

# Trends in mortality among decedents with coexisting neoplasms and cardiac arrhythmias in the United States, 1999–2024

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## Research Article

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# **Trends in mortality among decedents with coexisting neoplasms and cardiac arrhythmias in the United States, 1999–2024**

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## Abstract

**Background:** Cardiac arrhythmias and neoplasms are common among older adults and are associated with increased mortality. As cancer survival improves, the burden of cardiovascular complications rises continuously. However, national mortality trends in this population are not fully understood. This study evaluates mortality trends in the United States from 1999 to 2024 using CDC Wonder Data.

**Methods:** A retrospective analysis of United States mortality was performed by using the CDC WONDER multiple cause of death database(1999-2024) for adults aged  $\geq 65$  years with coexisting neoplasm and cardiac arrhythmias by using ICD-10 codes(neoplasms: C00–D48; arrhythmias: I44.0–I49.9) listed on death certificates were identified. Age-adjusted mortality rates and crude mortality rates (AAMRs, CMRs) per 100,000 population was calculated. Trends were analyzed by sex, race, age group, geographic region, state, and place of death. Annual percent change (APC) and average annual percent change (AAPC) in age-adjusted mortality rates (AAMRs) were calculated using joinpoint regression, with statistical significance set at  $p < 0.05$ .

**Results:** A total of 616,985 deaths were identified from 1999 to 2024 among adults aged 65 years and older in the United States with coexisting neoplasms and cardiac arrhythmias. Overall AAMRs increased from 43.67 in 1999 to 74.88 in 2024 (AAPC: 2.14; 95% CI: 1.71–2.58;  $p < 0.001$ ). From 1999 to 2010, mortality increased steadily, followed by a sharper rise from 2010 to 2018 (APC: 2.14;  $p < 0.001$ ) and a surge marked between 2018 and 2021 (APC: 10.16;  $p < 0.001$ ) before stabilizing from 2021 to 2024. Adults aged  $\geq 85$  years experienced the greatest mortality burden, with rising AAMR from 119.62 to 233.75. Mortality was higher among males compared to females (104.96 vs. 52.92 in 2024). Among racial groups, non-Hispanic white individuals accounted for the highest AAMR in 2024 (81.06) while Non-Hispanic Asian or Pacific Islander had the lowest (28.53). Geographically, the south showed the largest increase in AAMR(37.55 to 75.43), while non-metropolitan areas showed higher rates than metropolitan regions (82.39 vs. 63.77 in 2020).

**Conclusions:** Mortality among older adults with coexisting neoplasms and cardiac arrhythmias increased substantially in the United States from 1999 to 2024, with the greatest burden observed among the oldest age groups, males, non-Hispanic White individuals, residents of the South, and those living in non-metropolitan areas. Persistent demographic and geographic disparities underscore the need for targeted cardio-oncology strategies, improved arrhythmia surveillance, and equitable access to specialized cardiovascular care to mitigate mortality in this high-risk population.

**Keywords:** cardiac arrhythmias, neoplasms, mortality trends, health disparities, CDC

wonder,

## INTRODUCTION

Cancer and cardiovascular disease are the leading causes of morbidity and mortality among older adults worldwide. Improvements in cancer screening, diagnosis, and treatment have substantially increased survival, resulting in a growing population of older cancer survivors living with multiple chronic conditions. Among these, cardiovascular complications have emerged as a major determinant of long-term outcomes, contributing significantly to morbidity, healthcare utilization, and mortality. Consequently, the coexistence of neoplasms and cardiovascular disease has become an increasingly important public health concern (1,2). Cardiac arrhythmias are a diverse family of conditions that involve abnormalities in the generation or conduction of electrical impulses in the heart that produce an irregular heart rhythm that can be too fast, too slow, or unpredictable. These can vary in severity from minor “premature beats” to serious arrhythmias like atrial fibrillation, ventricular tachycardia, and sudden cardiac arrest. The higher prevalence of arrhythmias in older people is linked to a higher prevalence of cardiovascular risk factors, myocardial fibrosis, changes in the cardiac conduction system, changes in autonomic control, and autonomic aging. Therefore, arrhythmias have been linked to an increased risk of stroke, heart failure, rehospitalization, decreased quality of life, and death (3,4).

Cancer and cardiac arrhythmia are now growing areas of interest, with the development of the cardio-oncology field. Patients with malignancies commonly have traditional cardiovascular risk factors and may experience arrhythmia in several ways, such as systemic inflammatory response, autonomic dysfunction, electrolyte disturbances, metabolic disturbances, direct cardiac involvement by malignancy, and occur as a result of treatment-related cardiotoxicity. In addition, improvements in cancer treatment have also led to a growing number of long-term survivors who continue to be at risk for cardiovascular disease many years after their diagnosis and treatment. This situation of simultaneous occurrence of neoplasms and cardiac arrhythmia will create a complex clinical scenario and can create difficulties in the treatment of cancer, contribute to higher health care utilization, and affect survival outcomes (5,6).

Older adults are particularly vulnerable to the combined effects of cancer and arrhythmias because of multimorbidity, frailty, and reduced physiological reserve. Despite growing recognition of the intersection between oncology and cardiovascular medicine, there remains limited population-level evidence describing long-term mortality trends among older adults with coexisting neoplasms and cardiac arrhythmias. Most previous studies have focused on individual arrhythmia subtypes, specific cancer populations, or clinical cohorts, leaving important gaps in understanding nationwide mortality patterns and demographic disparities among individuals affected by both conditions (7,8).

The Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) database provides comprehensive, standardized, and publicly available mortality data across the United States, offering a valuable resource for evaluating long-term epidemiological trends. By analyzing mortality data derived from death certificates, this study captures the population-level burden of coexisting neoplasms and cardiac arrhythmias rather than relying solely on clinical cohorts (9)

Using CDC WONDER data from 1999 through 2024, this study evaluates temporal trends in mortality among U.S. adults aged 65 years and older with coexisting neoplasms and cardiac arrhythmias. Understanding these patterns is essential for identifying high-risk populations, characterizing demographic and geographic disparities, and informing evidence-based prevention strategies, cardio-oncology care, and public health policies aimed at reducing mortality among this growing and vulnerable population (10).

## **METHODS**

### **STUDY DESIGN AND DATA SOURCE**

This retrospective analysis used data obtained from the Centers for Disease Control and Prevention's Wide-ranging Online Data for the Epidemiologic Research (CDC WONDER) database to assess the U.S. mortality trends of adults with neoplasms and cardiac arrhythmias from 1999 to 2024 (11). The CDC WONDER provides a standard dataset for national-level epidemiological analyses by compiling mortality data encompassing death certificates from every U.S. state and the District of Columbia

### **STUDY POPULATION**

Records from the Multiple Cause-of-Death (MCD) were analyzed for decedents aged  $\geq 65$  years with documented neoplasms and cardiac arrhythmias in any listed cause-of-death field. Mortality data were obtained using International Classification of Diseases, 10th Revision (ICD-10) codes, where neoplasms were identified using the ICD codes (C00-D48), and the ICD code (I44.0-I49.9) referred to cardiac arrhythmias. Mortality events were considered if the condition of interest appeared anywhere on the death certificate, whether as a primary or contributing cause of death.

### **DATA ABSTRACTION**

Data extracted comprised variables such as year of death, demographic factors like age, sex, and race/ethnicity; U.S. state of residence and geographical region classification; and urbanicity. The

places of death were classified as medical facilities (including outpatient, emergency room, inpatient, death on arrival, or status unknown), home, hospice, and long-term care facilities. The age category included older adults (65+). Race and ethnicity categories included Hispanics/Latinos, NH American Indian or Alaska Native, NH Asian or Pacific Islander, NH White, and NH Black or African American. Geographic variable included the census regions designated according to the U.S. Census Bureau's regional designations (Northeast, Midwest, South, and West), which were available for the entire study period(1999-2024), while county-level urbanization classifications, which were available only for 1999–2020; data beyond 2020 were excluded due to reliability concerns. The 2013 National Center for Health Statistics Metropolitan Non-metropolitan Classification Scheme was applied to assign Urban and Rural classification (12)

The study was conducted in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (13), and since it relied on anonymized, publicly accessible data, it was exempt from IRB approval.

## STATISTICAL ANALYSIS

Age-adjusted mortality rates(AAMR) per 100,000 were computed annually and were categorized by demographic and geographic factors such as sex, race/ethnicity, U.S. state, and urban-rural classification, with 95% Confidence Intervals. The direct standardization method, referencing the 2000 U.S. population, was applied to all the mortality rates. Temporal analysis of the mortality trends was conducted using the JoinPoint Regression Program (version 5.4.0; National Cancer Institute) (14), which was used to determine the annual percent change (APC) with 95% CI in AAMR. This method identifies significant changes in AAMR over time by fitting log-linear regression models where temporal variation occurred. APCs were considered increasing or decreasing if the slope describing the change in mortality was significantly different from zero using 2-tailed *t*-testing. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

Between 1999 and 2024, neoplasms associated with arrhythmias accounted for 616,985 deaths among adults aged 65 years and older in the United States. The AAMR increased from 43.67 (95% CI: 42.98 to 44.37) in 1999 to 74.88 (95% CI: 74.17 to 75.60) in 2024, with an overall significant increase (AAPC: 2.14; 95% CI: 1.71 to 2.58; P-value: <0.001). From 1999 to 2010, mortality increased significantly (APC: 0.54; 95% CI: 0.24 to 0.84; P-value: 0.001), followed by a further increase from 2010 to 2018 (APC: 2.14; 95% CI: 1.63 to 2.65; P-value: <0.001). Mortality rose sharply between 2018 and 2021 (APC: 10.16; 95% CI: 6.78 to 13.65; P-value: <0.001), followed by a stable trend from 2021 to 2024 (APC: 0.38; 95% CI: -1.01 to 1.79; P-

value: 0.567). (**supplemental table 1; Fig. 1; Table 1**).

### **Stratified by Sex:**

The AAMR increased among both females and males between 1999 and 2024. In females, the AAMR increased from 30.71 (95% CI: 29.97 to 31.45) in 1999 to 52.92 (95% CI: 52.13 to 53.73) in 2024. Similarly, among males, the AAMR increased from 66.23 (95% CI: 64.78 to 67.67) in 1999 to 104.96 (95% CI: 103.65 to 106.29) in 2024.

Among females, mortality demonstrated a significant increase from 1999 to 2017 (APC: 1.00; 95% CI: 0.81 to 1.20; P-value: <0.001), followed by a marked increase between 2017 and 2021 (APC: 8.48; 95% CI: 5.94 to 11.09; P-value: <0.001). From 2021 to 2024, a non-significant increasing trend was observed (APC: 0.91; 95% CI: -1.17 to 3.03; P-value: 0.371). Overall, females exhibited a significant upward trend across the study period (AAPC: 2.15; 95% CI: 1.70 to 2.61; P-value: <0.001).

Among males, mortality remained stable between 1999 and 2009 (APC: -0.001; 95% CI: -0.33 to 0.33; P-value: 0.995), followed by a significant increase from 2009 to 2015 (APC: 1.51; 95% CI: 0.67 to 2.35; P-value: 0.002). A non-significant increasing trend was observed between 2015 and 2018 (APC: 3.15; 95% CI: -0.18 to 6.60; P-value: 0.062), followed by a sharp, significant increase from 2018 to 2021 (APC: 9.78; 95% CI: 6.67 to 12.99; P-value: <0.001). Mortality remained stable from 2021 to 2024 (APC: 0.08; 95% CI: -1.21 to 1.38; P-value: 0.899). Overall, males demonstrated a significant increasing trend throughout the study period (AAPC: 1.88; 95% CI: 1.33 to 2.43; P-value: <0.001). (**supplemental table 1; Fig. 1; Table 1**).

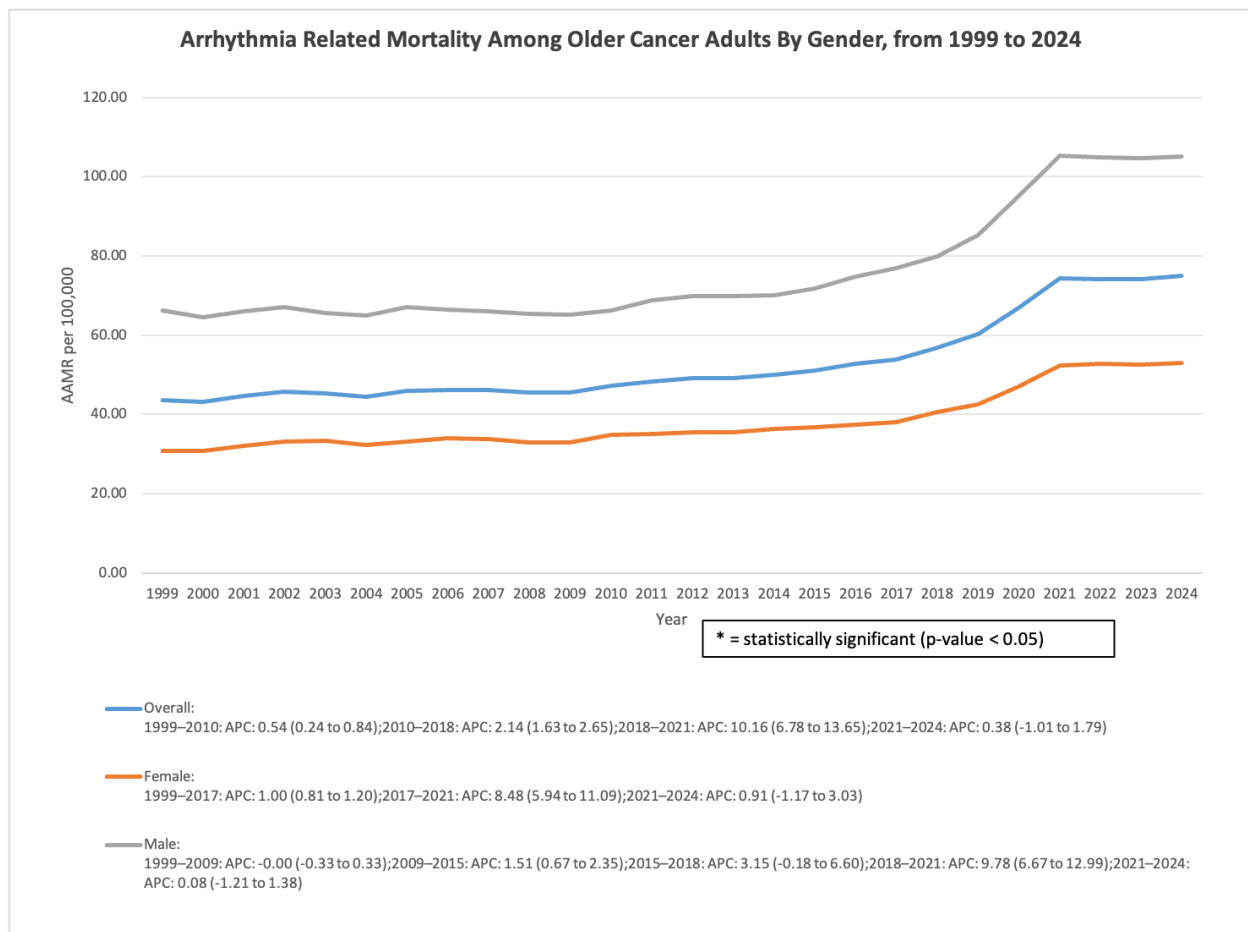


**Fig. 1: Neoplasms and cardiac arrhythmias AAMR among older adults stratified by overall and sex, per 100,000 population.**

### Stratified by Race:

Between 1999 and 2024, the AAMR increased across all racial and ethnic groups. Among Non-Hispanic American Indian or Alaska Native individuals, the AAMR increased from 17.73 (95% CI: 11.11 to 26.85) in 1999 to 35.39 (95% CI: 30.12 to 41.35) in 2024. Among Non-Hispanic Asian or Pacific Islander individuals, the AAMR increased from 21.08 (95% CI: 17.54 to 24.62) to 28.53 (95% CI: 26.67 to 30.48). Among Non-Hispanic Black or African American individuals, the AAMR increased from 38.21 (95% CI: 35.88 to 40.55) to 54.90 (95% CI: 52.91 to 56.94). Similarly, among Non-Hispanic White individuals, the AAMR increased from 44.71 (95% CI: 43.96 to 45.45) to 81.06 (95% CI: 80.24 to 81.88), while among Hispanic or Latino individuals, the AAMR increased from 19.60 (95% CI: 17.26 to 21.95) to 36.79 (95% CI: 35.15 to 38.50) over the study period.

Among Non-Hispanic American Indian or Alaska Native individuals, mortality demonstrated a continuous significant increase throughout the study period without any identified join points (AAPC: 2.74; 95% CI: 2.13 to 3.34; P-value: <0.001).

Among Non-Hispanic Asian or Pacific Islander individuals, mortality remained stable from 1999 to 2018 (APC: 0.17; 95% CI: -0.25 to 0.59; P-value: 0.411), followed by a significant increase between 2018 and 2021 (APC: 10.25; 95% CI: 0.69 to 20.71; P-value: 0.036). From 2021 to 2024, a non-significant declining trend was observed (APC: -2.24; 95% CI: -5.99 to 1.67; P-value: 0.240). Overall, the increasing trend did not reach statistical significance (AAPC: 1.03; 95% CI: -0.12 to 2.20; P-value: 0.079).

Among Non-Hispanic Black or African American individuals, mortality remained stable between 1999 and 2018 (APC: -0.03; 95% CI: -0.42 to 0.35; P-value: 0.851), followed by a significant increase from 2018 to 2021 (APC: 12.91; 95% CI: 2.20 to 24.75; P-value: 0.020). From 2021 to 2024, a non-significant increasing trend was observed (APC: 1.39; 95% CI: -2.91 to 5.87; P-value: 0.512). Overall, mortality demonstrated a significant upward trend across the study period (AAPC: 1.61; 95% CI: 0.35 to 2.88; P-value: 0.012).

Among Non-Hispanic White individuals, mortality increased significantly from 1999 to 2010 (APC: 0.70; 95% CI: 0.40 to 0.99; P-value: <0.001), followed by a further increase from 2010 to 2018 (APC: 2.43; 95% CI: 1.92 to 2.95; P-value: <0.001). A marked increase was observed between 2018 and 2021 (APC: 10.41; 95% CI: 6.99 to 13.94; P-value: <0.001), followed by a stable trend between 2021 and 2024 (APC: 0.62; 95% CI: -0.79 to 2.06; P-value: 0.364). Overall, Non-Hispanic White individuals demonstrated a significant increasing trend throughout the study period (AAPC: 2.36; 95% CI: 1.93 to 2.80; P-value: <0.001).

Among Hispanic or Latino individuals, mortality demonstrated a stable trend from 1999 to 2008 (APC: -0.28; 95% CI: -1.55 to 1.01; P-value: 0.648), followed by a significant increase between 2008 and 2018 (APC: 2.47; 95% CI: 1.54 to 3.41; P-value: <0.001). Mortality increased significantly from 2018 to 2021 (APC: 10.26; 95% CI: 2.50 to 18.61; P-value: 0.012), followed by a stable trend from 2021 to 2024 (APC: 0.70; 95% CI: -2.41 to 3.92; P-value: 0.641). Overall, Hispanic or Latino individuals demonstrated a significant upward trend during the study period (AAPC: 2.15; 95% CI: 1.11 to 3.21; P-value: <0.001). **(supplemental table 2; Fig. 2; Table 1).**

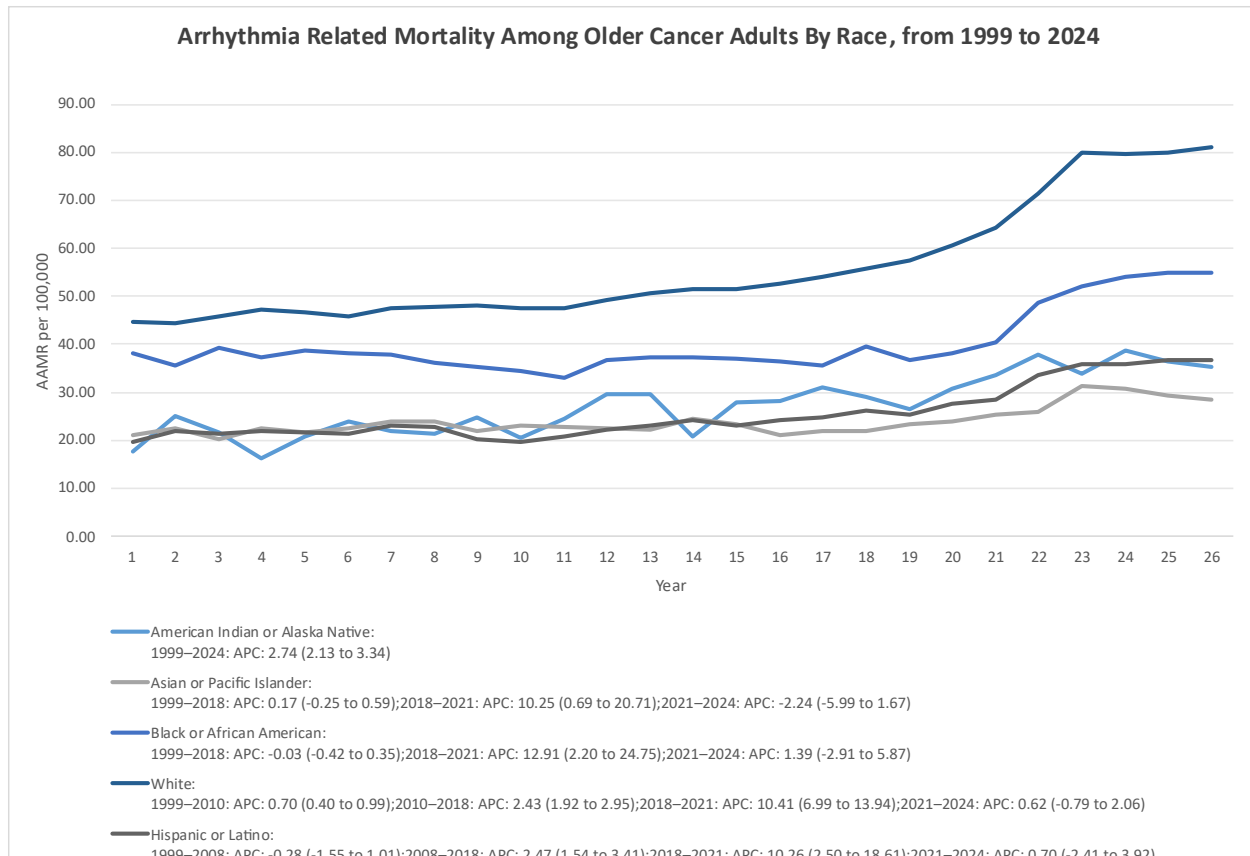


**Fig. 2: Neoplasms and cardiac arrhythmias AAMR among older adults stratified by race, per 100,000 population.**

### Stratified by Age:

Between 1999 and 2024, the AAMR increased across all age groups among older adults. Among adults aged 65–74 years, the AAMR increased from 19.08 (95% CI: 18.45 to 19.71) in 1999 to 28.22 (95% CI: 27.67 to 28.77) in 2024. Among adults aged 75–84 years, the AAMR increased from 53.58 (95% CI: 52.28 to 54.88) in 1999 to 88.66 (95% CI: 87.34 to 89.99) in 2024. Similarly, among adults aged 85 years and older, the AAMR increased from 119.62 (95% CI: 116.29 to 122.95) in 1999 to 233.75 (95% CI: 230.01 to 237.48) in 2024.

Among adults aged 65–74 years, mortality demonstrated a significant decline from 1999 to 2009 (APC: -0.84; 95% CI: -1.36 to -0.31; P-value: 0.004), followed by a significant increase between 2009 and 2017 (APC: 2.18; 95% CI: 1.40 to 2.98; P-value: <0.001). A marked increase was observed from 2017 to 2022 (APC: 7.42; 95% CI: 5.91 to 8.96; P-value: <0.001), followed by a non-significant declining trend from 2022 to 2024 (APC: -2.53; 95% CI: -6.35 to 1.44; P-value:

0.191). Overall, this age group demonstrated a significant upward trend throughout the study period (AAPC: 1.59; 95% CI: 1.09 to 2.10; P-value: <0.001).

Among adults aged 75–84 years, mortality increased significantly from 1999 to 2009 (APC: 0.71; 95% CI: 0.37 to 1.05; P-value: <0.001), followed by a continued increase between 2009 and 2018 (APC: 1.72; 95% CI: 1.28 to 2.17; P-value: <0.001). Mortality rose sharply from 2018 to 2021 (APC: 9.57; 95% CI: 6.00 to 13.26; P-value: <0.001), followed by a stable trend between 2021 and 2024 (APC: -0.21; 95% CI: -1.64 to 1.24; P-value: 0.762). Overall, adults aged 75–84 years demonstrated a significant increasing trend during the study period (AAPC: 1.99; 95% CI: 1.54 to 2.44; P-value: <0.001).

Among adults aged 85 years and older, mortality increased significantly from 1999 to 2017 (APC: 1.35; 95% CI: 1.15 to 1.55; P-value: <0.001), followed by a marked increase between 2017 and 2021 (APC: 9.65; 95% CI: 7.10 to 12.25; P-value: <0.001). From 2021 to 2024, a non-significant increasing trend was observed (APC: 1.64; 95% CI: -0.50 to 3.82; P-value: 0.125). Overall, this age group exhibited the greatest increase in mortality across the study period (AAPC: 2.67; 95% CI: 2.22 to 3.13; P-value: <0.001). (**supplemental table 3; Fig. 3; Table 1**).

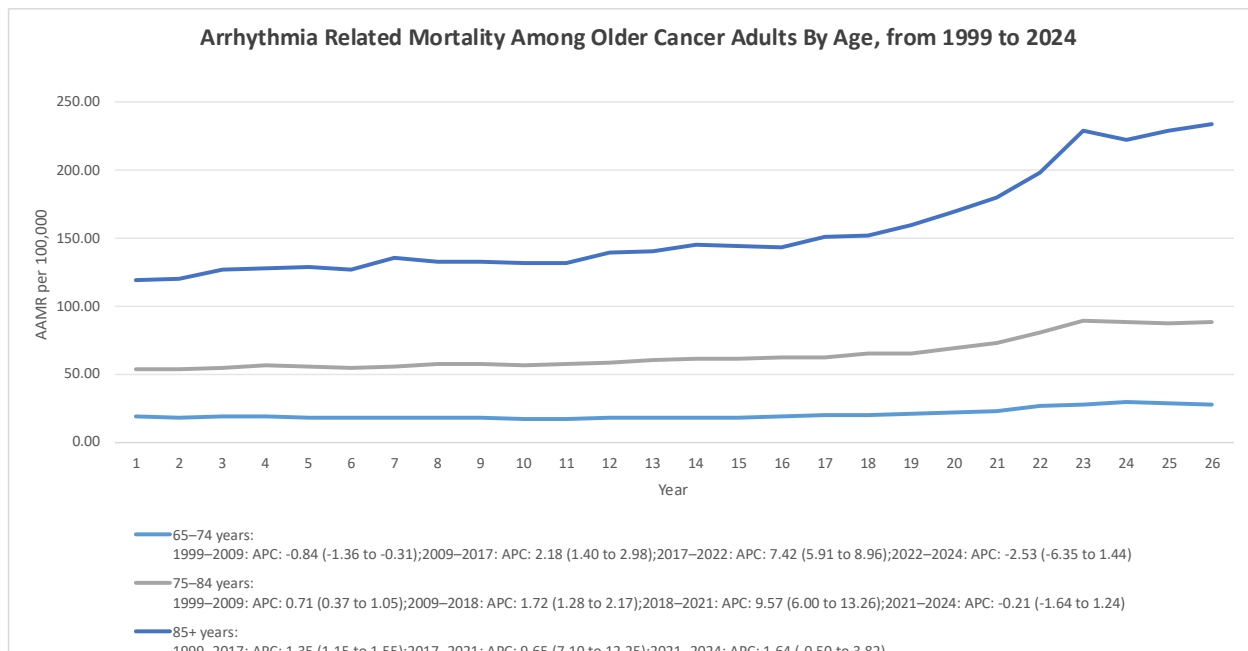


**Fig. 3: Neoplasms and cardiac arrhythmias AAMR among older adults stratified by age, per 100,000 population.**

## Regional Variation

### Stratified by Urbanization

Between 1999 and 2020, the AAMR increased in both metropolitan and non-metropolitan areas. In metropolitan areas, the AAMR increased from 43.40 (95% CI: 42.63 to 44.18) in 1999 to 48.65 (95% CI: 48.50 to 48.81) in 2020. In non-metropolitan areas, the AAMR increased more substantially from 44.56 (95% CI: 42.96 to 46.16) in 1999 to 82.39 (95% CI: 80.49 to 84.29) in 2020.

Among metropolitan areas, mortality demonstrated a stable trend between 1999 and 2009 (APC: 0.33; 95% CI: -0.06 to 0.72; P-value: 0.093), followed by a significant increase from 2009 to 2018 (APC: 1.88; 95% CI: 1.41 to 2.36; P-value: <0.001). A marked increase was observed between 2018 and 2020 (APC: 9.04; 95% CI: 5.23 to 12.99; P-value: <0.001). Overall, metropolitan regions demonstrated a significant upward trend during the study period (AAPC: 1.79; 95% CI: 1.39 to 2.20; P-value: <0.001).

Among non-metropolitan areas, mortality increased significantly from 1999 to 2013 (APC: 1.18; 95% CI: 0.87 to 1.50; P-value: <0.001), followed by a continued increase between 2013 and 2017 (APC: 3.46; 95% CI: 0.54 to 6.47; P-value: 0.023). Mortality rose sharply between 2017 and 2020 (APC: 9.85; 95% CI: 7.21 to 12.55; P-value: <0.001). Overall, non-metropolitan areas exhibited a significantly greater upward trend compared with metropolitan regions throughout the study period (AAPC: 2.81; 95% CI: 2.18 to 3.45; P-value: <0.001). (**supplemental table 4; Fig. 4; Table 1**).

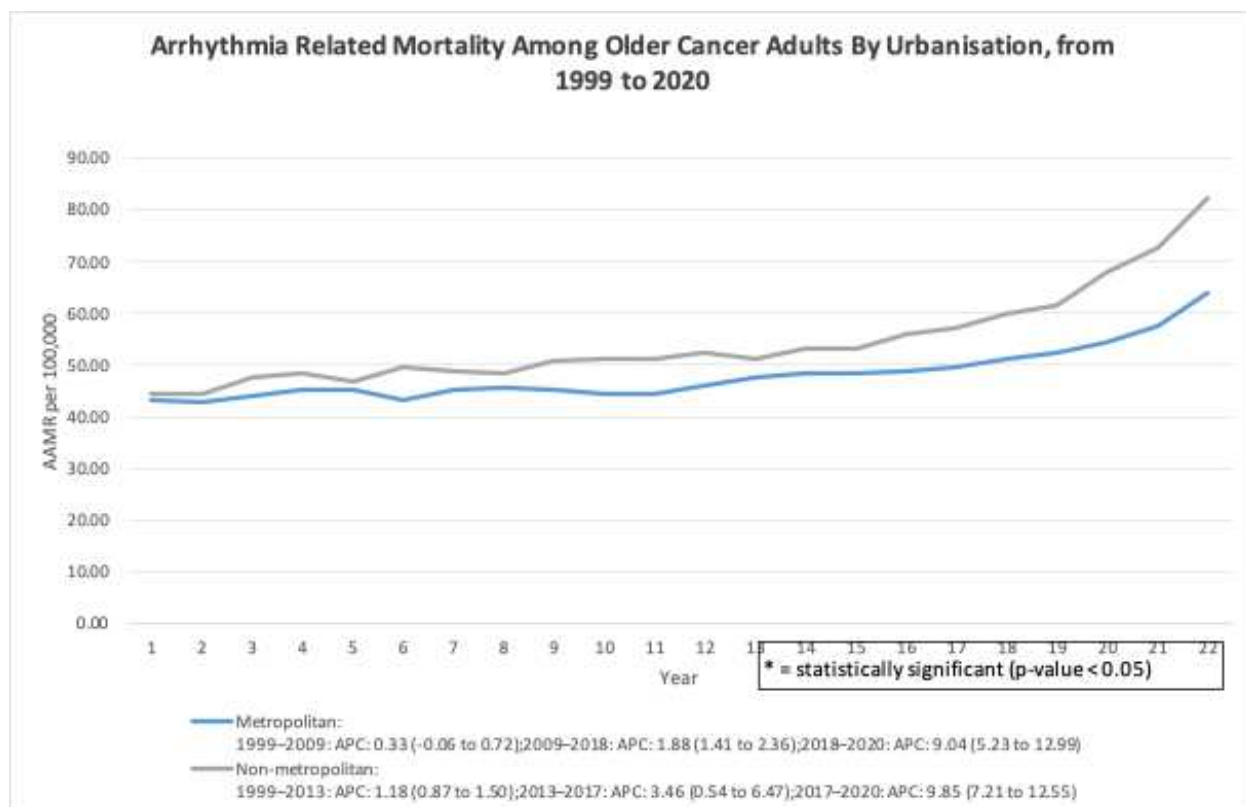


**Fig. 4: Neoplasms and cardiac arrhythmias AAMR among older adults stratified by urbanization, per 100,000 population.**

### Stratified by Census Region:

Between 1999 and 2024, the AAMR increased across all United States census regions. In the Northeast, the AAMR increased from 48.79 (95% CI: 47.20 to 50.38) in 1999 to 66.31 (95% CI: 64.75 to 67.89) in 2024. In the Midwest, the AAMR increased from 49.50 (95% CI: 47.99 to 51.01) to 78.64 (95% CI: 77.04 to 80.26). In the South, the AAMR increased from 37.55 (95% CI: 36.45 to 38.64) to 75.43 (95% CI: 74.26 to 76.61), while in the West, the AAMR increased from 41.71 (95% CI: 40.16 to 43.26) to 77.59 (95% CI: 76.05 to 79.15) during the study period.

In the Northeast, mortality demonstrated a significant decline from 1999 to 2008 (APC: -0.78; 95% CI: -1.26 to -0.30; P-value: 0.004), followed by a non-significant increase from 2008 to 2011 (APC: 3.82; 95% CI: -1.37 to 9.29; P-value: 0.137). Mortality remained stable between 2011 and 2018 (APC: 0.41; 95% CI: -0.39 to 1.22; P-value: 0.286), followed by a significant increase from 2018 to 2021 (APC: 9.10; 95% CI: 4.59 to 13.81; P-value: <0.001). A stable trend was subsequently observed from 2021 to 2024 (APC: -0.71; 95% CI: -2.61 to 1.23; P-value:

0.439). Overall, the Northeast demonstrated a significant increasing trend throughout the study period (AAPC: 1.25; 95% CI: 0.46 to 2.05; P-value: 0.002).

In the Midwest, mortality increased significantly from 1999 to 2013 (APC: 0.38; 95% CI: 0.16 to 0.59; P-value: 0.002), followed by a further increase between 2013 and 2018 (APC: 2.74; 95% CI: 1.41 to 4.09; P-value: <0.001). Mortality rose markedly from 2018 to 2021 (APC: 9.50; 95% CI: 5.68 to 13.45; P-value: <0.001), followed by a stable trend from 2021 to 2024 (APC: -0.78; 95% CI: -2.39 to 0.86; P-value: 0.323). Overall, the Midwest exhibited a significant upward trend during the study period (AAPC: 1.76; 95% CI: 1.25 to 2.28; P-value: <0.001).

In the South, mortality increased significantly from 1999 to 2009 (APC: 0.70; 95% CI: 0.20 to 1.21; P-value: 0.010), followed by a continued increase between 2009 and 2017 (APC: 2.22; 95% CI: 1.47 to 2.97; P-value: <0.001). A sharp increase was observed from 2017 to 2021 (APC: 10.04; 95% CI: 7.66 to 12.47; P-value: <0.001), followed by a further significant increase between 2021 and 2024 (APC: 2.36; 95% CI: 0.48 to 4.27; P-value: 0.017). Overall, the South demonstrated the greatest increase in mortality among all census regions (AAPC: 2.83; 95% CI: 2.34 to 3.32; P-value: <0.001).

In the West, mortality increased significantly from 1999 to 2002 (APC: 4.48; 95% CI: 1.32 to 7.73; P-value: 0.009), followed by a stable trend between 2002 and 2009 (APC: 0.39; 95% CI: -0.55 to 1.33; P-value: 0.386). Mortality subsequently increased significantly from 2009 to 2018 (APC: 2.36; 95% CI: 1.84 to 2.88; P-value: <0.001), followed by a marked increase between 2018 and 2021 (APC: 9.06; 95% CI: 4.95 to 13.33; P-value: <0.001). A stable trend was observed from 2021 to 2024 (APC: -0.05; 95% CI: -1.74 to 1.68; P-value: 0.955). Overall, the West exhibited a significant increasing trend throughout the study period (AAPC: 2.54; 95% CI: 1.89 to 3.19; P-value: <0.001). **(supplemental table 5; Fig. 5; Table 1).**

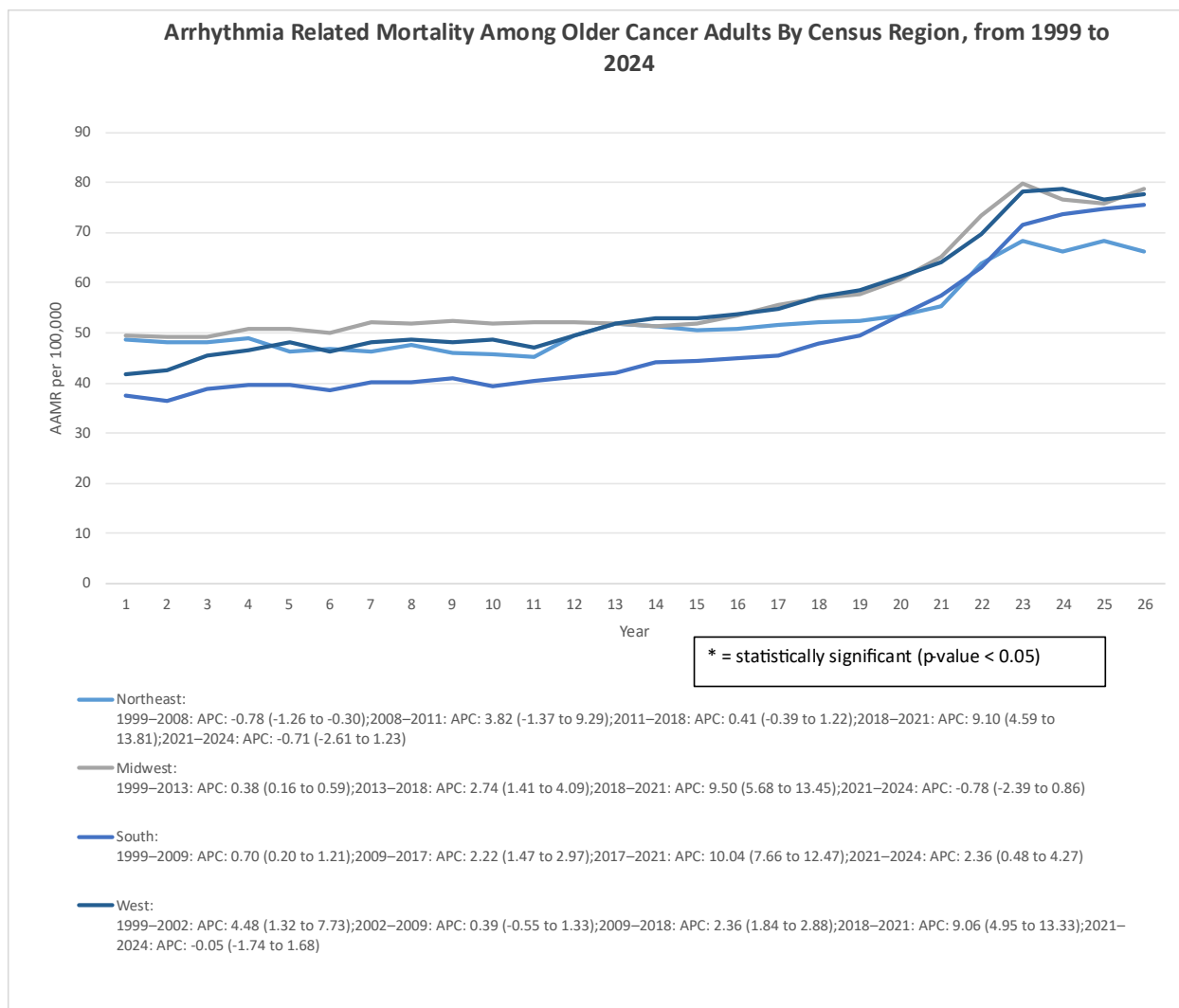


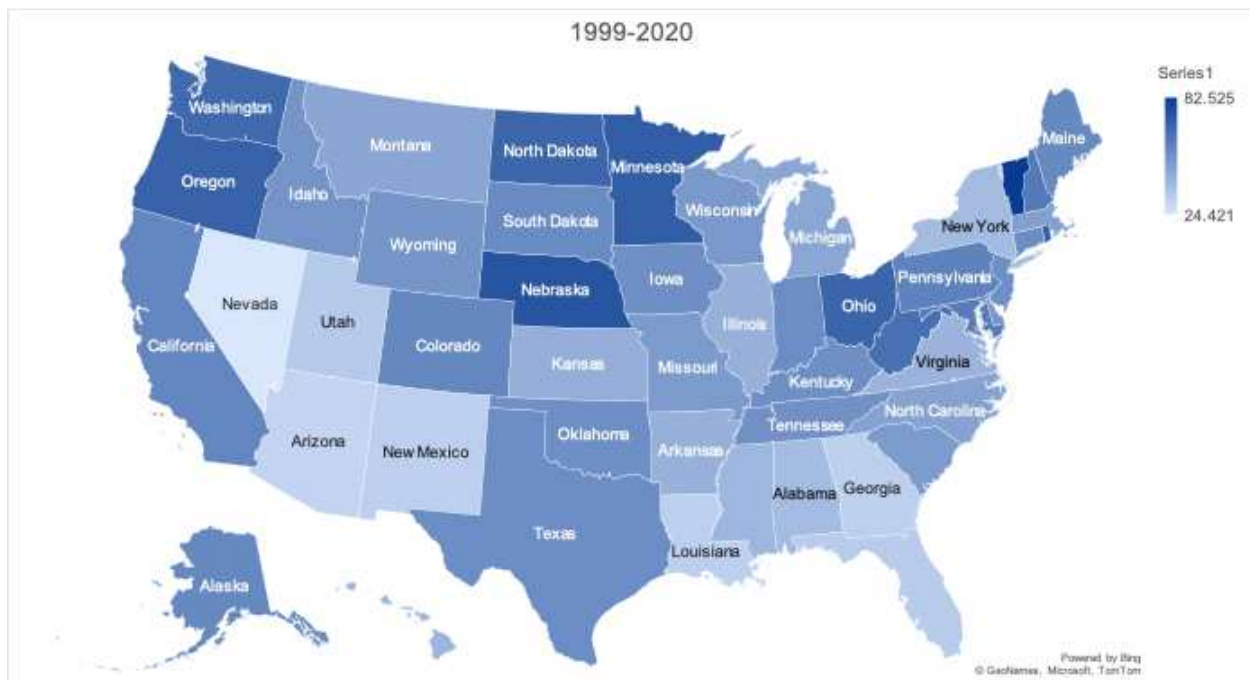
**Fig. 5: Neoplasms and cardiac arrhythmias AAMR among older adults stratified by census, per 100,000 population.**

### Stratified by States

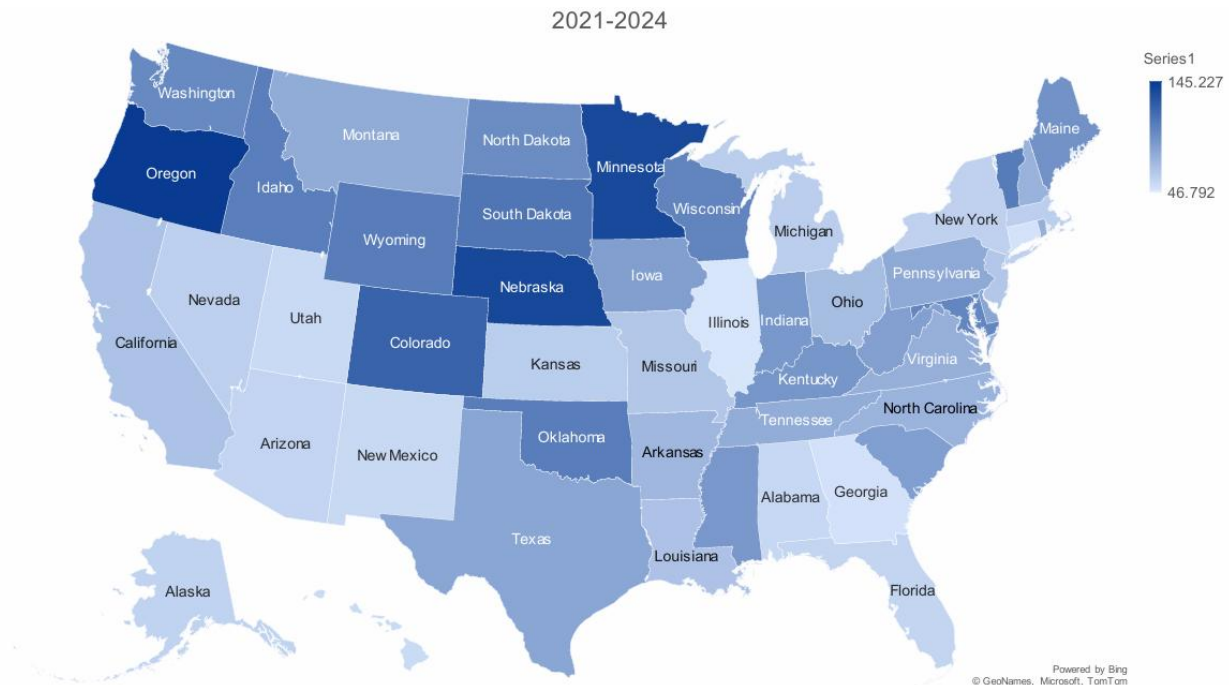
Marked geographic variation in arrhythmia-related mortality associated with neoplasms was observed across the United States.

From 1999 to 2020, states with the highest mortality burden percentile included Minnesota (70.94), Nebraska (73.90), Ohio (68.19), Oregon (69.28), Rhode Island (70.22), and Vermont (82.53). In contrast, states in the lowest mortality burden percentile included Arizona (30.53), Florida (33.47), Georgia (32.36), Louisiana (32.18), Nevada (24.42), and New Mexico (32.29).

Similarly, between 2021 and 2024, the highest mortality burden was observed in Colorado (122.36), Minnesota (137.43), Nebraska (138.00), Oregon (145.23), South Dakota (111.42), and Vermont (108.34). Conversely, states with comparatively lower mortality rates included Connecticut (49.02), Georgia (49.21), Hawaii (53.52), Illinois (46.79), New Mexico (54.45), and Utah (54.10). These findings highlight persistent and substantial geographic disparities in arrhythmia-related mortality among older adults across the United States. (**supplemental table 6; Fig. 6; Table 1**).



a) 1999-2020



b)2021-2024

**Fig. 6: Neoplasms and cardiac arrhythmias AAMR among older adults stratified by states, per 100,000 population.**

#### **Stratified by Place of Deaths:**

By location of death, the majority occurred in medical facilities (n=236,920; 38.40%), followed by the decedent's home (n=191,272; 31.00%), nursing homes or long-term care facilities (n=126,391; 20.48%), and hospice facilities (n=37,201; 6.03%). A smaller proportion of deaths occurred in other locations (n=24,402; 3.96%), while the place of death was unknown in a minimal number of cases (n=799; 0.13%). **(supplemental table 7).**

## **DISCUSSION**

In this nationwide population-based analysis spanning 1999–2024, mortality among older adults with coexisting neoplasms and cardiac arrhythmias demonstrated a substantial and persistent increase over time, with age-adjusted mortality rates increasing from 43.67 to 74.88 per 100,000 population and an overall annual increase of 2.14%. There was a slight trend of mortality increase during the early years of the study period, followed by a dramatic increase during the

last few years after 2018, with the steepest increase observed between 2018 and 2021; however, afterwards, mortality did not demonstrate any changes that were statistically significant. In summary, these results highlight the fact that despite remarkable progress in oncological and cardiovascular medicine, mortality linked to combined diseases of cancer and arrhythmia continues to represent an increasing health problem among older people (15,16).

Several mechanisms may explain the progressive increase in mortality observed over the study period. Aging may be considered as one of the principal contributors (17). Advancing age is accompanied by myocardial remodeling, including the development of atrial and ventricular fibrosis, disturbances in calcium homeostasis, and increasing electrical instability (18). Aging is also associated with progressive degeneration of the cardiac conduction system (19). These age-related changes create an arrhythmogenic substrate predisposing individuals to arrhythmia by promoting conduction heterogeneity and reentry mechanisms (18). In addition, previous research suggests that compared to other individuals, older adults are more likely to suffer from hypertension, coronary artery disease, heart failure, diabetes mellitus, as well as chronic kidney disease, all being potent risk factors for arrhythmias (17).

Several other mechanisms may contribute to the increased risk for arrhythmias in cancer patients. Cancer itself has increasingly been recognized as a pro-arrhythmic state due to systemic inflammation, metabolic disturbances, autonomic dysregulation, hypercoagulability, and direct or indirect myocardial injury (16,20–23). In addition, patients undergoing cancer treatment may experience higher rates of atrial and ventricular arrhythmias because of the use of chemotherapy, targeted therapy, radiotherapy, and cumulative cardiotoxicity (21–23). The development of cancer treatment strategies has resulted in a population of patients who not only survive cancer but also suffer from cardiac side effects of the treatment, which increases the prevalence of cardiac rhythm disorders (22). Accordingly, the observed increase in mortality may reflect evolving survivorship patterns and the growing population of high-risk individuals rather than deterioration in the quality of cardiovascular care.

The observed acceleration in mortality during the COVID-19 era deserves particular consideration. COVID-19 is known to increase the risk of both atrial and ventricular arrhythmias through multiple mechanisms, including systemic inflammation, autonomic dysregulation, myocardial injury, endothelial dysfunction, electrolyte abnormalities, hypoxemia, and thromboinflammatory states (24). According to experimental evidence, inflammatory cytokines may have a direct influence on ion channels and electrical stability, resulting in arrhythmogenic risk in humans (17). In addition, patients with severe COVID-19 and myocardial injury consistently demonstrated greater risks of arrhythmias and adverse cardiovascular events (25,26). Populations of patients with cancer may be especially prone to these events because of potential interruption of chemotherapy regimens, delayed cancer care visits, lack of access to procedures, and disruption of longitudinal treatment (24). In addition to biological reasons, disruption of care, including delays in seeking medical help, postponed procedures, decreased outpatient visits, and general pressure on the health care system, may result in poorer outcomes (24). The

stabilization observed after 2021 may reflect the gradual adaptation of healthcare systems and recovery of healthcare delivery, but no causal relationship can be ascertained in an ecological study design.

Sex-based disparities persisted throughout the study period, with men experiencing nearly double the mortality burden observed among women. Mortality increased from 66.23 to 104.96 per 100,000 among men compared with 30.71 to 52.92 among women. Despite the presence of accelerated trends in both sexes beginning in 2018, the observed persistently high mortality rates among men could be related to possible biological and behavioral factors. There are well-known differences and cardiovascular disease presentations, risk profiles, and clinical outcomes that result from intricate interplays between the effects of biological sex, hormones, and inequalities in healthcare delivery and use (27,28). Hormonal mechanisms may also contribute, as estrogen is thought to have cardioprotective effects on the body mediated by modulating autonomic nervous system activity, endothelial function, inflammatory pathways, and electrophysiologic properties (27,28). Differences in healthcare utilization and preventive care engagement may additionally influence long-term outcomes (27). The persistence of these disparities despite therapeutic advances suggests that both biological and social determinants continue to influence outcomes.

Ratio and ethnic differences have remained substantial over the whole study period. While people of non-Hispanic White ethnicity were the largest group experiencing mortality and had the highest rates, other ethnic groups demonstrated heterogeneous time dynamics and changes in mortality rates. These differences should be interpreted cautiously because subgroup trajectories varied, and some trends did not achieve statistical significance. Literature reviews suggest that the majority of the disparities in cardiovascular disease outcomes among different groups of people are attributable to social, structural, socioeconomic, and medical factors, including differences in socioeconomic status, healthcare access, referral patterns, preventive screening utilization, and specialty care access (29,30). Differences in access to rhythm monitoring, electrophysiology consultation, catheter ablation, and advanced cardiac therapies may further contribute to disparities in outcomes (19,29). Disparities in oncologic treatment and cancer survivorship services can also affect cardiovascular outcomes through the development of complications associated with chemotherapy and radiotherapy (31,32). Importantly, race and ethnicity likely function primarily as markers of broader social and structural determinants rather than independent factors.

Age represented one of the strongest determinants of mortality burden. Mortality progressively increased across age categories and was highest among adults aged 85 years and older, in whom mortality rates nearly doubled during the study period. Individuals aged 85 years and older also demonstrated the largest overall increase in mortality burden. These findings correlate with current biological plausibility and knowledge about cardiovascular aging. Aging is associated with progressive conduction system degeneration, increasing myocardial fibrosis, declining physiologic reserve, and an increased vulnerability to multimorbidity (17,18). Older adults with cancer frequently experience higher rates of frailty, polypharmacy, multiple co-existing diseases,

and more extensive medical history, thus complicating the diagnosis and treatment of arrhythmias (22). A substantial increase in mortality burden among the most elderly people indicates that growing longevity can be associated with higher levels of cancer survivorship and cardiovascular mortality burden.

Pronounced geographic disparities were also evident. Both metropolitan and non-metropolitan regions experienced mortality growth, although relative increases were more prominent in non-metropolitan areas. These findings are consistent with the current literature describing persistent rural-urban health disparities (31,32). Individuals living in rural regions frequently experience reduced access to cardiologists and electrophysiologists, delayed emergency services, transportation barriers, healthcare workforce shortages, and increasing hospital closures (15,16). Lack of cardio-oncology services and specialized cancer centers may also play their role.

The regional analyses revealed additional important patterns. Firstly, the South demonstrated the largest increase in mortality burden over time. Secondly, states within the Upper Midwest, Mountain West, and Pacific Northwest frequently appeared among regions with the highest mortality rates. These findings are likely influenced by demographic distribution, cardiovascular risk prevalence, healthcare delivery system, and specialized cardiovascular and oncologic care (19,31).

Place-of-death patterns provide additional clinical insight. The majority of people died in hospitals; however, there was a considerable percentage of deaths recorded in the homes of the patients and in nursing homes. Such a trend is indicative of different aspects, including but not limited to varying disease progression, patterns of health service utilization, and individual preferences regarding end-of-life care in older people with complicated diseases.

However, several limitations should be considered. First, this analysis relied on death certificate data and therefore remains susceptible to coding inaccuracies and misclassification bias. Arrhythmias frequently coexist with other cardiovascular conditions, and attribution of a single underlying cause of death may not fully capture disease complexity. Second, there was no information available regarding individual patient-level variables such as specific subtype of arrhythmia, type and intensity of care provided, procedure performed, and socioeconomic status that might help understand underlying mechanisms, and also the neoplasm category encompassed a broad spectrum of malignant, benign, in situ, and uncertain-behavior neoplasms, preventing assessment of mortality according to specific cancer types, stages, or treatment exposures. Thirdly, the way of coding and diagnosing has evolved during the period of observation, which could affect mortality rates. Finally, because this represents an ecological observational study, causal relationships cannot be established.

Despite these limitations, this study provides a comprehensive national assessment of long-term arrhythmia mortality trends among older adults and demonstrates a substantial and increasing burden characterized by persistent demographic and geographic disparities. As the population continues to age and more individuals survive chronic cardiovascular disease, the number of

patients living with conditions that predispose to arrhythmias is likely to increase. Identifying high-risk groups and improving equitable access to specialized cardiovascular care may therefore play an important role in reducing future mortality.

## **Abbreviation**

AAMR – Age-adjusted mortality rate

AAPC – Average annual percent change

APC – Annual Percent Change

CDC – Centers for Disease Control and Prevention

CI – Confidence Interval

ICD-10 – International Classification of Diseases, Tenth Revision

IRB – Institutional Review Board

NH – Non-Hispanic

STROBE – Strengthening the Reporting of Observational Studies in Epidemiology

U.S. – United States

WONDER – Wide-ranging Online Data for Epidemiologic Research

## **Statements and Declarations**

### **Funding:**

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### **Conflict of Interest / Competing Interests:**

The authors declare no competing interests.

### **Financial Disclosure:**

The authors have no relevant financial or non-financial interests to disclose.

### **Ethics Approval:**

This study used publicly available, de-identified data from the CDC WONDER database. As no human participants were directly involved, ethical approval and institutional review board (IRB) approval were not required.

**Informed Consent:**

Not applicable, as the study was based on publicly available, anonymized secondary data.

**Consent for Publication:**

Not applicable.

**Consent to participate:**

Not applicable.

**Data Availability:**

All data used in this study are publicly available through the CDC WONDER (Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research) database: <https://wonder.cdc.gov/>

**Code Availability:**

No custom software or code was required for this study. All analyses were conducted using publicly available tools, including CDC WONDER and Joinpoint Regression Program (version 5.4.0).

**Authors' Contributions:**

PK: Conceptualization, methodology, formal analysis, writing—original draft.

AS: Writing—review and editing.

SSA: Data curation, formal analysis.

MV: Writing—original draft.

MW: Writing—original draft.

MJ: Visualization, writing—original draft.

AK: Investigation, writing—original draft.

FUN: Writing—review and editing.

All authors contributed to the interpretation, critically revised the manuscript, and approved the final version.

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**TABLE 1: Annual percentage change for neoplasms and cardiac arrhythmias-related mortality among U.S. adults aged ≥65 years, 1999–2024.**

| Demographics | AAPC          |                          | Trend 1       |                                   | Trend 2       |                           | Trend 3       |                            | Trend 4       |                               | Trend 5       |                              |
|--------------|---------------|--------------------------|---------------|-----------------------------------|---------------|---------------------------|---------------|----------------------------|---------------|-------------------------------|---------------|------------------------------|
| Demographics | Year          | AAPC<br>(95%<br>CI)      | (Year)        | APC<br>(95%<br>CI)                | (Year)        | APC<br>(95%<br>CI)        | (Year)        | APC<br>(95%<br>CI)         | (Year)        | APC<br>(95%<br>CI)            | Year          | APC<br>(95%<br>CI)           |
| Overall      | 1999–<br>2024 | 2.14*<br>(1.71–<br>2.58) | 1999–<br>2010 | 0.54*<br>(0.24–<br>0.84)          | 2010–<br>2018 | 2.14*<br>(1.63–<br>2.65)  | 2018–<br>2021 | 10.16*<br>(6.78–<br>13.65) | 2021–<br>2024 | 0.38<br>(-<br>1.01–<br>1.79)  | —             | —                            |
| Sex          |               |                          |               |                                   |               |                           |               |                            |               |                               |               |                              |
| Female       | 1999–<br>2024 | 2.15*<br>(1.70–<br>2.61) | 1999–<br>2017 | 1.00*<br>(0.81–<br>1.20)          | 2017–<br>2021 | 8.48*<br>(5.94–<br>11.09) | 2021–<br>2024 | 0.91 (-<br>1.17–<br>3.03)  | —             | —                             | —             | —                            |
| Male         | 1999–<br>2024 | 1.88*<br>(1.33–<br>2.43) | 1999–<br>2009 | -0.00<br>(-<br>0.33–<br>0.33)     | 2009–<br>2015 | 1.51*<br>(0.67–<br>2.35)  | 2015–<br>2018 | 3.15 (-<br>0.18–<br>6.60)  | 2018–<br>2021 | 9.78*<br>(6.67–<br>12.99)     | 2021–<br>2024 | 0.08<br>(-<br>1.21–<br>1.38) |
| Age Groups   |               |                          |               |                                   |               |                           |               |                            |               |                               |               |                              |
| 65–74 years  | 1999–<br>2024 | 1.59*<br>(1.09–<br>2.10) | 1999–<br>2009 | -0.84*<br>(-1.36<br>to -<br>0.31) | 2009–<br>2017 | 2.18*<br>(1.40–<br>2.98)  | 2017–<br>2022 | 7.42*<br>(5.91–<br>8.96)   | 2022–<br>2024 | -2.53<br>(-<br>6.35–<br>1.44) | —             | —                            |
| 75–84 years  | 1999–<br>2024 | 1.99*<br>(1.54–<br>2.44) | 1999–<br>2009 | 0.71*<br>(0.37–<br>1.05)          | 2009–<br>2018 | 1.72*<br>(1.28–<br>2.17)  | 2018–<br>2021 | 9.57*<br>(6.00–<br>13.26)  | 2021–<br>2024 | -0.21<br>(-<br>1.64–<br>1.24) | —             | —                            |

|                                        |               |                           |               |                                   |               |                            |               |                               |               |                               |               |                               |
|----------------------------------------|---------------|---------------------------|---------------|-----------------------------------|---------------|----------------------------|---------------|-------------------------------|---------------|-------------------------------|---------------|-------------------------------|
| ≥85 years                              | 1999–<br>2024 | 2.67*<br>(2.22–<br>3.13)  | 1999–<br>2017 | 1.35*<br>(1.15–<br>1.55)          | 2017–<br>2021 | 9.65*<br>(7.10–<br>12.25)  | 2021–<br>2024 | 1.64 (-<br>0.50–<br>3.82)     | —             | —                             | —             | —                             |
| <b>Census Region</b>                   |               |                           |               |                                   |               |                            |               |                               |               |                               |               |                               |
| Northeast                              | 1999–<br>2024 | 1.25*<br>(0.46–<br>2.05)  | 1999–<br>2008 | -0.78*<br>(-1.26<br>to -<br>0.30) | 2008–<br>2011 | 3.82 (-<br>1.37–<br>9.29)  | 2011–<br>2018 | 0.41 (-<br>0.39–<br>1.22)     | 2018–<br>2021 | 9.10*<br>(4.59–<br>13.81)     | 2021–<br>2024 | -0.71<br>(-<br>2.61–<br>1.23) |
| Midwest                                | 1999–<br>2024 | 1.76*<br>(1.25–<br>2.28)  | 1999–<br>2013 | 0.38*<br>(0.16–<br>0.59)          | 2013–<br>2018 | 2.74*<br>(1.41–<br>4.09)   | 2018–<br>2021 | 9.50*<br>(5.68–<br>13.45)     | 2021–<br>2024 | -0.78<br>(-<br>2.39–<br>0.86) | —             | —                             |
| South                                  | 1999–<br>2024 | 2.83*<br>(2.34–<br>3.32)  | 1999–<br>2009 | 0.70*<br>(0.20–<br>1.21)          | 2009–<br>2017 | 2.22*<br>(1.47–<br>2.97)   | 2017–<br>2021 | 10.04*<br>(7.66–<br>12.47)    | 2021–<br>2024 | 2.36*<br>(0.48–<br>4.27)      | —             | —                             |
| West                                   | 1999–<br>2024 | 2.54*<br>(1.89–<br>3.19)  | 1999–<br>2002 | 4.48*<br>(1.32–<br>7.73)          | 2002–<br>2009 | 0.39 (-<br>0.55–<br>1.33)  | 2009–<br>2018 | 2.36*<br>(1.84–<br>2.88)      | 2018–<br>2021 | 9.06*<br>(4.95–<br>13.33)     | 2021–<br>2024 | -0.05<br>(-<br>1.74–<br>1.68) |
| <b>Race/Ethnicity</b>                  |               |                           |               |                                   |               |                            |               |                               |               |                               |               |                               |
| American<br>Indian or<br>Alaska Native | 1999–<br>2024 | 2.74*<br>(2.13–<br>3.34)  | 1999–<br>2024 | 2.74*<br>(2.13–<br>3.34)          | —             | —                          | —             | —                             | —             | —                             | —             | —                             |
| Asian or<br>Pacific<br>Islander        | 1999–<br>2024 | 1.03 (-<br>0.12–<br>2.20) | 1999–<br>2018 | 0.17<br>(-<br>0.25–<br>0.59)      | 2018–<br>2021 | 10.25*<br>(0.69–<br>20.71) | 2021–<br>2024 | -2.24<br>(-<br>5.99–<br>1.67) | —             | —                             | —             | —                             |
| Black or<br>African<br>American        | 1999–<br>2024 | 1.61*<br>(0.35–<br>2.88)  | 1999–<br>2018 | -0.03<br>(-<br>0.42–<br>0.35)     | 2018–<br>2021 | 12.91*<br>(2.20–<br>24.75) | 2021–<br>2024 | 1.39 (-<br>2.91–<br>5.87)     | —             | —                             | —             | —                             |
| White                                  | 1999–<br>2024 | 2.36*<br>(1.93–<br>2.80)  | 1999–<br>2010 | 0.70*<br>(0.40–<br>0.99)          | 2010–<br>2018 | 2.43*<br>(1.92–<br>2.95)   | 2018–<br>2021 | 10.41*<br>(6.99–<br>13.94)    | 2021–<br>2024 | 0.62<br>(-<br>—)              | —             | —                             |

|                     |               |                          |               |                           |               |                          |               |                            |               |                          |   |   |
|---------------------|---------------|--------------------------|---------------|---------------------------|---------------|--------------------------|---------------|----------------------------|---------------|--------------------------|---|---|
|                     |               |                          |               |                           |               |                          |               |                            |               | 0.79–<br>2.06)           |   |   |
| Hispanic or Latino  | 1999–<br>2024 | 2.15*<br>(1.11–<br>3.21) | 1999–<br>2008 | -0.28<br>(-1.55–<br>1.01) | 2008–<br>2018 | 2.47*<br>(1.54–<br>3.41) | 2018–<br>2021 | 10.26*<br>(2.50–<br>18.61) | 2021–<br>2024 | 0.70<br>(-2.41–<br>3.92) | — | — |
| <b>Urbanization</b> |               |                          |               |                           |               |                          |               |                            |               |                          |   |   |
| Metropolitan        | 1999–<br>2020 | 1.79*<br>(1.39–<br>2.20) | 1999–<br>2009 | 0.33<br>(-0.06–<br>0.72)  | 2009–<br>2018 | 1.88*<br>(1.41–<br>2.36) | 2018–<br>2020 | 9.04*<br>(5.23–<br>12.99)  | —             | —                        | — | — |
| Non-metropolitan    | 1999–<br>2020 | 2.81*<br>(2.18–<br>3.45) | 1999–<br>2013 | 1.18*<br>(0.87–<br>1.50)  | 2013–<br>2017 | 3.46*<br>(0.54–<br>6.47) | 2017–<br>2020 | 9.85*<br>(7.21–<br>12.55)  | —             | —                        | — | — |

LEGENDS

**Fig. 1:** Neoplasms and cardiac arrhythmias AAMR among older adults stratified by overall and sex, per 100,000 population.

**Fig. 2:** Neoplasms and cardiac arrhythmias AAMR among older adults stratified by race, per 100,000 population.

**Fig. 3:** Neoplasms and cardiac arrhythmias AAMR among older adults stratified by age, per 100,000 population.

**Fig. 4:** Neoplasms and cardiac arrhythmias AAMR among older adults stratified by urbanization, per 100,000 population.

**Fig. 5:** Neoplasms and cardiac arrhythmias AAMR among older adults stratified by census, per 100,000 population.

**Fig. 6:** Neoplasms and cardiac arrhythmias AAMR among older adults stratified by states, per 100,000 population.

Table 1

**Table 1: Annual Percentage Change in Neoplasm- and Cardiac Arrhythmia–Associated Mortality Among U.S. Adults Aged  $\geq 65$  Years, 1999–2024**

**Supplemental Tables**

**Supplemental Table 1:** Overall and sex-stratified trends in neoplasm- and cardiac arrhythmia–associated mortality, shown as age-adjusted mortality rates per 100,000 among adults aged  $\geq 65$  years in the United States, 1999–2024.

**Supplemental Table 2:** Race/ethnicity-stratified trends in neoplasm- and cardiac arrhythmia–associated mortality, shown as age-adjusted mortality rates per 100,000 among adults aged  $\geq 65$  years in the United States, 1999–2024.

**Supplemental Table 3:** Age-stratified trends in neoplasm- and cardiac arrhythmia–associated mortality, shown as age-adjusted mortality rates per 100,000 among adults aged  $\geq 65$  years in the United States, 1999–2024.

**Supplemental Table 4:** Urbanization-stratified trends in neoplasm- and cardiac arrhythmia–associated mortality, shown as age-adjusted mortality rates per 100,000 among adults aged  $\geq 65$  years in the United States, 1999–2024.

**Supplemental Table 5:** Census region-stratified trends in neoplasm- and cardiac arrhythmia–associated mortality, shown as age-adjusted mortality rates per 100,000 among adults aged  $\geq 65$  years in the United States, 1999–2024.

**Supplemental Table 6:** State-level trends in neoplasm- and cardiac arrhythmia–associated mortality, shown as age-adjusted mortality rates per 100,000 among adults aged  $\geq 65$  years in the United States, 1999–2024.

**Supplemental Table 7:** Percentage distribution of place of death among decedents with neoplasms and cardiac arrhythmias in the United States, 1999–2024.

## Supplementary Files

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