

The Lethal Convergence: Premature Mortality Surges and Widening Disparities in Concomitant Atherosclerotic Heart Disease and Heart Failure: A CDC WONDER Analysis (1999–2023)

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**The Lethal Convergence: Premature Mortality Surges and Widening Disparities in Concomitant
Atherosclerotic Heart Disease and Heart Failure: A CDC WONDER Analysis (1999–2023)**

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Abstract

Background

Concurrent atherosclerotic heart disease (ASHD) and heart failure (HF) represent a high-burden clinical phenotype, yet long-term national trends and subgroup disparities remain insufficiently characterized.

Methods

We analyzed CDC WONDER mortality data for U.S. adults with ASHD and HF, using Joinpoint regression to calculate age-adjusted mortality trends (APC and AAPC) across demographic subgroups.

Results

Overall AAMR declined from 1999–2012 (APC: –4.09%), stabilized through 2018 (APC: –0.40%; $p = 0.44$), increased during 2018–2021 (APC: 4.69%), and restabilized during 2021–2023 (APC: –3.78%; $p = 0.08$). Males had higher overall AAMRs and steeper 2018–2021 increases (APC: 5.21%), while females exhibited steeper long-term declines (AAPC: –2.88% vs. –1.43%). By race/ethnicity, AAMR was highest in non-Hispanic (NH) Whites (41.6) and lowest in NH Asians (18.46); long-term declines were steepest for Hispanic and NH Asian populations, yet 2018–2021 saw significant increases among NH Whites (APC: 5.15%) and NH Blacks (APC: 5.95%). Geographically, the Midwest recorded the highest AAMR, and non-metropolitan rates were higher overall, increasing post-2013 while metropolitan rates stabilized. Over the full 1999–2023 period, AAMR increased among adults aged 25–54 years but declined for those aged ≥ 55 years.

Conclusion

The stalled decline in U.S. mortality from concurrent ASHD and HF, marked by widening disparities and alarming increases in younger adults, necessitates targeted prevention.

Keywords

Atherosclerotic Heart Disease; Heart Failure; Mortality Trends; Epidemiology; Cardiovascular Health Disparities; Joinpoint Regression; Premature Cardiovascular Mortality; CDC WONDER

Abbreviations

AA: African American

AAMR: Age-Adjusted Mortality Rate

AAPC: Average Annual Percent Change

AHA: American Heart Association

AI/AN: American Indian/Alaskan Native

APC: Annual Percent Change

ASCVD: Atherosclerotic Cardiovascular Disease

ASHD: Atherosclerotic Heart Disease

CABG: Coronary Artery Bypass Grafting

CDC WONDER: Centers for Disease Control and Prevention Wide-ranging ONline Data for Epidemiologic Research

CI: Confidence Interval

CMR: Crude Mortality Rate

GDMT: Guideline-Directed Medical Therapy

HF: Heart Failure

HFpEF: Heart Failure with preserved Ejection Fraction

ICD-10: International Classification of Diseases, Tenth Revision

IHS: Indian Health Service

NCHS: National Center for Health Statistics

NH: Non-Hispanic

STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

1.0 Introduction

Cardiovascular disease remains the leading cause of mortality in the United States, with atherosclerotic heart disease (ASHD) and heart failure (HF) representing its most formidable manifestations [1]. Far from independent entities, these conditions are closely interconnected in a pathophysiological continuum. Coronary atherosclerosis restricts myocardial blood flow, driving chronic ischemia, adverse ventricular remodeling, and irreversible myocyte loss that ultimately culminate in ischemic cardiomyopathy [2]. The failing heart, in turn, reduces coronary perfusion pressure, deepening ischemic injury and accelerating disease progression. This bidirectional, self-reinforcing cycle defines a distinct dual phenotype-concomitant ASHD and HF-that carries substantially greater mortality risk, healthcare utilization, and therapeutic complexity than either condition in isolation [2,3]. Yet despite its clinical gravity, this combined phenotype has been largely invisible to epidemiological surveillance, which has historically tracked ASHD and HF as independent entities [1,4]. The long-term national mortality trajectory of their convergence and how it has evolved across key demographic subgroups under the weight of modern systemic pressures remains a critical blind spot in cardiovascular public health.

Decades of progress in statin therapy [5], percutaneous coronary intervention, coronary artery revascularization [6], and guideline-directed medical therapy drove meaningful reductions in isolated ASHD-related mortality through the early 2000s [1]. Parallel advances in HF pharmacotherapy and device therapy, codified in the 2022 AHA/ACC/HFSA Heart Failure Guideline [7], produced similar gains in disease-specific survival. However, these successes have been hypothesized to yield an epidemiological paradox: as therapeutic advances extended survival after initial ischemic events, a growing pool of post-infarction survivors may have progressed to HF, while simultaneously confronting

accelerating cardiometabolic risk factors; obesity, hypertension, and diabetes- that fueled further myocardial dysfunction [3,8].

Tracking this lethal convergence is urgent, as these patients represent the highest-risk stratum of end-stage cardiometabolic disease, having exhausted the benefits of early-stage interventions [2,3,7].

Currently, it is unknown whether the post-2012 HF mortality resurgence [9] is amplified when ASHD co-occurs, or how this burden shifts across sex, race/ethnicity, age, and geography. Furthermore, characterizing this cohort over the last two decades is necessary to answer critical questions: whether younger adults—a group already exhibiting alarming premature cardiovascular mortality trends [4,8]—are experiencing accelerating ASHD-HF mortality independent of older cohort trends; how demographic subgroups diverged during the COVID-19 pandemic [10]; and whether the post-pandemic era (2021–2023) reflects genuine recovery. It also attempts to establish an indispensable baseline prior to the population-level impact of novel therapies like SGLT2 inhibitors and GLP-1 receptor agonists [7]. These gaps carry direct implications for equitable resource allocation, pharmacotherapy prioritization, and the disruption of the atherosclerosis-to-HF continuum before it reaches its terminal stage [2,3].

Accordingly, this study leverages 25 years of nationally representative data from the CDC WONDER database (1999–2023) to characterize the full epidemiological trajectory of concomitant ASHD and HF mortality in the United States. By identifying inflection points and mapping granular demographic contours, we provide an actionable public health foundation, oriented not toward conditions in isolation, but toward the lethal convergence that represents their most advanced clinical expression.

2.0 Methods

2.1 Study setting and population

We conducted a retrospective mortality analysis using death certificate data from 1999 to 2023 across all 50 U.S. states and the District of Columbia to evaluate mortality involving ASHD and HF. Mortality data were obtained from the National Vital Statistics System (NVSS) via the CDC WONDER database on April 1, 2026 [11]. ASHD mortality was identified using International Classification of Diseases, Tenth Revision (ICD-10) codes I25.0 (atherosclerotic cardiovascular disease) and I25.1 (atherosclerotic heart disease). These codes were selected to capture chronic ischemic ASHD with greater specificity within the broader ischemic heart disease category. HF mortality was defined using ICD-10 code I50 (all subcategories). This methodology has been used in previous studies [9,12]

The analysis used the Multiple Cause of Death (MCOB) database. Decedents were included if ICD-10 codes for ASHD and HF were reported anywhere on the death certificate, either as the underlying or a contributing cause of death. Co-occurrence reflects co-mention on death certificates and does not imply temporal, clinical, or causal association between conditions.

A sensitivity analysis was conducted in which mortality trends for ASHD and HF were evaluated separately to assess the robustness of temporal patterns. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [13] and was exempt from institutional review board approval due to the use of de-identified, publicly available data.

2.2 Data abstraction

Mortality data were stratified by year, sex (male/female), age, race/ethnicity, and geographic characteristics, including state, U.S. census region, and urban–rural classification. Age was restricted to ≥ 25 years and categorized into 10-year intervals to ensure comparability across the study period.

Race/ethnicity was defined using the National Center for Health Statistics (NCHS) bridged-race categories available in CDC WONDER, including Hispanic or Latino, non-Hispanic (NH) White, NH Black or

African American (AA), NH Asian or Pacific Islander, and NH American Indian/Alaskan Native (AI/AN).

Place of death was classified as a medical facility (outpatient, emergency department, inpatient, death on arrival, or unknown), home, hospice, or nursing home/long-term care facility. Urban–rural status was categorized according to the NCHS classification into metropolitan ($\geq 50,000$ population) and non-metropolitan ($< 50,000$ population) areas [14]. Geographic regions were defined per the U.S. Census Bureau as Northeast, Midwest, South, and West [15].

2.3 Statistical analysis

Crude mortality rates (CMRs) and age-adjusted mortality rates (AAMRs), along with their 95% confidence intervals (CIs), were calculated per 100,000 population. CMRs were calculated as the annual number of deaths divided by the corresponding U.S. population, with AAMRs standardized to the 2000 U.S. population. Temporal trends were assessed using the Joinpoint Regression Program (Version 5.4.0, National Cancer Institute) to estimate annual percent changes (APCs) and average annual percent changes (AAPCs) via log-linear models [16]. APCs and their 95% CIs were derived for each segment between joinpoints using the “Monte Carlo permutation test” to identify the optimal number of inflection points, conducting 4,499 permutations [17]. Statistical significance of variations from baseline mortality was determined by the Joinpoint Regression Program (two-tailed t-tests), with p-values < 0.05 considered significant. Models were fitted using the grid search method, assuming homoscedasticity and independence of errors. Statistical significance was defined as a two-sided p-value < 0.05 . For stratified analyses, identical model specifications were applied; however, models were fitted independently for each subgroup, allowing for detection of distinct temporal patterns without enforcing parallel trends or shared joinpoint locations.

3.0 Results

3.1 Annual Mortality Trends

From 1999 to 2023, concomitant ASHD and HF mortality declined overall, with AAMR decreasing from 56.59 to 34.79 per 100,000 (AAPC: -2.09; 95% CI: -2.75 to -1.43). AAMR declined significantly from 1999 to 2012 (APC: -4.09; 95% CI: -4.33 to -3.86), remained stable during 2012–2018 (APC: -0.40; 95% CI: -1.46 to 0.68; $p = 0.44$), increased from 2018 to 2021 (APC: 4.69; 95% CI: 0.04 to 9.57; $p = 0.048$), and stabilized again during 2021–2023 (APC: -3.78; 95% CI: -7.83 to 0.44; $p = 0.08$). **(Figure 1,**

Supplementary Table 1, Supplementary Table 2)

3.2 Sex-Stratified Mortality Trends

Males had higher overall AAMR than females (52.01 vs. 30.51). Among males, AAMR declined from 69.34 per 100,000 in 1999 to 49.34 in 2023, remaining consistently higher than in females. Mortality decreased significantly from 1999 to 2012 (APC: -3.32; 95% CI: -3.52 to -3.12), remained stable during 2012–2018 (APC: 0.26; 95% CI: -0.56 to 1.10; $p = 0.51$), increased from 2018 to 2021 (APC: 5.21; 95% CI: 1.64 to 8.90), and declined during 2021–2023 (APC: -3.68; 95% CI: -6.85 to -0.39).

Among females, AAMR declined from 48.25 in 1999 to 24.15 in 2023, with significant decreases during 1999–2003 (APC: -3.86; 95% CI: -5.33 to -2.36), 2003–2012 (APC: -5.27; 95% CI: -5.84 to -4.70), and 2012–2018 (APC: -1.42; 95% CI: -2.76 to -0.05), followed by stable trends during 2018–2021 (APC: 3.71; 95% CI: -2.05 to 9.79; $p = 0.18$) and 2021–2023 (APC: -3.92; 95% CI: -9.07 to 1.51; $p = 0.14$). Overall, females experienced a greater mortality reduction than males (Females: AAPC: -2.88; 95% CI: -3.72 to -2.03; Males: AAPC: -1.43; 95% CI: -1.94 to -0.92). **(Figure 2, Supplementary Table 1, Supplementary**

Table 2)

3.3 Race-Stratified Mortality Trends

The highest AAMR was observed among NH White individuals (41.6), followed by NH AI/AN (36.8), NH Black individuals (33.52), Hispanic individuals (27.92), and NH Asian or Pacific Islanders (18.46) (**Figure 3, Supplementary Table 3**)

NH White and NH Black populations showed nearly identical trajectories, with early declines (1999–2012; APC: –3.98 and –3.75), stabilization through 2018, a resurgence during 2018–2021 (APC: 5.15 and 5.95), and subsequent stabilization. In contrast, NH AI/AN individuals experienced a continuous decline in AAMR throughout the study period (APC: –1.13; 95% CI: –1.57 to –0.69), while mortality for NH Asian or Pacific Islander individuals declined until 2014 (APC: –3.86; 95% CI: –4.42 to –3.29) before plateauing till 2023 (APC: 0.91; 95% CI: –0.06 to 1.88; $p = 0.06$). Among Hispanic individuals, mortality declined from 1999–2012 (APC: –4.44; 95% CI: –4.79 to –4.09), remained stable during 2012–2018 (APC: –0.60; 95% CI: –1.94 to 0.75; $p = 0.35$) and 2018–2021 (APC: 4.40; 95% CI: –0.99 to 10.07; $p = 0.10$), and declined again from 2021–2023 (APC: –6.28; 95% CI: –11.01 to –1.31) (**Figure 3, Supplementary Table 2**)

Overall, all racial and ethnic groups demonstrated significant mortality reductions, greatest among Hispanic individuals (AAPC: –2.58; 95% CI: –3.36 to –1.79), followed by NH Asian or Pacific Islanders (AAPC: –2.09; 95% CI: –2.57 to –1.63), NH Whites (AAPC: –1.88; 95% CI: –2.53 to –1.22), NH Blacks (AAPC: –1.71; 95% CI: –2.51 to –0.90), and NH AI/AN individuals (AAPC: –1.13; 95% CI: –1.57 to –0.69) (**Supplementary Table 2**)

3.4 Census Region-Stratified Mortality Trends

The Midwest had the highest AAMR (42.3), followed by the West (39.37), South (37.90), and Northeast (37.71). AAMRs declined from 1999 to 2023 from 60.40 to 39.26 (Midwest), 58.12 to 33.55 (West), 56.72 to 28.46 (Northeast), and 52.81 to 36.09 (South) (**Figure 4, Supplementary Table 4**)

Mortality declined in Midwest during 1999–2012 (APC: –4.02; 95% CI: –4.28 to –3.75), remained stable in 2012–2018 (APC: –0.02; 95% CI: –1.28 to 1.26; $p = 0.98$), increased in 2018–2021 (APC: 5.68; 95% CI: 0.25 to 11.40), and stabilized thereafter (APC: –3.47; 95% CI: –8.29 to 1.61; $p = 0.16$). The West showed declines in AAMR during 1999–2012 (APC: –4.16; 95% CI: –4.43 to –3.88), followed by stable trends during 2012–2018 (APC: –0.88; 95% CI: –2.10 to 0.35; $p = 0.15$), 2018–2021 (APC: 4.45; 95% CI: –0.81 to 9.99; $p = 0.09$), and 2021–2023 (APC: –4.68; 95% CI: –9.48 to 0.37; $p = 0.06$). In the South, mortality declined during 1999–2005 (APC: –3.42; 95% CI: –3.97 to –2.87) and 2005–2011 (APC: –4.77; 95% CI: –5.53 to –4.01), remained stable in 2011–2018 (APC: –0.06; 95% CI: –0.66 to 0.55; $p = 0.83$), increased in 2018–2021 (APC: 5.92; 95% CI: 2.51 to 9.43), and stabilized in 2021–2023 (APC: –2.89; 95% CI: –5.85 to 0.16; $p = 0.06$). The Northeast exhibited the most favorable trajectory, with declines during 1999–2005 (APC: –3.81; 95% CI: –4.34 to –3.28), 2005–2009 (APC: –5.64; 95% CI: –7.30 to –3.94), and 2009–2017 (APC: –2.34; 95% CI: –2.83 to –1.84), followed by stability in 2017–2020 (APC: 2.36; 95% CI: –1.42 to 6.28; $p = 0.20$) and a renewed decline during 2020–2023 (APC: –3.55; 95% CI: –5.37 to –1.70) (**Figure 4, Supplementary Table 2**)

Overall, the greatest mortality reduction was observed in the Northeast (AAPC: –2.85; 95% CI: –3.40 to –2.29), followed by the West (AAPC: –2.35; 95% CI: –3.10 to –1.59), Midwest (AAPC: –1.81; 95% CI: –2.58 to –1.04), and South (AAPC: –1.62; 95% CI: –2.12 to –1.12) (**Supplementary Table 2**)

3.5 Age-Stratified Mortality Trends

In 1999, CMRs were 0.08 (25–34 years), 0.54 (35–44), 3.49 (45–54), 18.67 (55–64), 78.01 (65–74), 276.12 (75–84), and 1087.38 (≥ 85 years), changing to 0.09, 0.73, 3.89, 15.50, 48.52, 162.48, and 644.99, respectively, by 2023, reflecting increases in younger but declines in older adults. (**Figure 5, Supplemental Table 5**)

Mortality increased overall among adults aged 25–34 years (AAPC: 0.95; 95% CI: 0.21–1.70). In those aged 35–44 years, rates were stable during 1999–2014 (APC: –0.86; 95% CI: –1.81 to 0.11; $p = 0.08$) before increasing during 2014–2023 (APC: 5.29; 95% CI: 3.13–7.49) (AAPC: 1.40; 95% CI: 0.47–2.35). Among individuals aged 45–54 years, mortality declined during 1999–2012 (APC: –2.04; 95% CI: –2.80 to –1.27) and increased during 2012–2023 (APC: 4.07; 95% CI: 3.10–5.06) (AAPC: 0.72; 95% CI: 0.15–1.29) **(Figure 5, Supplementary Table 2).**

For those aged 55–64 years, mortality declined during 1999–2010 (APC: –4.23; 95% CI: –4.51 to –3.95), remained stable during 2010–2013 (APC: –0.28; 95% CI: –4.48 to 4.10; $p = 0.89$), increased during 2013–2018 (APC: 2.98; 95% CI: 1.67–4.30) and 2018–2021 (APC: 7.40; 95% CI: 3.63–11.30), and declined during 2021–2023 (APC: –3.90; 95% CI: –7.20 to –0.49) (AAPC: –0.84; 95% CI: –1.56 to –0.12). Among adults aged 65–74 years, mortality declined during 1999–2009 (APC: –5.13; 95% CI: –5.46 to –4.79), was stable during 2009–2013 (APC: –2.27; 95% CI: –4.67 to 0.20; $p = 0.07$) and 2013–2018 (APC: 1.31; 95% CI: –0.10 to 2.75; $p = 0.07$), increased during 2018–2021 (APC: 5.40; 95% CI: 1.32–9.64), and declined during 2021–2023 (APC: –4.28; 95% CI: –7.81 to –0.61) (AAPC: –1.99; 95% CI: –2.68 to –1.30) **(Figure 5, Supplementary Table 2).**

Among those aged 75–84 years, mortality declined during 1999–2004 (APC: –3.24; 95% CI: –4.03 to –2.45), 2004–2011 (APC: –4.57; 95% CI: –5.23 to –3.91), and 2011–2018 (APC: –1.14; 95% CI: –1.86 to –0.40), increased during 2018–2021 (APC: 4.86; 95% CI: 0.73–9.16; $p = 0.03$), and declined during 2021–2023 (APC: –4.86; 95% CI: –8.42 to –1.16) (AAPC: –2.18; 95% CI: –2.78 to –1.58) **(Figure 5, Supplementary Table 2).**

In adults aged ≥ 85 years, mortality declined during 1999–2014 (APC: –3.95; 95% CI: –4.24 to –3.65) before increasing during 2014–2023 (APC: 0.96; 95% CI: 0.28–1.65) (AAPC: –2.13; 95% CI: –2.43 to –1.84) **(Supplementary Table 2)**

3.6 Urbanization-Stratified Mortality Trends

AAMR remained consistently higher in non-metropolitan than metropolitan areas, decreasing from 63.65 vs. 54.88 in 1999 to 45.28 vs. 34.03 in 2020. Metropolitan areas experienced a significant decline during 1999–2012 (APC: -4.20 ; 95% CI: -4.44 to -3.96), followed by stability in 2012–2018 (APC: -0.47 ; 95% CI: -1.54 to 0.61 ; $p = 0.37$) and 2018–2020 (APC: 4.39 ; 95% CI: -0.19 to 9.18 ; $p = 0.06$). Non-metropolitan areas declined during 1999–2013 (APC: -3.53 ; 95% CI: -3.81 to -3.25) but increased during 2013–2020 (APC: 1.57 ; 95% CI: 0.72 to 2.42). Overall, mortality reductions were greater in metropolitan (AAPC: -2.35 ; 95% CI: -2.84 to -1.86) than non-metropolitan areas (AAPC: -1.86 ; 95% CI: -2.17 to -1.55)

(Figure 6, Supplementary Table 2, Supplementary Table 6)

3.7 State-Stratified Mortality Trends

From 1999–2023, states in the lowest 10th percentile included Hawaii (AAMR: 22.02), Alaska (27.76), Alabama (28.09), Nevada (28.56), and District of Columbia (28.6), whereas the highest 90th percentile included West Virginia (60.0), Oklahoma (58.95), Rhode Island (56.86), Ohio (52.66), and Tennessee (52.3). (Figure 7, Supplementary Table 7)

3.8 Condition-Specific Sensitivity Analysis

For the HF cohort, AAMR declined from 1999–2012 (APC: -2.13%), increased from 2012–2018 (APC: 1.89%), rose further during 2018–2021 (APC: 4.87%), and subsequently stabilized from 2021–2023 (APC: -2.73% ; $p=0.15$). Overall, no significant change was observed across the study period (AAPC: -0.33% ; $p=0.282$). In the atherosclerotic heart disease cohort, AAMR declined from 1999–2012 (APC: -3.79%) and continued to decrease through 2018 (APC: -2.01%), followed by a transient increase during 2018–2021 (APC: 5.17%) and a subsequent decline from 2021–2023 (APC: -6.19%). Overall mortality decreased significantly over the study period (AAPC: -2.47%) (Figure 1, Supplementary Table 8)

3.9 Mortality trends for Atherosclerotic heart disease (underlying cause) with heart failure as a contributing cause of death

From 1999 to 2012, the AAMR declined substantially (APC: -4.84 ; 95% CI: -5.12 to -4.55). However, from 2012 to 2023, the rate of decline slowed markedly (APC: -0.52 ; 95% CI: -0.94 to -0.11)

(Supplementary Table 9)

4.0 Discussion

In this nationwide 25-year analysis, we found that concomitant ASHD and HF may represent a distinct high-risk cardiovascular phenotype with epidemiologic characteristics that differ from either condition alone. Although overall mortality declined substantially between 1999 and 2023, these gains were largely confined to the pre-2012 era and were followed by a period of stagnation, a pandemic-associated resurgence, and only partial recovery. Importantly, this overall trend masked several important epidemiologic shifts. We identified a striking age-based divergence, whereby mortality continued to decline among older adults but increased among younger populations, suggesting a possible generational shift in cardiovascular risk. Demographic disparities remain entrenched; males consistently experienced higher mortality than females (despite steeper long-term female declines), while NH White and NH AI/AN populations bore the greatest burden; the largest mortality reductions occurred among Hispanic and NH Asian/Pacific Islander individuals. The Midwest experienced the highest mortality, while the Northeast achieved the greatest improvements, and a widening rural-urban penalty has emerged, driven by escalating non-metropolitan mortality since 2013, alongside considerable state-level variation **(Figure 8)**.

The substantial mortality decline observed between 1999 and 2012 coincided with major public health improvements and advances in cardiovascular care. First, statin utilization expanded markedly,

increasing by nearly 80% between 2002 and 2013 (from 21.8 to 39.2 million U.S. adults) [18]. Supported by evidence from more than 170,000 patients demonstrating proportional reductions in cardiovascular events with LDL-C lowering [5], widespread statin use likely contributed to slowing atherosclerotic progression and reducing recurrent ischemic events. Second, evidence-based revascularization strategies, including PCI and CABG, became increasingly standardized and have been associated with improved survival following ischemic heart disease [6]. Third, broader adoption of guideline-directed medical therapy for HF, including renin–angiotensin–aldosterone system inhibitors, beta-blockers, and device-based therapies, likely further reduced mortality [7]. These therapeutic advances were complemented by population-level improvements in hypertension control and declining smoking prevalence [19], which may have reinforced the downward mortality trend.

This decline phase varied significantly across demographic subgroups. Females experienced a steeper proportional mortality reduction than males, although males maintained a substantially higher absolute AAMR throughout the period. This proportional female advantage may reflect their historically lower baseline burden of obstructive coronary atherosclerosis and higher prevalence of microvascular disease [20], phenotypes that align with the systemic benefits of statins [5] and antihypertensives. Conversely, the persistently elevated absolute male mortality parallels their higher baseline ASHD burden [21], earlier onset of risk factors, and greater historical prevalence of adverse behavioral exposures like smoking. Crucially, these trajectories sharply uncoupled after 2012: male mortality abruptly plateaued, while female mortality continued to decline steadily until 2018. This divergence suggests that the systemic cardiovascular stagnation of the 2010s [1, 4] may have been predominantly driven by deteriorating male cardiovascular health, potentially because the modern cardiometabolic epidemic (e.g., central adiposity, diabetes) accelerates male-pattern macrovascular disease more aggressively [21, 22]. Compounded by behavioral vulnerabilities, such as lower screening compliance and fragmented

primary care engagement [23], males may have exhausted the protective buffer of existing therapies faster.

Notably, women and racial/ethnic minorities received high-intensity statins at significantly lower rates during this era [18, 24, 25]. Therefore, it can be hypothesized that female mortality gains occurred despite relative pharmacotherapy undertreatment; equitable prescribing might have widened their survival advantage over males even further. Despite mortality improvements, women remain uniquely vulnerable to the under-recognition of ischemic symptoms, delayed diagnosis, and a higher prevalence of HF with preserved ejection fraction (HFpEF) [22], all of which may continue to drive their residual mortality burden.

The mortality stagnation observed from 2012 to 2018 coincides with a rising cardiometabolic burden that may have neutralized prior therapeutic gains. During this period, U.S. adult obesity prevalence rose from 34.9% (2011–2012) to 42.4% (2017–2018) [26], paralleling increases in sedentary behaviors and caloric excess [8]. These trends were particularly pronounced among younger adults, who experienced increases in diabetes (3.0% to 4.1%), obesity (32.7% to 40.9%), and hypertension (9.3% to 11.5%) between 2009 and 2020 [27]. This aligns with broader national declines in blood pressure control after the early 2010s, often attributed to therapeutic inertia, nonadherence, and systemic healthcare barriers [27]. Consequently, this accelerating cardiometabolic profile likely expanded the cohort vulnerable to premature ASHD-to-HF progression [3], consistent with evidence identifying obesity as the fastest-growing independent predictor of incident HF globally [3]. Furthermore, this mortality plateau temporally preceded the widespread adoption of SGLT2 inhibitors. At the plateau's onset, the landmark 2015 EMPA-REG OUTCOME trial, which demonstrated 38% and 35% reductions in cardiovascular death and HF hospitalization among ASCVD patients, respectively [28], had not yet been published, and official guideline incorporation of these therapies [7] remained years away.

The transient mortality increase observed between 2018 and 2021 coincided with both pre-existing adverse cardiovascular trends and the disruptions of the COVID-19 pandemic. First, SARS-CoV-2 infection is associated with direct cardiovascular mechanisms, including myocardial injury, endothelial dysfunction, and inflammation [29], that likely disproportionately impacted patients with this dual-phenotype burden, given that pre-existing CVD was present in 20–35% of critically ill COVID-19 patients. Second, pandemic-related healthcare shifts disrupted the continuous GDMT optimization critical for managing concomitant ASHD and HF [30], while deferred emergency care paralleled a rise in out-of-hospital cardiac deaths [31]. Third, pandemic-era lifestyle changes (e.g., physical inactivity, psychological stress) aligned with an accelerating cardiometabolic risk trajectory [8], factors known to independently correlate with atherosclerotic progression and HF decompensation [3]. Importantly, because mortality began rising in several subgroups prior to 2020, the pandemic may have only amplified, rather than solely initiated, this reversal in cardiovascular progress.

The sex-stratified data reveal a novel trend for the concomitant ASHD and HF phenotype: the pandemic-era mortality surge was statistically significant in males (APC +5.21; $p = 0.006$) but not in females (APC +3.71; $p = 0.18$). This differential aligns with evidence associating male sex with higher odds of myocardial injury, ischemic stroke, and all-cause mortality during COVID-19 [32], alongside male-predominant hyperinflammatory and prothrombotic profiles (e.g., elevated D-dimer, troponin T, C-reactive protein, and ferritin) [33]. In patients with concomitant ASHD and HF, these pathways may further exacerbate the pre-existing vulnerability of a failing heart supplied by stenotic coronaries. Furthermore, system-wide pandemic healthcare disruptions likely amplified the male tendency to delay medical attention, potentially converting manageable HF exacerbations into out-of-hospital fatalities. In contrast, stronger female antiviral immune responses and a predominance of HFpEF may have conferred marginal resilience against acute viral cardiogenic shock.

Beyond sex differences, all racial and ethnic groups demonstrated significant mortality reductions over the study period, yet their trajectories reveal persistent and widening inequities. Hispanic individuals achieved the greatest reduction and the steepest post-pandemic decline. This aligns with the "Hispanic Paradox"—a phenomenon where Hispanic populations exhibit lower CVD mortality despite higher cardiometabolic and socioeconomic risks [34], historically attributed to healthy migrant effects, lower tobacco use, and strong social cohesion [35]. The sharp post-2021 decline may reflect accelerated healthcare re-engagement and vaccination uptake [10]. However, evidence suggests this advantage may be attenuating as acculturation alters behavioral patterns [36]. Furthermore, broad ethnic aggregation in databases may obscure subgroup-specific risks within both Hispanic and NH Asian/Pacific Islander populations, the latter of which maintained the lowest overall mortality, likely reflecting lower population-level smoking and obesity prevalence.

Conversely, NH Black individuals experienced the steepest pandemic-era mortality surge without a statistically significant post-2021 recovery. This disproportionate trajectory parallels an established vulnerability: Black adults experience higher national CVD mortality [37] and persistently higher rates of uncontrolled hypertension [27]. The AHA's 2020 Presidential Advisory identified structural racism, affecting housing, care access, and insurance, as a fundamental driver of these disparities [38], including structurally determined gaps in access to novel agents like SGLT2 inhibitors [39]. Within the ASHD-HF phenotype, these barriers likely manifest as GDMT underoptimization [7], exacerbating baseline cardiometabolic risks [3]. Notably, while NH Black populations bear a severe burden of HF (often driven by non-ischemic, hypertensive etiologies), the absolute predominance of ASHD-HF mortality among NH White populations indicates that ischemic cardiomyopathy remains deeply rooted in this demographic.

Finally, although NH AI/AN individuals were the only group to experience a continuous statistical decline without a pandemic-era spike, they maintained the second-highest absolute mortality rate and achieved

the smallest overall reduction. This sluggish progress highlights an ongoing crisis of healthcare inequity and systemic marginalization [40]. The persistently high mortality burden in this population parallels the chronic under-resourcing of the Indian Health Service (IHS), geographic barriers to advanced cardiac centers, lower GDMT prescription rates, and a high prevalence of competing risks like diabetes [40].

Age-stratified findings were particularly concerning: while mortality declined in older adults, it increased significantly among adults aged 25–34 years and accelerated sharply after 2012–2014 in those aged 35–64. The emergence of the concomitant ASHD-HF phenotype in these cohorts suggests a dangerous compression of the disease trajectory [2]. The pathophysiological cycle culminating in end-stage cardiovascular disease is increasingly completed in patients' 30s and 40s rather than their 60s and 70s, a fundamental demographic shift previously obscured by tracking ASHD and HF independently [1, 4]. This premature clinical manifestation parallels the accelerating cardiometabolic epidemic in younger populations. Between 2009 and 2020, adults aged 20–44 experienced rising diabetes (3.0% to 4.1%) and obesity (32.7% to 40.9%) alongside persistently uncontrolled hypertension, with the highest burden observed in Black young adults [27]. These trends align with concurrent population-level rises in obesity and HF-related mortality [8] and correspond to the leading modifiable drivers of incident HF globally [3].

Furthermore, clinical and systemic factors likely compound these risks. Younger adults frequently face delayed diagnosis and undertreatment, potentially exacerbated by insurance gaps and declining healthcare access [41, 42]. Notably, traditional 10-year ASCVD risk calculators often underestimate lifetime risk in younger individuals [43, 44]. This underestimation may contribute to therapeutic inertia and to delayed initiation of aggressive lipid-lowering therapies and novel cardioprotective agents, such as SGLT2 inhibitors or GLP-1 receptor agonists. Because premature cardiovascular death results in a profound loss of potential life-years, this demographic shift threatens to dramatically amplify the future

burden of ASHD-HF, underscoring an urgent need for earlier cardiometabolic risk reduction strategies [45].

The rural disadvantage in the concomitant ASHD-HF phenotype is particularly consequential, as effective management relies on coordinated access to interventional cardiology for revascularization [6], electrophysiology for device therapy, and HF specialist oversight for GDMT optimization [7]. Notably, these services are less available per capita in rural versus urban counties [46]. Global literature identifies systems-level access to multidisciplinary care as a strong independent predictor of HF outcomes [3], highlighting a deeply inequitable resource distribution in the United States. Furthermore, rural communities exhibit higher population-level rates of smoking, obesity, physical inactivity, and poorly controlled hypertension, factors inherently associated with accelerated disease progression. Importantly, non-metropolitan mortality transitioned from decline to significant increase after 2013; this inflection aligns with a wave of rural hospital closures and rising metabolic dysfunction, suggesting these populations may not have equitably benefited from recent cardiovascular therapeutic advances [46].

Regional and state-level differences further parallel the structural determinants of cardiovascular health. The Midwest consistently exhibited the highest mortality rates, alongside persistently elevated burdens in several Southern and Appalachian states. These geographic patterns overlap substantially with areas reporting higher prevalences of obesity, diabetes, smoking, and poverty, coupled with reduced preventive healthcare access. For example, West Virginia and Oklahoma remained in the highest 10th percentile across both study epochs, a finding that aligns with their well-documented convergence of high behavioral risk factors and limited subspecialty access [4]. These state-level differentials extend the cardiometabolic mortality patterns previously documented by Shah et al. (1999–2017) through 2023 [4]. Conversely, states like Hawaii and California consistently maintained lower mortality, potentially reflecting healthier population-level behaviors and more robust public health infrastructure. In contrast,

the Northeast achieved the lowest absolute mortality, the greatest overall reduction, and a resumption of its downward trajectory following the initial pandemic shock. This favorable pattern likely parallels high geographical proximity to tertiary cardiovascular centers for acute myocardial infarctions [47]. Such infrastructural density facilitates the high-frequency outpatient visits necessary for safely titrating complex GDMT and often coincides with higher socioeconomic baselines and robust state-level public health initiatives, including the widespread early adoption of Medicaid expansion [48].

The post-2021 mortality stabilization is directionally encouraging and temporally aligns with two concurrent developments. First, it coincides with maximal COVID-19 vaccination penetration and the restoration of cardiovascular care infrastructure, factors previously associated with declining excess cardiovascular mortality during the later pandemic period [10]. Second, this era marks the broader population-level deployment of SGLT2 inhibitors. Clinical trials—including DAPA-HF [49], EMPEROR-Reduced [50], EMPEROR-Preserved [51], and DELIVER [50, 52], have associated these agents with 25–26% reductions in composite cardiovascular death or worsening HF across the ejection fraction spectrum. Now codified in the 2022 AHA/ACC/HFSA guidelines [7], these disease-modifying therapies, combined with their demonstrated ASCVD event reductions, align mechanistically with the dual pathophysiology of the concomitant ASHD-HF phenotype.

However, this stabilization has not been uniform: premature mortality among adults aged 25–54 continued to rise through 2023, and NH Black individuals experienced an incomplete recovery. These divergences caution against interpreting aggregate improvements as equitable population-wide benefits. As Sajid et al. noted regarding obesity-related HF management [8], the uneven distribution of therapeutic advances, combined with persistent, structurally determined barriers to prescribing novel agents [38, 39], parallels observable mortality disparities along racial, socioeconomic, and geographic lines. Consequently, this study establishes a critical pre-SGLT2 era mortality baseline against which the

future population-level impact of these therapies on the concomitant ASHD-HF cohort can be longitudinally assessed.

Our findings hold several urgent implications for clinical practice and public health policy, necessitating a shift from reactive to proactive cardiovascular care;

Early-Life Intervention: The escalating ASHD and HF mortality among young adults demands a reevaluation of primary prevention guidelines. Clinicians must lower the threshold for early cardiometabolic screening. At the same time, payers should reduce administrative barriers to initiating novel, disease-modifying therapies (such as SGLT2 inhibitors and GLP-1 receptor agonists) in younger patients to prevent the progression to ischemic cardiomyopathy.

Rural Healthcare Infrastructure: Reversing the widening rural-urban mortality penalty requires aggressive investments to ensure patients are not geographically penalized. Federal reimbursement models must be restructured to financially sustain rural critical access hospitals. Furthermore, expanding tele-cardiology through permanent payment parity and federally subsidized hub-and-spoke networks will allow urban advanced HF specialists to co-manage complex patients alongside rural providers. At the community level, deploying mobile units for routine cholesterol, blood pressure, and ankle-brachial index (ABI) screening can capture at-risk patients early [61].

Demographic Equity and Representation: The stark disparities observed in NH AI/AN populations demand sustained legislative funding for the IHS to bridge regional gaps in specialty care. Broader state-level variations in care must also be addressed through evidence-based reforms, particularly nationwide Medicaid expansion, to close the insurance gap and ensure equitable access to specialist care for low-income populations. Additionally, future cardiovascular trial designs must mandate diverse

demographics and balanced gender representation to widen the evidence base for historically underserved communities.

Longitudinal Value-Based Care: Realigning financial incentives to reward long-term GDMT adherence, reduced readmissions, and multidisciplinary outpatient management is crucial for building resilient healthcare systems capable of maintaining chronic care during public health emergencies.

4.1 Limitations

We acknowledge several limitations inherent to the CDC WONDER database and the retrospective observational design. First, reliance on death certificates introduces the risk of ICD-10 misclassification and coding errors by certifiers, particularly regarding the precise clinical sequencing of underlying versus contributing causes of death. Second, the registry lacks granular, patient-level clinical data, such as left ventricular ejection fraction (precluding the critical distinction between HFrEF and HFpEF), specific medication dosages, or laboratory values, restricting our ability to adjust for disease severity or establish causal inference. Third, the dataset lacks individual-level socio-demographic variables, such as socioeconomic status, insurance coverage, health literacy, and behavioral risk factors (e.g., smoking status, diet), leaving the potential for unmeasured confounding. Fourth, racial and ethnic misclassification on death certificates is a documented systemic issue, which may lead to the underestimation of mortality burdens in certain minority populations, particularly among NH AI/AN and Hispanic cohorts. Finally, although clear pandemic-era inflections were observed, the database cannot distinguish between direct effects of SARS-CoV-2 infection and indirect effects related to healthcare disruptions, delayed presentations, and deferred chronic care. Additionally, the post-2021 period includes only two years of data, limiting statistical power for evaluating recent trends. Despite these limitations, the major strength of this study is its nationwide, 25-year scope, providing a comprehensive assessment of mortality trends across the United States. The large, population-based dataset minimizes

selection bias and enhances generalizability compared with localized registries or clinical cohorts. This robust analysis offers valuable epidemiological insight into the burden of concomitant ASHD and HF, enabling evaluation of the long-term impact of therapeutic advances, healthcare disparities, and major public health events on mortality patterns over time.

5.0 Conclusion

Mortality associated with concomitant ASHD and HF declined substantially in the United States from 1999 to 2023. However, these gains slowed in the last decade, were markedly disrupted by the COVID-19 pandemic, and remain challenged by persistent demographic and geographic disparities, particularly among younger adults, males, rural populations, and certain racial and regional subgroups. The rising burden of premature mortality and widening rural disparities suggest that current prevention strategies are insufficient. Future efforts should prioritize early identification and management of cardiometabolic risk factors, strengthening rural healthcare access, and ensuring equitable delivery of advanced cardiovascular care to prevent progression from atherosclerotic disease to HF.

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Consent for Publication: Not applicable. This study did not involve the publication of identifiable personal data.

Data Availability: The data that support the findings of this study are publicly available from the CDC WONDER online database (<https://wonder.cdc.gov/>). The authors did not generate any new data.

Authors' Contributions

AC: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization. **PR:** Writing - Original Draft. **PK:** Writing - Original Draft, Writing - Review & Editing. **MIK:** Writing - Original Draft. **MST:** Writing - Original Draft, Writing - Review & Editing. **BN:** Writing - Original Draft. **SA:** Writing - Original Draft, Writing - Review & Editing. **AC:** Writing - Original Draft, Writing - Review & Editing. **RS:** Writing - Original Draft, Writing - Review & Editing. **SB:** Writing - Original Draft, Writing - Review & Editing.

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Figure Captions

Figure 1: Overall trends in atherosclerotic Heart disease (ASHD), heart failure (HF) and concomitant ASHD and HF mortality, shown as age-adjusted mortality rates (AAMR) per 100,000 among adults aged ≥ 25 in the United States, 1999–2023

Figure 2: Sex-stratified trends in atherosclerotic Heart disease (ASHD) and heart failure (HF) mortality shown as age-adjusted mortality rates per 100,000 among adults aged ≥ 25 in the United States, 1999–2023

Figure 3: Race-stratified trends in atherosclerotic Heart disease (ASHD) and heart failure (HF) mortality shown as age-adjusted mortality rates per 100,000 among adults aged ≥ 25 in the United States, 1999–2023

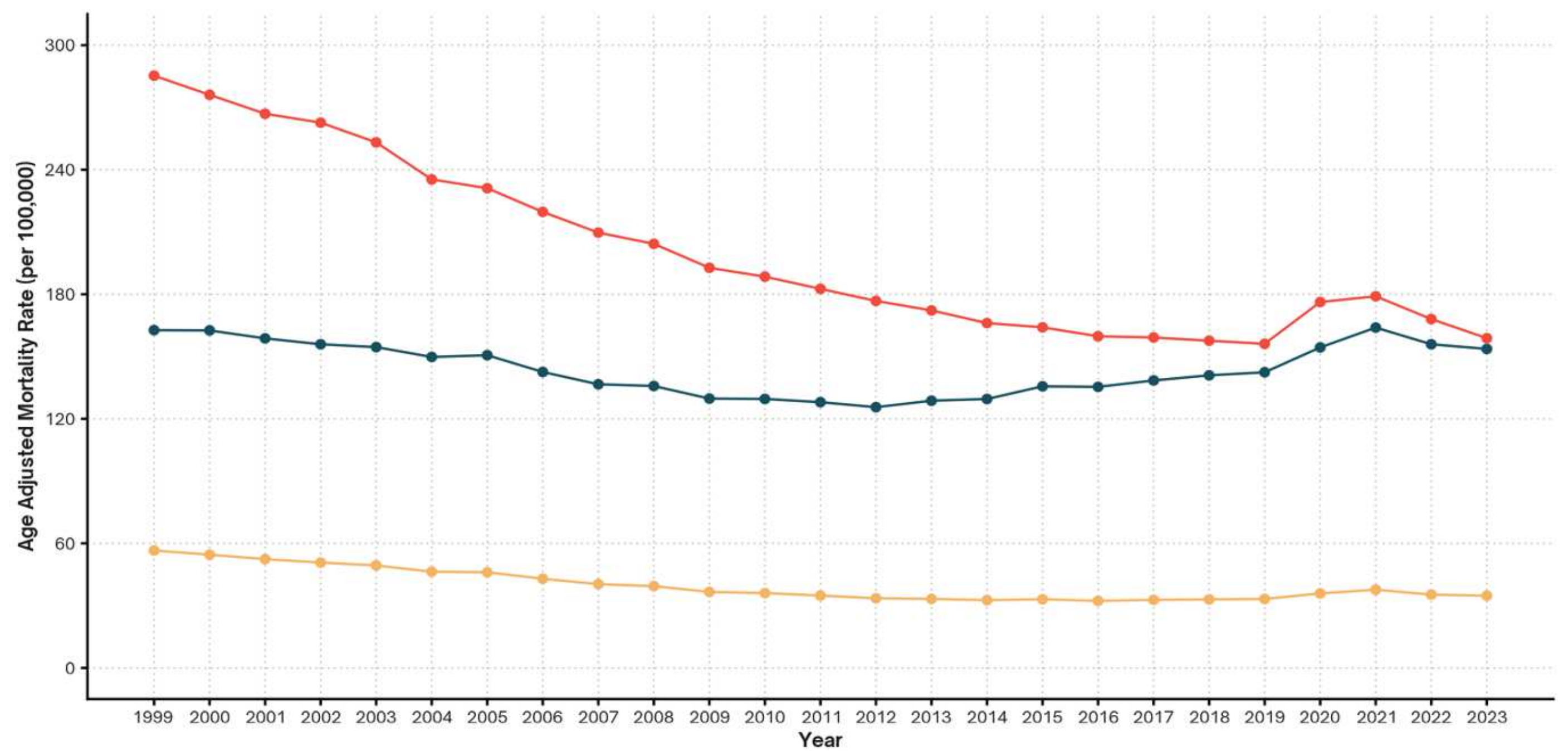
Figure 4: Census region-stratified trends in atherosclerotic Heart disease (ASHD) and heart failure (HF) mortality shown as age-adjusted mortality rates per 100,000 among adults aged ≥ 25 in the United States, 1999–2023

Figure 5: Age-stratified trends in atherosclerotic Heart disease (ASHD) and heart failure (HF) mortality shown as age-adjusted mortality rates per 100,000 among adults aged ≥ 25 in the United States, 1999–2023

Figure 6: Urbanisation-stratified trends in atherosclerotic Heart disease (ASHD) and heart failure (HF) mortality shown as age-adjusted mortality rates per 100,000 among adults aged ≥ 25 in the United States, 1999–2023

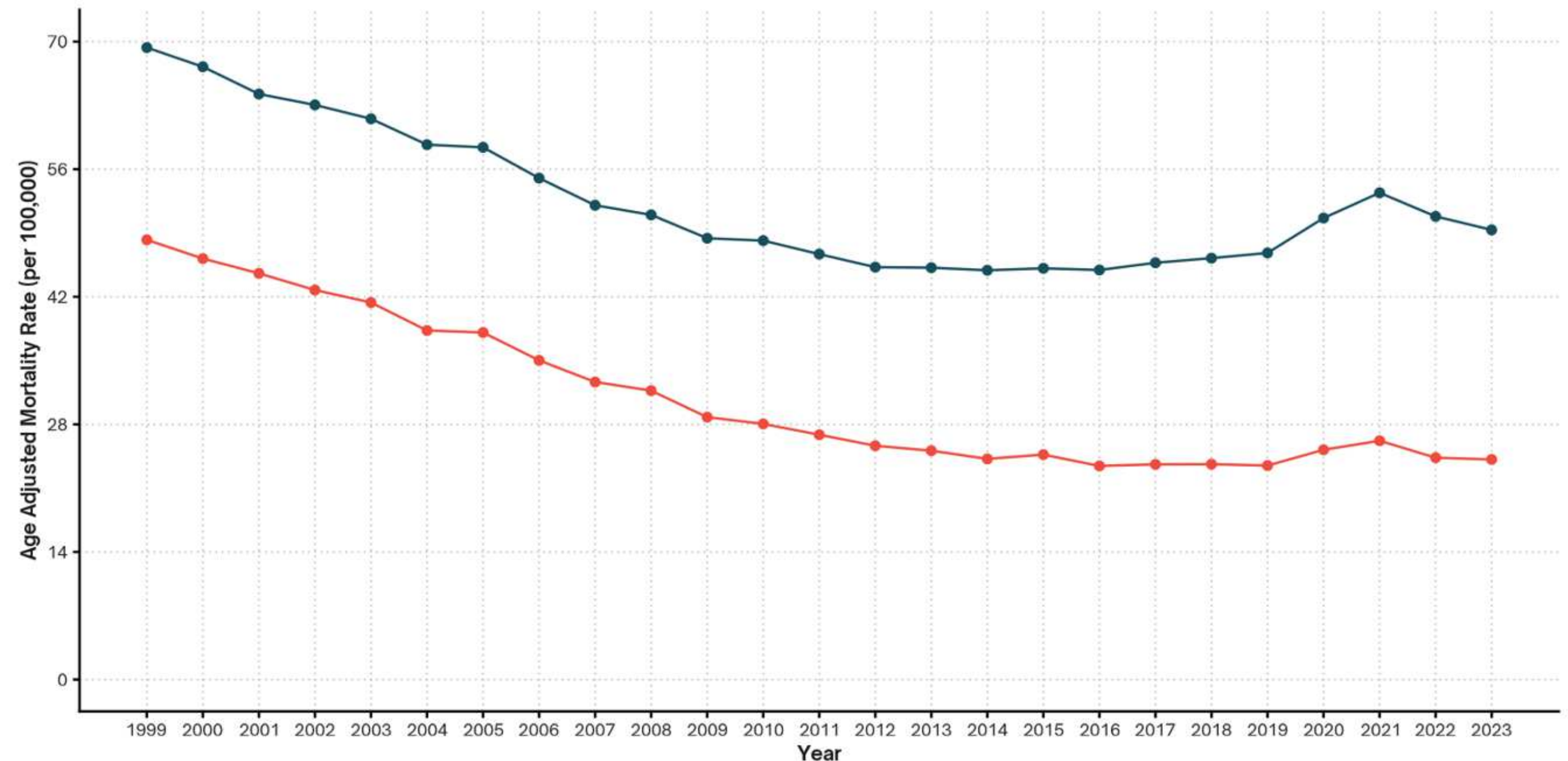
Figure 7: States-stratified trends in atherosclerotic Heart disease (ASHD) and heart failure (HF) mortality shown as age-adjusted mortality rates per 100,000 among adults aged ≥ 25 in the United States, 1999–2023

Figure 8: Central Illustration, Trends in demographics and disparities in concurrent atherosclerotic heart disease (ASHD) and heart failure (HF)-related mortality among the United States adults, 1999-2023.



- **ASCVD**
1999–2012 (APC: -3.79* [95% CI: -3.98 to -3.60]), **2012–2018** (APC: -2.01* [95% CI: -2.88 to -1.13]), **2018–2021** (APC: 5.17* [95% CI: 1.21 to 9.29]), **2021–2023** (APC: -6.19* [95% CI: -9.64 to -2.62])
- **HF**
1999–2012 (APC: -2.13* [95% CI: -2.38 to -1.89]), **2012–2018** (APC: 1.89* [95% CI: 0.85 to 2.94]), **2018–2021** (APC: 4.87* [95% CI: 0.72 to 9.19]), **2021–2023** (APC: -2.73 [95% CI: -6.50 to 1.19])
- **ASCVD and HF**
1999–2012 (APC: -4.09* [95% CI: -4.33 to -3.86]), **2012–2018** (APC: -0.40 [95% CI: -1.46 to 0.68]), **2018–2021** (APC: 4.69* [95% CI: 0.04 to 9.57]), **2021–2023** (APC: -3.78 [95% CI: -7.83 to 0.44])

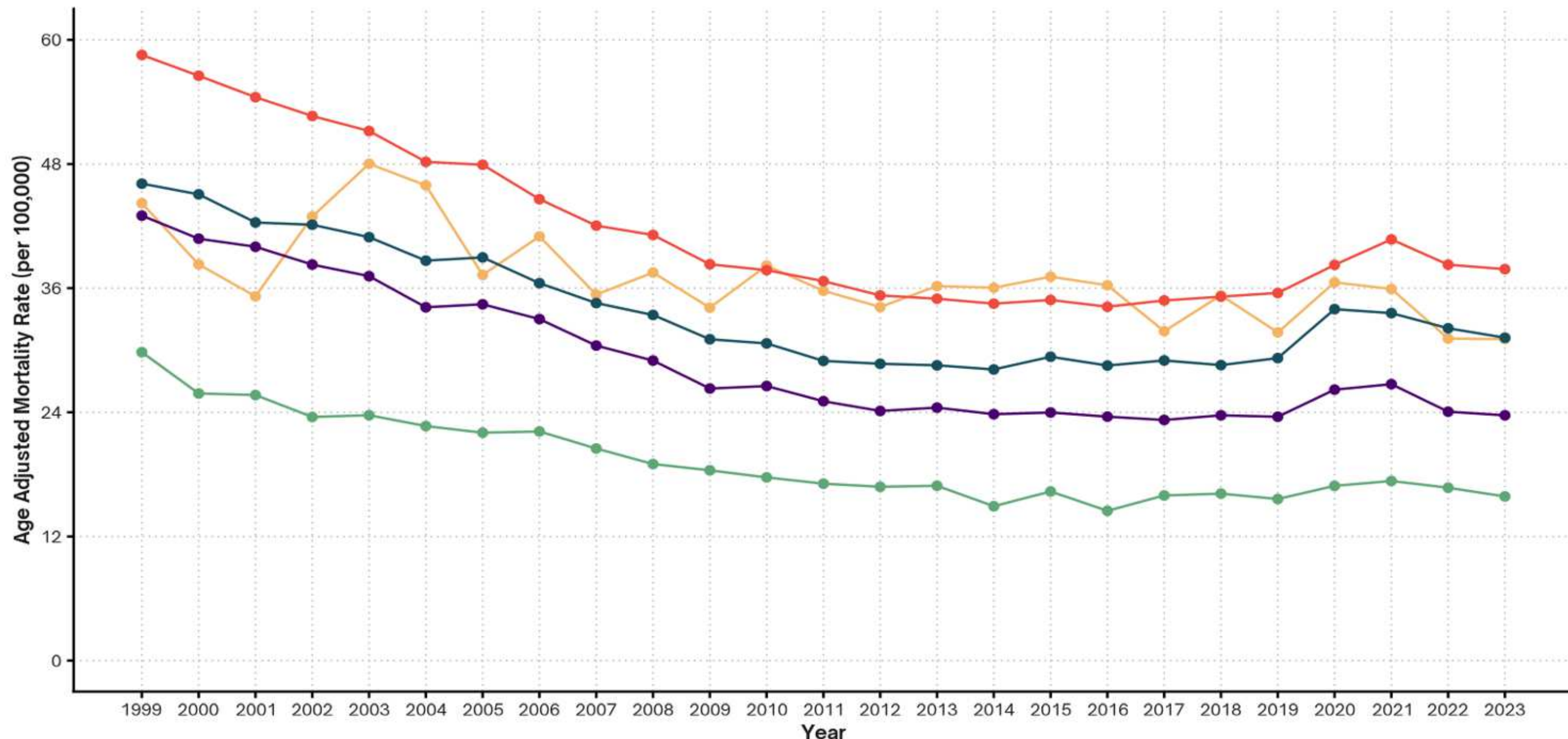
* Indicates that Annual Percentage Change (APC) is significant (p value < 0.05)



Female 1999–2003 (APC: -3.86* [95% CI: -5.33 to -2.36]), 2003–2012 (APC: -5.27* [95% CI: -5.84 to -4.70]), 2012–2018 (APC: -1.42* [95% CI: -2.76 to -0.05]), 2018–2021 (APC: 3.71 [95% CI: -2.05 to 9.80]), 2021–2023 (APC: -3.92 [95% CI: -9.07 to 1.51])

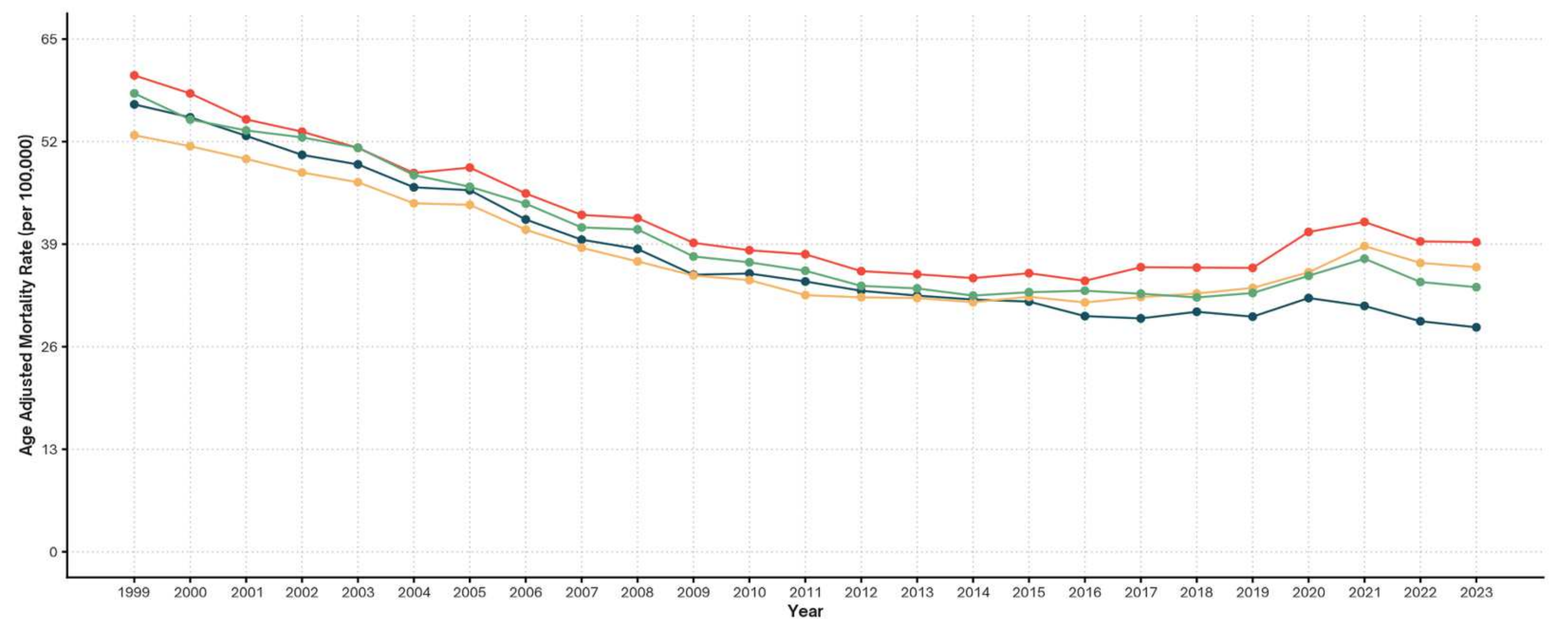
Male 1999–2012 (APC: -3.32* [95% CI: -3.52 to -3.12]), 2012–2018 (APC: 0.26 [95% CI: -0.56 to 1.10]), 2018–2021 (APC: 5.21* [95% CI: 1.64 to 8.90]), 2021–2023 (APC: -3.68* [95% CI: -6.85 to -0.39])

* Indicates that Annual Percentage Change (APC) is significant (p value < 0.05)

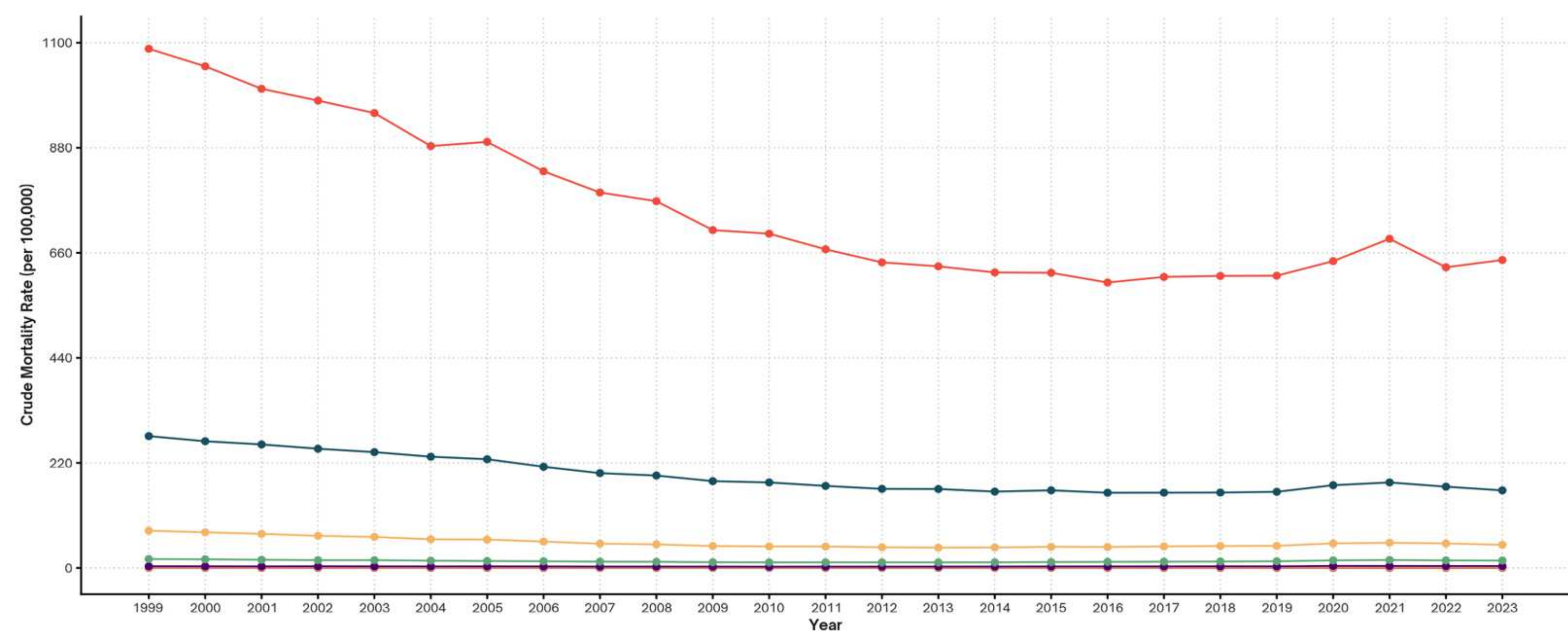


 <i>NH White</i>	1999–2012 (APC: -3.98* [95% CI: -4.20 to -3.75]), 2012–2018 (APC: -0.19 [95% CI: -1.24 to 0.87]), 2018–2021 (APC: 5.15* [95% CI: 0.57 to 9.95]), 2021–2023 (APC: -3.29 [95% CI: -7.53 to 1.14])
 <i>NH Black or African American</i>	1999–2012 (APC: -3.75* [95% CI: -4.06 to -3.44]), 2012–2018 (APC: 0.11 [95% CI: -1.25 to 1.49]), 2018–2021 (APC: 5.95* [95% CI: 0.35 to 11.86]), 2021–2023 (APC: -4.73 [95% CI: -9.61 to 0.40])
 <i>NH American Indian or Alaska Native</i>	1999–2023 (APC: -1.13* [95% CI: -1.57 to -0.69])
 <i>NH Asian or Pacific Islander</i>	1999–2014 (APC: -3.86* [95% CI: -4.42 to -3.29]), 2014–2023 (APC: 0.91 [95% CI: -0.06 to 1.88])
 <i>Hispanic or Latino</i>	1999–2012 (APC: -4.44* [95% CI: -4.79 to -4.09]), 2012–2018 (APC: -0.60 [95% CI: -1.94 to 0.75]), 2018–2021 (APC: 4.40 [95% CI: -0.99 to 10.07]), 2021–2023 (APC: -6.28* [95% CI: -11.01 to -1.31])

* Indicates that Annual Percentage Change (APC) is significant (p value < 0.05)

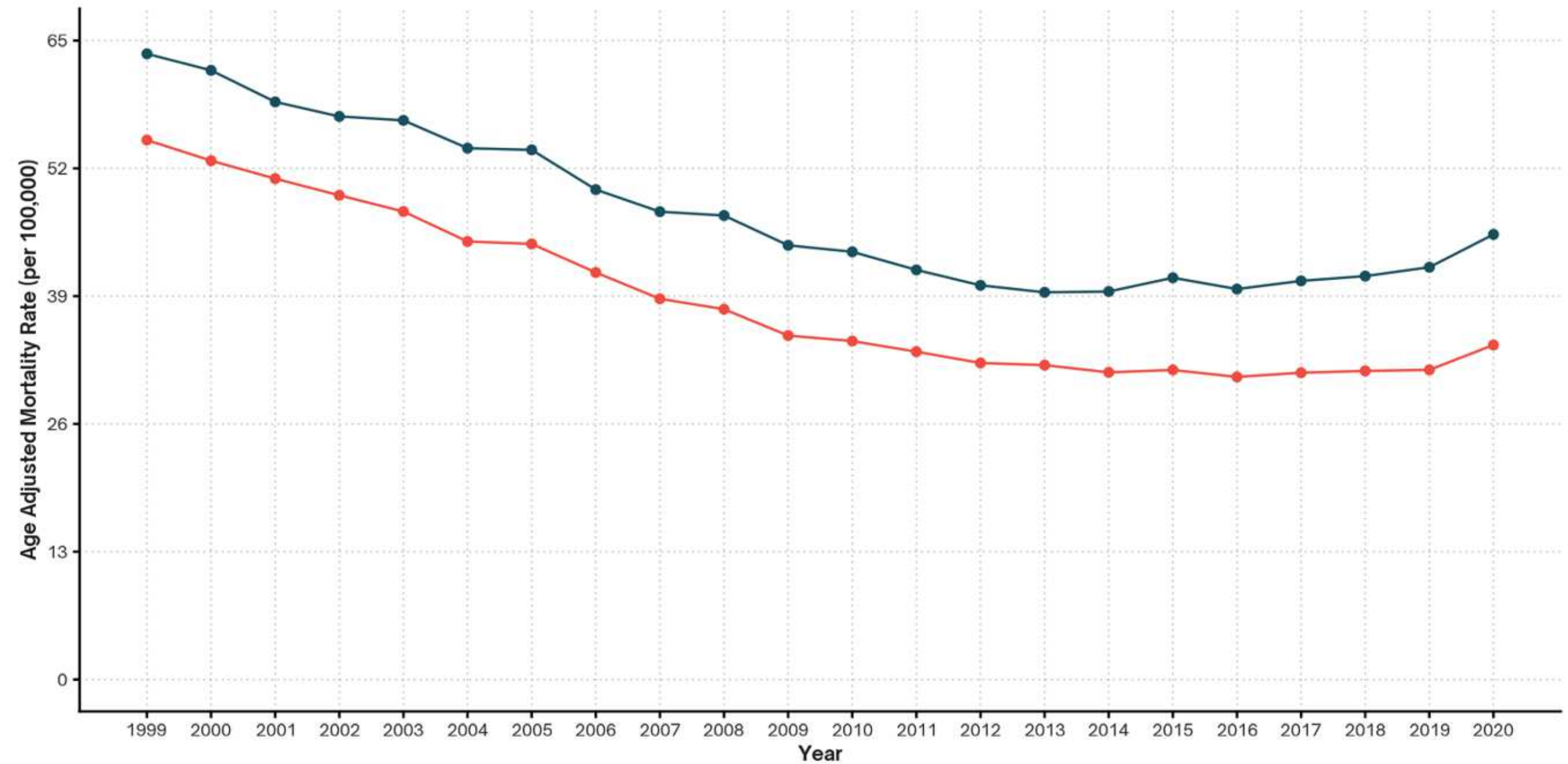


- **Midwest**
1999–2012 (APC: -4.0* [95% CI: -4.3 to -3.8]), **2012–2018** (APC: -0.02 [95% CI: -1.3 to 1.3]), **2018–2021** (APC: 5.7* [95% CI: 0.3 to 11.4]), **2021–2023** (APC: -3.47 [95% CI: -8.29 to 1.61])
 - **Northeast**
1999–2005 (APC: -3.8* [95% CI: -4.3 to -3.3]), **2005–2009** (APC: -5.6* [95% CI: -7.3 to -3.9]), **2009–2017** (APC: -2.3* [95% CI: -2.8 to -1.8]), **2017–2020** (APC: 2.4 [95% CI: -1.4 to 6.3]), **2020–2023** (APC: -3.6* [95% CI: -5.4 to -1.7])
 - **South**
1999–2005 (APC: -3.4* [95% CI: -4.0 to -2.9]), **2005–2011** (APC: -4.8* [95% CI: -5.5 to -4.0]), **2011–2018** (APC: -0.1 [95% CI: -0.7 to 0.6]), **2018–2021** (APC: 5.9* [95% CI: 2.5 to 9.4]), **2021–2023** (APC: -2.9 [95% CI: -5.9 to 0.2])
 - **West**
1999–2012 (APC: -4.2* [95% CI: -4.4 to -3.9]), **2012–2018** (APC: -0.9 [95% CI: -2.1 to 0.4]), **2018–2021** (APC: 4.5 [95% CI: -0.8 to 10.0]), **2021–2023** (APC: -4.7 [95% CI: -9.5 to 0.4])
- * Indicates that Annual Percentage Change (APC) is significant (p value < 0.05)



- **85+ years** **1999–2014** (APC: -4.0* [95% CI: -4.2 to -3.7]), **2014–2023** (APC: 1.0* [95% CI: 0.3 to 1.7])
- **75-84 years** **1999–2004** (APC: -3.3* [95% CI: -4.0 to -2.5]), **2004–2011** (APC: -4.6* [95% CI: -5.2 to -3.9]), **2011–2018** (APC: -1.1* [95% CI: -1.9 to -0.4]), **2018–2021** (APC: 4.9* [95% CI: 0.7 to 9.2]), **2021–2023** (APC: -4.9* [95% CI: -8.4 to -1.2])
- **65-74 years** **1999–2009** (APC: -5.1* [95% CI: -5.5 to -4.8]), **2009–2013** (APC: -2.3 [95% CI: -4.7 to 0.2]), **2013–2018** (APC: 1.3 [95% CI: -0.1 to 2.8]), **2018–2021** (APC: 5.4* [95% CI: 1.3 to 9.6]), **2021–2023** (APC: -4.3* [95% CI: -7.8 to -0.6])
- **55-64 years** **1999–2010** (APC: -4.2* [95% CI: -4.5 to -4.0]), **2010–2013** (APC: -0.3 [95% CI: -4.5 to 4.1]), **2013–2018** (APC: 3.0* [95% CI: 1.7 to 4.3]), **2018–2021** (APC: 7.4* [95% CI: 3.6 to 11.3]), **2021–2023** (APC: -3.9* [95% CI: -7.2 to -0.5])
- **45-54 years** **1999–2012** (APC: -2.0* [95% CI: -2.8 to -1.3]), **2012–2023** (APC: 4.1* [95% CI: 3.1 to 5.1])
- **35-44 years** **1999–2014** (APC: -0.9 [95% CI: -1.8 to 0.1]), **2014–2023** (APC: 5.3* [95% CI: 3.1 to 7.5])
- **25-34 years** **1999–2023** (APC: 1.0* [95% CI: 0.2 to 1.7])

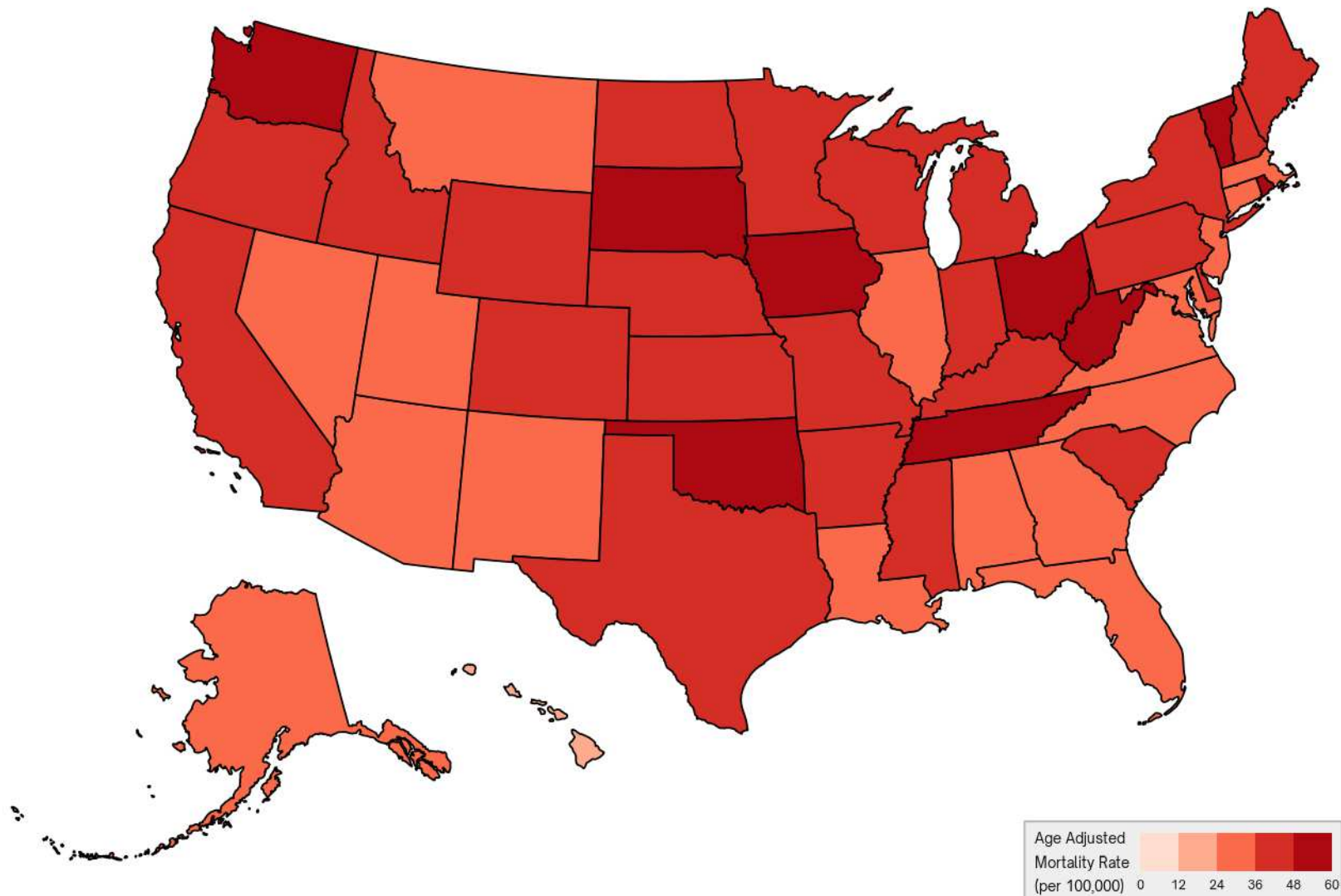
* Indicates that Annual Percentage Change (APC) is significant (p value < 0.05)



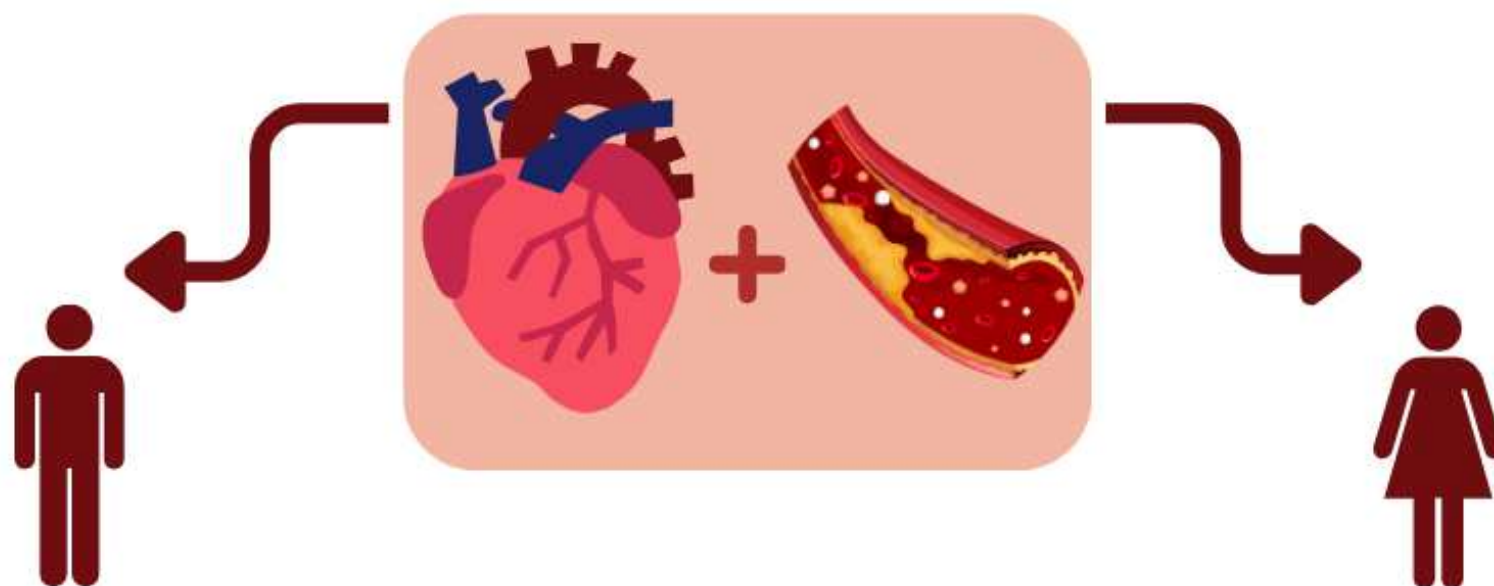
 **Metropolitan** 1999–2012 (APC: -4.20* [95% CI: -4.44 to -3.96]), 2012–2018 (APC: -0.47 [95% CI: -1.54 to 0.61]), 2018–2020 (APC: 4.39 [95% CI: -0.19 to 9.18])

 **Non-Metropolitan** 1999–2013 (APC: -3.53* [95% CI: -3.81 to -3.25]), 2013–2020 (APC: 1.57* [95% CI: 0.72 to 2.42])

* Indicates that Annual Percentage Change (APC) is significant (p value < 0.05)



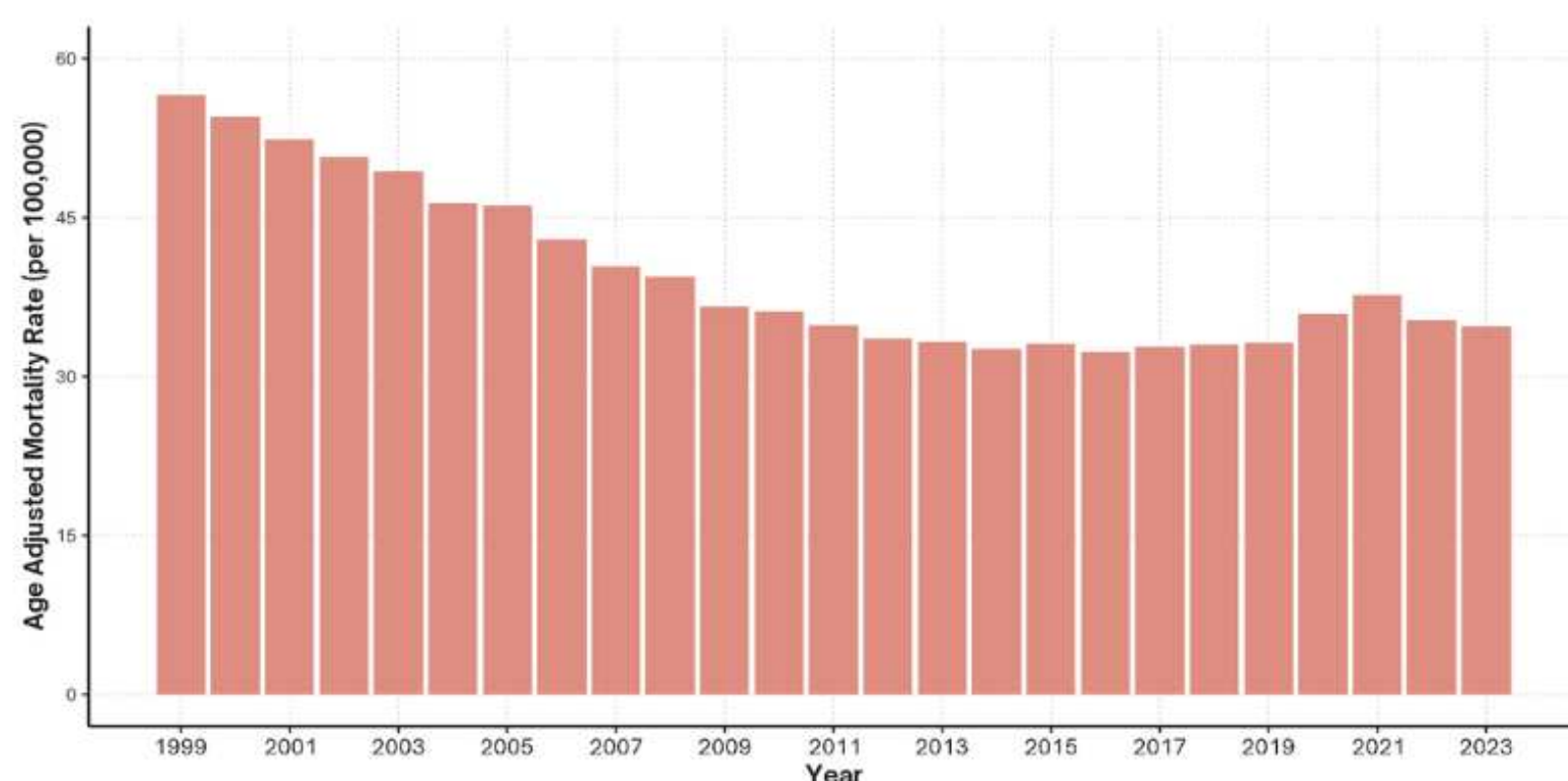
Men
1999: 69.3 AAMR
2023: 49.3 AAMR
Overall: 52.0 AAMR



Women
1999: 48.3 AAMR
2023: 24.2 AAMR
Overall: 30.5 AAMR

Female mortality **declined** more steeply than male mortality (AAPC -2.88% vs. -1.43% ; both $p < 0.001$). Among males, the 2018–2021 increase was pronounced (APC 5.21% ; $p = 0.007$), whereas female trends after 2018 were nonsignificant.

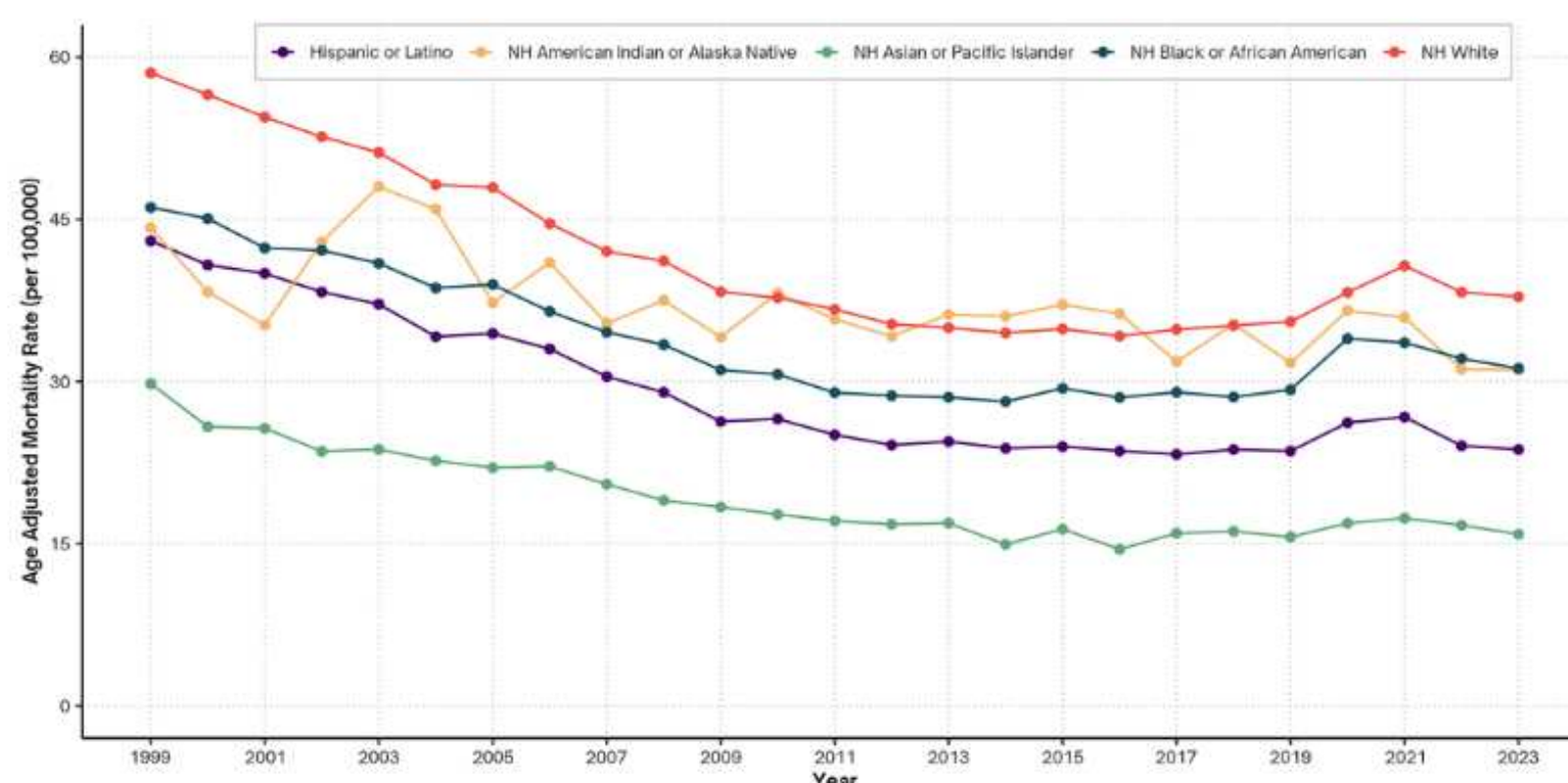
Overall Trend (1999-2023)



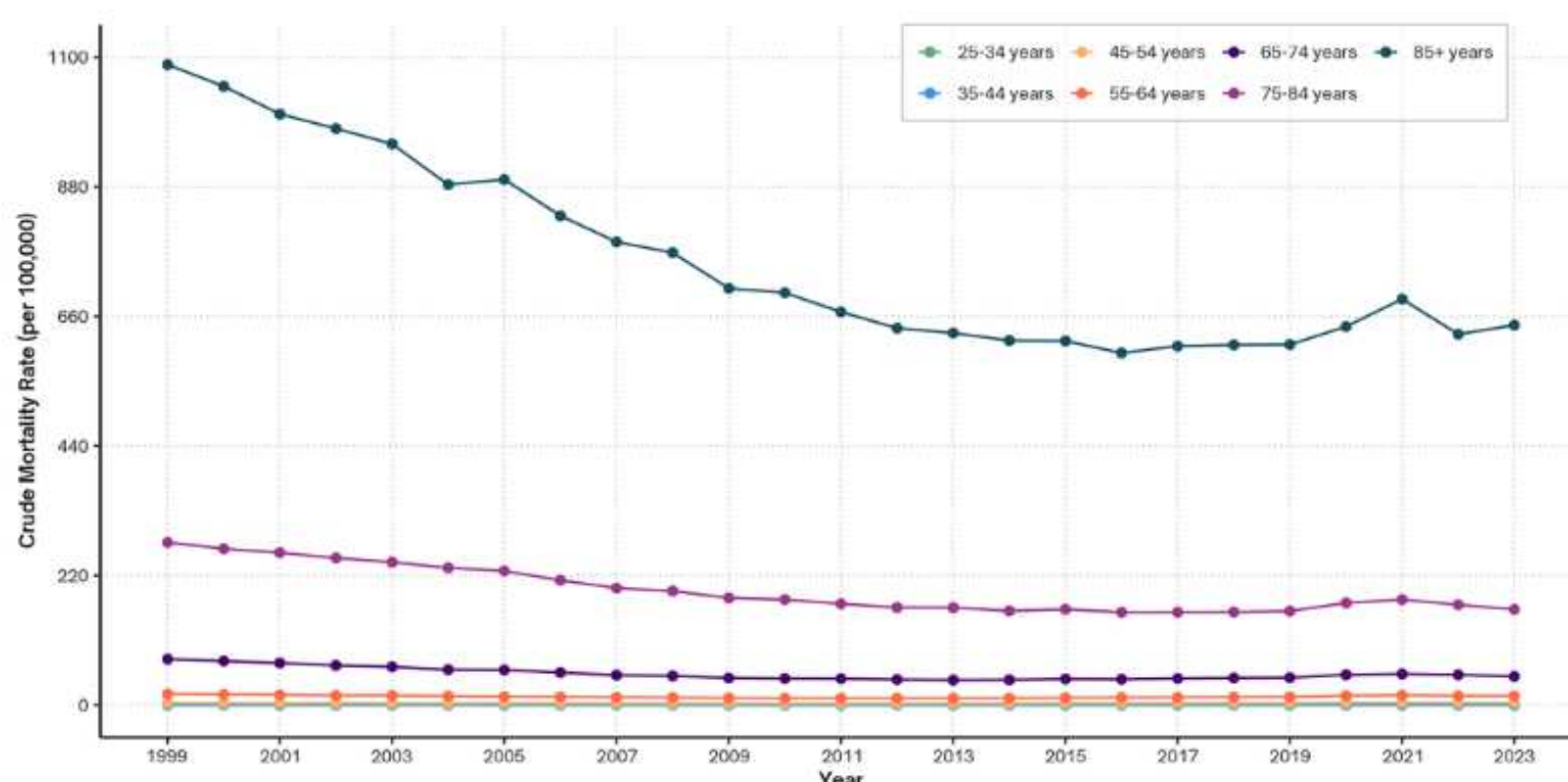
From 1999 to 2023, overall mortality **declined** significantly (AAPC -2.09% ; $p < 0.001$), characterized by a steep reduction through 2012 (APC -4.09), stabilization between 2012 and 2018 (APC -0.40), and a significant increase from 2018 to 2021 (APC 4.69%), followed by a nonsignificant decline thereafter.

Race-Stratified Age-Adjusted Mortality Rates

From 1999 to 2023, mortality **declined** across all racial/ethnic groups, most notably among Hispanics and Asians. Between 2018–2021, rates rose significantly for Whites ($+5.15\%$) and Blacks ($+5.95\%$), with nonsignificant increases in others, followed by uneven declines after 2021.



Tenth Age Groups-Stratified Crude Mortality Rates



From 1999 to 2023, mortality **rose** in younger and middle-aged adults (25–54 years), driven by post-2012 increases, while adults ≥ 55 years showed **sustained decline** with a transient 2018–2021 spike. Rising mortality in younger and midlife groups signals a generational shift that may offset overall progress.

Supplementary Files

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

- [SupplementaryMaterial.docx](#)