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Original Article

Trends in Mortality Co-Reporting Heart Failure and Metabolic Syndrome–Related Conditions Among U.S. Adults Aged ≥25 Years, 1999–2023: A CDC WONDER Analysis

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ABSTRACT

Background: Heart failure frequently coexists with cardiometabolic conditions commonly associated with metabolic syndrome. Characterizing long-term mortality patterns involving these co-reported conditions may help identify populations with a disproportionate burden.
Methods: We performed a national serial cross-sectional analysis using the CDC WONDER Multiple Cause of Death database to examine mortality among U.S. adults aged ≥25 years from 1999 to 2023. Eligible deaths included those with at least one heart failure ICD–10 code and at least one metabolic syndrome–related ICD–10 code recorded anywhere on the death record. Age-adjusted mortality rates (AAMRs) per 100,000 population were calculated using the 2000 U.S. standard population. Temporal trends were assessed using Joinpoint regression and stratified by sex, race/ethnicity, U.S. Census region, urbanization (1999–2020), and state.
Results: A total of 1,562,715 deaths co-reporting heart failure and metabolic syndrome–related conditions were identified. The overall AAMR increased from 24.7 in 1999 to 38.3 in 2023. After declining from 2005 to 2012, mortality increased beginning in the mid-2010s, with a pronounced acceleration during 2018–2021 and a modest decline thereafter. AAMRs were higher among men, non-Hispanic Black and American Indian or Alaska Native populations, residents of the Midwest (with comparatively elevated rates also observed in the West and South), and individuals in nonmetropolitan areas.
Conclusions: Mortality involving deaths co-reporting heart failure and metabolic syndrome–related conditions increased substantially after 2012, with marked disparities by sex, race/ethnicity, geography, and urbanization, underscoring the need for equity-focused cardiometabolic prevention strategies.

1. Introduction

Heart failure (HF) is a major public health problem and a leading cause of morbidity and mortality globally. Cardiometabolic conditions commonly associated with metabolic syndrome – including diabetes mellitus, obesity, dyslipidemia, and related metabolic disorders – frequently coexist with HF and are associated with substantial mortality in the US population [1]. The prevalence of cardiometabolic conditions commonly associated with metabolic syndrome has risen over the past two decades, driven largely by increases in obesity and diabetes. It is strongly associated with cardiovascular risk, including heart failure [2].

Demographic factors, including age, sex, and race/ethnicity, play an important role in the mortality involving heart failure. For instance, males have shown higher mortality involving heart failure than females, which could be attributed to the early onset of risk factors associated with metabolic syndrome and sex differences in cardiac remodeling [3, 4]. Similarly, racial and ethnic differences have been observed in the mortality involving heart failure, with the NH Black and NH American Indian or Alaska Native (AI/AN) populations showing increased mortality from heart failure, which could be attributed to structural factors including access to healthcare and the prevalence of uncontrolled risk factors associated with metabolic syndrome [5, 6].

Geographic variation also contributes to differential risk, as the South and Midwest regions consistently report increased mortality

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rates involving HF, which may be attributed to the increased rates of obesity, diabetes, and other factors [7]. Additionally, there are disparities in rural vs. urban populations, as rural populations have less access to health care, resulting in increased mortality from HF compared to those living in metropolitan regions [8].

Identifying demographic, racial, and geographic patterns of mortality involving death certificates, co reported heart failure, and metabolic syndrome – related conditions can help identify populations for targeted interventions aimed at reducing disparities and improving cardiovascular outcomes. Accordingly, this study aims to examine national trends and disparities in mortality involving death certificates that co report heart failure and metabolic syndrome – related conditions among U.S. adults aged 25 years and older from 1999 to 2023.

2. Methods

2.1. Study design, data source, and reporting framework

We performed a serial cross-sectional (time-trend) analysis using the National Vital Statistics System (NVSS) Multiple-Cause-of-Death (MCD) files accessed through the Centers for Disease Control and Prevention (CDC) Wide-ranging Online Data for Epidemiologic Research (WONDER). To cover the complete study period (1999 – 2023), we queried the Multiple-Cause-of-Death 1999 – 2020 (bridged-race) series and the Multiple-Cause-of-Death 2018 – 2023 (single-race) series [9, 10]. Each U.S. death certificate includes one underlying cause of death (UCD) and up to 20 multiple (contributing) causes, along with demographic and geographic variables [11]. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline [12]. Because the data are deidentified and publicly available, institutional review board approval was not required. All data were accessed on February 1, 2026.

2.2. Study population

The study population included U.S. residents aged ≥25 years. We identified eligible deaths using a multiple-cause-of-death (MCD) all-mentions approach within the National Vital Statistics System database, accessed through CDC WONDER. Heart failure (HF) was identified using International Classification of Diseases, Tenth Revision (ICD 10) codes I11.0, I13.0, I13.2, and I50.x [2]. Metabolic syndrome – related conditions were defined by the presence of ICD 10 codes for diabetes mellitus (E10 – E14), obesity (E66), dyslipidemia (E78), and other disorders of metabolism (E88) [13].

Eligible deaths were those in which at least one HF code and at least one metabolic syndrome – related condition code were recorded anywhere on the death certificate, regardless of whether either condition was listed as the underlying cause of death or as a contributing cause. This operational definition captures a heterogeneous group of cardiometabolic comorbidities commonly associated with metabolic syndrome but does not represent clinically adjudicated metabolic syndrome as defined by established diagnostic criteria. Accordingly, all analyses reflect mortality involving death certificates that co reported HF and metabolic syndrome – related conditions, rather than cause specific mortality attributable to metabolic syndrome or HF alone. All analyses were conducted using a multiple cause of death, all mentions approach and describe death certificates on which both heart failure and metabolic syndrome – related conditions were recorded, without attributing causality or underlying cause of death to either condition.

2.3. Variables and stratification

We extracted annual death counts and mortality measures stratified by year, sex, race/ethnicity, U.S. Census region, urbanization, and state [9–11]. U.S. Census regions (Northeast, Midwest, South, West) were classified according to the Census Bureau's definitions [14]. Race and ethnicity were combined, bridged-race categories for 1999 – 2020 and single-race categories for 2018 – 2023 [9, 10]. Urbanization was defined using the 2013 National Center for Health Statistics (NCHS) Urban – Rural Classification Scheme and collapsed into metropolitan (large central, large fringe, medium, small metro) versus nonmetropolitan (micropolitan, noncore) categories [15, 16]. Because county-level identifiers are not available in the 2018 – 2023 single-race MCD series, urbanization analyses were restricted to 1999 – 2020.

Race and ethnicity data were obtained from CDC WONDER using two mortality data series to cover the full study period. For analyses spanning 1999 – 2020, we used the Multiple Cause of Death 1999 – 2020 bridged race series. For analyses spanning 2021 – 2023, we used the Multiple Cause of Death 2018 – 2023 single race series. Although both datasets include overlapping calendar years from 2018 to 2020, death counts for these years were identical across the two series. Therefore, estimates for 2018 – 2020 were taken from a single series, and the single race series was used beginning in 2021 to extend analyses through 2023. This approach preserves continuity while avoiding duplication or artificial discontinuities across the race coding transition.

2.4. Mortality measures and scaling

We extracted crude mortality rates (CMRs) and age-adjusted mortality rates (AAMRs) with 95% confidence intervals (CIs), standardized to the 2000 U.S. standard population [17]. Rates were expressed per 100,000 population. Although CDC WONDER suppresses death counts of fewer than 10 and flags rates based on fewer than 20 deaths as unreliable, no suppressed or unreliable estimates occurred in this study, and complete annual rates were available for all included strata.

2.5. Urbanization-specific considerations

Urbanization analyses were limited to 1999 – 2020, the only period for which county-level identifiers were available. The 2018 – 2023 single-race dataset does not provide county or urbanization variables; therefore, urbanization trends were not evaluated beyond 2020. Joinpoint modeling for urbanization was performed solely for the 1999 – 2020 interval.

2.6. Statistical analysis

Temporal trends in AAMRs were evaluated using the Joinpoint Regression Program (version 4.9.0.0) from the National Cancer Institute [18]. Log linear segmented regression models were used to identify statistically significant changes in mortality trends over time, with calendar year as the independent variable and the natural logarithm of the AAMR as the dependent variable. A maximum of four joinpoints was allowed, consistent with recommendations for analyses spanning more than two decades.

Model selection was conducted using Monte Carlo permutation testing with 4,499 replications and an overall two sided significance level of 0.05. The minimum number of observations required between joinpoints was four years, with at least two observations at each end of the data series. Heteroscedastic error variance was assumed, and standard errors were estimated using the Joinpoint program's default variance option based on reported AAMR confidence intervals.

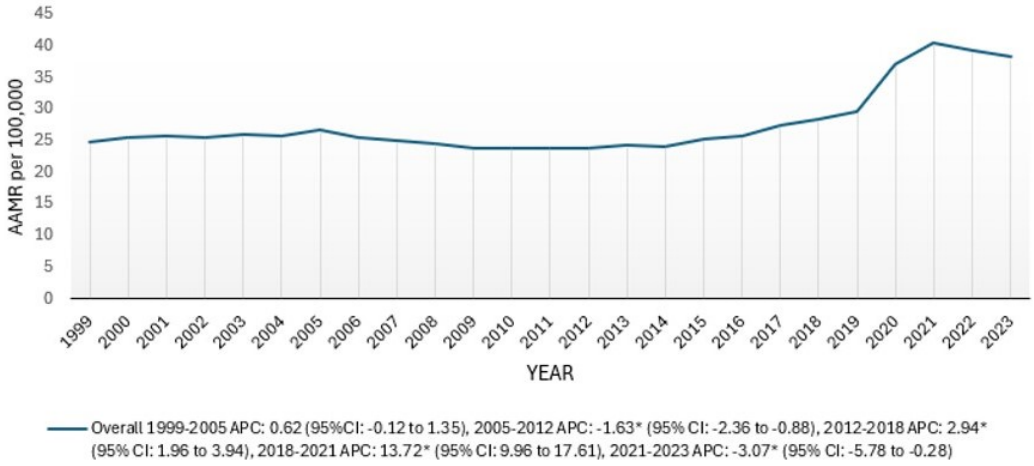

Figure 1: Overall Annual Trends in Mortality Involving Co-Reported Heart Failure And Metabolic Syndrome–Related Conditions, 1999-2023.
* Indicates that the annual percentage change (APC) is significantly different from zero at $\alpha = 0.05$. AAMR = age-adjusted mortality rate.

Annual percent change (APC) estimates with 95% confidence intervals (CIs) were calculated for each identified time segment, and statistical significance was defined as a two-sided p-value < 0.05. Subgroup analyses were performed by sex, race and ethnicity, U.S. Census region, urbanization status, and state. State-level results were summarized using average AAMRs and percentile-based rankings to identify the highest and lowest-burden states.

3. Results

Between 1999 and 2023, a total of 1,562,715 death certificates co reported heart failure and metabolic syndrome – related conditions in the studied population aged 25 and above **(Supplemental Table 1)**.

3.1. Overall annual trends in mortality involving co reported heart failure and metabolic syndrome – related conditions

Across the study period, mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions demonstrated substantial temporal variation in age adjusted mortality rates. The AAMR for overall deaths was 24.7 in 1999 and 38.3 in 2023. From 1999 to 2005, the AAMRs increased, although the change was not statistically significant (APC: 0.62; 95% CI: -0.12 to 1.35). This was followed by a significant decline between 2005 and 2012 (APC: -1.63; 95% CI: -2.36 to -0.88). Beginning in 2012, AAMR increased significantly through 2018 (APC: 2.94; 95% CI: 1.96 to 3.94). The upward trend then accelerated sharply from 2018 to 2021 (APC: 13.72; 95% CI: 9.96 to 17.61). After 2021, the overall AAMR decreased significantly through 2023 (APC: -3.07; 95% CI: -5.78 to -0.28) **(Figure 1)** and **(Supplemental Tables 2 and 3)**.

3.2. Mortality involving co reported heart failure and metabolic syndrome – related conditions, stratified by sex

When stratified by sex, mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions was consistently higher among men than women throughout the study period (overall AAMR for men: 33.0; 95% CI: 32.7 to 33.4; women: 23.5; 95% CI: 23.2 to 23.8).

Among men, the AAMR was 27.4 (95% CI: 27.0 to 27.8) in 1999, increasing to 29.8 (95% CI: 29.4 to 30.2) in 2004 (APC: 1.70; 95% CI: 0.69 to 2.71), followed by a significant decrease to 28.7 in 2012 (APC: -0.85; 95% CI: -1.42 to -0.26). AAMR then increased significantly to 35.3 in 2018 (APC: 3.42; 95% CI: 2.48 to 4.36), followed by a sharp rise to 50.3 in 2021 (APC: 13.71; 95% CI: 10.21 to 17.31), and then decreased significantly to 48.1 in 2023 (APC: -2.71; 95% CI: -5.23 to -0.11).

Among women, the AAMR was 22.8 (95% CI: 22.5 to 23.1) in 1999, showing no significant change to 23.8 in 2005 (APC: 0.0; 95% CI: -0.82 to 0.82). This was followed by a significant decline to 20.2 in 2012 (APC: -2.31; 95% CI: -3.17 to -1.44), then a significant increase to 23.0 in 2018 (APC: 2.20; 95% CI: 1.00 to 3.40). This rise steepened substantially to 32.7 in 2021 (APC: 13.73; 95% CI: 9.01 to 18.66). After 2021, the trend shifted downward with a significant decrease to 30.7 in 2023 (APC: -3.70; 95% CI: -7.10 to -0.18) **(Figure 2)** and **(Supplemental Tables 2 and 3)**.

3.3. Mortality involving co reported heart failure and metabolic syndrome – related conditions, stratified by race/ethnicity

Marked racial and ethnic disparities were observed in mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions over the study period. Across the study period, the highest AAMRs occurred among NH Black, followed by NH American Indian or Alaska Native (AI/AN), NH White, Hispanic, and NH Asian or Pacific Islander (API) populations (Overall AAMR, NH Black 37.1; 95% CI: 36.3 to 38.0, NH American Indian or Alaska Native (AI/AN) 34.0; 95% CI: 30.6 to 37.1, NH White 27.0; 95% CI: 26.7 to 27.2, Hispanic 26.1; 95% CI: 25.3 to 27.0, and NH Asian or pacific Islanders (API) 15.9; 95% CI: 15.0 to 16.8). The AAMR among Black individuals declined significantly from 1999 to 2013 (APC: -0.62; 95% CI: -1.04 to -0.19). Rates then showed a nonsignificant rise until 2018 (APC: 2.47; 95% CI: -0.03 to 5.04). From 2018 to 2021, mortality increased sharply (APC: 16.19; 95% CI: 9.22 to 23.59). And a nonsignificant decline in AAMRs was observed until 2023 (APC: -4.08; 95% CI: -9.92 to 2.14). Among NH American Indian or Alaska Native (AI/AN) individuals, the AAMR declined non-significantly from 1999 to 2018 (APC: -0.47; 95% CI: -1.09 to 0.16). This was followed by a sharp, significant increase until 2021 (APC: 25.22; 95% CI: 8.62 to 44.36). From 2021 to 2023, AAMRs declined again, though not significantly (APC: -5.76; 95% CI: -17.86 to 8.12). NH White individuals demonstrated several inflection points. AAMRs increased nonsignificantly from 1999 to 2005 (APC: 0.61; 95% CI: -0.22 to 1.44), followed by a

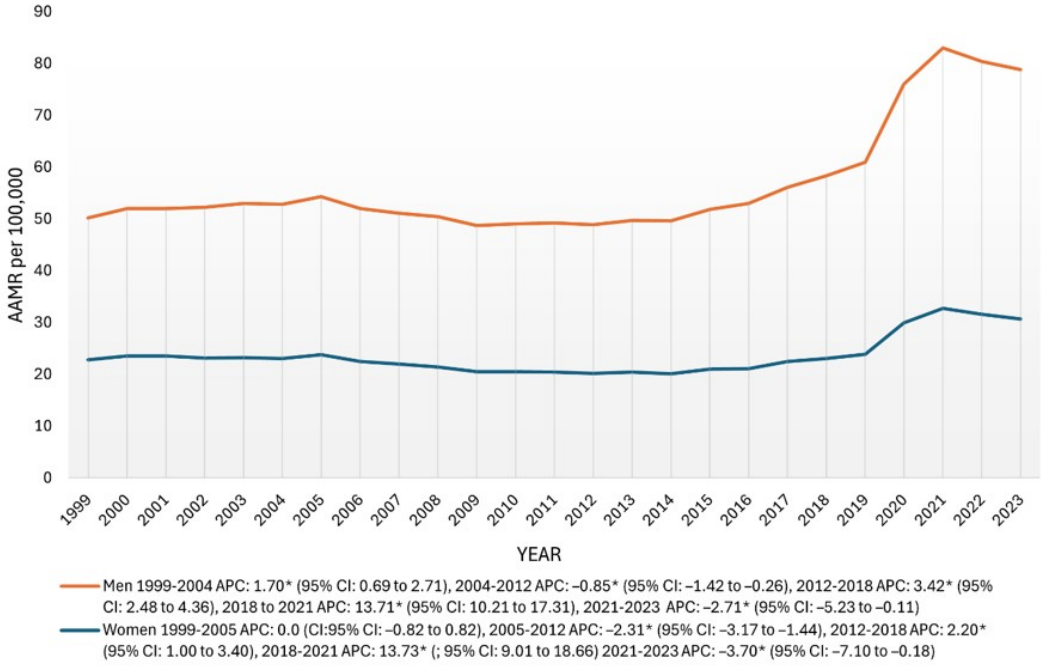

Figure 2: Mortality Trends Involving Co-Reported Heart Failure and Metabolic Syndrome–related Conditions, Stratified by Sex, 1999–2023.
* Indicates that the annual percentage change (APC) is significantly different from zero, $\alpha = 0.05$. AAMR = age-adjusted mortality rate.

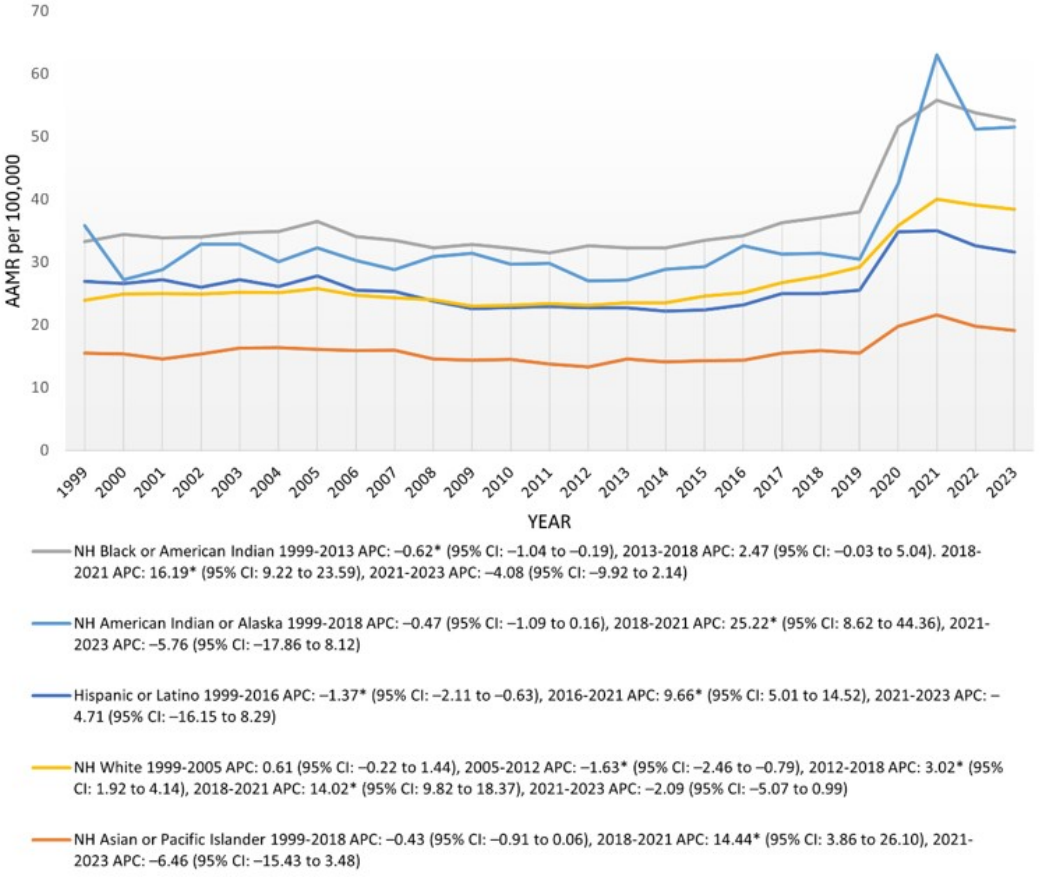

Figure 3: Mortality Trends Involving Co-Reported Heart Failure and Metabolic Syndrome–Related Conditions, Stratified by Race/Ethnicity, 1999–2023.
* Indicates that the annual percentage change (APC) is significantly different from zero, $\alpha = 0.05$. AAMR = age-adjusted mortality rate, NH = Non-Hispanic.

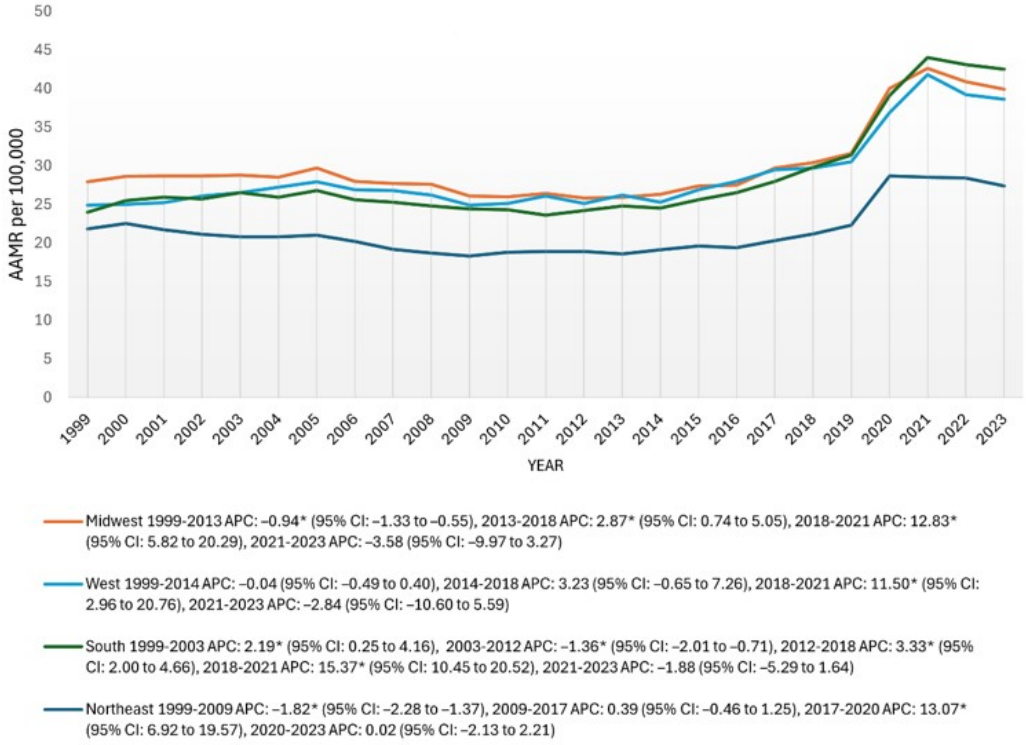

Figure 4: Mortality Trends Involving Co-Reported Heart Failure and Metabolic Syndrome–Related Conditions, Stratified by Census Region, 1999–2023. * Indicates that the annual percentage change (APC) is significantly different from zero, $\alpha = 0.05$. AAMR = age-adjusted mortality rate.

significant decline until 2012 (APC: -1.63; 95% CI: -2.46 to -0.79). Rates rose significantly from 2012 to 2018 (APC: 3.02; 95% CI: 1.92 to 4.14), with a further steep rise until 2021 (APC: 14.02; 95% CI: 9.82 to 18.37). A nonsignificant decrease followed from 2021 to 2023 (APC: -2.09; 95% CI: -5.07 to 0.99). Among Hispanic individuals, the AAMR declined significantly from 1999 to 2016 (APC: -1.37; 95% CI: -2.11 to -0.63). This was followed by a significant increase from 2016 to 2021 (APC: 9.66; 95% CI: 5.01 to 14.52). From 2021 to 2023, AAMRs decreased, though not significantly (APC: -4.71; 95% CI: -16.15 to 8.29). For NH Asian or Pacific Islander (API) individuals, the AAMR decreased slightly from 1999 to 2018 (APC: -0.43; 95% CI: -0.91 to 0.06), though this decline was not statistically significant. A significant rise then occurred from 2018 to 2021 (APC: 14.44; 95% CI: 3.86 to 26.10). The trend reversed from 2021 to 2023, with a nonsignificant decline (APC: -6.46; 95% CI: -15.43 to 3.48) **(Figure 3)** and **(Supplemental table 2 and 4)**.

3.4. Mortality involving co reported heart failure and metabolic syndrome – related conditions, stratified by census region

Significant regional variation was observed in mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions across the four U.S. Census regions. During the study period, the highest AAMR was observed in the Midwest, 30.0 (95% CI: 29.5 to 30.5), followed by the West, 28.7 (95% CI: 28.2 to 29.1), South, 28.5 (95% CI: 28.1 to 28.8), and Northeast, 21.4 (95% CI: 21 to 21.9). In the Midwest, AAMRs decreased significantly from 1999 to 2013 (APC: -0.94; 95% CI: -1.33 to -0.55). The trend reversed from 2013 to 2018, showing a significant increase (APC: 2.87; 95% CI: 0.74 to 5.05). A much steeper rise occurred from 2018 to 2021 (APC: 12.83; 95% CI: 5.82 to 20.29). From 2021 to 2023, AAMRs decreased, although the change was not statistically significant (APC: -3.58; 95% CI: -9.97 to 3.27). In the West, AAMRs remained stable from 1999 to 2014 (APC: -0.04; 95% CI: -0.49 to 0.40). A non-significant increase was observed from 2014 to 2018 (APC: 3.23; 95% CI: -0.65 to 7.26). This was followed by a significant rise from 2018 to 2021 (APC: 11.50; 95% CI: 2.96 to 20.76). Rates decreased afterward from 2021 to 2023, though non-significantly (APC: -2.84; 95% CI: -10.60 to 5.59). The South exhibited multiple inflection points. From 1999 to 2003, AAMR increased significantly (APC: 2.19; 95% CI: 0.25 to 4.16), followed by a significant decline between 2003 and 2012 (APC: -1.36; 95% CI: -2.01 to -0.71). AAMRs then increased again from 2012 to 2018 (APC: 3.33; 95% CI: 2.00 to 4.66), followed by a marked surge between 2018 and 2021 (APC: 15.37; 95% CI: 10.45 to 20.52). From 2021 to 2023, AAMRs declined, although the change was not statistically significant (APC: -1.88; 95% CI: -5.29 to 1.64). In the Northeast, AAMRs declined steadily from 1999 to 2009 (APC: -1.82; 95% CI: -2.28 to -1.37). This was followed by a period of stability from 2009 to 2017, with no significant change (APC: 0.39; 95% CI: -0.46 to 1.25). From 2017 to 2020, AAMR increased sharply (APC: 13.07; 95% CI: 6.92 to 19.57), before stabilizing again from 2020 to 2023 (APC: 0.02; 95% CI: -2.13 to 2.21) **(Figure 4)** and **(Supplemental table 2 and 5)**.

3.5. Mortality involving co reported heart failure and metabolic syndrome – related conditions, stratified by urbanization

During the 1999 – 2020 study period, mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions differed substantially by urbanization status, with consistently higher rates observed in nonmetropolitan areas than metropolitan areas, with overall AAMRs of 34.1 (95% CI: 33.9 to 34.2) and 24.4 (95% CI: 24.4 to 25.5), respectively. In nonmetropolitan areas from 1999 to 2005, AAMRs increased significantly (APC: 1.26; 95% CI: 0.42 to 2.10). This was followed

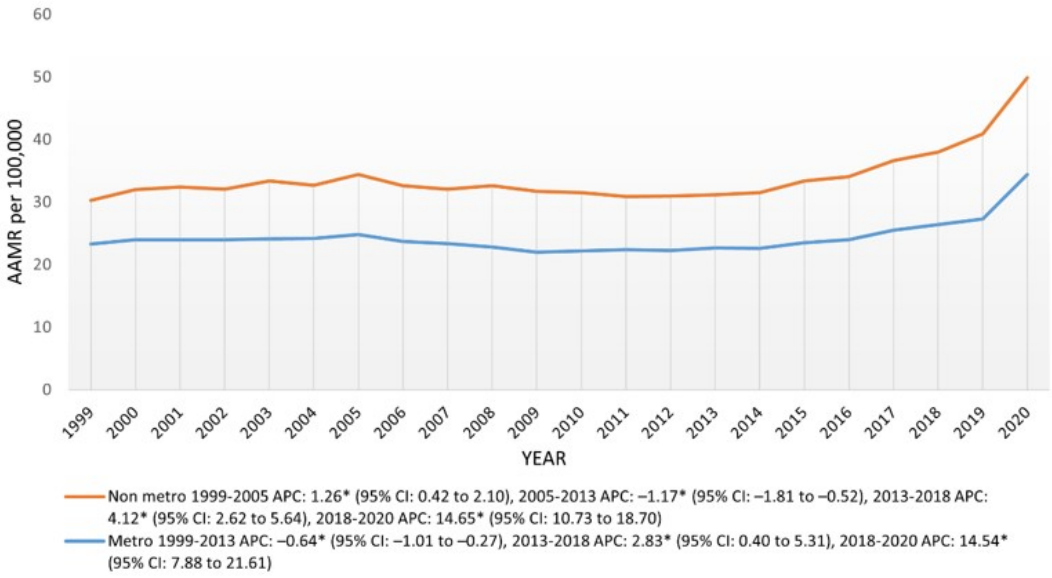

Figure 5: Mortality involving co-reported heart failure and metabolic syndrome–related conditions, stratified by urbanization, 1999–2020.
* Indicates that the annual percentage change (APC) is significantly different from zero, $\alpha = 0.05$. AAMR = age-adjusted mortality rate.

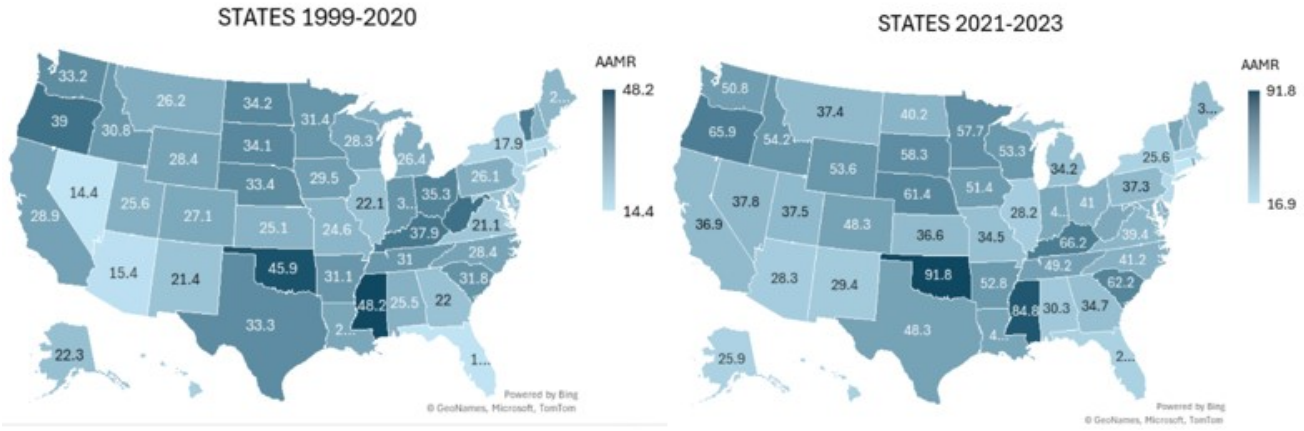

Figure 6: State-Stratified Heart Failure With Metabolic Syndrome–Related AAMRs per 100,000 Among Adults Aged 25 Years and Older in the United States, 1999–2023.

by a significant decline between 2005 and 2013 (APC: -1.17; 95% CI: -1.81 to -0.52). Rates then increased markedly from 2013 to 2018 (APC: 4.12; 95% CI: 2.62 to 5.64), and a sharp surge occurred from 2018 to 2020 (APC: 14.65; 95% CI: 10.73 to 18.70). In metropolitan areas, AAMRs decreased significantly from 1999 to 2013 (APC: -0.64; 95% CI: -1.01 to -0.27). This was followed by a significant rise from 2013 to 2018 (APC: 2.83; 95% CI: 0.40 to 5.31). Mortality surged sharply between 2018 and 2020 (APC: 14.54; 95% CI: 7.88 to 21.61) **(Figure 5)** and **(Supplemental Table 2 and 6)**.

3.6. Mortality involving co reported heart failure and metabolic syndrome – related conditions, stratified by state

State level analyses revealed considerable geographic heterogeneity in mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions across the United States. During 1999 – 2020, AAMR values ranged from a low of 14.4 deaths per 100,000 in Nevada to a high of 48.2 in Mississippi. States in the highest (≥90th) percentile were Mississippi, Oklahoma, West Virginia, Oregon, Kentucky, and Vermont, while Nevada, Florida, Arizona, Massachusetts, and New York fell within the lowest (≤10th) percentile.

In 2021 – 2023, AAMR values increased substantially, ranging from a low of 16.9 in Connecticut to a high of 91.8 in Oklahoma. States in the ≥90th percentile included Oklahoma, Mississippi, Kentucky, Oregon, South Carolina, and Nebraska, whereas Connecticut, New Jersey, Massachusetts, New York, and Alaska comprised the lowest (≤10th) percentile.

Several states were in the highest-burden group in both analytic periods, although the periods differed in duration. Oklahoma, Mississippi, Kentucky, and Oregon ranked within the highest percentile group in both the 1999 – 2020 and 2021 – 2023 analyses

periods. Conversely, several states fell into the lowest-burden group in both analytic periods. Massachusetts and New York ranked within the lowest percentile group in both periods **(Figure 6)** and **(Supplemental Table 7)**.

4. Discussion

This integrative study of mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions among the adult population (age 25 and above) in the United States from 1999 to 2023 indicates epidemiological trends and existing inequalities that require immediate societal intervention. Our results reveal a complex trend: first, a period of stability, followed by a considerable decrease in mortality rates, and then a sharp increase beginning around 2012, with the steepest rise occurring between 2018 and 2021. These time trends are consistent with and expand upon findings from recent national studies of cardiometabolic mortality [1, 19].

The overall age adjusted mortality rate increased from 24.7 in 1999 to 38.3 in 2023, representing a 55% increase over the study period. Joinpoint regression identified five phases: a nonsignificant increase (1999 – 2005), a significant decrease (2005 – 2012), a significant increase (2012 – 2018), a sharp acceleration (2018 – 2021), and a recent decline (2021 – 2023). These patterns align with recent national analyses using CDC WONDER data that have documented accelerating cardiometabolic and heart failure – related mortality trends beginning in the early to mid-2010s [19, 20]. The decline observed between 2005 and 2012 has been described in prior literature and may plausibly relate to contemporaneous improvements in cardiovascular prevention and management; however, such mechanisms cannot be evaluated directly in the present analysis. The reversal and subsequent rise after 2012, therefore, warrant careful interpretation. The sharp acceleration observed between 2018 and 2021 should be interpreted in the context of the COVID 19 pandemic as a potential structural disruption rather than as a stable continuation of the underlying secular trend. Joinpoint regression identifies statistically significant changes in slope but does not distinguish between endogenous trend shifts and extraordinary exogenous shocks. Importantly, increases in age adjusted mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions were already evident beginning in the mid-2010s, before the onset of the pandemic. Thus, the post-2012 upward trajectory persists qualitatively outside the 2020 – 2021 period, while the pandemic years likely represent a superimposed perturbation that amplifies – but does not solely define – the longer term trend.

The years 2018 – 2021 overlap with the COVID 19 pandemic and coincide with a marked increase in mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions. Although the present analysis cannot evaluate mechanisms, prior studies have suggested that pandemic related disruptions in healthcare access, delayed presentations, and acute cardiovascular complications of SARS CoV 2 infection may have plausibly influenced mortality patterns during this period [21, 22]. Previously declining trends reversed sharply after 2020, with a marked increase in mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions, with the most pronounced increases among non-Hispanic American Indian and Hispanic populations [22]. Prior studies have suggested that the pandemic period was associated with disruptions in access to routine care, delayed presentations for acute decompensated HF, and introduced direct viral effects such as myocardial injury and inflammation [21]. Additionally, the pandemic exacerbated social determinants of health. Prior studies have described worsening social determinants of health, including food insecurity, housing instability, and limited access to preventive care during this period [23]. Similar inflection points around 2012 have been reported in mortality studies involving HF, atrial fibrillation, and sepsis, with continued increases through 2023 [20]. These factors are discussed here as contextual explanations rather than inferences derived from the present certificate based data.

Sex specific patterns were also evident. Men consistently exhibited higher AAMRs than women, with sharper increases in the mid-2010s. Potential mechanisms include earlier onset and greater severity of metabolic abnormalities, higher prevalence of obstructive coronary artery disease, and sex specific differences in cardiac remodeling under metabolic stress [3]. Prior observational studies indicate that heart failure with preserved ejection fraction represents a growing proportion of heart failure – related morbidity and mortality, particularly among older adults. However, absolute mortality remains high across heart failure phenotypes [24]. However, the present analysis does not include individual level clinical or treatment data, and these proposed mechanisms cannot be directly assessed.

Racial and ethnic disparities were among the most striking findings, with generally higher AAMRs observed among NH Black and NH American Indian or Alaska Native (AI/AN) populations. However, estimates for smaller racial and ethnic groups were characterized by wider uncertainty and greater temporal variability, reflecting smaller underlying death counts. Accordingly, findings for NH American Indian or Alaska Native (AI/AN) and NH Asian or Pacific Islander (API) populations are best interpreted as indicating elevated or variable mortality involvement rather than stable or persistent rank ordering over time.

The most pronounced relative increases between 2018 and 2021 were observed among NH Black and NH AI/AN populations, although estimates for NH AI/AN individuals exhibited greater year to year variability. These findings are consistent with national studies of heart failure mortality in non alcoholic fatty liver disease, anemia related heart failure mortality, and other cardiometabolic conditions [1, 25]. These disparities reflect cumulative structural inequities, including limited access to healthcare, socioeconomic disadvantage, higher rates of uncontrolled hypertension and diabetes, and historical residential segregation [5]. The American Heart Association's cardiovascular kidney metabolic syndrome framework highlights how NH Black and NH AI/AN individuals are more likely to be in advanced stages of CKM syndrome, which carries exponentially higher mortality risk [6, 26]. Hispanic individuals showed a different temporal pattern, with declines until approximately 2016 followed by a rise through 2021, which may reflect broader increases in cardiometabolic risk and persistent barriers to preventive care described in prior literature.

Geographic disparities were pronounced throughout the study period. The Midwest exhibited the highest AAMR, followed by the West and the South. Although the Midwest consistently ranked highest, both the West and South experienced substantial increases in mortality over time, particularly after 2018, highlighting important regional variation in cardiometabolic and heart failure – related mortality patterns. These disparities align with patterns described in prior literature, including regional clustering of cardiovascular and metabolic risk in the southeastern United States [27]. The South and Midwest experienced the steepest increases after 2018. State-level patterns revealed that Oklahoma, Mississippi, Kentucky, and Oregon ranked among the highest burden states across both analytic periods, while Massachusetts and New York consistently ranked among the lowest. Oklahoma's exceptionally high rates in 2021 – 2023 warrant

further investigation into state-specific policies, healthcare access, and the prevalence of metabolic risk.

Urbanization analyses limited to 1999 – 2020 revealed higher mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions in nonmetropolitan areas compared with metropolitan areas. These differences may reflect contextual factors described in prior literature, including differences in healthcare access, availability of cardiology subspecialty services, and broader socioeconomic conditions. Although both metro and non-metro areas saw sharp rises between 2018 and 2020, rural areas carried a substantially higher burden. These findings align with prior studies reporting increases in heart failure mortality. However, in the present analysis, this increase may reflect patterns described in the prior literature, including differences in healthcare access, geographic distance to care, and socioeconomic conditions in rural populations [28]. Recent observational and health systems – based studies have reported reduced outpatient utilization and higher mortality among rural cardiac populations, even after adjustment for demographic and clinical factors [28]. Ongoing rural hospital closures and financial instability of rural health systems have been described as potential contributors to disparities in access to acute cardiac care in broader cardiovascular health system analyses [29]. There are several clinical and public health implications of these findings. First, the dramatic rise in mortality since 2018 – especially among Black and AI/AN populations and in the South and Midwest – warrants urgent public health attention, particularly among high-burden populations identified in this analysis, including NH Black and NH AI/AN populations and residents of the Midwest, West, and South. The AHA's cardiovascular kidney metabolic syndrome framework emphasizes early identification and management of metabolic risk factors, incorporating social determinants of health into prevention and treatment strategies [6, 30]. Second, targeted interventions are needed for high risk populations. For Black and American Indian or Alaska Native communities, culturally tailored strategies that address social determinants of health and promote equitable access to evidence based cardiometabolic care have been emphasized in national frameworks [6]. In parallel, observational studies linking advanced cardiovascular , kidney , and metabolic risk to substantially higher mortality underscore the importance of strengthening prevention and long term chronic disease management in these populations [31]. For rural populations, expanding telehealth, mobile health units, and rural healthcare infrastructure is critical [8]. Third, the decline in mortality between 2021 and 2023 is encouraging but requires careful evaluation to determine whether it reflects improved COVID-19 management, catch-up healthcare utilization, or stabilization of pandemic-related disruptions. It is too early to determine whether this represents a sustained reversal.

This study is subject to limitations inherent to death certificate – based analyses, including potential misclassification and underreporting. The operational definition captures a heterogeneous group of cardiometabolic conditions and does not represent clinically adjudicated metabolic syndrome. The use of a multiple-cause-of-death design also introduces the possibility that observed trends reflect changes in coding or documentation practices (ascertainment drift) rather than true changes in mortality burden. Additionally, the composite metabolic syndrome – related category was not decomposed into individual components or overlap patterns, limiting insight into specific drivers of trends. CDC WONDER lacks individual-level clinical and socioeconomic data, and urbanization analyses were restricted to 1999 – 2020. Estimates for smaller populations may be more variable. Finally, underlying-cause-specific analyses were not performed; thus, the relative contribution of heart failure as the underlying cause of death could not be determined. Despite these limitations, consistency with prior national studies supports the reliability of the observed patterns.

5. Conclusion

Following a decline until 2012, mortality involving death certificates that co reported heart failure and metabolic syndrome – related conditions increased substantially, particularly between 2018 and 2021, before declining modestly in more recent years. The highest observed mortality rates occurred among men, NH Black and NH American Indian or Alaska Native (AI/AN) populations, residents of the Midwest (with comparatively elevated rates also observed in the West and South), and individuals living in nonmetropolitan areas. These findings highlight population level inequities in cardiometabolic health and heart failure burden. Importantly, the use of a multiple cause of death, co mention design reflects patterns of mortality involving death certificates co reporting heart failure and metabolic syndrome – related conditions, rather than clinically adjudicated metabolic syndrome or cause specific attribution.

Taken together, these results underscore the need for targeted public health strategies aimed at reducing cardiometabolic risk and addressing structural and geographic disparities associated with heart failure – related mortality in the United States. Continued surveillance using transparent, methodologically rigorous approaches will be essential to monitor evolving trends and inform equitable prevention and management efforts.

Conflicts of Interest

The authors declare no competing interests that could have influenced the objectivity or outcome of this research.

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Author Contributions

Conceptualization was performed by ZA and FN. Methodology was carried out by ZA and FN. Data curation involved ZA, FN, MA, AR, FNUA, FNUS and FNUB. Formal analysis was conducted by ZA and FN. The original draft was written by ZA, FN, FNUB, MA, MR, SS and LKA. Review and editing were performed by ZA, FN, KO, KC, SA, FNUB, MR, SS, AR, FNUA, FNUS, MA and LKA. Supervision was provided by ZA and FN.

Data Availability

The mortality data analyzed in this study are publicly available through the Centers for Disease Control and Prevention (CDC)

Wide-ranging Online Data for Epidemiologic Research (WONDER) platform using National Vital Statistics System multiple-cause-of-death files. All data are deidentified and accessible without restriction.

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