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Mortality trends in Ischemic heart diseases and new infectious triggers (Influenza & Pneumonia), A CDC Wonder Analysis (1999-2020)

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Abstract

Background: The risk for ischemic heart disease increases after contracting pneumonia and influenza. This association poses major clinical challenges and complicates management. This study quantified and analyzed mortality trends in ischemic heart disease and infectious triggers (pneumonia+influenza) with attention to disparities by sex, race/ethnicity, region, state, and urban-rural status.

Methods: We used the CDC WONDER multiple-cause mortality database (1999-2020) to find Age-adjusted mortality rates (AAMRs) per 100,000 among individuals aged 15 and older, with 95% confidence intervals (CIs), calculated across demographic, geographic, and temporal variables using ICD-10 codes. Joinpoint regression identified statistically significant ($p < 0.05$) trend changes and annual percent changes (APCs).

Results: A total of 567,770 deaths occurred between 1999 and 2020, primarily in inpatient medical facilities and nursing homes. The overall age-adjusted mortality rate (AAMR) declined from 17.58 in 1999 to 10.35 in 2020, with significant reductions through 2018 followed by a sharp increase thereafter. Males consistently had higher AAMRs than females, while White and non-Hispanic populations and nonmetropolitan areas exhibited the highest mortality rates. West Virginia and Rhode Island had the highest state-level AAMR. At the regional level, the Northeast exhibited the highest AAMR. Across all demographic and geographic subgroups, mortality trends reversed after 2018, indicating worsening outcomes in recent years.

Conclusions: From 1999 to 2018, mortality rates declined but increased sharply after 2018. Persistent disparities were observed across sex, race/ethnicity, geography, and urban-rural status. These findings underscore the need for targeted public health strategies to reduce mortality and narrow disparities among at risk populations.

INTRODUCTION

Cardiovascular diseases still remain the leading cause of death, with ischemic heart disease being most prevalent with significant morbidity [1]. Ischemic heart disease occurs when the blood flow to the heart is blocked or reduced. It leads to shortness of breath, pain and discomfort in the chest, jaw, shoulder, back, or arms if ischemia is severe, heart attack or death occurs. Risk factors for ischemic heart disease include hypertension, smoking, obesity, dyslipidemia, diabetes, and physical inactivity. In addition to these factors, growing evidence indicates that respiratory diseases like influenza and pneumonia may be triggers for acute cardiac events. Previous studies have suggested an association between influenza and acute myocardial infarction [2]. Unlike the common cold, Pneumonia and Influenza can cause severe illness, pneumonia, or death, particularly in high-risk groups. It affects millions of patients every year. But there are also a number of studies proving that the risk of Acute myocardial infarction (AMI) and stroke is increased not only in bacterial pneumonia but also in viral infections, especially influenza [3]. AMI risks have been shown to be significantly raised during days 1–3 after acute respiratory infection [4]. Which is why vaccination for influenza has shown to reduce the risk for acute myocardial infarction [5]. Influenza

and pneumonia are known to induce systemic inflammation, endothelial dysfunction, increase the chance for blood clots, and free up the atherosclerotic plaques in the vessels. Pneumonia may lead to a systemic inflammatory response inducing severe hypo-perfusion and multi-organ failure that may affect the flow of blood through the vessels [6]. Transient rises in cardiovascular morbidity are seen when seasonal respiratory infections are on the rise. By analyzing the CDC Wonder database and examining data collected from 1999 to 2020, this study aims to provide an understanding for the trends in ischemic heart disease and the role of influenza and pneumonia as acute triggers of serious cardiac events investigating the temporal patterns in IHD related deaths.

Materials and Methods

Study design and Population

We conducted an observational analysis using death records from the CDC WONDER Multiple Cause of Death database for the period 1999–2020 [7], focusing on individuals aged 15–85 + years in the United States. Mortality records were reviewed for cases in which both Ischemic heart disease and Infectious triggers (influenza and pneumonia) were listed among the causes of death. The 10th edition of the International Classification of Diseases (ICD-10) was used to identify relevant cases. Ischemic heart disease was classified under I20-I25 codes. Infectious triggers were classified under J09-J18 codes [8]. Deaths were included only if both ischemic heart diseases and infections (influenza and pneumonia) codes appeared; those without both codes were excluded. Because this study used publicly available, de-identified government data, Institutional Review Board approval was not required.

Data abstraction:

The CDC WONDER dataset includes information on sex, race/ethnicity, urban-rural classification, region, state, age group, and place of death [7]. Sex was classified as male or female based on death certificate records. Race/ethnicity followed the Office of Management and Budget (1997) standards: Hispanic or Latino, non-Hispanic (NH) White, NH Black or African American, NH American Indian or Alaska Native, and NH Asian or Pacific Islander. Urban-rural status was defined according to the National Center for Health Statistics (2013) scheme, which classifies urban areas as large metropolitan regions (≥ 1 million population) or medium/small metropolitan regions (50,000-999,999 population). Rural areas are defined as non-metropolitan regions with < 50,000 population. Geographic regions were categorized by the US Census Bureau (2013) as West, Midwest, South, or Northeast. Place of death was grouped into healthcare settings (including outpatient, emergency department, inpatient, dead on arrival, or unknown status), home, hospice/palliative care, and nursing/extended care facilities. Data covered all 50 states and Washington, D.C. The mortality variables available through CDC WONDER have been widely used in prior epidemiologic studies and form the basis of the present analysis.

Statistical analysis

National trends were evaluated using age-adjusted mortality rates (AAMRs) per 100,000 individuals for Ischemic heart disease and Infectious triggers (influenza and pneumonia), adjusted for population age structure using the 2000 U.S. standard population as the reference. Mortality rates were analyzed for 1999–2020 by sex, race/ethnicity, age group, urban-rural status, state, and year. Temporal patterns in AAMRs were assessed using the Joinpoint Regression Program (Version 5.3.0.0) [9], which applies log-linear regression models to identify statistically significant changes in trends. Annual percent changes (APCs) with 95% confidence intervals (CIs) were calculated, and trends were classified as increasing or decreasing when the slope significantly differed from zero. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 567,770 deaths occurred between 1999 and 2020 with the majority occurring in Medical Facility – Inpatient (64.22%), and Nursing home/long term care (20.22%)(refer to supplementary table 1)

Overall Mortality Trends:

The overall age-adjusted mortality rate (AAMR) declined from 17.58 (95% CI: 17.41–17.76) in 1999 to 10.35 (95% CI: 10.24–10.46) in 2020. (Refer to Figure 1).

Mortality rates decreased significantly from 1999 to 2018 (APC: −6.45 95% CI: −6.94 to −5.94) but increased sharply between 2018 and 2020 (APC: 35.30 95% CI: 10.79 to 65.22), indicating worsening trends in recent years (refer to supplementary figure 1)

Figure 1: Overall trends in AAMRs for IHD and pneumonia + influenza

AAMRs: age-adjusted mortality rates,.

Overall Mortality Trends Stratified by Sex

In 1999, the AAMR among females was 13.49 (95% CI: 13.29–13.68), which declined to 6.45 (95% CI: 6.33–6.56) in 2020. Among males, the AAMR decreased from 24.44 (95% CI: 24.08–24.79) in 1999 to 15.60 (95% CI: 15.39–15.81) in 2020.

From 1999 to 2018, mortality rates declined significantly among both females (APC: −6.97 95% CI: −7.50 to −6.44) and males (APC: −6.40 95% CI: −6.93 to −5.86). However, from 2018 to 2020, mortality rates increased substantially in both groups, with a more prominent rise among males (APC: 39.98 95% CI: 14.48 to 71.16) compared to females (APC: 28.78 95% CI: 4.69 to 58.39).(refer to supplementary figure 2) Overall, males consistently exhibited higher AAMRs than females . Although both sexes experienced long-term declines in mortality, a marked reversal of trends occurred after 2018. (Refer to Figure 2, supplementary table 2).

Figure 2: Sex-specific trends in AAMRs for IHD and pneumonia + influenza

AAMRs: age-adjusted mortality rates

Overall Mortality Trends Stratified by Race:

White and non-Hispanic populations consistently exhibited the highest AAMRs, whereas Asian or Pacific Islander populations had the lowest AAMRs. Overall AAMRs were 8.25 (95% CI: 7.94–8.57) among American Indian or Alaska Native individuals, 7.31 (95% CI: 7.19–7.42) among Asian or Pacific Islanders, 8.39 (95% CI: 8.31–8.47) among Black or African American individuals, and 10.05 (95% CI: 10.02–10.08) among White individuals, who accounted for 89.37% of total deaths. (refer to supplementary figure 3) Hispanic or Latino individuals had a lower AAMR(8.55 95% CI: 8.45–8.64) compared with non-Hispanic or Latino individuals, who exhibited a higher AAMR (9.89 95% CI: 9.87–9.92) Sharp increases in AAMRs were observed in most groups after 2018. From 2018 to 2020, all racial and ethnic groups experienced significant upward trends, with particularly pronounced increases among Hispanic/Latino (APC=82.40%, 95% CI: 60.21–107.57) and Black/African American populations (APC=58.55%, 95% CI: 38.08–82.05), indicating that the trends have worsened in recent years especially after 2018.(Refer to figure 3, supplementary table 3)

Figure 3: AAMR trends for IHD and pneumonia + influenza stratified by race/ethnicity.

Overall Mortality Trends Stratified By Urbanization:

The highest overall AAMR was in Noncore (Nonmetro) areas, followed by Micropolitan (Nonmetro), Large Central Metro, Small Metro, Medium Metro, and Large Fringe Metro regions. The AAMR was highest in Noncore (Nonmetro) (12.11; 95% CI: 12.01–12.21) and Micropolitan (Nonmetro) (11.80; 95% CI: 11.71–11.89), followed by Large Central Metro (9.73; 95% CI: 9.68–9.78), Small Metro (9.68; 95% CI: 9.60–9.76), Medium Metro (9.17; 95% CI: 9.12–9.23), and Large Fringe Metro (9.09; 95% CI: 9.04–9.14).

From 1999 to 2018, mortality rates declined significantly in Large Central, Large Fringe, Medium, and Small Metropolitan regions, with sustained decreases observed in Large Fringe Metro (APC: −7.13%), Large Central Metro (APC: −6.79%), , Medium Metro (APC: −6.32%), and Small Metro (APC: −5.76%). However, after 2018, a significant increase in mortality was observed across all regions upto 2020, including Large Central Metro (APC: 45.02%), Large Fringe Metro (APC: 39.40%), Medium Metro (APC: 31.18%), and Small Metro (APC: 32.49%).

Micropolitan (Nonmetro) regions demonstrated multiple joinpoints, with declines from 1999 to 2005 (APC: −2.38%), 2005 to 2009 (APC: −11.49%), and 2009 to 2018 (APC: −3.95%), followed by a significant increase from 2018 to 2020 (APC: 27.10%). Similarly, Noncore (Nonmetro) areas showed a sustained decrease from 1999 to 2018 (APC: −5.52%) and a subsequent increase from 2018 to 2020 (APC: 29.42%).(Refer to supplementary figure 4)

Overall, mortality showed a consistent decline from 1999 to 2018 across metropolitan and nonmetropolitan regions, followed by a significant reversal after 2018. (refer to figure 4)

Figure 4: AAMR trends associated with urbanization

Overall Mortality Trends stratified by States and Census Region:

West Virginia had highest age-adjusted mortality rate (AAMR) (17.39), followed by Rhode Island (16.27), Vermont (14.74), and Oklahoma (13.48)(refer to supplementary table 4). At the regional level, the Northeast exhibited the highest AAMR (10.29; 95% CI: 10.23–10.34), followed by the Midwest (10.07; 95% CI: 10.01–10.12), the West (9.74; 95% CI: 9.68–9.79). South had the lowest AAMR (9.44; 95% CI: 9.40–9.48). (refer to supplementary table 5) There were significant declines in mortality across all census regions from 1999 to 2018, including the Northeast (APC: −6.92%), Midwest (APC: −6.40%), South (APC: −5.86%), and West (APC: −7.09%), On the contrary , reversal in trends was observed after 2018, with mortality rates increasing through 2020 in the Northeast (APC: 35.95%), Midwest (APC: 37.03%), South (APC: 39.91%), and West (APC: 28.32%). (refer to figure 5, supplementary figure 5)

Figure 5: AAMR trends across different US census regions

AAMR: age-adjusted mortality rate

DISCUSSION

In this national analysis of mortality trends from 1999 to 2020, we observed a substantial long term decline in age adjusted mortality rates from ischemic heart disease associated with influenza and pneumonia, followed by a sharp and concerning reversal after 2018. Although overall mortality decreased steadily for nearly two decades, the pronounced increase in mortality between 2018 and 2020 highlights a period of renewed vulnerability and suggests that infectious respiratory illnesses may play an increasingly important role as acute triggers for fatal ischemic cardiac events. (Fig. 6)

The sustained decline in ischemic heart disease mortality from 1999 through 2018 is consistent with prior national trends and likely reflects improvements in cardiovascular risk factor control, widespread use of statins and The Sustained decline in ischemic heart disease mortality from 1999 through 2018 is consistent with prior national trends and likely reflects improvements in cardiovascular risk factor control, widespread use of statins and antihypertensive therapies, advances in acute coronary care, and declining smoking prevalence [10–12]. However, the abrupt increase in mortality observed after 2018 represents a clear departure from these long-standing gains. The burden of cardiovascular disease is influenced directly by social and psychological factors and indirectly by economic stressors, including reduced access to preventive care, increased sedentary lifestyles, and widening income inequality [13].

This reversal also coincides temporally with heightened circulation of respiratory infections and culminates during the early phase of the COVID 19 pandemic. The COVID 19 pandemic, a major confounding factor for mortality data from 2020 onward, likely exacerbated existing social and healthcare disparities. In addition to systemic impacts on healthcare access and delivery, COVID 19 has been well documented to cause cardiovascular complications, including myocarditis, heart failure,

cardiomyopathy, and myocardial infarction during both acute illness and the post acute phase [14]. A growing body of literature suggests that indirect effects of the pandemic, such as interruptions in care for chronic conditions, healthcare workforce shortages, and patient hesitancy to seek medical attention, may have contributed to the reversal of long-standing improvements in cardiovascular mortality [15,16].

Influenza and pneumonia are well recognized precipitants of acute ischemic events through mechanisms including systemic inflammation, endothelial dysfunction, prothrombotic states, increased myocardial oxygen demand, and destabilization of atherosclerotic plaques [17]. The sharp increase in mortality between 2018 and 2020 suggests that acute infectious triggers may have amplified ischemic risk in susceptible individuals, particularly older adults and those with preexisting cardiovascular disease. Although causal inference cannot be established using death certificate data, the temporal alignment supports the role of respiratory infections as contributors to excess ischemic heart disease mortality during this period.

Throughout the study period, males consistently exhibited higher age-adjusted mortality rates than females, reflecting established sex differences in ischemic heart disease risk, including higher prevalence of smoking, occupational exposures, and cardiometabolic comorbidities among men [18–20]. Both sexes experienced substantial declines in mortality prior to 2018, followed by a marked reversal thereafter. Notably, the post 2018 increase was more pronounced among males, suggesting greater vulnerability to infection-related ischemic complications or higher likelihood of severe disease following respiratory infections.

Significant racial and ethnic disparities were evident in both baseline mortality rates and recent trend reversals. White and non Hispanic populations accounted for the majority of deaths and exhibited higher overall mortality rates, likely reflecting population age structure. However, the most striking increases were observed among Black and Hispanic or Latino populations, who experienced disproportionately steep rises in mortality after 2018. These trends likely reflect the intersection of structural inequities, higher cardiometabolic risk burden, differential exposure to respiratory infections, and disparities in access to timely preventive and acute care [21]. Living in disadvantaged neighborhoods is an independent risk factor for coronary heart disease, and Black individuals are more than four times as likely as White individuals to reside in these areas, further increasing cardiovascular risk and subsequent mortality [22].

The pronounced post 2018 increase among Hispanic or Latino populations is particularly notable and may reflect occupational exposure risks, reduced access to healthcare, and lower vaccination uptake [23]. These findings underscore the importance of addressing social determinants of health when evaluating infection associated cardiovascular risk.

A clear urban rural gradient was observed, with the highest mortality rates occurring in noncore and micropolitan regions, consistent with prior studies [24]. Although mortality declined across all urbanization levels prior to 2018, rural and nonmetropolitan areas experienced persistently higher baseline mortality and substantial increases in later years. These disparities likely reflect limited access

to preventive care, fewer cardiology services, delayed treatment for acute coronary syndromes, and higher prevalence of smoking and chronic disease in rural populations [25–27]. Rural populations may therefore be at heightened risk for cardiovascular complications of influenza and pneumonia. These findings highlight the need for targeted public health interventions and resource allocation to address the unique challenges faced by rural communities.

At the regional and state levels, mortality varied considerably. States such as West Virginia, Rhode Island, Vermont, and Oklahoma exhibited the highest mortality rates. These patterns parallel known distributions of smoking prevalence, poverty, environmental exposures, and healthcare access inequities [28, 29]. The South paradoxically demonstrated the lowest overall age adjusted mortality despite experiencing one of the steepest post 2018 increases. Regional differences likely reflect variation in population demographics, healthcare infrastructure, environmental exposures, and infectious disease burden, emphasizing the need for region specific cardiovascular prevention strategies.

Clinical and Public Health Implications

These findings have important clinical and public health implications. The sharp reversal in ischemic heart disease mortality following respiratory infections highlights the need for improved prevention strategies, particularly among high risk populations. Influenza vaccination has been shown to reduce the risk of acute myocardial infarction and should be prioritized as a cardiovascular preventive intervention, especially for older adults and individuals with established heart disease [30]. Early recognition and aggressive management of respiratory infections in patients with cardiovascular risk factors may further mitigate infection associated ischemic complications.

From a public health perspective, strengthening vaccination programs, improving access to primary and preventive care, and addressing healthcare disparities in rural and underserved communities are critical steps toward reducing infection associated cardiovascular mortality.

Limitations

This study has several limitations. Mortality data derived from CDC WONDER rely on death certificate coding, which is subject to misclassification and variability in reporting of ischemic heart disease, influenza, and pneumonia. The database lacks clinical detail, including infection severity, vaccination status, comorbid conditions, and timing of infection relative to cardiac events, limiting causal interpretation. Additionally, the observed post 2018 increase may partially reflect disruptions in healthcare access and reporting during the COVID 19 pandemic. Despite these limitations, the large national sample and extended study period provide valuable insight into long term mortality patterns.

Conclusion

In conclusion, ischemic heart disease mortality associated with influenza and pneumonia declined substantially in the United States from 1999 to 2018 but increased sharply thereafter, with pronounced

worsening between 2018 and 2020. This reversal disproportionately affected males, Black and Hispanic populations, rural communities, and residents of high burden states.

These findings highlight the growing importance of infectious respiratory illnesses as potential triggers for fatal ischemic events and highlight the need for integrated cardiovascular and infectious disease prevention strategies to mitigate future mortality. Coordinated cardiovascular risk management, vaccination efforts, early infection control, and targeted public health interventions are essential to mitigate future mortality and reduce inequities among vulnerable populations.

Declarations

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Figures

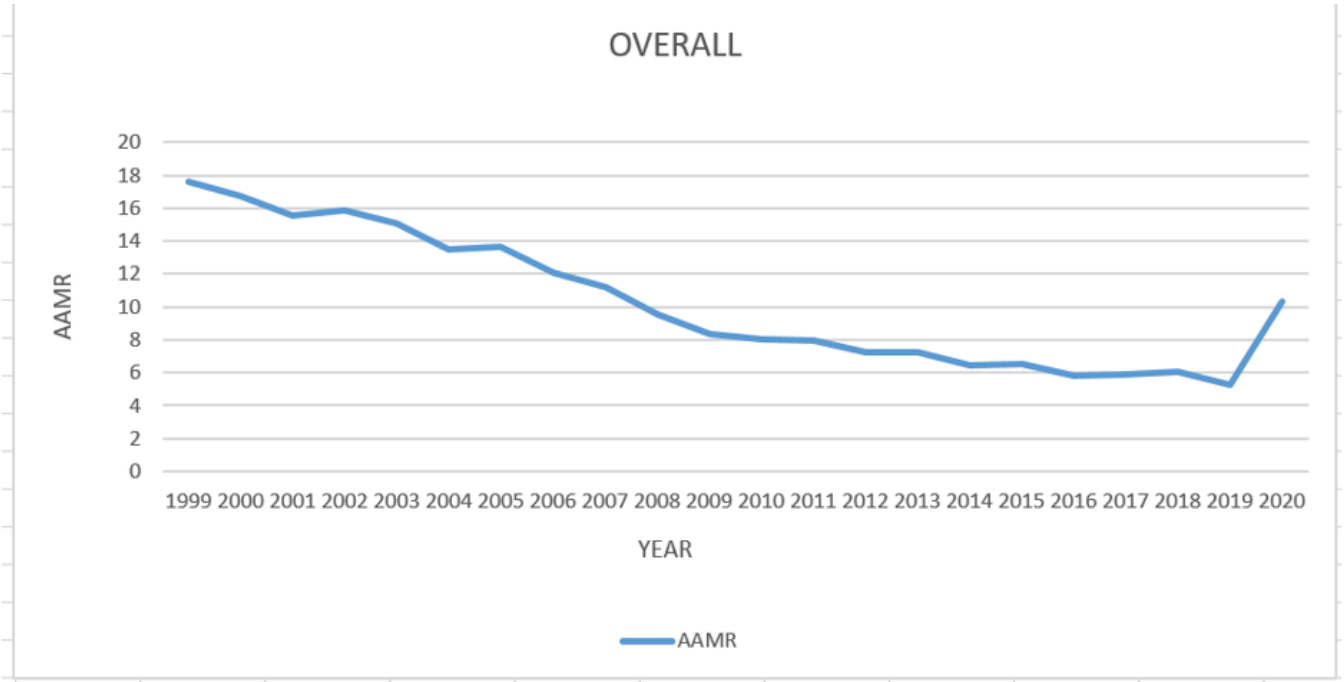


Figure 1

Overall trends in AAMRs for IHD and pneumonia + influenza

AAMRs: age-adjusted mortality rates,.

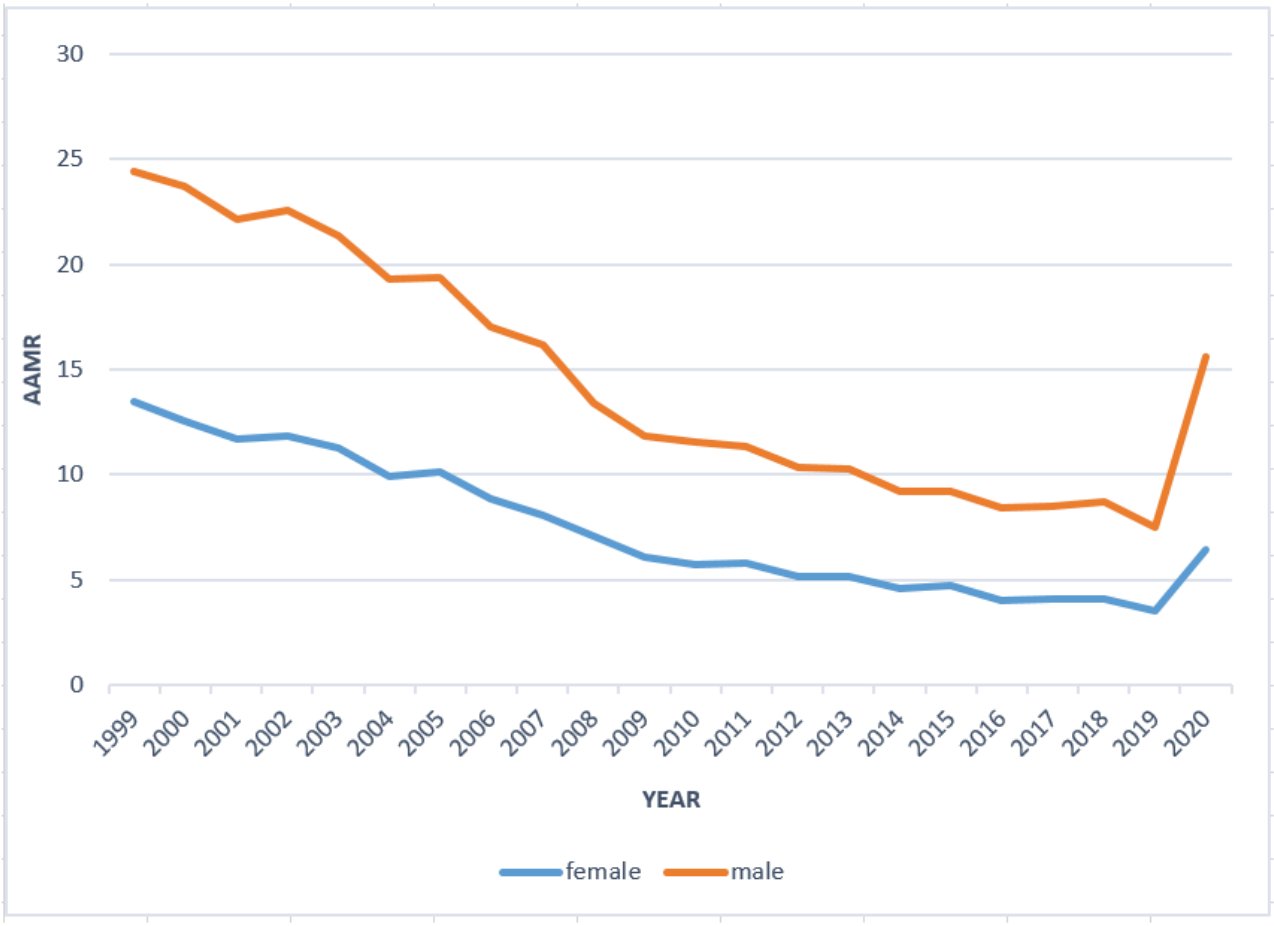


Figure 2

Sex-specific trends in AAMRs for IHD and pneumonia + influenza

AAMRs: age-adjusted mortality rates

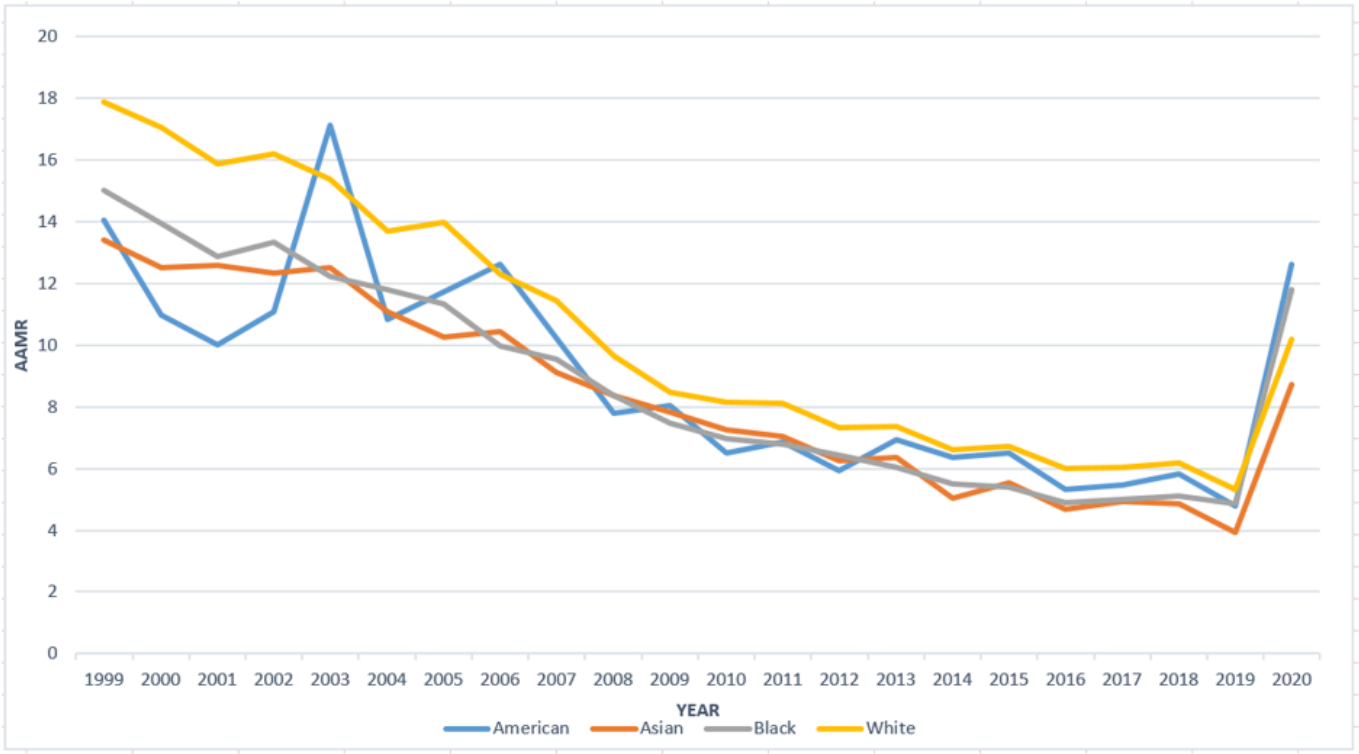


Figure 3

AAMR trends for IHD and pneumonia + influenza stratified by race/ethnicity.

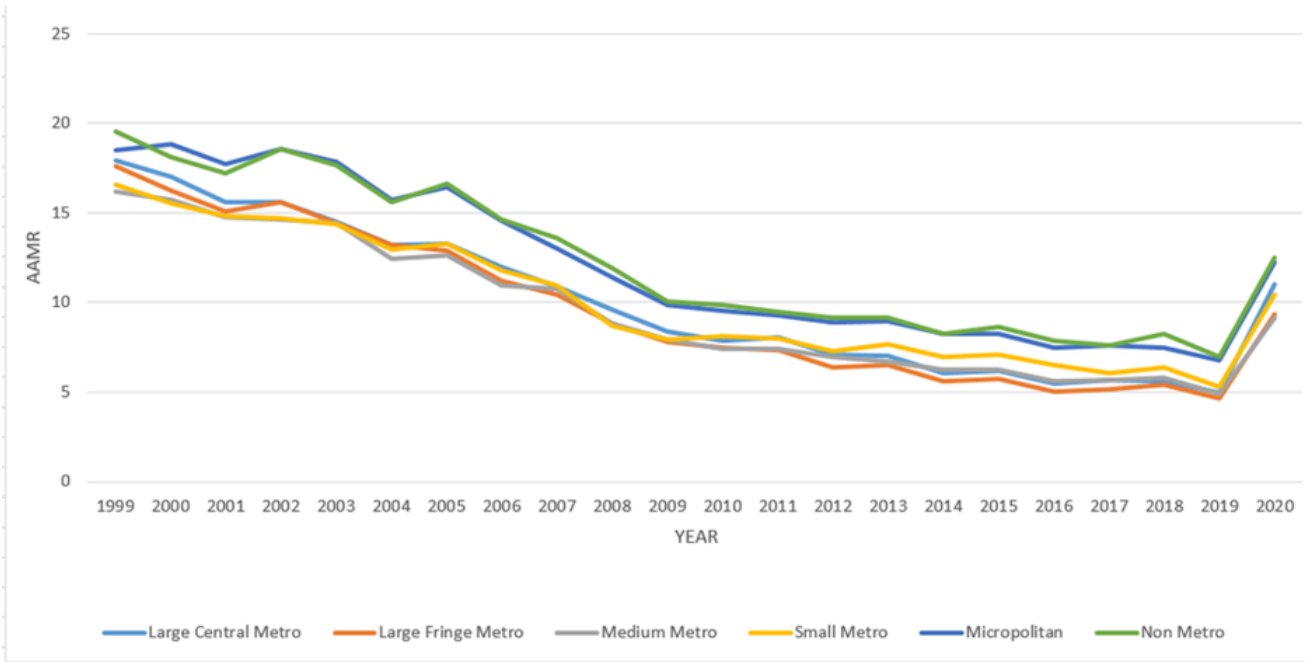


Figure 4

AAMR trends associated with urbanization

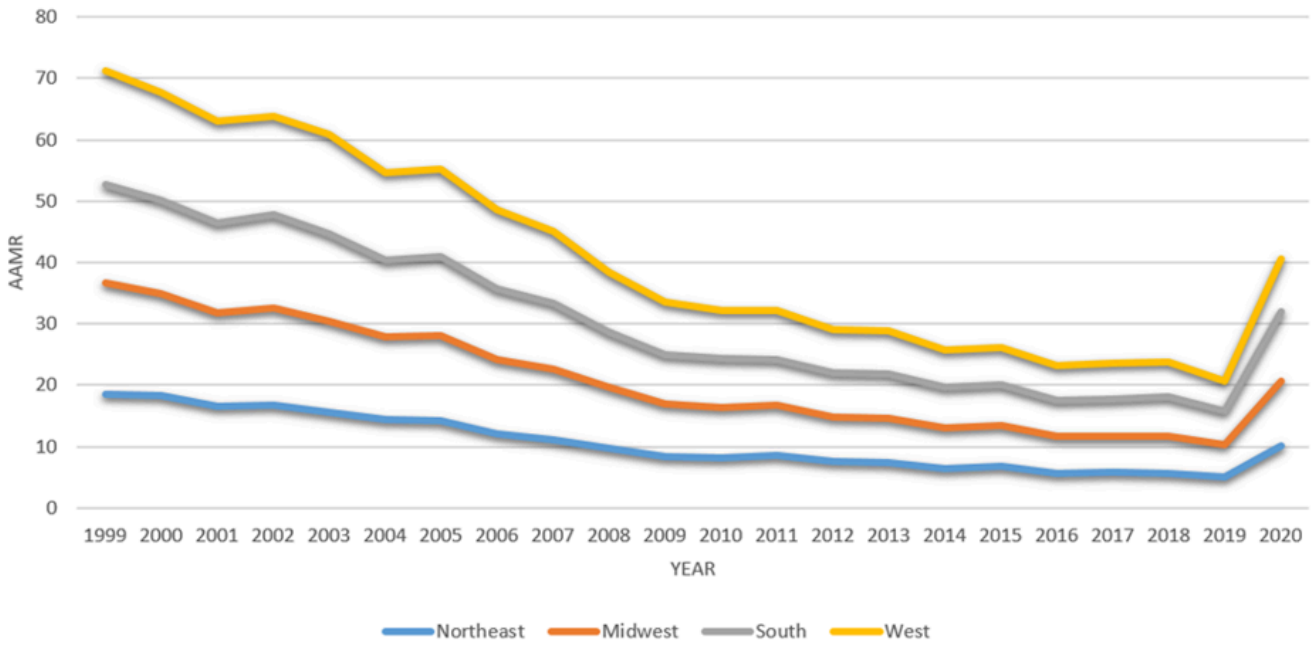


Figure 5

AAMR trends across different US census regions

AAMR: age-adjusted mortality rate

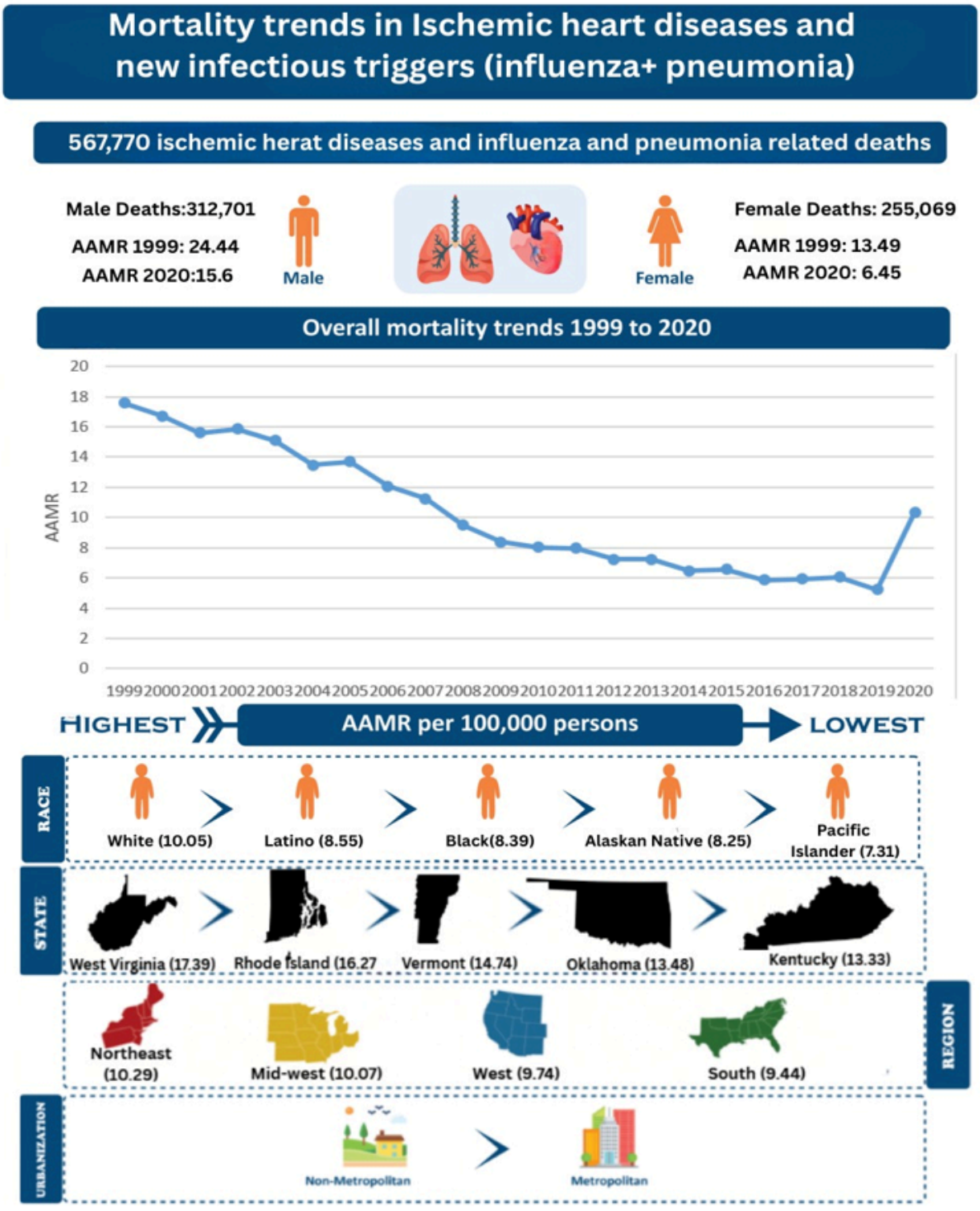


Figure 6

Central illustration showing mortality trends in ischemic heart disease and pneumonia +influenza among US adults aged 15 and older. AAMR: age-adjusted mortality rate.

Image Credit: This figure was created by the authors and has not been previously published.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplemntarytablesinfluenza.xlsx
- jpsinfluandpneu.docx