


## RAPID COMMUNICATION

# Trends in comorbid chronic kidney disease and atrial fibrillation-related cardiovascular mortality in the United States

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## Abstract

**Background:** The impact of chronic kidney disease (CKD) on atrial fibrillation outcomes (AF) is not well understood.

**Methods:** We conducted analyses of comorbid AF and CKD related death in the United States from 1999 to 2020 using descriptive epidemiology.

**Results:** Age-adjusted mortality rates (AAMR) per 100,000 increased from 0.39 in 1999 to 1.65 in 2020. Non-Hispanic populations (1.01) and nonmetropolitan areas (1.08) had higher AAMRs compared to Hispanic (0.62) and metropolitan (0.97) areas. Midwestern (1.11) and Western (1.13) US regions recorded the highest AAMRs.

**Conclusions:** These findings highlight the need for interventions to address AF death disparities in patients with CKD.

## KEYWORDS

atrial, disparities, epidemiology, fibrillation, gender

Atrial fibrillation (AF) and chronic kidney disease (CKD) share common risk factors and frequently co-exist. These conditions also share similar outcomes including thromboembolic phenomena and bleeding complications, demonstrating a bidirectional relationship.<sup>1-4</sup> Little is known about mortality trends and disparities related to AF and CKD in the United States (US). Therefore, we sought to conduct cross sectional analyses of AF-related cardiovascular death with co-existing CKD.

Data were obtained from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research database to capture all deaths using US death certificate information.<sup>5</sup> All diagnoses were based on the *International Classification of Diseases, Tenth Revision* (ICD10). Race and ethnicity were made available on death certificates. We utilized the US census regions and

the 2013 National Center for Health Statistics (NCHS) Urban–Rural Classification Scheme for Counties among our included subpopulations analyses.

Mortality rates with cardiovascular disease (I00–I78) as the underlying cause of death and AF (I48) and CKD (N18) as the multiple causes of death were queried from 1999 to 2020. Age-adjusted mortality rates (AAMR) were calculated using the direct method with the US population in 2000 as the standard population. Subgroup analyses were conducted by comparing AAMR using descriptive epidemiology across gender, race, and geographic subpopulations. We used log-linear regression models via Joinpoint Regression (National Cancer Institute) to analyze trends in AAMR over time, with inflection points and average annual percentage change (AAPC) estimated through use of the Monte-Carlo permutation test. To determine

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whether the slope of the change was significantly different from zero, we conducted two-tailed t-testing, with statistical significance set at  $p < .05$ .

Data visualization was done using Stata (Release 17.0; StataCorp LLC). Institutional review board approval was not required as the data collected is publicly available and de-identified.

From 1999 to 2020, there were a total of 73,321 AF-related cardiovascular deaths in individuals with comorbid CKD in the United States. Yearly death counts, population sizes, crude mortality rates, and AAMR are depicted in Table S1. The AAMR increased from 0.39 in 1999 to 1.65 in 2020, with an AAPC of +6.65% ( $p < .001$ ). Inflection points were observed in 2010 to 2011 and 2012 to 2013. While males had higher overall AAMR (AAMR: 1.35) compared to females (AAMR: 0.76), while both genders showed a similar AAPC of +6.18% ( $p < .001$ ) and +6.73% ( $p < .001$ ), respectively (Figure 1).

Non-Hispanic populations (AAMR: 1.01) had a higher AAMR compared to Hispanic populations (AAMR: 0.62); however, AAPC was similar among both groups (6.78% [ $p < .001$ ] and 5.21% [ $p < .001$ ], respectively). AAMR between Black (AAMR: 1.04) and White (AAMR: 1.00) populations were similar and higher than Asian/Pacific Islander (AAMR: 0.67) populations. No differences in AAPC were

observed for the three racial subgroups (+4.55% [ $p < .001$ ], +6.99% [ $p < .001$ ], and +2.5% [ $p = .456$ ], respectively). Nonmetropolitan regions (AAMR: 1.08) were disproportionately affected compared to metropolitan regions (AAMR: 0.97). AAPC among nonmetropolitan (+6.97% [ $p < .001$ ]) and metropolitan (+6.55% [ $p < .001$ ]) regions were similar. The Midwest (AAMR: 1.11) and West (AAMR: 1.13) had a similar AAMR, greater than the AAMR in the Northeast (AAMR: 0.90) and South (AAMR: 0.89) regions. AAPC was similar among all four US census regions (+7.25% [ $p < .001$ ], +6.76% [ $p < .001$ ], +5.76% [ $p < .001$ ], and +6.42% [ $p < .001$ ], respectively).

The present study investigated AF-related mortality in individuals with CKD. Our findings indicate that mortality rates have increased over time among individuals with CKD, with certain subpopulations disproportionately affected.

The rising prevalence of shared risk factors including hypertension, obesity, and diabetes in the United States suggests that AF and CKD rates will likely increase, contributing to higher morbidity and mortality.<sup>6,7</sup> Earlier onset of AF in males and gender differences related to the susceptibility of atrial arrhythmias may explain the higher AAMR among male populations.<sup>8,9</sup> Furthermore, our analysis found no major mortality differences between Black and White populations, contrary to the REasons for Geographic and Racial Differences in Stroke (REGARDS) study.<sup>10</sup> However, non-Hispanic populations had disproportionately higher AF-related cardiovascular mortality, reflecting ethnic disparities in cardiovascular outcomes.<sup>11</sup> Geographic variability in AF and CKD mortality stem from differences in care quality, access to healthcare, and risk profiles.<sup>10,12</sup> The two observed inflection points from 2010 to 2013 may have resulted from various factors, including changes in CKD evaluation and management guidelines, risk factors prevalence, and year-to-year variation.<sup>13-15</sup>

Limitations of our analysis includes the use of death certificate information, which are subjected to inaccuracies. However, it is unlikely that this limitation could account for the observed disparities. Additionally, other covariates such as anticoagulation therapy, use of dialysis, and etiology of CKD were not available in the data repositories, which may have a significant impact on outcomes because of AF and CKD.

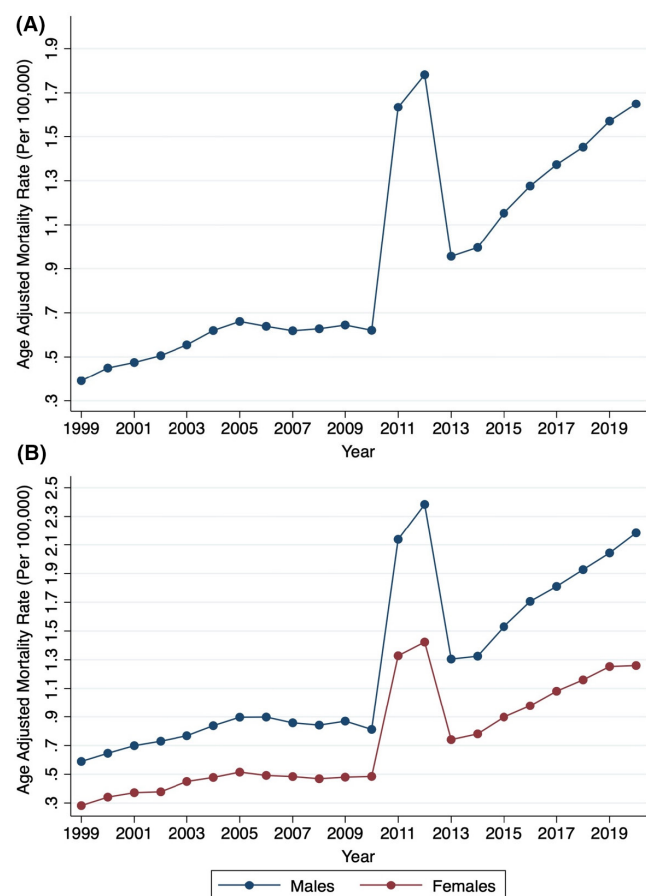
Our findings indicate that AF-related cardiovascular death in individuals with CKD has increased over time with significant disparities among gender, racial/ethnic, and regional subpopulations, underscoring the importance of healthcare access issues and unique risk factor profiles. These conclusions emphasize the need for targeted interventions to reduce the burden of AF-related cardiovascular mortality in individuals with CKD.

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**FIGURE 1** Yearly Mortality Data. Yearly age-adjusted cardiovascular mortality trends in decedents with chronic kidney disease and atrial fibrillation from 1999 to 2020. (A) Cumulative population (B) Gender subpopulations.

**CONFLICT OF INTEREST STATEMENT**

Authors have no conflict of interest.

**DATA AVAILABILITY STATEMENT**

All data used in this study are publicly available and deidentified in the CDC WONDER database.

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**SUPPORTING INFORMATION**

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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