

Rising Female Mortality in Combined Ischemic Heart Disease and Chronic Kidney Disease in the United States (1999–2023)

Hassaan Abid

habid@iu.edu

Indiana University

Muhammad Vazaym

Liaquat University of Medical & Health Sciences

Muhammad Jawad

Liaquat University of Medical & Health Sciences

Gaaitri Lohano

Liaquat University of Medical & Health Sciences

Syed Mohamin Abbas Shah

King Edward Medical University

Naveed Ahmed Khan

Khyber Medical College

Research Article

Keywords: Ischemic heart disease, chronic kidney disease, Mortality trends, Sex differences, CDC WONDER

Posted Date: March 27th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-8993837/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Although age-adjusted mortality from ischemic heart disease (IHD) has declined in the United States over recent decades, the coexistence of chronic kidney disease (CKD) may be reshaping mortality patterns. Emerging data suggest that improvements in cardiovascular survival may not be uniform across sexes.

Methods

We conducted a retrospective population-based study using CDC WONDER multiple cause-of-death data from 1999–2023. Deaths mentioning IHD (ICD-10 codes I20–I25) and CKD (ICD-10 code N18) were identified. Age-adjusted mortality rates (AAMRs) per 1,000,000 population were calculated using the 2000 U.S. standard population. Temporal trends were evaluated using Joinpoint Regression Program version 5.0 (National Cancer Institute) to estimate annual percent change (APC) and average annual percent change (AAPC) with 95% confidence intervals (CIs).

Results

Between 1999 and 2023, 633,221 deaths involved both IHD and CKD. Overall AAMR declined modestly (AAPC – 1.13%; 95% CI – 2.46 to 0.21; $p = 0.093$). Male mortality declined significantly (APC – 1.12%; 95% CI – 2.19 to – 0.03; $p = 0.044$). In contrast, female mortality increased significantly from 2015 to 2023 (APC 3.25%; 95% CI 0.78 to 5.79; $p = 0.013$). Similar increases were observed among middle-aged adults. Persistent regional and racial disparities were noted.

Conclusions

Despite modest national declines in cardiorenal mortality, a sustained rise in female mortality since 2015 signals a concerning reversal of cardiovascular progress. Targeted sex-specific prevention strategies are urgently needed.

Background

Ischemic heart disease (IHD) remains a significant public health concern and continues to be the leading cause of death in the United States, accounting for more than 300,000 deaths annually [1]. Although age-adjusted IHD mortality rates have declined over recent decades due to advances in preventive strategies, early diagnosis, pharmacologic therapy, and interventional cardiology [1, 2], the absolute burden of disease remains substantial.

Chronic kidney disease (CKD) represents another major and growing contributor to morbidity and mortality, affecting nearly 14% of U.S. adults [3]. From 1999 to 2020, CKD has been associated with approximately 1.94 million deaths nationwide [4]. CKD is widely recognized not only as a progressive renal condition but also as a powerful and independent risk factor for cardiovascular disease [3, 5]. Individuals with CKD experience substantially higher rates of cardiovascular events and premature mortality compared with those without kidney dysfunction [5].

The pathophysiological relationship between CKD and IHD is multifactorial. Beyond shared risk factors such as hypertension, diabetes mellitus, and dyslipidemia, CKD accelerates atherosclerosis through chronic inflammation, endothelial dysfunction, oxidative stress, vascular calcification, and disordered mineral metabolism [6, 7]. Consequently, cardiovascular disease, particularly IHD, remains the leading cause of death among patients with CKD [4, 5].

Long-term analyses of mortality trends have demonstrated overall declines in cardiovascular mortality [3]. However, improvements are not uniform across demographic groups [5]. Mortality patterns may differ by sex, race, geography, and age, and multiple cause-of-death analyses allow more comprehensive assessment of CKD's contributory role in cardiovascular mortality [3, 5].

While overall IHD mortality has declined nationally [1, 2], emerging evidence suggests that cardiovascular gains among women may be slowing or reversing. Sex differences in cardiovascular risk recognition and treatment remain well documented [22, 23], and recent nephrology data indicate that CKD may confer greater excess cardiovascular risk in women compared with men [24]. Despite this, few studies have evaluated long-term sex-specific trends in combined IHD and CKD mortality.

This study uses CDC WONDER data from 1999 to 2023 to evaluate national trends in IHD- and CKD-related mortality, with primary focus on emerging increases in female mortality and secondary examination of demographic and geographic disparities.

Methods

Study Design and Data Source

We performed a retrospective, population-based study examining U.S. mortality trends from 1999 through 2023 using the Centers for Disease Control and Prevention (CDC) Wide-ranging Online Data for Epidemiologic Research (WONDER) Multiple Cause-of-Death database. This publicly accessible dataset compiles information from national death certificates and allows identification of both underlying and contributing causes of death.

Deaths were included if ischemic heart disease (IHD; ICD-10 codes I20–I25) and chronic kidney disease (CKD; ICD-10 code N18) were documented anywhere on the death certificate. Because the database contains de-identified, publicly available data, this study was exempt from Institutional Review Board

oversight. The general analytic framework applied in this study has been described previously in similar CDC WONDER mortality analyses. [45]

Variables and Definitions

Mortality data were stratified by demographic and geographic characteristics, including sex, race/ethnicity, age group, U.S. Census region, state, urban–rural classification, and place of death.

Race and ethnicity categories were defined according to CDC classifications as non-Hispanic (NH) White, NH Black or African American, Hispanic or Latino, NH American Indian or Alaska Native, and NH Asian or Pacific Islander. Age was categorized into three predefined groups: 25–44 years, 45–64 years, and ≥ 65 years.

Geographic regions were classified according to U.S. Census Bureau definitions (Northeast, Midwest, South, and West). Urbanization status was determined using the 2013 National Center for Health Statistics Urban–Rural Classification Scheme for Counties. Place of death categories included inpatient medical facilities, outpatient or emergency departments, home, hospice, nursing home or long-term care facilities, and other specified locations.

Statistical Analysis

Crude mortality rates and age-adjusted mortality rates (AAMRs) per 1,000,000 population were calculated annually. Age adjustment was performed using the direct standardization method with the 2000 U.S. standard population as reference.

Temporal trends in AAMRs were evaluated using the Joinpoint Regression Program (Version 5.0, National Cancer Institute). This approach applies segmented log-linear regression modeling to identify statistically significant changes in mortality trends over time. Annual percent change (APC) and average annual percent change (AAPC) were estimated with corresponding 95% confidence intervals (CIs). Statistical significance was assessed using permutation testing, and two-sided p-values < 0.05 were considered significant. A maximum of three joinpoints were permitted in model selection.

Results

Overall

Between 1999 and 2023, a total of 633,221 deaths in the United States involved both ischemic heart disease (IHD) and chronic kidney disease (CKD). During this period, age-adjusted mortality rates (AAMRs) declined from 13.1 (95% CI 13.0–13.3) per 1,000,000 in 1999 to 9.1 (95% CI 9.0–9.2) in 2023. The highest AAMR was observed in 2012 at 18.5 (95% CI 18.4–18.7). Overall, the trend demonstrated a non-significant decline, with an average annual percent change (AAPC) of -1.13% (95% CI -2.46 to 0.21 ; $p = 0.093$) (Fig. 1).

Gender

Mortality rates were consistently higher among males than females throughout the study period. From 1999 to 2023, 375,585 deaths occurred among males and 257,636 among females. Among males, the AAMR peaked at 26.9 (95% CI 26.6–27.3) in 2012. Male mortality declined significantly over the study period (APC – 1.12%; 95% CI – 2.19 to – 0.03; $p = 0.044$). Among females, the highest AAMR was 12.8 (95% CI 12.6–13.0) in 2012. Female mortality declined significantly from 1999 to 2009 (APC – 2.75%; 95% CI – 3.93 to – 1.55; $p < 0.001$), followed by a non-significant increase from 2009 to 2012 (APC 17.57%; 95% CI – 0.23 to 38.62; $p = 0.054$). A significant decline was observed from 2012 to 2015 (APC – 24.27%; 95% CI – 40.13 to – 4.23; $p = 0.024$). However, from 2015 to 2023, mortality increased significantly (APC 3.25%; 95% CI 0.78 to 5.79; $p = 0.013$) (Fig. 1).

Race and Ethnicity

Mortality trends were stratified by race and ethnicity. From 1999 to 2023, AAMRs were highest among non-Hispanic (NH) White adults, followed by NH Black or African American, Hispanic or Latino, NH Asian or Pacific Islander, and NH American Indian or Alaska Native populations. Among NH White adults, mortality demonstrated a non-significant decline (APC – 0.59%; 95% CI – 1.88 to 0.72; $p = 0.359$). NH Black or African American adults experienced a significant decline (APC – 3.33%; 95% CI – 4.40 to – 2.24; $p < 0.001$). Hispanic or Latino individuals also demonstrated a significant decline (APC – 3.69%; 95% CI – 4.97 to – 2.39; $p < 0.001$). Among NH Asian or Pacific Islanders, mortality declined significantly from 1999 to 2009 (APC – 4.68%; 95% CI – 6.49 to – 2.83; $p < 0.001$), followed by a non-significant increase from 2009 to 2012 (APC 15.82%; 95% CI – 7.08 to 44.38; $p = 0.175$). A significant decline was observed from 2012 to 2015 (APC – 25.76%; 95% CI – 42.23 to – 4.60; $p = 0.023$), followed by a non-significant increase through 2023 (APC 1.63%; 95% CI – 0.48 to 3.78; $p = 0.121$). NH American Indian or Alaska Native individuals experienced a significant decline over the study period (APC – 3.19%; 95% CI – 4.44 to – 1.91; $p < 0.001$) (Fig. 2).

Age Groups

Mortality trends were analyzed across three age groups: 25–44 years, 45–64 years, and ≥ 65 years. Crude mortality rates were highest among adults aged ≥ 65 years. Among adults aged ≥ 65 years, mortality declined significantly from 1999 to 2023 (APC – 1.40%; 95% CI – 2.75 to – 0.04; $p = 0.043$). Among adults aged 45–64 years, mortality declined significantly from 1999 to 2009 (APC – 3.97%; 95% CI – 5.05 to – 2.88; $p < 0.001$), followed by a non-significant change through 2012 (APC 15.49%; 95% CI – 1.04 to 34.79; $p = 0.065$). A significant decline occurred from 2012 to 2015 (APC – 25.29%; 95% CI – 43.31 to – 1.54; $p = 0.040$). However, mortality increased significantly from 2015 to 2023 (APC 3.88%; 95% CI 1.15 to 6.69; $p = 0.008$). Among adults aged 25–44 years, mortality declined significantly over the entire study period (APC – 3.16%; 95% CI – 4.52 to – 1.79; $p < 0.001$). The AAPC was – 1.40% (95% CI –

2.75 to - 0.05; $p = 0.043$) for adults aged ≥ 65 years, - 2.24% (95% CI - 5.82 to 1.47; $p = 0.234$) for those aged 45–64 years, and - 3.16% (95% CI - 4.51 to - 1.79; $p < 0.001$) for those aged 25–44 years (Fig. 3).

Geographic Region

Mortality trends were evaluated across U.S. Census regions. From 1999 to 2023, 121,088 deaths occurred in the Northeast, 153,259 in the Midwest, 226,223 in the South, and 132,651 in the West. The West demonstrated a significant decline (AAPC - 1.59%; 95% CI - 2.94 to - 0.24; $p = 0.023$), as did the Northeast (AAPC - 2.22%; 95% CI - 3.16 to - 1.26; $p < 0.001$). Declines in the Midwest (AAPC - 1.04%; 95% CI - 2.22 to 0.16; $p = 0.087$) and South (AAPC - 1.12%; 95% CI - 2.37 to 0.15; $p = 0.081$) were not statistically significant (Fig. 4). State-level analysis (1999–2021) demonstrated the highest age-adjusted mortality rate in West Virginia (39.2 per 1,000,000) and the lowest in Nevada (17.8 per 1,000,000) (Fig. 5).

Urbanization

From 1999 to 2020, 449,095 deaths occurred in metropolitan areas and 103,076 in non-metropolitan areas. Both metropolitan (AAPC - 1.35%; 95% CI - 4.48 to 1.89; $p = 0.410$) and non-metropolitan areas (AAPC - 0.16%; 95% CI - 3.23 to 3.00; $p = 0.918$) demonstrated non-significant overall declines (Fig. 6). Urbanization data were only available through 2020.

Place of Death

From 1999 to 2023, most deaths occurred in medical facility inpatient settings (281,811), followed by decedents' homes (133,292), nursing homes or long-term care facilities (122,525), medical facility outpatient or emergency departments (46,963), hospice facilities (24,483), other locations (19,251), medical facility deaths on arrival (3,236), place of death unknown (1,104), and medical facility status unknown (551).

Discussion

In this nationwide analysis of IHD- and CKD-related mortality from 1999 to 2023, we observed modest overall declines in age-adjusted mortality rates. However, this aggregate improvement concealed a critical and concerning finding: a statistically significant rise in female mortality during the 2015–2023 period, in contrast to continued improvement among males. This divergence suggests that prior gains in women's cardiovascular survival may be eroding in the context of combined cardiorenal disease.

The modest decline in overall IHD-CKD mortality likely reflects decades of progress in cardiovascular prevention and treatment, including widespread statin use, improved antihypertensive regimens, antiplatelet therapy, and advancements in revascularization strategies [8, 9]. Similarly, improvements in CKD management—particularly renin-angiotensin system blockade, glycemic control, and earlier detection—have contributed to enhanced survival [10, 11]. National surveillance has consistently

documented declining IHD mortality during this period [16, 17]. However, rising prevalence of obesity, diabetes, and metabolic syndrome has counterbalanced these gains [12–15]. The growing cardiometabolic burden may be particularly relevant in patients with concurrent CKD, where cardiovascular risk is already amplified [18–21]. As a result, overall mortality trends appear flattened rather than dramatically improved. Importantly, these aggregate patterns obscure meaningful subgroup divergence—most notably by sex.

The most consequential finding of this study is the sustained increase in female IHD-CKD mortality from 2015 to 2023. While women historically have lower absolute cardiovascular mortality compared with men [22], this survival advantage appears to be narrowing in the context of combined kidney and heart disease. Sex disparities in cardiovascular recognition and management are well documented. Women are more likely to present with atypical symptoms, experience delays in diagnosis, and receive fewer invasive procedures and guideline-directed medical therapies [23]. These disparities may become particularly consequential in high-risk populations such as those with CKD. Emerging nephrology literature further suggests that CKD may confer greater excess cardiovascular mortality risk in women than in men [24]. Potential mechanisms include sex-specific differences in vascular biology, inflammatory response, hormonal changes, and progression of kidney dysfunction. In post-menopausal women, accelerated metabolic dysregulation may further compound cardiovascular risk. The temporal pattern observed, early decline followed by post-2015 increase, raises concern that recent cardiometabolic trends may be disproportionately affecting women. Rising rates of obesity and diabetes [14, 15, 29, 30], particularly in midlife women, may be contributing to the parallel increase observed in the 45–64 age group. If this trajectory continues, women with combined IHD and CKD may face increasing mortality risk over the next decade, potentially reversing decades of progress in cardiovascular survival.

Although older adults bore the highest absolute mortality burden, middle-aged adults demonstrated a concerning post-2015 increase. Obesity, insulin resistance, and poorly controlled hypertension in midlife accelerate both CKD progression and atherosclerotic disease [29, 30]. Given that women often experience delayed recognition of cardiovascular risk during midlife, this intersection may represent a critical window of vulnerability. These findings underscore the importance of early cardiovascular risk assessment and aggressive CKD management in middle-aged populations, particularly women.

Consistent with prior literature, racial disparities persisted, with non-Hispanic White adults exhibiting the highest absolute mortality rates and minority populations demonstrating significant long-term declines [25, 26]. Structural determinants of health, including socioeconomic status, healthcare access, and neighborhood disadvantage, continue to shape cardiovascular outcomes [27, 28]. Regional variation was also evident, with the South experiencing the greatest mortality burden. Geographic differences in cardiometabolic risk factor prevalence, healthcare infrastructure, and specialty access likely contribute to these disparities [31–33]. Rural populations demonstrated slower improvement, consistent with limited access to cardiology and nephrology services [34]. Importantly, although these disparities remain substantial, most racial and regional groups demonstrated overall improvement rather than reversal. In contrast, the rise in female mortality represents a unique and emergent divergence.

The interaction between CKD and IHD presents unique therapeutic challenges. CKD complicates cardiovascular management through altered pharmacokinetics, increased bleeding risk, and limitations in revascularization options [37]. As CKD prevalence continues to rise, cardiovascular mortality attributable to kidney dysfunction is projected to increase globally [38].

Given this landscape, sex-specific prevention strategies should include earlier cardiovascular risk screening in women with CKD, improved recognition of atypical ischemic symptoms, aggressive management of midlife cardiometabolic risk factors, integrated cardio-renal care pathways, and reduction of structural barriers to specialty care. Addressing inequities in cardio-renal care delivery remains essential [40, 41].

A key strength of this study is the use of multiple cause-of-death methodology, which captures deaths in which CKD contributed even if not listed as the underlying cause [43, 44]. This approach provides a more comprehensive estimate of cardiorenal mortality burden. However, limitations include reliance on death certificate data, potential misclassification, and lack of granular clinical detail regarding disease severity, treatment patterns, and risk factor control [39].

Conclusion

Although overall IHD-CKD mortality declined modestly from 1999 to 2023, these aggregate trends conceal a concerning and statistically significant rise in female mortality since 2015. While racial and regional disparities persist, none demonstrated the sustained reversal observed among women.

This emerging sex-specific divergence suggests that women with combined cardiovascular and renal disease may be entering a new phase of vulnerability. Without targeted prevention, earlier CKD detection, and improved cardiovascular risk recognition in women, prior survival gains may continue to erode.

Abbreviations

IHD: Ischemic heart disease

CKD: Chronic kidney disease

AAMR: Age-adjusted mortality rate

APC: Annual percent change

AAPC: Average annual percent change

CDC: Centers for Disease Control and Prevention

CI: Confidence interval

Declarations

Ethics approval and consent to participate

This study used publicly available, de-identified data from the CDC WONDER database. Institutional Review Board approval and informed consent were not required.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are publicly available in the CDC WONDER database (<https://wonder.cdc.gov/>).

Competing interests

The authors declare that they have no competing interests.

Funding

The authors received no specific funding for this work.

Authors' contributions

HA conceptualized the study. HA and MV performed data extraction and statistical analyses. MJ and GL contributed to interpretation of results. SMAS and NAK drafted and critically revised the manuscript. All authors reviewed and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Nowbar AN, Gitto M, Howard JP, Francis DP, Al-Lamee R. Mortality From Ischemic Heart Disease: Analysis of Data From the World Health Organization and Coronary Artery Disease Risk Factors From NCD Risk Factor Collaboration. *Circ: Cardiovascular Quality and Outcomes*. 2019;12(6):e005375.
2. King SJ, Wangdak Yuthok TY, Bacong AM, Khandelwal A, Kazi DS, Mussolino ME, et al. Heart Disease Mortality in the United States, 1970 to 2022. *JAHA*. 2025;14(13):e038644.

3. Ahmad E, Ahmad S, Naeem A, Ahmed S, Shehzad M, Akram U, et al. Trends in Cardiovascular Mortality in Patients With Chronic Kidney Disease From 1999 to 2020: A Retrospective Study in the United States. *Clin Cardiol.* 2025;48(8):e70174.
4. Shahzad M, Ahmed S, Ahsan M, Zulfiqar E, Hurjkaliani S, Thakur T, et al. Trends and disparities in heart failure mortality with and without chronic kidney disease in a nationwide retrospective analysis. *Sci Rep.* 2025;15(1):29103.
5. Kobo O, Abramov D, Davies S, Ahmed SB, Sun LY, Mieres JH, et al. CKD-Associated Cardiovascular Mortality in the United States: Temporal Trends From 1999 to 2020. *Kidney Med.* 2023;5(3):100597.
6. Carracedo J, Alique M, Vida C, Bodega G, Ceprián N, Morales E, et al. Mechanisms of Cardiovascular Disorders in Patients With Chronic Kidney Disease: A Process Related to Accelerated Senescence. *Front Cell Dev Biol.* 2020;8:185.
7. Gollie JM, Mahalwar G. Cardiovascular Disease in Chronic Kidney Disease: Implications of Cardiorespiratory Fitness, Race, and Sex. *Rev Cardiovasc Med.* 2024;25(10):365.
8. Andersson T, Nåtman J, Mourtzinis G, Bager JE, Bengtsson Boström K, Franzén S, et al. The effect of statins on mortality and cardiovascular disease in primary care hypertensive patients without other cardiovascular disease or diabetes. *Eur J Prev Cardiol.* 2023;30(17):1883–94.
9. Mensah GA, Wei GS, Sorlie PD, Fine LJ, Rosenberg Y, Kaufmann PG, et al. Decline in Cardiovascular Mortality: Possible Causes and Implications. *Circul Res.* 2017;120(2):366–80.
10. Pozo Garcia L, Thomas SS, Rajesh H, Navaneethan SD. Progress in the management of patients with diabetes and chronic kidney disease. *Curr Opin Nephrol Hypertens.* 2022;31(5):456–63.
11. Garcia Sanchez JJ, Thompson J, Scott DA, Evans R, Rao N, Sörstadius E, et al. Treatments for Chronic Kidney Disease: A Systematic Literature Review of Randomized Controlled Trials. *Adv Ther.* 2022;39(1):193–220.
12. Goyal A, Saeed H, Sulaiman SA, Sultan W, Siddiqui MR, Kan Changez MI et al. Emerging trends and disparities in cardiovascular, kidney, and diabetes-related mortality: A retrospective analysis of the wide-ranging online data for epidemiologic research database. Ghimire A, editor. *PLoS One.* 2025;20(5):e0320670.
13. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: a comparative risk assessment. *Lancet Diabetes Endocrinol.* 2014;2(8):634–47.
14. Scurt FG, Ganz MJ, Herzog C, Bose K, Mertens PR, Chatzikyrkou C. Association of metabolic syndrome and chronic kidney disease. *Obes Rev.* 2024;25(1):e13649.
15. Grant CH, Bell S. Obesity and Chronic Kidney Disease: The Dual Epidemic in Cardiovascular Health. *Eur Cardiol.* 2025;20:e28.
16. Burzyńska M, Jankowski P, Pikala M. Two Decades of Progress in Cardiovascular Health: Declining Mortality and Years of Life Lost from Acute Myocardial Infarction in Poland. *JCM.* 2026;15(2):838.
17. Khalid N, Higgins SC, Abdullah M, Munshi H, Hasnat M, Doshi R, et al. Ischemic heart disease-related mortality trends in the United States (1999–2020) and prediction using machine learning. *Annals*

Med Surg. 2025;87(7):4145–51.

18. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. yuan. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. *N Engl J Med*. 2004;351(13):1296–305.
19. Navaneethan SD, Schold JD, Arrigain S, Jolly SE, Nally JV. Cause-Specific Deaths in Non–Dialysis-Dependent CKD. *J Am Soc Nephrol*. 2015;26(10):2512–20.
20. Matsushita K, Ballew SH, Wang AYM, Kalyesubula R, Schaeffner E, Agarwal R. Epidemiology and risk of cardiovascular disease in populations with chronic kidney disease. *Nat Rev Nephrol*. 2022;18(11):696–707.
21. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular Disease in Chronic Kidney Disease: Pathophysiological Insights and Therapeutic Options. *Circulation*. 2021;143(11):1157–72.
22. Mikkola TS, Gissler M, Merikukka M, Tuomikoski P, Ylikorkala O. Sex Differences in Age-Related Cardiovascular Mortality. Onland-Moret NC, editor. *PLoS ONE*. 2013;8(5):e63347.
23. El Bassiri Y, Azeem A, Sharma AC, Hassan M, Hassan M, Omari I. Gender Disparities in Ischemic Heart Disease Management: Underdiagnosis in Women and Differences in Treatment. *Cureus* [Internet]. 2025 Aug 12 [cited 2026 Feb 7]; Available from: <https://www.cureus.com/articles/387114-gender-disparities-in-ischemic-heart-disease-management-underdiagnosis-in-women-and-differences-in-treatment>
24. Tian Z, Hillebrand UC, Casper J, Schmidt-Ott KM, Melk A, Schmidt BMW. Chronic kidney disease confers increased excess risks of mortality and cardiovascular events in women compared with men. *Nephrol Dialysis Transplantation*. 2025;gfaf217.
25. Kyalwazi AN, Loccoh EC, Brewer LC, Ofili EO, Xu J, Song Y, et al. Disparities in Cardiovascular Mortality Between Black and White Adults in the United States, 1999 to 2019. *Circulation*. 2022;146(3):211–28.
26. Tran HHV, Thu A, Twayana AR, Fuertes A, Gonzalez M, Mehta KA et al. Improving Access and Outcomes in Cardiovascular Care for Racial and Ethnic Minorities. *Cardiology in Review* [Internet]. 2025 Oct 9 [cited 2026 Feb 7]; Available from: <https://journals.lww.com/10.1097/CRD.0000000000001073>
27. Powell-Wiley TM, Baumer Y, Baah FO, Baez AS, Farmer N, Mahlobo CT, et al. Social Determinants of Cardiovascular Disease. *Circul Res*. 2022;130(5):782–99.
28. Acquah I, Hagan K, Javed Z, Taha MB, Valero-Elizondo J, Nwana N, et al. Social Determinants of Cardiovascular Risk, Subclinical Cardiovascular Disease, and Cardiovascular Events. *JAHA*. 2023;12(6):e025581.
29. Maric-Bilkan C. Obesity and Diabetic Kidney Disease. *Med Clin North Am*. 2013;97(1):59–74.
30. Nawaz S, Chinnadurai R, Al-Chalabi S, Evans P, Kalra PA, Syed AA, et al. Obesity and chronic kidney disease: A current review. *Obes Sci Pract*. 2023;9(2):61–74.
31. Tu JV, Chu A, MacLagan L, Austin PC, Johnston S, Ko DT, et al. Regional variations in ambulatory care and incidence of cardiovascular events. *CMAJ*. 2017;189(13):E494–501.

32. Zupa MF, Rothenberger SD, Bauer JG, Zheng Y, Johnson AE, Kinnee E, et al. Geographic and Sociodemographic Factors and Receipt of Metabolic Disease Specialty Care. *JAMA Netw Open*. 2025;8(5):e2511559.
33. Parcha V, Kalra R, Suri SS, Malla G, Wang TJ, Arora G et al. Geographic Variation in Cardiovascular Health Among American Adults. *Mayo Clinic Proceedings*. 2021;96(7):1770–81.
34. Loccoh EC, Joynt Maddox KE, Wang Y, Kazi DS, Yeh RW, Wadhera RK. Rural-Urban Disparities in Outcomes of Myocardial Infarction, Heart Failure, and Stroke in the United States. *J Am Coll Cardiol*. 2022;79(3):267–79.
35. Kerr M, Matthews B, Medcalf JF, O'Donoghue D. End-of-life care for people with chronic kidney disease: cause of death, place of death and hospital costs. *Nephrol Dialysis Transplantation*. 2017;32(9):1504–9.
36. Combs SA, Davison SN. Palliative and end-of-life care issues in chronic kidney disease. *Curr Opin Supportive Palliat Care*. 2015;9(1):14–9.
37. Coyle M, Flaherty G, Jennings C. A critical review of chronic kidney disease as a risk factor for coronary artery disease. *IJC Heart Vasculature*. 2021;35:100822.
38. Zhang T, Li T, Jin P. Global, regional, and national burden of cardiovascular disease attributable to kidney dysfunction (1990–2021) with projections to 2050: analysis of the 2021 Global Burden of Disease study. *Ren Fail*. 2025;47(1):2472039.
39. Pagidipati NJ, Gaziano TA. Estimating Deaths From Cardiovascular Disease: A Review of Global Methodologies of Mortality Measurement. *Circulation*. 2013;127(6):749–56.
40. Mohottige D. Paving a Path to Equity in Cardiorenal Care. *Semin Nephrol*. 2024;44(2):151519.
41. Lamprea-Montealegre JA, Shlipak MG, Estrella MM. Chronic kidney disease detection, staging and treatment in cardiovascular disease prevention. *Heart*. 2021;107(16):1282–8.
42. Ahmed M, Zulfiqar E, Shafiq A, Shahzad M, Hashmi TM, Raja HAA et al. Chronic Kidney Disease and Ischemic Heart Disease Mortality in the United States: A 25-Year Review of Racial and Geographic Disparities. *Cardiology in Review [Internet]*. 2025 Aug 20 [cited 2026 Feb 7]; Available from: <https://journals.lww.com/10.1097/CRD.0000000000001028>
43. Bishop K, Balogun S, Eynstone-Hinkins J, Moran L, Martin M, Banks E, et al. Analysis of Multiple Causes of Death: A Review of Methods and Practices. *Epidemiology*. 2023;34(3):333–44.
44. Redelings MD, Sorvillo F, Simon P. A Comparison of Underlying Cause and Multiple Causes of Death: US Vital Statistics, 2000–2001. *Epidemiology*. 2006;17(1):100–3.
45. Khan S, Najam F, Shakil R, Javed M, Anwar T, Zafar S, et al. Epidemiological trends and demographic disparities in type 1 diabetes-related mortality in the United States (1999–2020): a CDC WONDER analysis. *Diabetes Epidemiol Manag*. 2026;21:100300. 10.1016/j.deman.2026.100300.

Tables

Table 1 to 7 are available in the Supplementary Files section.

Figures

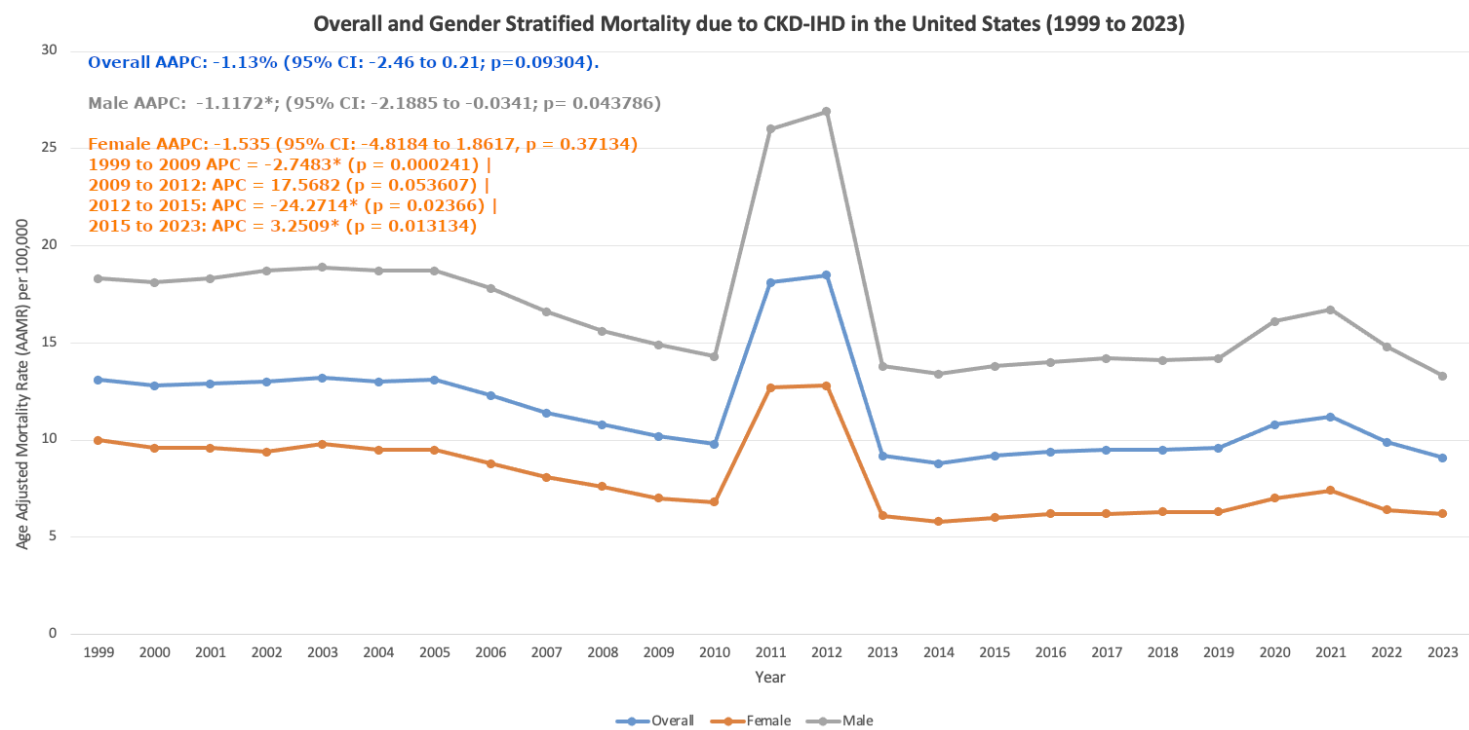


Figure 1

Trends in age-adjusted mortality rates for combined ischemic heart disease and chronic kidney disease overall and stratified by sex, United States, 1999–2023.

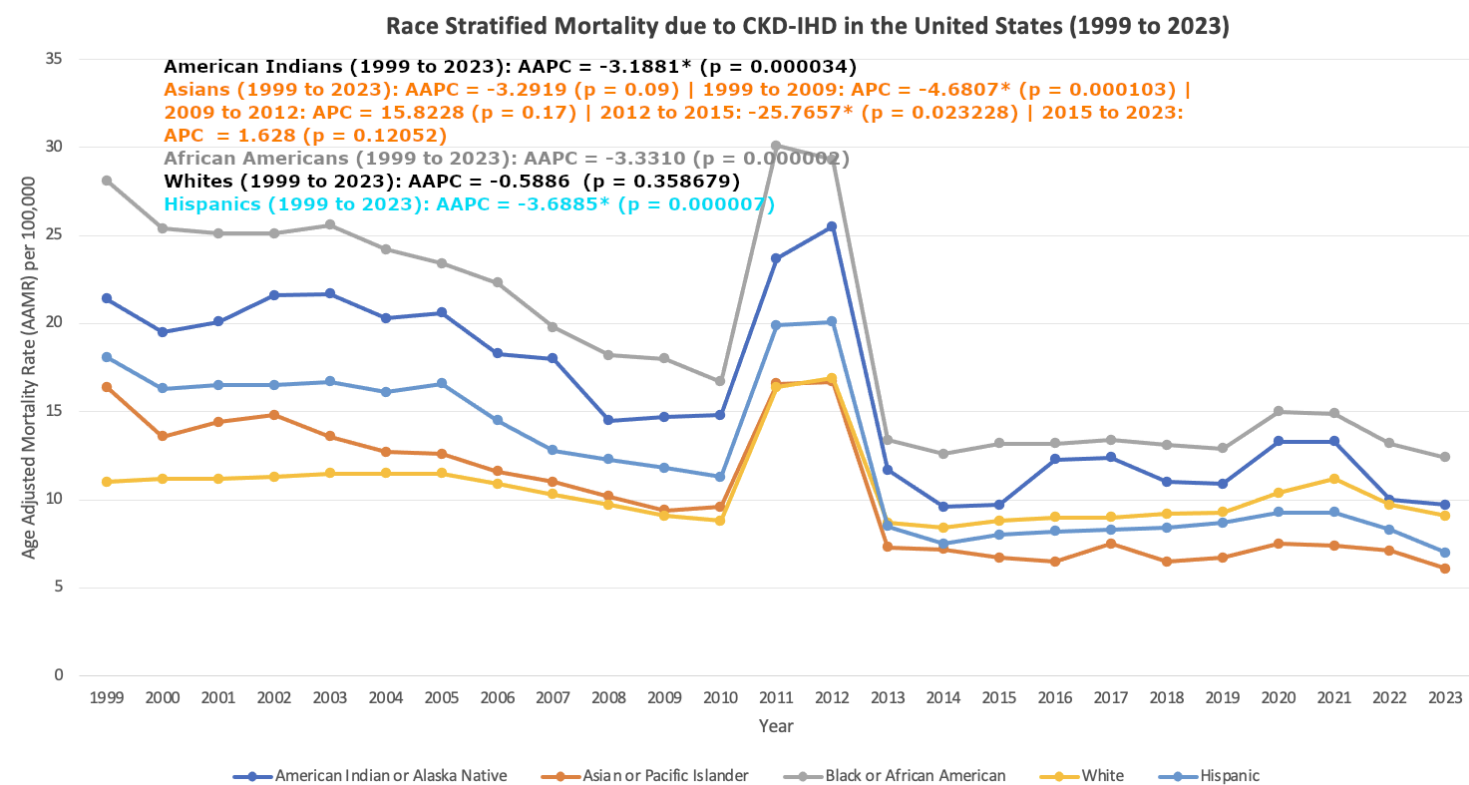


Figure 2

Race- and ethnicity-stratified age-adjusted mortality rates for IHD and CKD, 1999–2023.

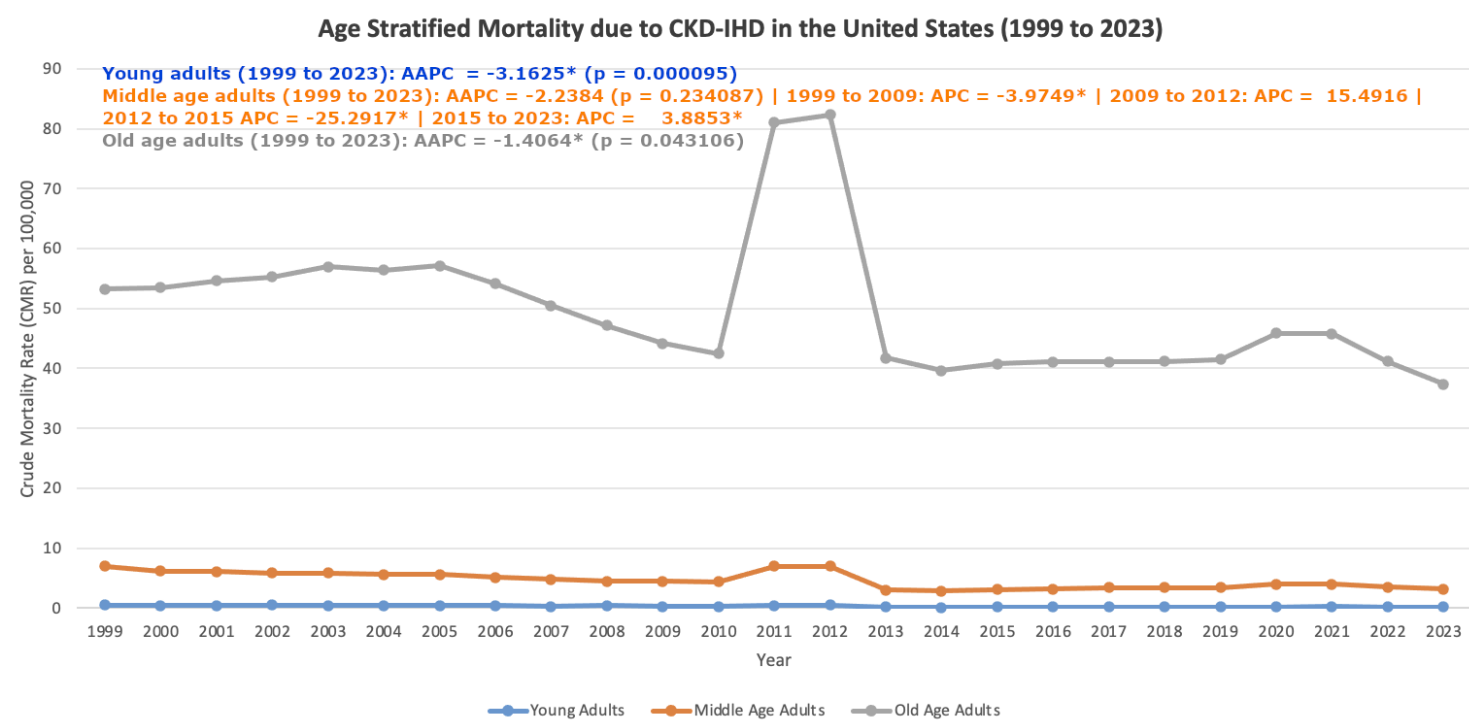


Figure 3

Age group–stratified mortality trends, 1999–2023.



Region Stratified Mortality due to CKD-IHD in the United States (1999 to 2023)

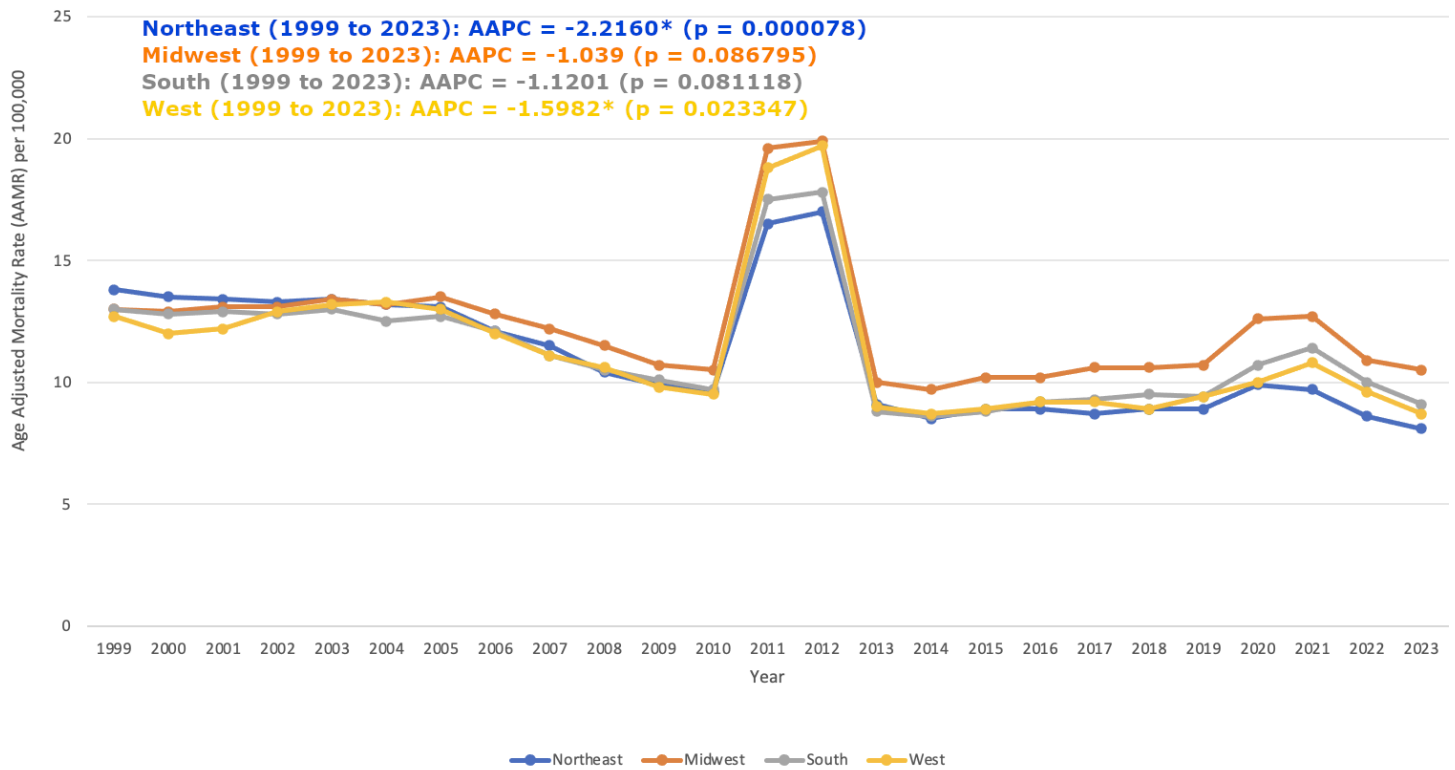


Figure 4

Regional mortality trends by U.S. Census region.

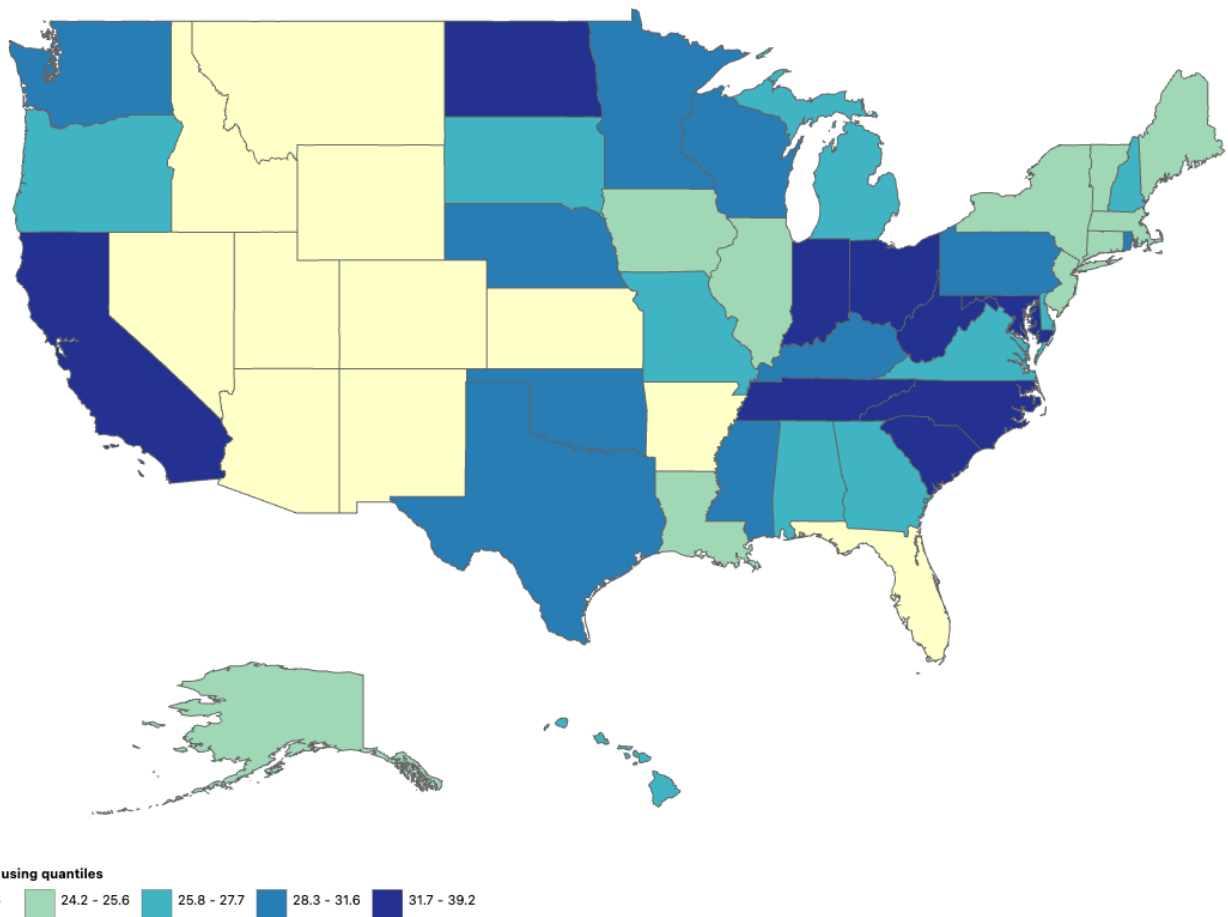


Figure 5

State-level age-adjusted mortality rates.

Urbanization Stratified Mortality due to CKD-IHD in the United States (1999 to 2023)

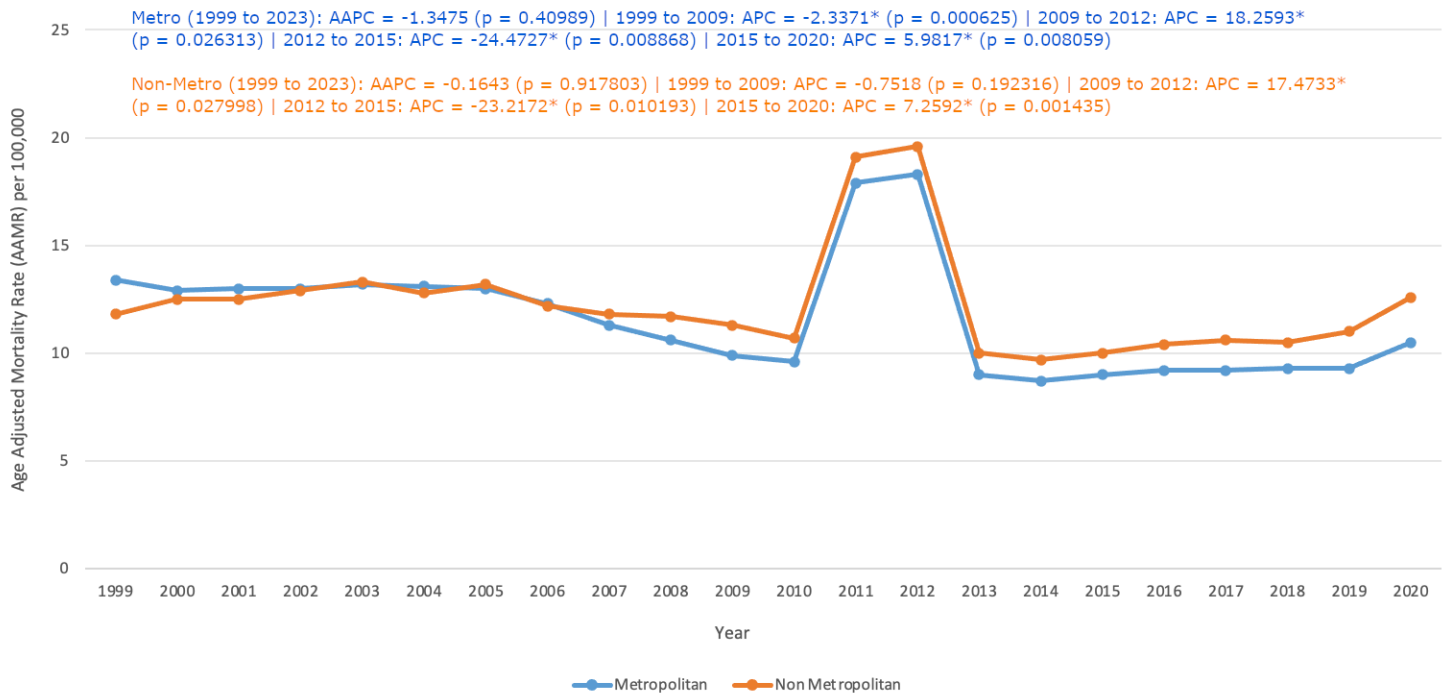


Figure 6

Urban–rural stratified mortality trends.

Supplementary Files

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

- [Table1OverallandGender.xlsx](#)
- [Table2Race.xlsx](#)
- [Table3Regions.xlsx](#)
- [Table4AgeGroups.xlsx](#)
- [Table5States.xlsx](#)
- [Table6PlaceofDeath.xlsx](#)
- [Table7Urbanization.xlsx](#)
- [JPUrbanization.bmp](#)
- [JPAgeGroups.bmp](#)
- [JPRace.bmp](#)
- [JPRegion.bmp](#)
- [JPOverall.bmp](#)