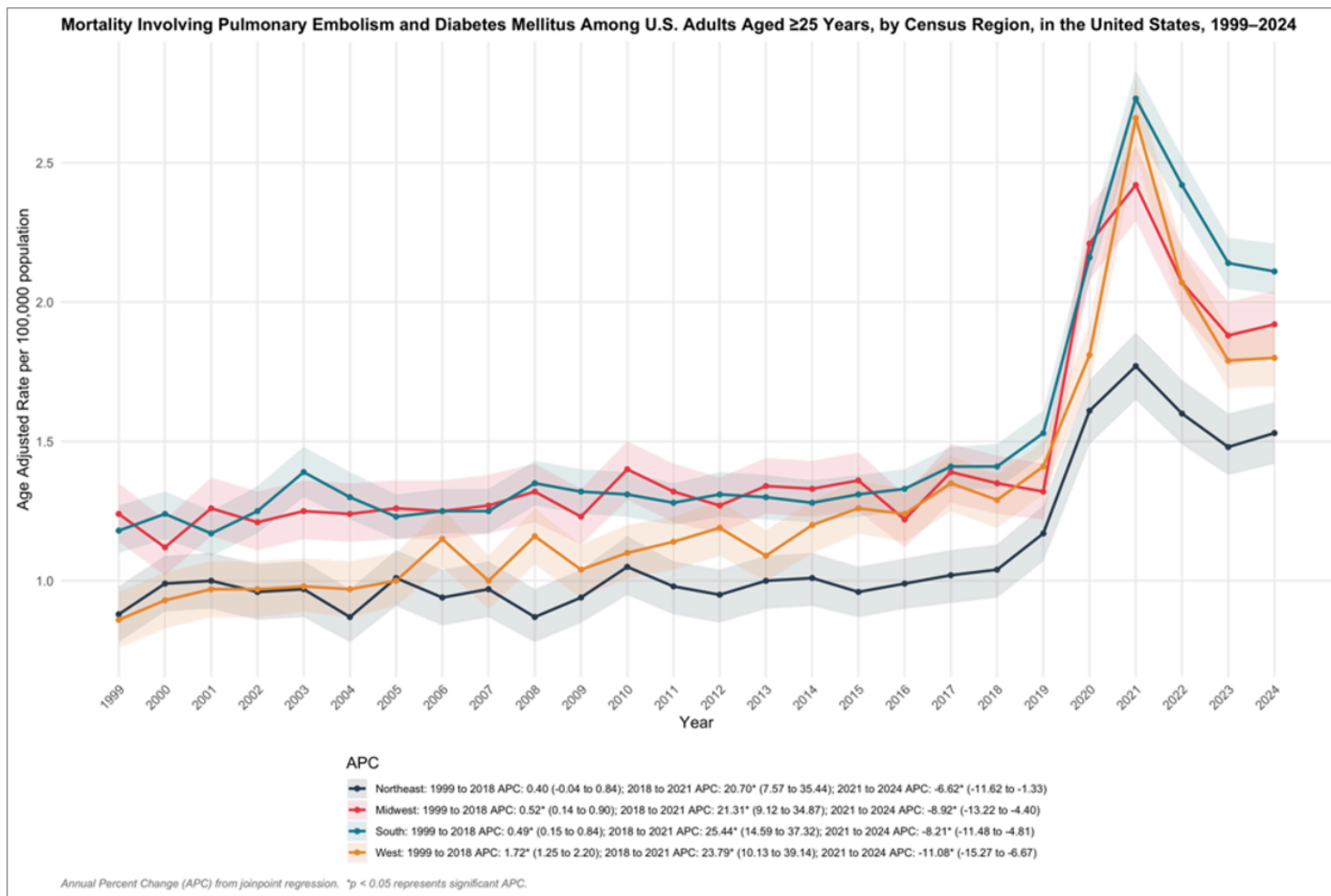


Figure 3

Census Region-Stratified Age-Adjusted Mortality Rates (per 100,000 Population) for Mortality Involving Pulmonary Embolism and Diabetes Mellitus Among U.S. Adults Aged ≥ 25 Years, United States, 1999–2024.

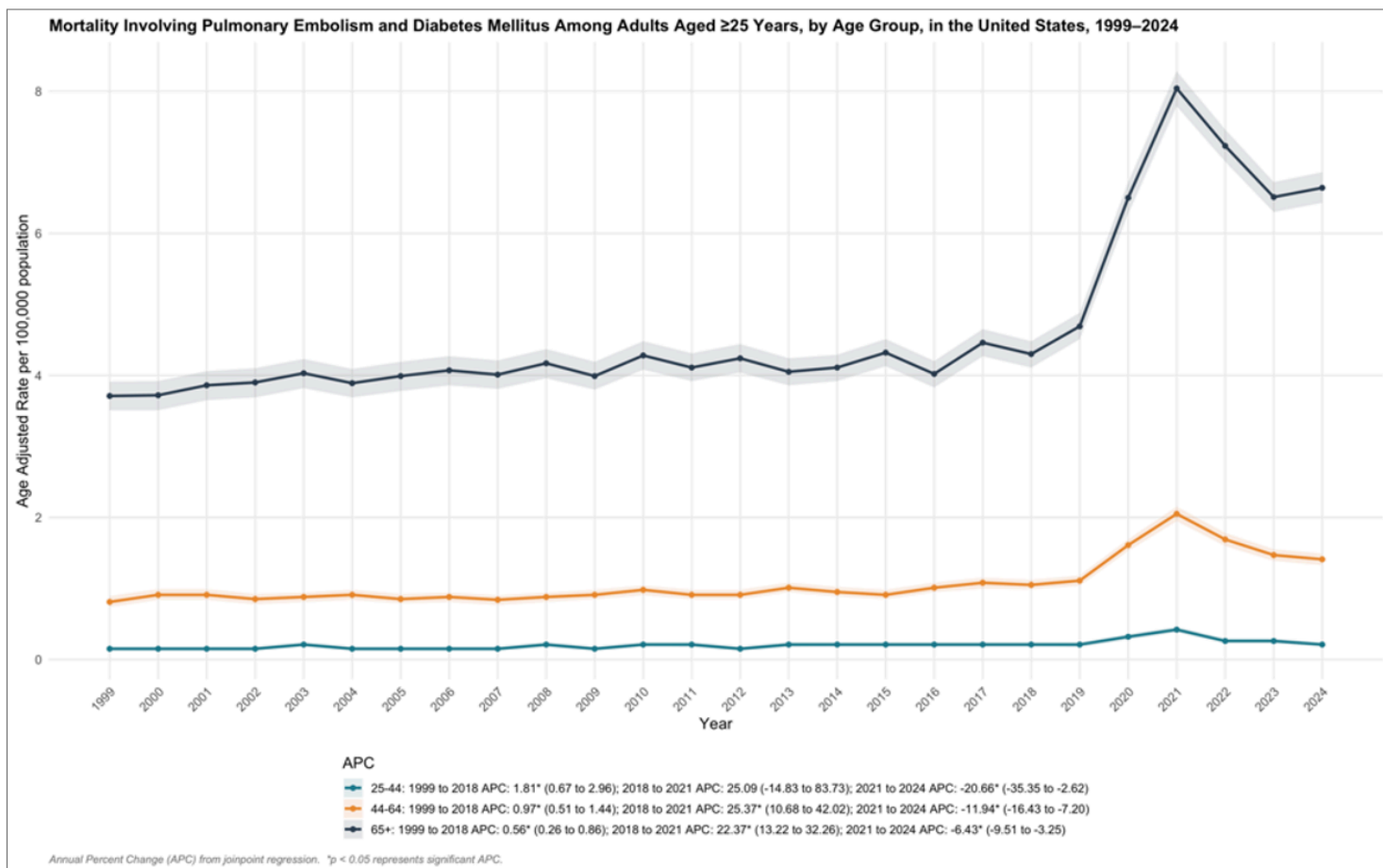


Figure 4

Age group-Stratified Age-Adjusted Mortality Rates (per 100,000 Population) for Mortality Involving Pulmonary Embolism and Diabetes Mellitus Among U.S. Adults Aged ≥25 Years, United States, 1999–2024.

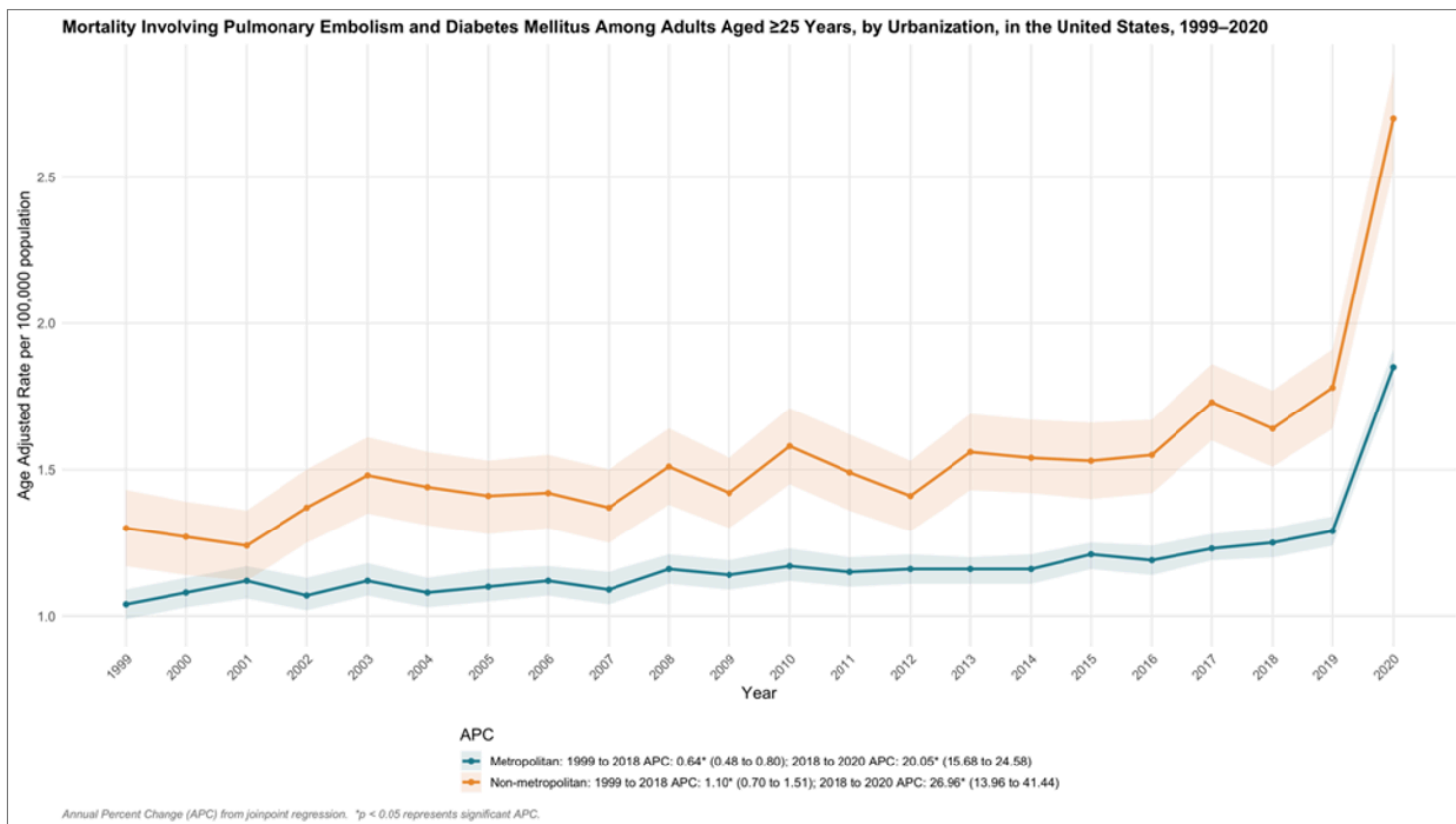


Figure 5

Urbanization-Stratified Age-Adjusted Mortality Rates (per 100,000 Population) for Mortality Involving Pulmonary Embolism and Diabetes Mellitus Among U.S. Adults Aged ≥ 25 Years, United States, 1999–2020.

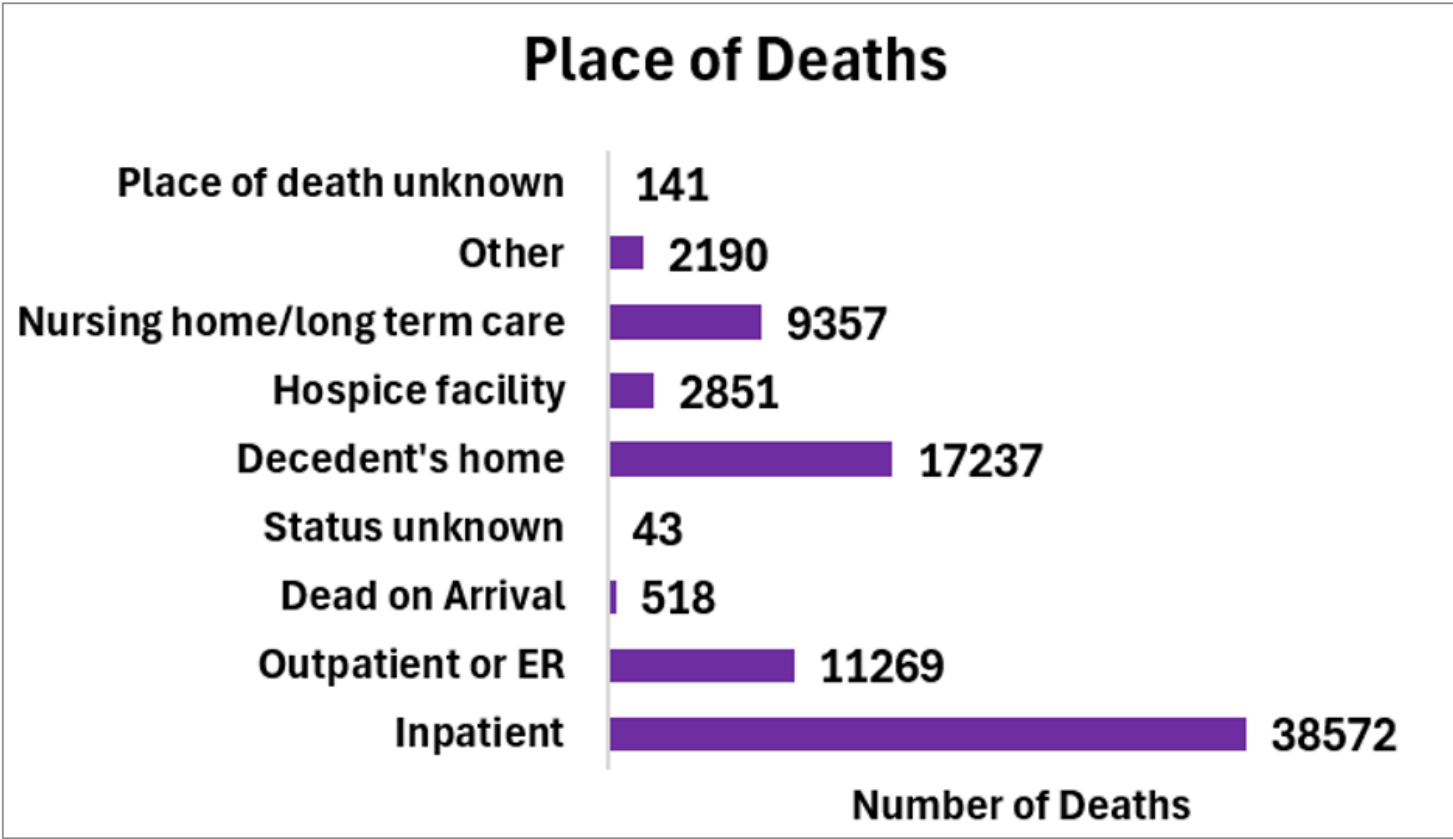


Figure 6

Distribution of place of death among decedents with mortality involving pulmonary embolism and diabetes mellitus in the United States, 1999–2024.

2021-2024

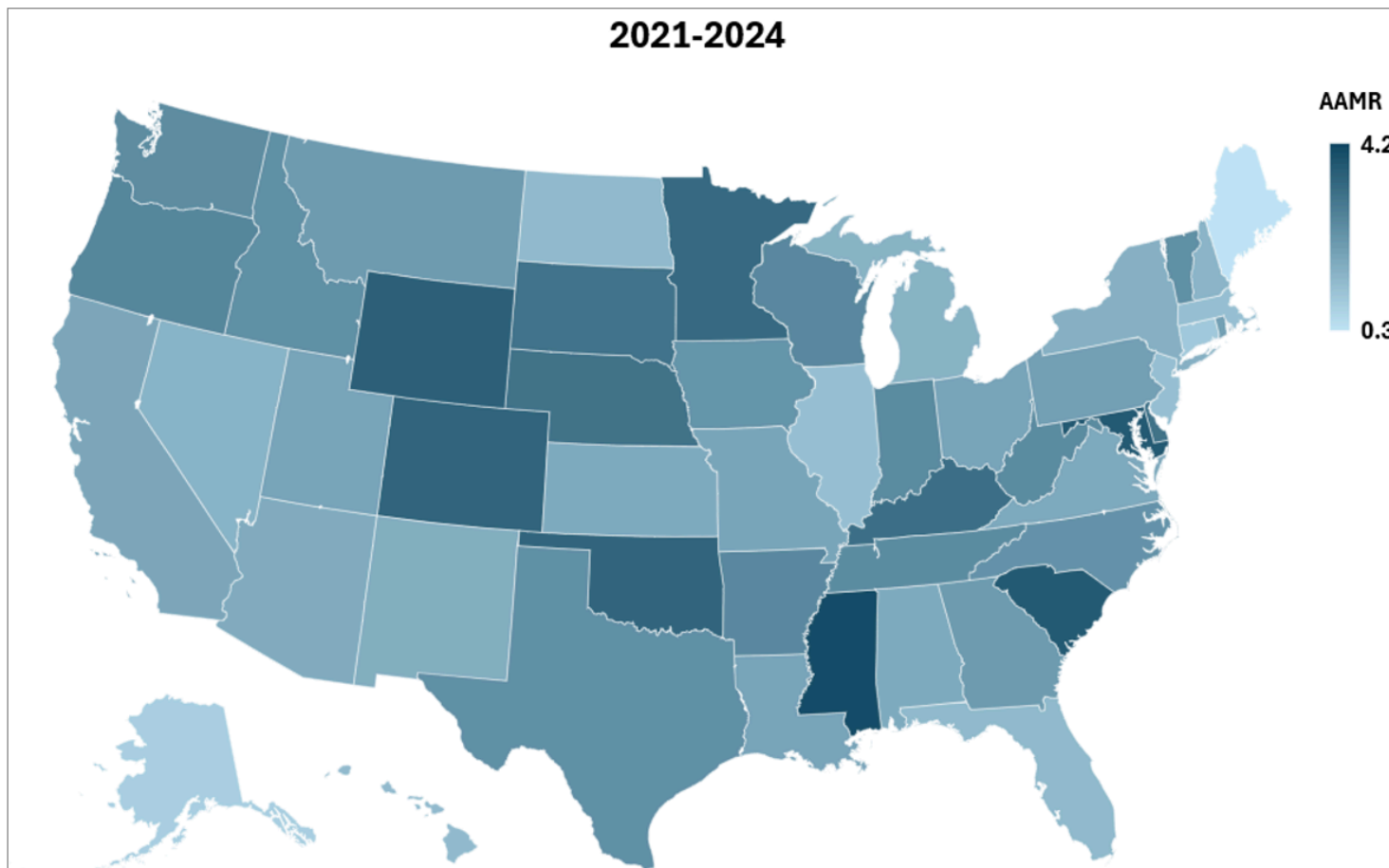


Figure 8

Geographic distribution of state-level age-adjusted mortality rates (AAMRs) for mortality involving pulmonary embolism and diabetes mellitus among U.S. adults aged ≥ 25 years, 2021–2024.

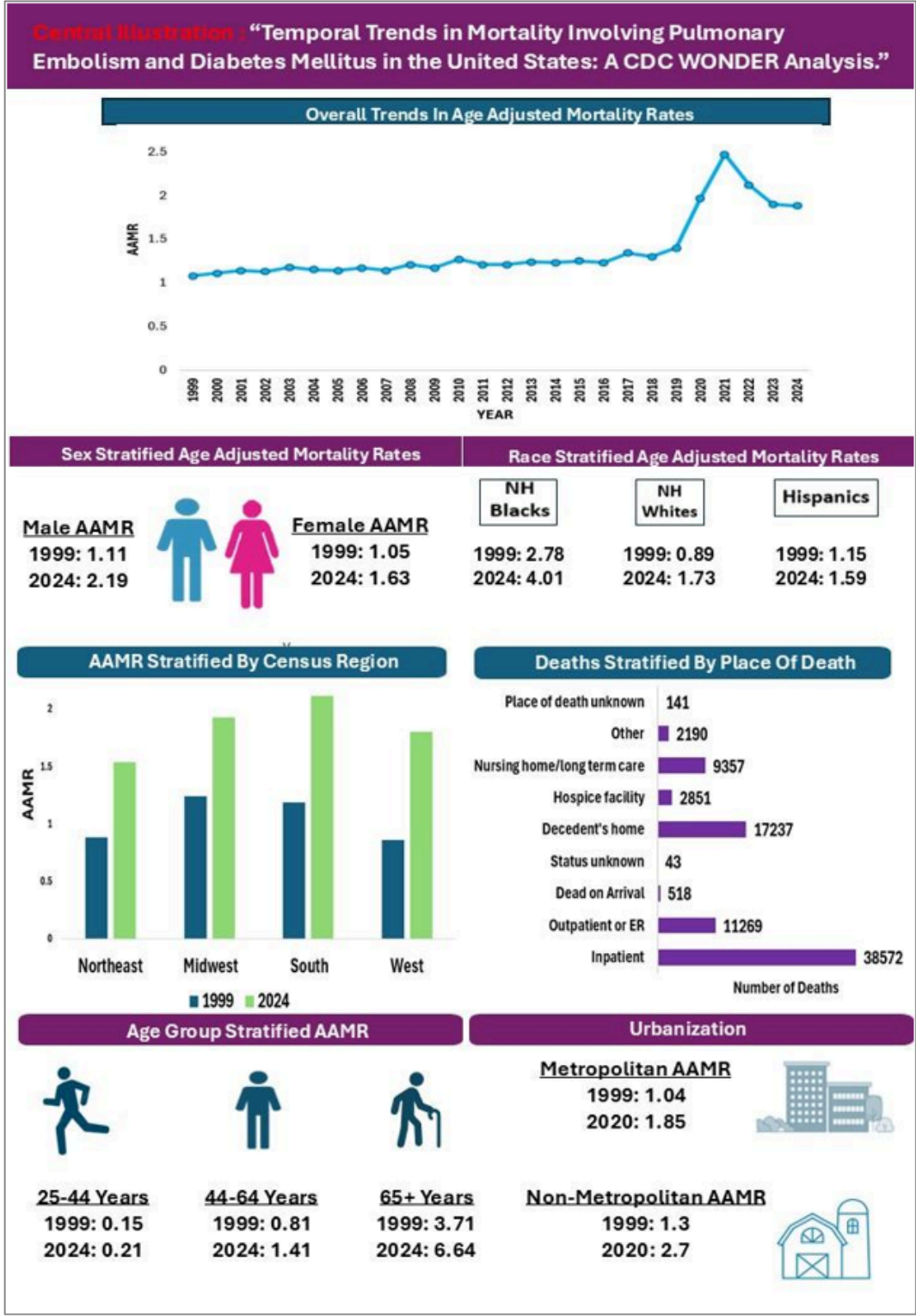


Figure 9

Central Illustration. Overview of temporal trends, demographic and geographic disparities in mortality involving pulmonary embolism and diabetes mellitus among U.S. adults aged ≥ 25 years in the United States, 1999–2024

Supplementary Files

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