Clinical research

Mortality from coexisting cancer and ischaemic heart disease in the United States: national trends from 1999 to 2023

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Abstract

Introduction: Cancer and ischaemic heart disease (IHD) are associated with an increased risk of mortality. This study aims to assess long-term mortality trends among adults with cancer and IHD in the US from 1999 to 2023.
Material and methods: The CDC-WONDER database was used to extract death certificate information for individuals aged 25 years and older with cancer and IHD. Age-adjusted mortality rates (AAMRs) were estimated per 100,000 individuals, and the annual percent change (APC) was determined using JoinPoint.
Results: From 1999 to 2023, cancer and IHD were associated with 65,692 deaths in the US. During this period, the AAMR increased from 1.03 in 1999 to 1.69 in 2023. The AAMR remained stable from 1999 to 2016 but rose significantly from 1.09 in 2016 to 1.64 in 2023, with an APC of 7.7% (95% CI: 6.55 to 9.15). Males had higher AAMR compared to females (2.2 vs. 1.3, respectively, in 2023). Among racial/ethnic groups, the highest mortality was observed in NH Blacks or African Americans and NH Whites (2.8 vs. 1.6 in 2023). Geographic variations were evident, with the Western region and urban areas having higher AAMRs.
Conclusions: We observed an overall increase in cancer and IHD mortality in the US over the study period, especially after 2016. Mortality was higher among males, NH Blacks, and NH Whites. Geographic disparities were observed, with higher AAMRs in the Western region and urban areas.

Key words: cancer, ischaemic heart disease, United States, mortality.

Introduction

Ischaemic heart disease (IHD) and cancer are both well-known to be the leading causes of mortality in the USA [1, 2]. Risk factors that can increase the likelihood of developing IHD include smoking, obesity, sedentary lifestyle, hyperlipidaemia, hypertension, and diabetes. These risk factors are also shared commonly with the development of cancer [3, 4].

Advances in the treatment of cancer have proven to increase survival rates in many cancers [5–7]. However, despite this progress, cardiovascular disease, namely IHD, has been a major cause of mortality amongst cancer survivors [8–10]. The association between these diseases is important to consider, especially how cancer increases the likelihood of IHD. Several anti-cancer drugs, such as tyrosine kinase inhibitors and platinum-based drugs, have been shown to cause cardiac ischaemia and atherosclerosis, leading to possible myocardial infarction [11]. Radiation-induced heart disease is also evident and can occur due to damaged vascular endothelium, manifesting as possible peripheral, coronary, and carotid artery disease [12].

Additionally, patients with malignancy are at risk of being in a prothrombotic state due to cancer cells activating the coagulation system via tissue factor and other pathways increasing VTE risk, which can then lead to prominent cardiovascular complications like IHD [13].

Despite substantial research on cancer and IHD association, few studies have comprehensively evaluated long-term mortality trends for patients with concomitant cancer- and IHD-related mortality. This study aims to address these important literature gaps by analysing cancer- and IHD-related mortality from 1999 to 2023. We also assess trends, demographic factors, and regional differences, which provide better insights on this vital topic. This can help guide policymakers and clinicians to improve patient care and spread awareness on this topic.

Material and methods

Study setting and population

This study examined cancer- and IHD-related mortality across the United States using data from the CDC WONDER (Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research) database. This database includes comprehensive death certificate data from all 50 states and the District of Columbia.

Mortality from IHD was identified using ICD-10 codes I20–I25, while cancer-related deaths were categorised under ICD-10 codes C00–D48. These codes are validated, and they have been used in previous published works [14–17]. The analysis encompassed all age groups between 1999 and 2023. Since this research utilised publicly available and de-identified government data, institutional review board approval was not required. To ensure methodological accuracy, the study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [18].

Data collection

Data on cancer- and IHD-related deaths, population sizes, and demographic characteristics (including age, sex, race/ethnicity, and regional details) were gathered for the period 1999–2023. The racial and ethnic groups analysed included non-Hispanic (NH) White, NH Black or African American, NH others (e.g. NH Asian or Pacific Islander, NH American Indian or Alaska Native), and Hispanic or Latino populations. These classifications align with prior research utilising CDC WONDER data derived from death certificates.

Mortality trends were further analysed by state, U.S. Census regions (Northeast, Midwest, South, and West), and urbanisation levels of counties. Counties were categorised as rural (micropolitan and noncore regions) or urban (large central metro, large fringe metro, medium metro, and small metro) using the 2013 National Center for Health Statistics Urban-Rural Classification Scheme [19]. Similar stratification has been used in earlier studies [20, 21].

Statistical analysis

Crude mortality rates (CMRs) and age-adjusted mortality rates (AAMRs) were calculated per 100,000 population. CMRs were obtained by dividing the total number of cancer- and IHD-related deaths by the population of the respective year. AAMRs were calculated by adjusting deaths to the 2000 U.S. standard population to enable comparison across years [22]. To identify trends in mortality rates, the Joinpoint Regression Program (Joinpoint V 5.1.0.0, National Cancer Institute) was used [23]. This software identifies significant changes in AAMRs and CMRs over time using log-linear regression models applied to intervals where changes occurred. Annual percentage changes (APCs) and 95% confidence intervals (CIs) were calculated to assess these trends, with Joinpoints indicating significant shifts. The Monte Carlo permutation test was applied to determine statistical significance, with APCs considered meaningful if the slope differed significantly from zero in a two-tailed *t*-test. Statistical significance was defined as $p < 0.05$.

Results

Overall

From 1999 to 2023, cancer and IHD accounted for 65,692 deaths in the US. During this period, the AAMR increased from 1.03 in 1999 to 1.69 in 2023. The AAMR remained stable from 1999 to 2016 but rose significantly from 1.09 in 2016 to 1.64 in 2023, with an APC of 7.70* (95% CI: 6.55 to 9.15; $p < 0.00001$) (Supplementary Table SI, Figure 1).

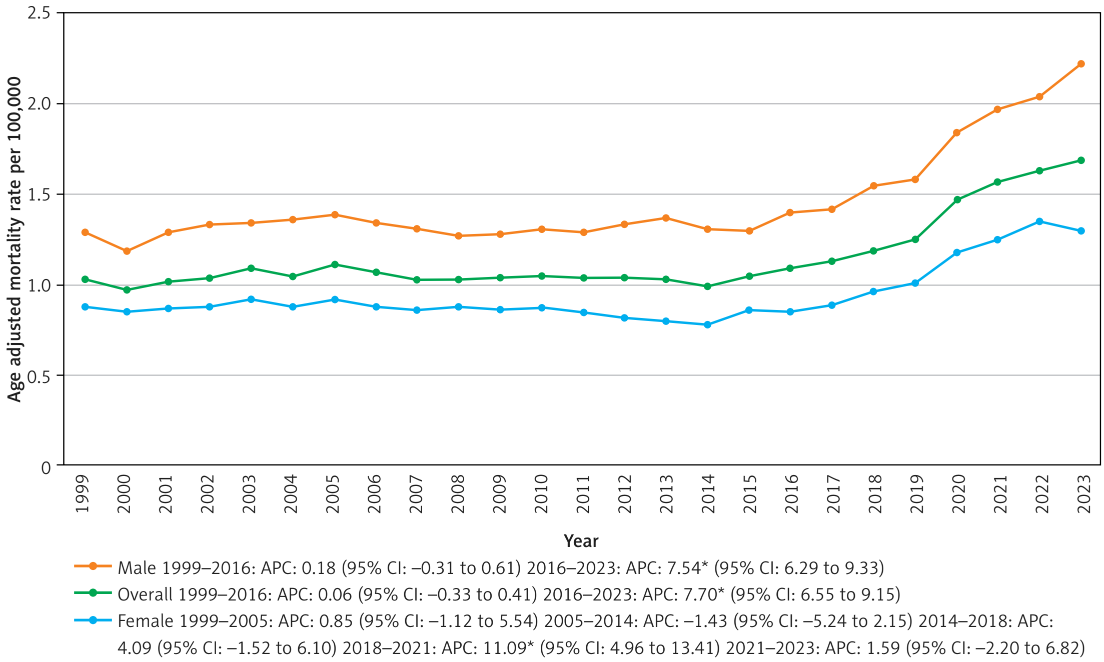

Figure 1. Overall and sex-stratified, age-adjusted mortality rates (AAMRs) per 100,000 individuals in the United States, 1999 to 2023

Cancer- and IHD-related AAMR stratified by sex

Throughout the study period, males consistently exhibited a notably higher AAMR compared to females. Among males, the AAMR remained unchanged from 1999 to 2016 but then increased significantly, rising from 1.4 in 2016 to 2.22 in 2023, with an APC of 7.54* (95% CI: 6.29 to 9.33; p < 0.000001). For females, the trend remained stable between 1999 and 2018, followed by a significant increase from 0.96 in 2018 to 1.3 in 2021, with an APC of 11.09* (95% CI: 4.96 to 13.41; p = 0.015) (Supplementary Table SII, SIII).

Cancer- and IHD-related AAMR stratified by race/ethnicity

Over the study period, the highest AAMR was consistently observed in the NH Black or African American group and NH White group.

In the NH Black or African American population, the AAMR initially declined from 2.69 in 1999 to 1.93 in 2015 (APC = –1.46*; 95% CI: –2.33 to –0.77; p < 0.000001) but subsequently increased, reaching 2.87 in 2023 (APC = 4.34*; 95% CI: 2.75 to 6.82; p < 0.000001). For NH White populations, the AAMR remained stable from 1999 to 2016, followed by an increase from 0.98 in 2016 to 1.63 in 2023 (APC = 8.35*; 95% CI: 7.07 to 9.96; p < 0.01). Among the Hispanic or Latino group, the AAMR was stagnant from 1999 to 2014 but rose from 0.71 in 2014 to 1.14 in 2023 (APC = 4.90*; 95% CI: 3.44 to 7.45; p < 0.000001). Lastly, for the NH Other population, the AAMR initially declined from 0.99 in 1999 to 0.64 in 2018 (APC = –1.39*; 95% CI: –4.37 to –0.06; p = 0.040) before increasing to 1.06 in 2023 (APC = 8.42*; 95% CI: 2.32 to 22.91; p = 0.002) (Supplementary Table SIV, Figure 2).

Cancer- and IHD-related AAMR stratified by geographical region

Statewide

Throughout the study period, significant statewide variation in cancer- and IHD-related mortality was observed. From 1999 to 2020, states falling within the top 90th percentile for mortality rates included the District of Columbia, Mississippi, Oklahoma, California, and Vermont, while those in the bottom 10th percentile were Delaware, Massachusetts, New Mexico, Alaska, and Utah. In the subsequent period from 2021 to 2023, the states with the highest mortality rates were Oklahoma, Mississippi, District of Columbia, and North Dakota, whereas Illinois, New Mexico, Connecticut, New Hampshire, and Alaska ranked in the lowest 10th percentile (Supplementary Table SV).

Census region

From 1999 to 2023, the highest cancer- and IHD-related mortality rates were recorded in the West, followed by the South, Midwest, and Northeast regions.

In the Northeast, the AAMR rose from 0.86 in 1999 to 1.11 in 2017 (APC = 0.96*; 95% CI: 0.04 to 1.53; p = 0.047) and further increased to 1.52

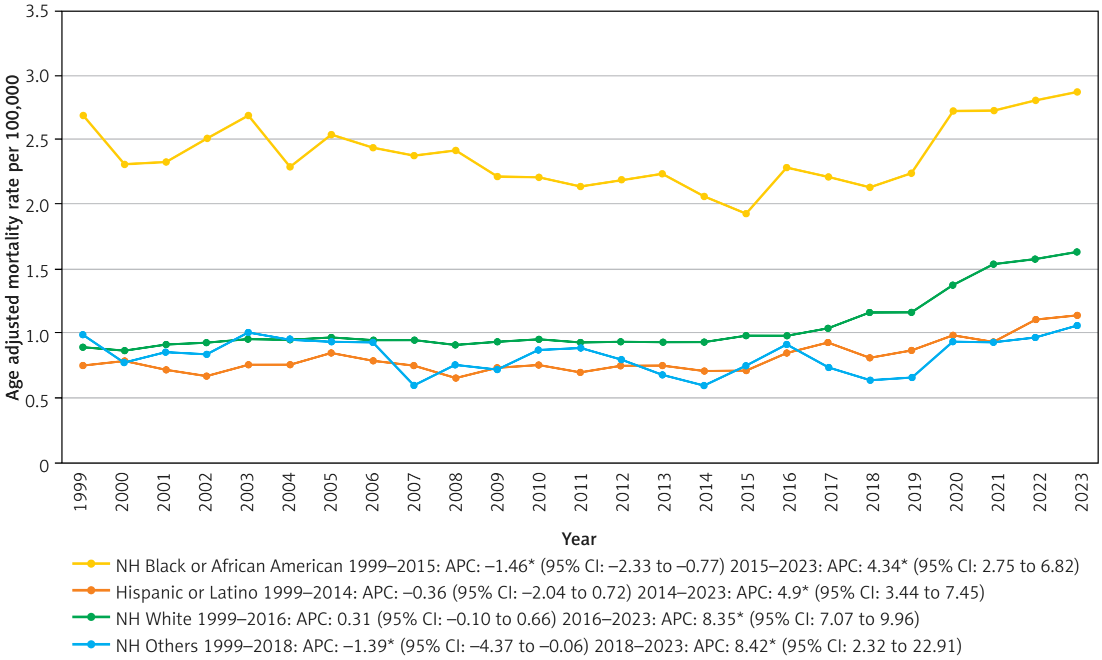

Figure 2. Age-adjusted mortality rates (AAMRs) per 100,000 individuals stratified by race/ethnicity in the United States, 1999 to 2023

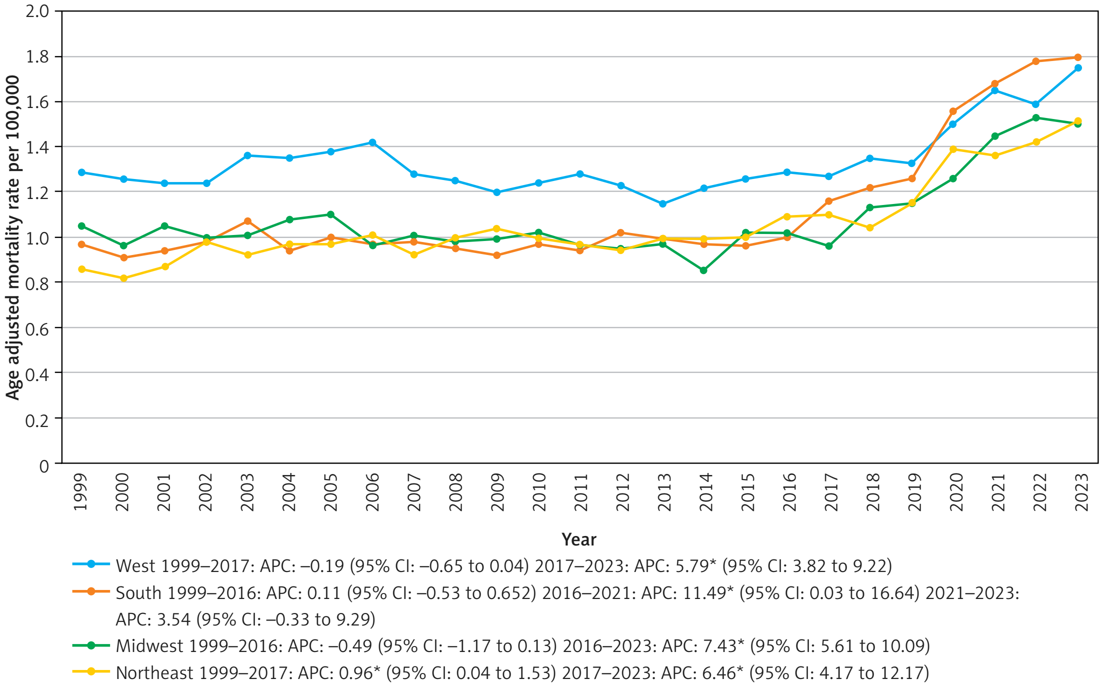

Figure 3. Age-adjusted mortality rates (AAMRs) per 100,000 individuals stratified by census region in the United States, 1999 to 2023

in 2023 (APC = 6.46*; 95% CI: 4.17 to 12.17; $p < 0.000001$). In the South, the AAMR remained stable from 1999 to 2016, then increased from 1.0 in 2016 to 1.68 in 2021 (APC = 11.49*; 95% CI: 0.03 to 16.64; $p = 0.050$), followed by stagnation from 2021 to 2023. For the Midwest, the AAMR was stagnant from 1999 to 2016 but rose from 1.02 in 2016 to 1.5 in 2023 (APC = 7.43*; 95% CI: 5.61 to 10.09; $p < 0.000001$). Lastly, for the West, the AAMR remained stable from 1999 to 2017, followed by an increase from 1.27 in 2017 to 1.75 in 2023 (APC = 5.79*; 95% CI: 3.82 to 9.22; $p < 0.000001$) (Figure 3, Supplementary Table SVI).

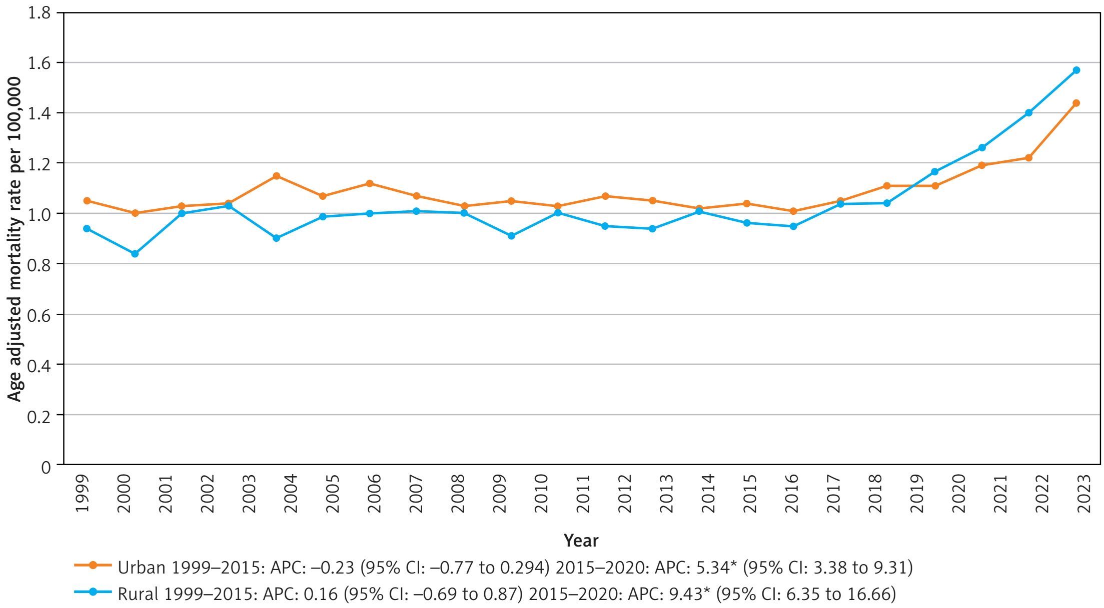

Figure 4. Age-adjusted mortality rates (AAMRs) per 100,000 individuals stratified by urbanisation in the United States, 1999 to 2020

**Data for urbanisation AAMRs was unavailable for 2021–2023.*

Urban-Rural

Over the study period, urban areas exhibited slightly higher AAMR compared to rural areas.

In urban areas, the AAMR remained stable from 1999 to 2015, followed by an increase from 1.05 in 2015 to 1.44 in 2020 (APC = 5.34*; 95% CI: 3.38 to 9.31; p < 0.000001). In rural areas, the AAMR was also stagnant from 1999 to 2015 but showed a sharper rise from 1.04 in 2015 to 1.57 in 2020 (APC = 9.43*; 95% CI: 6.35 to 16.66; p < 0.000001) (Figure 4, Supplementary Table SVII).

Discussion

This retrospective analysis of mortality data from the CDC WONDER database reveals several important findings regarding trends in cancer- and IHD-related deaths in the United States from 1999 to 2023. First, the overall AAMR for these conditions remained stable from 1999 to 2016 but experienced a significant upward trend thereafter, rising from 1.09 in 2016 to 1.64 in 2023. Second, sex-based disparities were evident, with males consistently exhibiting higher AAMRs than females. Third, racial and ethnic disparities were prominent, with non-Hispanic Black and non-Hispanic White populations experiencing the highest AAMRs compared to other groups. Additionally, significant geographical variations were observed, with states such as the District of Columbia, Mississippi, and Oklahoma consistently ranking among the highest in mortality rates, while states like New Mexico and Alaska were among the lowest. Furthermore, urban areas reported higher AAMRs than rural areas, although both settings experienced sharp increases in mortality rates after 2015.

In this study, we found an increase in the rates of cancer- and IHD-related mortality in the US after 2016. There are several factors that could have led to these findings. Potential pathways for IHD burden in cancer patients include shared underlying mechanisms such as systemic inflammation and oxidative stress [24, 25], as well as the pro-inflammatory and prothrombotic states often induced by cancer itself [26]. Additionally, cancer treatments, including chemotherapy and radiation, may contribute to IHD risk. Recent studies have shown a reversal in CVD mortality in the US, which could have led to the increased mortality observed in cancer patients [14, 27]. Additionally, the incidence of cancer is increasing in the US, including among young adults [28]. The period between 2019 and 2023 saw a notable surge in mortality rates and falls during the COVID-19 pandemic. This impacted critical health conditions, particularly patients with chronic diseases like cancer and IHD. In the US, the pandemic was closely linked to a marked increase in cancer- and IHD-related deaths because the virus worsened existing health issues [29–31]. The pandemic put an increased burden on healthcare systems worldwide during this time and led to significant disruptions in the delivery of medical care. In the U.S., patients with chronic medical conditions faced immense difficulties in accessing routine treatments, emergency services, and preventive care, which contributed to the worsening of their health outcomes [30]. Additionally, the pandemic intensified several cardiovascular risk factors, such as physical inactivity, poor dietary habits, and heightened stress levels, as lockdowns and social distancing measures altered daily lifestyles. These factors could have contributed to an increased mortality burden [32, 33].

We observed higher death rates among males compared to females. One potential explanation for this trend is the higher prevalence of IHD and cancer in men within the US [28, 34]. Moreover, studies have shown that men experience higher rates of CAD-related deaths than women [14]. Men are generally less likely than women to adopt preventive health behaviours and tend to utilise healthcare services less frequently [35]. NH Blacks had the highest mortality, which aligns with previous research showing that NH Blacks had higher and continuously increasing mortality rates for cancer, IHD, and obesity [14, 28, 36]. The differences in mortality across various regions can be attributed to variations in population demographics, the distribution of cancer risk factors, early detection efforts, and disparities in healthcare access, which vary significantly throughout the US [37]. State-level policies play a critical role in shaping health outcomes by regulating the availability and cost of health insurance options, such as those offered through Medicaid [38]. Notably, the 10 states in the South and Midwest that have chosen not to expand Medicaid eligibility report the highest cancer mortality rates and the lowest life expectancy [39, 40]. Beyond insurance, states also influence healthcare through legislation, programs, and regulations that affect the distribution of healthcare providers, particularly in underserved rural areas. Additionally, state-funded initiatives, such as Delaware's successful decade-long effort to eliminate racial disparities in cancer outcomes, demonstrate the impact of targeted policies on improving public health [41].

Our findings should be reconciled with recent population-level data from Rana *et al.* [2], who reported continued declines in US age-adjusted IHD mortality through 2024. The two analyses are complementary rather than contradictory: Rana *et al.* measured IHD as the underlying cause of death in the general population, whereas we captured the much smaller intersection cohort with both cancer and IHD recorded on death certificates. This intersection AAMR can rise even as overall IHD mortality falls, driven by the expanding population of cancer survivors at sustained ischaemic risk [8], broadening use of cardiotoxic therapies, the synergy of cancer-associated inflammation and prothrombotic state with conventional risk factors [24, 25], and the disproportionate pandemic-era impact on multimorbid patients. Our results thus identify a high-risk subgroup in whom population-level progress against IHD has not been achieved.

This study has several limitations that should be considered. We used the CDC WONDER database, which sources mortality data primarily from death certificates, raising concerns about potential misclassification. For instance, deaths attributed to conditions such as cancer or IHD may have been inaccurately recorded. There is also a risk of missing data if the treating physician does not list IHD and cancer as contributing causes of death. Furthermore, the database does not include critical clinical information, such as the severity of diseases, the presence of comorbidities, or details about treatments received, which restricts the ability to thoroughly analyse mortality trends. Important individual-level factors, including socioeconomic status, access to healthcare, and lifestyle behaviours, are also absent from the dataset. Although adjustments were made to account for variations in population age structure, these may not fully capture shifts in healthcare practices over time or changes in risk factors that could influence outcomes.

In conclusion, the study shows a notable increase in AAMR after 2016, with men, NH Black, and NH White populations bearing the highest burden. Geographic variations further highlight the impact of regional healthcare disparities, with states like Mississippi and Oklahoma reporting elevated mortality rates. These findings emphasise the need for targeted public health interventions to address rising mortality trends, reduce disparities, and improve outcomes across diverse populations and regions.

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Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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