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# Investigating mortality trends and disparities in tricuspid valve disorder: a U.S. nationwide study from 1999 to 2023

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### **Abstract**

Tricuspid valve disorder (TVD), a critical aspect of valvular heart disease (VHD), significantly impacts cardiovascular health, yet its mortality trends are not well understood. This study aimed to investigate demographic and geographic disparities in TVD-related mortality across the United States from 1999 to 2023. Using data from the CDC WONDER database, death certificates were analyzed to identify TVD-related fatalities, and age-adjusted mortality rates (AAMRs) were calculated per 1,000,000 individuals. Joinpoint regression analysis was conducted to assess annual percent changes (APCs) in mortality rates. A total of 72,805 deaths were attributed to TVD. An initial steep increase in mortality rate from 1999 to 2003 (APC: 7.9%; 95% CI: 3.9 to 14.1) followed by a stable period from 2003 to 2014 (APC: 0.1%; 95% CI: -2.7 to 1.0) and a sharp increase in AAMR from 2014 to 2023 (APC: 6.5%; 95% CI: 5.2 to 8.4). Females consistently had higher mortality rates than males, with a sharper increase after 2012. Racial and ethnic disparities were evident, with American Indian and white populations experiencing higher mortality rates than black populations. Geographic disparities were also noted, with states like Oregon, Minnesota, and Vermont, as well as the West census region, showing significantly higher mortality rates. Rural areas had higher mortality rates compared to urban areas. TVD-related mortality trends have followed a complex trajectory, with marked disparities across demographic and geographic factors. Further research is required to fully understand the factors driving these trends and their public health implications.

Keywords Tricuspid Valve Disorder, Tricuspid Valve Disease, Cardiovascular Health, CDC WONDER, Mortality

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### Introduction

Cardiovascular disease (CVD) remains the leading cause of disability and death in the United States, responsible for over 900,000 deaths in 2021 [1]. Valvular heart disease (VHD) plays a significant role in cardiovascular mortality, with approximately 2.5% of the U.S. population diagnosed with VHD and around 25,000 deaths annually from non-rheumatic VHD [2-4]. The tricuspid valve, located between the right atrium and right ventricle, facilitates blood flow for proper oxygenation [5]. Impairment of this function leads to a subset of VHD, namely Tricuspid valve disorders (TVDs) including tricuspid stenosis (TS) and tricuspid regurgitation (TR). TVD is a type of VHD that has historically remained significantly underexplored as compared to aortic valve diseases [6]. Aortic valve diseases have significantly declined over the past two decades with widespread adoption of Transcatheter Aortic Valve Replacement (TAVR) and surgical aortic valve replacement (SAVR). The age-standardized mortality rate (ASD) for nonrheumatic aortic stenosis is 1.5%, aortic insufficiency is 2.1%, and combined ASD of 2.3% [7]. In contrast, TVD have addressed a noticeable spike in mortality rate in the USA. Although existing literature lacks TVD related dermographic variations and potential risk factors contributing to upward trajectory of TVD related mortality trend in USA, creating a study gap. Our study aims to bridge this gap by providing a detailed analysis of the TVD-related mortality trend along with their contributing factors and variations among individuals, with advance analytical method.

TR, the most prevalent form, arises due to incomplete closure of the tricuspid valve, resulting in a backward flow of blood from the right ventricle. Primarily, TR is caused by intrinsic valve abnormalities like congenital malformations, endocarditis, etc. [5]. However, TR commonly occurs due to right ventricular or atrial dilation secondary to heart failure, pulmonary hypertension, or left-sided heart disease, affecting 0.9% of the U.S. population, with an estimated prevalence of up to 1.6 million individuals nationwide [8, 9]. On the other hand, a stiff and narrowed tricuspid valve leads to the prevention of blood flow in a forward direction from the right atrium to the right ventricle, causing Tricuspid Stenosis (TS) [5]. TS is rare, typically resulting from rheumatic heart disease or iatrogenic causes like permanent pacemaker implantation or TR-related valve repair, making up just 2.4% of all TVD cases [10]. Although only around 8,000 tricuspid valve surgeries are performed annually in the U.S., the emerging field of transcatheter tricuspid valve replacement is showing great promise and could potentially become the dominant treatment strategy [11, 12]. However, mortality trends associated with TVD remain underexplored.

As we move into an era where valve interventions are becoming more accessible, it is essential to examine trends to understand the mortality burden associated with tricuspid valve disease (TVD). Therefore, we aimed to analyze the demographic and geographic disparities in tricuspid valve-related mortality among individuals of all ages in the United States from 1999 to 2023. This analysis seeks to identify at-risk populations and enable timely interventions to improve outcomes.

### **Methods**

The Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database was accessed to obtain data on cardiovascular deaths related to Tricuspid Valve Disorder (TVD) in the United States [13]. To identify cases in which cardiovascular death was listed as the underlying cause of death and TVD was listed as a contributing cause of death, death certificates were used. This study specifically emphasizes the mortality trend of TVD without adjusting for comorbid conditions. A populationbased cohort study suggests that comorbidities like heart Failure, pulmonary diseases, and diabetes significantly increase the mortality risk in cardiac patients, similar mechanisms likely contribute to TVD-related mortality trends. This database has been used in previous studies to analyze cardiovascular mortality patterns related to heart failure or arrhythmias [14, 15]. To identify cardiovascular disease (CVD) patients, specific ICD-10-CM codes (I00-I99) were used. ICD-10-CM was officially introduced by the World Health Organization WHO) in 1994 and adopted by the United States on October 1, 2015. Prior to October 2015, ICD-9-CM codes were utilized by the U.S. healthcare system. As this study exclusively employs ICD-10-CM Codes for TVD-related mortality trends, deaths before ICD-10-CM code adoption are retrospectively classified using the ICD-10 code. Sensitivity analysis ensured no significant discrepancies or coding artifacts during a sudden shift in mortality trends around 2015, confirming data consistency. TVD patients were specifically identified using ICD-10-CM codes (Rheumatic tricuspid valve disease I07, Multiple valve diseases including TVD I08, Nonrheumatic tricuspid valve disorders I36, and Congenital malformations of the tricuspid valve Q22), focusing on patients aged between 1 year and 85+years. According to the U.S. Healthcare system, Echocardiography is recognized as a gold standard method of diagnosing tricuspid valve diseases (TVDs). The 2020 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines strongly recommend Transthoracic Echocardiography (TTE) as a first-line imaging modality and Transesophageal Echocardiography (TEE) as a detailed investigation of choice for valvular heart diseases [16]. To ensure accurate case identification in national health databases, TVD confirmed with echocardiography results are included in ICD-10-CM Codes. Institutional Review Board approval was exempt for this study, as it utilized anonymized publicly available data and adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Data from year (yr.) 1999 to 2023 were collected, including deaths caused by Tricuspid Valve Disorder, the location of the deaths (such as outpatient, emergency room, inpatient, death on arrival, or unknown status, as well as home, hospice, and nursing home/long-term care facility), demographic information (sex, race/ethnicity, and age), and regional information (urban-rural and state). Non-Hispanic individuals, who are those without ancestral ties to Spanish-speaking countries, particularly those in Latin America, were categorized into two groups: non-Hispanics and Latinos or Hispanics. The latter group includes persons of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish cultures or origins, regardless of race. The categories for race and ethnicity used in this context were White non-Hispanics, Black non-Hispanics or African American, Latino or Hispanics, American Indians non-Hispanics or Alaska Natives, and Asian non-Hispanics or Pacific Islander non-Hispanics, based on data reported on death certificates, which has been used in previous analyses of the WONDER database. The 2013 National Center for Health Statistics Urban-Rural Classification Scheme was used to categorize counties into metropolitan (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan) and non-metropolitan (micropolitan and non-core) regions [17]. The regions were classified into Northeast, Midwest, South, and West based on the Census Bureau definitions.

To investigate nationwide trends in mortality associated with tricuspid valve disorder (TVD), we calculated both the crude mortality (CMRS) and age-adjusted mortality rates (AAMRs) per 1,000,000 people from 1999 to 2023. These rates were further stratified by sex, race, ethnicity, state, and urban–rural status, along with 95% confidence intervals (CIs). We determined CMRs by dividing the number of TVD-related deaths by the corresponding U.S. population for each year. AAMRs were

calculated by standardizing TVD-related deaths to the 2000 U.S. standard population, as previously described [18]. To determine the annual trends in mortality, we used the Joinpoint Regression Program to determine the annual percentage change (APC) with a 95% CI in AAMRs from 1999 to 2023 [19]. We conducted a sensitivity analysis focusing on cardiovascular disease (CVD) deaths associated with tricuspid valve disorder, where TVD was recorded as the underlying cause of death and CVD (I00-I99) was noted as a contributing factor. Additionally, a subgroup analysis stratified by age category was conducted, dividing the age groups into four categories to observe APC and AAMRs/CMRs. These age groups included Infant to Adolescent (<1 yr to 19 yr), Younger Adults (20 yr to 39 yr), Middle-Aged Adults (40 yr to 64 yr), and Older Adults (65+yr). We used a 2-tailed t-testing to identify if the slope of annual percent change indicated that there was a significant difference in mortality from zero, with a P < 0.05 threshold for statistical significance.

### **Results**

TVD resulted in 72,805 fatalities among patients ranging from newborns to 85 + years of age between 1999 and 2023. This condition encompasses various health issues, with rheumatic cases affecting 23,995 individuals (32.3%) and having an average annual mortality rate (AAMR) of 2.71. Multiple valve diseases affected 41,770 people (58.0%) with an AAMR of 4.96, while nonrheumatic tricuspid disorders affected 3,579 individuals (4.90%) with an AAMR of 0.31. Additionally, congenital malformations affected 3,461 people (4.8%), with an AAMR of 0.51. Our analysis of the TVD mortality trend based on ICD-10-Code revealed that isolated TVDs (I07, I36, Q22) exhibited different mortality rates as compared to multiple valve diseases with TVD involvement (Q22). The TVD-related AAMRs/CMRs for the demographic characteristics of the United States for all age groups from 1999 to 2023 are depicted in Table 1.

### Overall

The overall AAMR for TVD-related deaths in patients rose from 5.7 in 1999 to 13.2 in 2023. Between 1999 and 2003, the AAMR increased with an APC of 7.9 and a 95% CI of 3.9 to 14.1. From 2003 to 2014, there was a slight increase in AAMR with an APC of 0.1 and a 95% CI of -2.7 to 1.0. Lastly, between 2014 and 2023, there was a steep incline in AAMR with an APC of 6.5, and a 95% CI of 5.2 to 8.4 These findings are illustrated in Fig. 1 and provided in Supplemental Tables 1 and 2. When focusing on CVD as the underlying cause of death in the sensitivity

 Table 1
 Demographic Characteristics of Deaths due to Tricuspid Valve Disorder Among All Ages in the USA from 1999 to 2023

Variable	Tricuspid Valve Disorder (TVD) Deaths (n)	AAMRs / CMRs (95% CI) per 1,000,000
Overall Population	72,805 (100%)	8.4 (8—8.7)
Tricuspid Valve Disorder <sup>a</sup>		
Rheumatic Tricuspid Valve Disorders	23,995 (32.3%)	2.71 (2.70—2.84)
Multiple Valve Diseases including TVD	41,770 (58.0)	4.96 (4.90—5.0)
Nonrheumatic Tricuspid Valve Disorders	3579 (4.90%)	0.31 (0.30—0.32)
Congenital Malformations of Tricuspid Valves	3461 (4.8%)	0.51 (0.50—0.52)
Sex <sup>a</sup>		
Male	27,741 (38.1%)	7.8 (7.3—8.2)
Female	45,064 (61.9%)	8.8 (8.4—9.2)
Census Region <sup>a</sup>		
Northeast	12,802 (17.8%)	7.5 (6.8—8.1)
Midwest	19,032 (26.1%)	9.8 (9.1—10.5)
South	21,356 (29.3%)	6.8 (6.4—7.3)
West	19,615 (26.8%)	10.4 (9.6—11.1)
Race / Ethnicity <sup>a</sup>		
NH American Indian or Alaska Native	327 (0.50%)	9.8 (5.6—14.7)
NH Asian or Pacific Islander	2,086 (2.87%)	5.8 (4.8—9.1)
NH Black or African American	6,066 (8.3%)	7.2 (6.2—8.1)
NH White	59,872 (82.52%)	8.8 (8.5—9.2)
Hispanic or Latino	4,227 (5.81%)	5.4 (4.5—6.3)
Age <sup>b</sup>		
<1 year	2,044 (2.81)	22.4 (20.4—24.4)
1–4 years	229 (0.32%)	0.7 (0.6—0.9)
5–14 years	198 (0.27)	0.2 (0.2—0.3)
15–24 years	447 (0.61%)	0.5 (0.5—0.6)
25–34 years	1,211 (1.66%)	1.7 (1.5—1.8)
35–44 years	1,680 (2.31%)	2.4 (2.2—2.5)
45–54 years	2,736 (3.76%)	3.3 (3—3.5)
55–64 years	5,428 (7.46%)	7.2 (6.9—7.5)
65–74 years	10,367 (14.20%)	18.7 (18.1—19.4)
75–84 years	19,936 (27.40%)	65.2 (63.6—66.9)
85 + years	28,528 (39.20%)	263 (257.6—268.4)
Age Categories <sup>b</sup>		
Infant to Adolescent	2,632 (3.47%)	1.3 (1.1—1.6)
Younger Adults	2,278 (3.1%)	1.1 (0.9—1.3)
Middle-Aged Adults	9,053 (12.43%)	3.6 (3.3- 4.0)
Older Adults	58,803 (81.0%)	52.0 (50.0—54.1)
Urbanization <sup>a</sup>		
Metropolitan	59,017 (81.1%)	8.5 (8.2—8.9)
Nonmetropolitan	13,788 (18.9%)	9.5 (8.7—10.2)
Place of Death <sup>c</sup>		
Medical Facility	39,385 (50,1%)	=
Decedent's Home	17,512 (24.1%)	=
Hospice Facility	3,416 (4.7%)	=
Nursing Home/Long-term Care Facility	9,697 (13.3%)	=
Others	2,664 (3.65%)	=

<sup>&</sup>lt;sup>a</sup> Age Adjusted Mortality Rates (AAMRs) is utilized

 $<sup>^{\</sup>rm b}$  Crude Mortality Rates (CMRs) is used for all age dependent analysis

<sup>&</sup>lt;sup>c</sup> Age Adjusted Mortality Rates (AAMRs) is not applicable for Place of Death

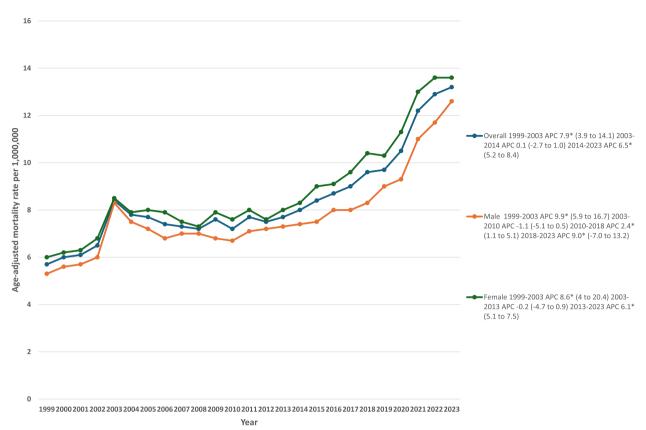


Fig. 1 Overall and Sex-Stratified TVD Related AAMRs per 1,000,000 in the US, 1999 to 2023

analysis, a unique trend emerged. There was an initial steep increase in deaths from 1999 to 2003 (APC: 13.9; 95% CI: 9.2–22.1), followed by a decrease between 2003 and 2014 (APC: –0.8; 95% CI: –5.3 to 0.7), and finally, an increase from 2014 to 2023 (APC: 3.2; 95% CI: 2.5–4.5) These findings are illustrated in Supplemental Fig. 1.

### Gender

Females consistently had more AAMRs than males during the analyzed years. The overall AAMR for females was 8.8, with a 95% confidence interval (CI) of 8.4–9.2, whereas the AAMR for males was 7.8, with a 95% CI of 7.3–8.2. Starting in 1999, the AAMR for females was 6, which increased to 13.6 in 2023. The annual percentage change (APC) showed a steep incline from 1999 to 2003 (APC: 8.6; 95% CI: 4 to 20.4), then slightly declined from 2003 to 2013 (APC: –0.2; 95% CI: –4.7 to 0.9), and then displayed a steep incline from 2013 to 2023 (APC: 6.1; 95% CI: 5.1 to 7.5). The AAMR for males related to total variable deaths (TVD) also increased from 5.3 in 1999 to 12.6 in 2023. The APC showed a steep incline from 1999 to 2003 (APC: 9.9; 95% CI: 5.9 to 16.7), then

slightly declined from 2003 to 2010 (APC: -1.1; 95% CI: -5.1 to 0.5), and then displayed an incline from 2010 to 2018 (APC: 2.4; 95% CI: 1.1 to 5.1), followed by a steep increase from 2018 to 2023 (APC: 9.0; 95% CI: -7.0 to 13.2). These findings are illustrated in Fig. 1 and in Supplemental Tables 1 and 2.

### Race/Ethnicity

The AAMR stratification by race/ethnicity revealed that American Indian or Alaska Native NH patients had the highest rates, followed by NH White, NH Black or African American, NH Asian or Pacific Islander, and Hispanic or Latino patients. The AAMR for NH American Indian or Alaska Native patients was 9.8, with a 95% CI of 5.6–14.7. The rate for NH White patients was 8.8, with a 95% CI of 8.5–9.2. For NH Black or African American patients, the rate was 7.2, with a 95% CI of 6.2–8.1. The rate for NH Asian or Pacific Islander patients was 5.8, with a 95% CI of 4.8–9.1. For Hispanic and Latino patients, the rate was 5.4, with a 95% CI of 4.5–6.3. Regarding the death rates for NH American Indian or Alaska Native patients, there was a drastic increase from

to 2008-2019 (APC: 1.6; 95% CI: -6.7 to 3.7), followed by a further deep increase from 2019 to 2023 (APC: 11.4; 95% CI: 4.4 to 25.3). The NH Black or African American community saw an increase in the trend from 1999-2003 (APC: 8.2; 95% CI: 1.7 to 24.0), followed by a gradual increase from 2003 to 2013 (APC: 1.6; 95% CI: -7.8 to -0.2), and then a steep incline from 2013 to 2023 (APC: 7.5; 95% CI: 5.8 to 10.0). A similar increase in AAMRs was observed in Hispanic or Latino patients from 1999 to 2018 (APC: 0.9; 95% CI: 0.1 to 1.6), followed by a sharp increase from 2018 to 2023 (APC: 9.3; 95% CI: 6.1 to 15.1). The trend for NH White patients showed an incline from 1999 to 2003 (APC: 10.2; 95% CI: 5.4 to 22.1), followed by a decline from 2003 to 2013 (APC: -0.3; 95% CI: -3.7 to 0.8), and lastly, an incline from 2013 to 2023 (APC: 6.4; 95% CI: 5.5 to 7.8). The trend for NH Asian or Pacific Islander patients showed a decline from 1999 to 2011 (APC: -1.5; 95% CI: -11.0 to 1.3), followed by a steep incline until 2023 (APC: 4.3; 95% CI: 1.4 to 12.5).

These findings are illustrated in Fig. 2 and provided in Supplemental Tables 1 and 3.

# Geographic region

### States

The states presented a wide array of AAMRs, with Georgia having the lowest value of 5.1 (95% CI: 4.5–5.7) and Oregon boasting the highest value of 25.4 (95% CI: 23.5–27.2). It is noteworthy that states with death rates in the top 90th percentile, namely Oregon, Minnesota, and Vermont, had AAMRs that were more than four-fold higher than those found in the states in the lower 10th percentile, namely Georgia, Alabama, and Louisiana as shown in Fig. 3 and provided in Supplemental Tables 4.

### Census region

We analyzed mortality rates across the different census regions in the United States, and the results showed

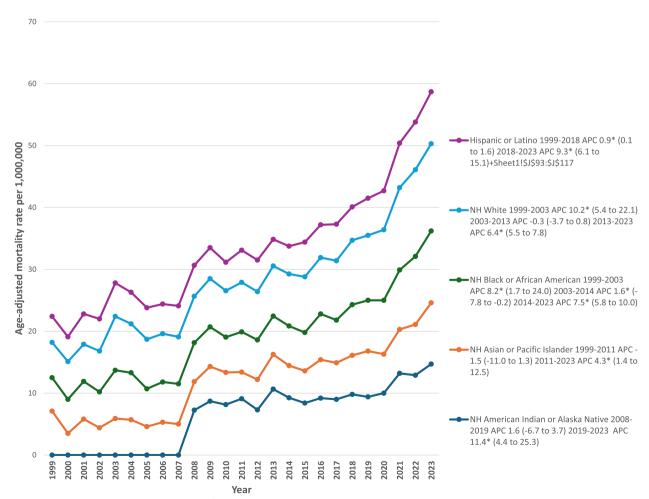


Fig. 2 TVD Related AAMRs per 1,000,000 Stratified by Race in the US, 1999 to 2023

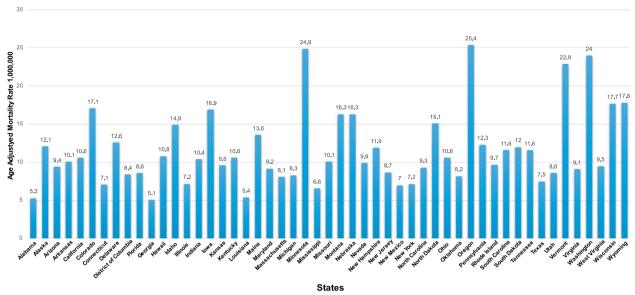


Fig. 3 TVD Related AAMRs per 1,000,000 Stratified by State in the US, 1999 to 2023

that the highest mortality rates were found in the West region (AAMR: 10.4; 95% CI: 9.6-11.1), followed by the Midwest region (AAMR: 9.8; 95% CI: 9.1-10.5), the Northeast region (AAMR: 7.5; 95% CI: 6.8-8.1), and the South region (AAMR: 6.8; 95% CI: 6.4-7.3). Our analysis also revealed that the death rates for the West region increased steadily from 1999 to 2015 (APC: 1.4; 95% CI: 0.2 to 2.4), and then experienced a steep incline from 2015 to 2023 (APC: 7.1; 95% CI: 5.5 to 10.0). The Midwest region also witnessed a steep incline in deaths from 1999 to 2003 (APC: 12.5; 95% CI: 7.0 to 22.9), followed by a slight decline from 2003 to 2013 (APC: -0.5; 95% CI: -3.7 to 0.7), and then a further increase from 2013 to 2023 (APC: 5.9; 95% CI: 4.7 to 7.7). In contrast, the Northeast region showed a continuous increase in death rates from 1999 to 2023, with a steady growth from 1999 to 2017 (APC: 1.6; 95% CI: 0.3 to 2.4), followed by a steeper increase from 2017 to 2023 (APC: 8.5; 95% CI: 5.4 to 19.0). The South region exhibited a unique trend, with a significant increase in death rates from 1999 to 2003 (APC: 8.4; 95% CI: 4.3 to 14.7), followed by a decline from 2003 to 2012 (APC: -0.7; 95% CI: -4.2 to 0.4), a slight increase from 2012 to 2019 (APC: 3.4; 95% CI: 1.3 to 5.4), and a significant increase from 2019 to 2023 (APC: 9.8; 95% CI: 7.1 to 15.7). These findings are illustrated in Fig. 4 and provided in Supplemental Tables 1 and 5.

# Urbanization

Between 1999 and 2023, the mortality rates increased in both metropolitan and non-metropolitan areas, with non-metropolitan areas ending the study period with the highest rates. Specifically, the Nonmetropolitan AAMR was 9.5 (95% CI: 8.7–10.2), while the Metropolitan AAMR was 8.5 (95% CI: 8.2–8.9). Non-metropolitan areas consistently showed an increase in AAMRs from 1999 to 2023, with APC of 12.3 (95% CI: 5.8 to 28.7) from 1999 to 2003, 0.1 (95% CI: -4.1 to 1.2) from 2003 to 2015, and 8.1 (95% CI: 6.8 to 10.6) from 2015 to 2023. In contrast, metropolitan areas showed a similar trend throughout the study period, with a slight incline from 1999 to 2018 (APC: 1.65; 95% CI: 0.8 to 2.5) followed by a steep increase from 2018 to 2023 (APC: 14.1; 95% CI: 10.8 to 19.5) These findings are illustrated in Fig. 5 and provided in Supplemental Tables 1 and 6.

### Subgroup analysis stratified by age categories

Our analysis of mortality rates by age categories revealed that the highest CMRs were found in older adults (CMR: 52.0; 95% CI: 50.0–54.1), followed by middle-aged adults (CMR: 3.6; 95% CI: 3.3–4.0), infants to adolescents (CMR: 1.3; 95% CI: 1.1–1.6), and younger adults (CMR: 1.1; 95% CI: 0.9–1.3). The death rates for older adults increased from 1999–2003 (APC: 13.0; 95% CI: 9.5 to 18.5), showed a slight decline from 2003 to 2010 (APC: –0.7; 95% CI: –4.1 to 0.5), a slight incline from 2010 to 2019 (APC: 2.1; 95% CI: 1.1 to 3.9), and a steeper curve from 2019 to 2023 (APC: 8.1; 95% CI: 6.1 to 12.6). The death rates for middle-aged adults increased in all stages from to 1999–2013 (APC: 0.4; 95% CI: –1.8 to 1.8), and then showed a steep incline from 2013 to 2023 (APC: 7.2; 95% CI: 5.7 to 10.0).

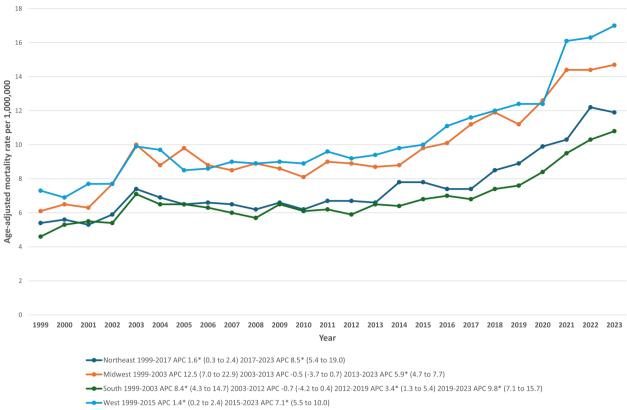


Fig. 4 TVD Related AAMRs per 1,000,000 Stratified by Census Region in the US, 1999 to 2023

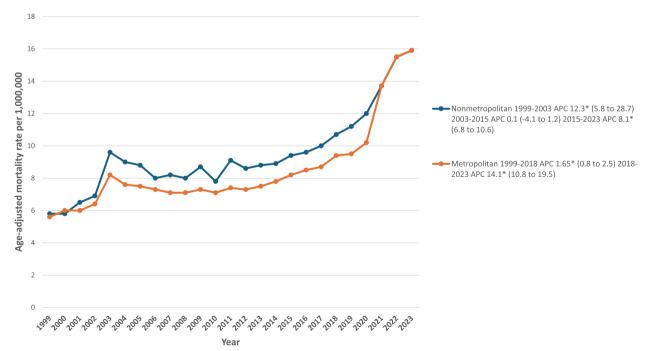


Fig. 5 TVD Related AAMRs per 1,000,000 Stratified by Urbanization in the US, 1999 to 2023

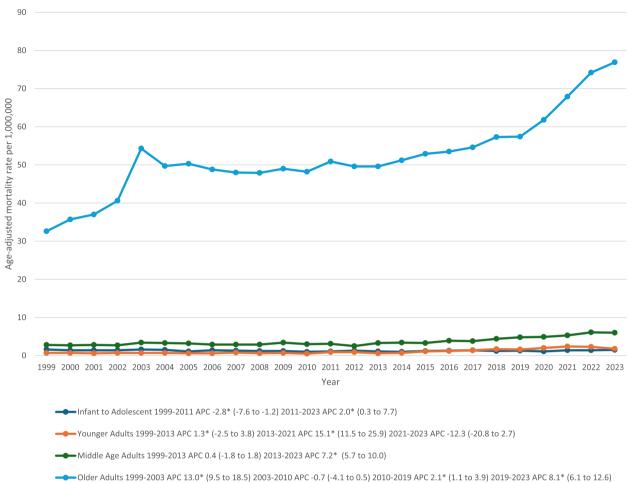


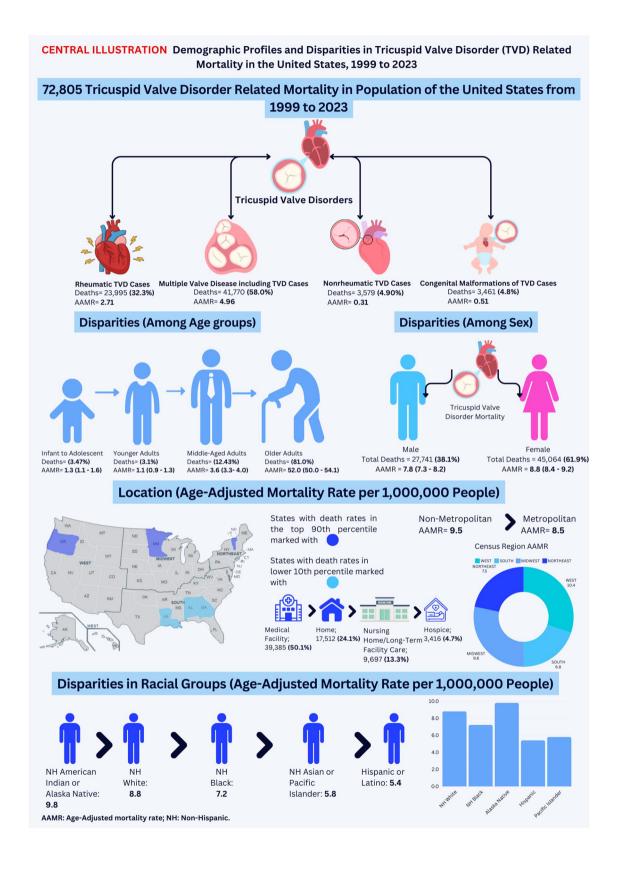
Fig. 6 Subgroup Analysis Stratified by Age Categories, TVD Related CMR per 1,000,000 in the US, 1999 to 2023

For infants to adolescents, a unique trend was observed from 1999–2011 (APC: -2.8; 95% CI: -7.6 to -1.2), followed by an incline from 2011 to 2023 (APC: 2; 95% CI: 0.3 to 7.7). The death rates for younger adults increased from to 1999–2013 (APC: 1.3; 95% CI: -2.5 to 3.8), and showed a steep incline from 2013 to 2021 (APC: 15.1; 95% CI: 11.5 to 25.9), and then decreased drastically from 2021 to 2023 (APC: -12.3; 95% CI: -20.8 to 2.7). These findings are illustrated in Fig. 6 and provided in Tables 1 and Supplementary Table 1.

# Discussion

Based on mortality data sourced from the Centers for Disease Control and Prevention (CDC) spanning 1999 to 2023, several noteworthy observations were made. Initially, there was a progressive increase observed in AAMRS from 1999 to 2002, followed by a notable spike

in mortality in 2003. Subsequently, a period of consistent decline ensued until 2012. However, from 2012 onwards, there was a discernible upward trajectory, particularly accentuated during the COVID era. This pattern remained consistent across various demographic subgroups. Notably, mortality rates were notably higher among females and older age cohorts. Additionally, there were disparities among racial groups, with American Indian and white populations experiencing higher mortality rates compared to black populations. Moreover, mortality rates tended to be elevated in Oregon, Minnesota and non-metropolitan areas. Rheumatic cases accounted for a significant proportion of TVD-related deaths, highlighting the persistent impact of this preventable disease in certain populations. The overall ageadjusted mortality rate for TVD showed a concerning upward trend over the study period, indicating a growing burden of the disease (CENTRAL ILLUSTRATION).



The increasing mortality rates associated with TVD may be attributed to a combination of factors, including demographic shifts, changes in disease prevalence and incidence, improvements in diagnostic sensitivity, and advancements in treatment modalities [20]. The aging population, coupled with the increasing prevalence of risk factors such as hypertension, obesity, and diabetes, may contribute to the rising burden of TVD-related mortality [21]. In our study, we initially observed a small increase in death rates up to 2012, which may be related to the increased use of cardiac artificial implants. However, starting in 2012, we noticed a significant shift in this trend, with a steeper rise in death rates observed thereafter. This change may be attributed to the aging population, which is more likely to have multiple comorbidities. Our analysis of age demographics supports this idea. The rising mortality rates due to non-rheumatic tricuspid regurgitation (TR) may be caused by several factors. Firstly, there is a possible link between the increase in TR cases and the surge in heart failure incidence [22, 23]. Additionally, the increase in pacemaker implantations and the rise in cor pulmonale cases may contribute to this phenomenon [24]. Furthermore, the use of left ventricular assist devices over the past decade may worsen mild TR by inducing interventricular septal shift, further exacerbating mortality rates associated with this condition [25]. Moreover, during the COVID era, we observed a significant spike in mortality rates, which may be influenced by the implementation of lockdown measures and the suspected interaction of COVID-19 among patients. Several studies have emphasized the impact of COVID-19 on individuals with various heart conditions, particularly TVD [26-28].

The mortality rates were higher among females during the period, which can be attributed to several factors. One reason is that there are differences in the presentation and characteristics of TVD between genders [29, 30]. Men usually present with more calcified valve lesions, leading to distinct pathophysiological processes [31, 32]. Women often develop more fibrosed aortic valve lesions, leading to distinct clinical manifestations and outcomes. Similar mechanisms may play a role in TVD, but direct evidence remains limited, highlighting the need for further research [31]. Additionally, the type and severity of regurgitation associated with TVD differ between males and females. Women are more likely to experience significant regurgitation, particularly in cases with rheumatic and Barlow etiologies [33]. In contrast, men are more prone to fibroelastic deficiency and posterior leaflet prolapse or flail, which may have varying implications for disease progression and mortality.

Disparities in TVD were also observed among different racial groups, with whites and American Indians being the most affected. Factors contributing to the prevalence of TVD among white individuals in the United States may include demographic distribution, genetic predispositions, access to healthcare, lifestyle and environmental factors, comorbidities, and healthcare utilization patterns [34]. Whites constitute a significant portion of the population, have greater access to healthcare resources, and may exhibit distinct genetic susceptibilities and lifestyle behaviors compared to other racial groups, leading to disparities in TVD prevalence [35, 36]. Additionally, variations in the prevalence of comorbid conditions and healthcare-seeking behaviors may also play a role in these differences [37]. Our investigation revealed a higher overall mortality rate among rural inhabitants with TVD when compared to their urban counterparts. This disparity might be connected to persistent obstacles to efficient healthcare in rural regions of the US. Despite attempts to address these disparities via public health policy modifications, rural-urban inequities continue to persist [38, 39]. The shutdown of nearly 130 hospitals since 2010 has further intensified these challenges, resulting in restricted access to primary and cardiology care, longer travel times for healthcare access, and reduced follow-up prospects [40]. Hence, rural residents with TVD experience worse outcomes due to disparities like limited healthcare access, older population, reduced healthcare awareness, variability in diagnostic protocols, and socioeconomic issues [41]. Additionally, rural population are known contributors of cardiovascular mortality due to high burden of hypertension, diabetes and obesity [41]. Mortality trends for TVD among the urban population exhibited a gradual increase from 1999 to 2019 contributed by well awareness and improved diagnosis with increase availability of advanced diagnostic protocols resulting in higher detection rate of Valvular heart diseases including TVD. Rising cardiovascular risk factors like obesity, diabetes and hypertension among urban population have contributed in upward trajectory of TVD mortality trend. Healthcare access disparities among economically different populations results in limited access to early cardiovascular care and progressing to worse outcomes like TVD related mortality. However, a remarkable increase was observed in mortality rates within urban metropolitan areas from 2019 to 2023, potentially attributable to the influence of COVID-19. This surge led to mortality rates comparable to those seen in rural populations [42]. Recent treatment advances like tricuspid transcatheter edge-to-edge repair (TEER) and transcatheter valve replacement have shown promising results as minimally invasive alternatives for high-risk surgical patients. The TRILUMINATE (Trial to Evaluate Treatment With Abbott Transcatheter Clip Repair System in Patients With Moderate or Greater Tricuspid Regurgitation) pivotal trial, conducted across

leading centers in the U.S. and Europe, has demonstrated long-term benefits of transcatheter tricuspid valve repair (TTVR) in high surgical risk patients with symptomatic tricuspid regurgitation (TR). At three-year follow-up, 79% of patients exhibited a reduction in TR severity to moderate or less, with 92% showing at least a one-grade improvement. The trial also highlighted significant improvements in quality of life and reduced hospitalizations, though long-term mortality benefits remain under investigation [43].

Meanwhile, the TRISCEND II pivotal trial has shown that transcatheter tricuspid valve replacement (TTVR) with the EVOQUE valve significantly improves quality of life, symptoms, and functional capacity compared to optimal medical therapy (OMT) alone. At one-year follow-up, 64.6% of TTVR patients were "alive and well," with Kansas City Cardiomyopathy Questionnaire (KCCQ) scores improving by 17.8 points [44]. These findings underscore the need for innovative, patient-specific treatment strategies and emphasize the importance of future studies to refine tailored therapeutic approaches and conduct comparative analyses.

### Limitations

This analysis has several limitations that need to be acknowledged. First, using mortality data from death certificates may result in biases due to misclassification or underreporting of deaths related to TVD. Second, the study focuses only on mortality outcomes, ignoring nonfatal TVD cases and trends in disease incidence, which limits the scope of the findings. Additionally, the retrospective design prevents causal conclusions and may miss temporal relationships between exposures and outcomes. Furthermore, relying on CDC data may involve limitations inherent to surveillance and reporting systems, affecting the accuracy and reliability of the results. Other issues include potential errors in ICD coding, the impact of unmeasured co-existing conditions such as other valvular diseases, and the lack of important investigational and diagnostic variables, all of which further limit the study. This study exclusively concentrates on tricuspid valve diseases neglecting comparative analysis with other valvular heart diseases. This standardized focus may limit the generalizability of our findings across all valvular diseases. Future studies should aim to include comparative studies among various valvular heart diseases to provide a broad spectrum of results. This study solely focuses on TVDrelated mortality trend and lacks individual level data on comorbid conditions, limiting our study to assess their impact on outcomes.

### **Conclusion**

In summary, the analysis of mortality data from 1999 to 2023 reveals a complex pattern in deaths related to tricuspid valve disorder (TVD). The data show an initial increase in mortality rates followed by a decline, but a significant rise in mortality was observed starting in 2012, which worsened during the COVID-19 pandemic. Several factors contribute to these trends, including demographic changes, variations in disease prevalence, advancements in medical technology, and the effects of COVID-19. Disparities are evident, with higher age-adjusted mortality rates among females, older adults, Native American populations, and residents of states like Oregon, Minnesota, and Vermont, particularly in the Western region and rural areas. This underscores the complex impact of TVD. Nevertheless, the study's limitations and its retrospective nature indicate the need for further research to fully understand the dynamics of TVD and its public health implications.

### **Abbreviations**

TVD Tricuspid Valve Disease
VHD Vascular Heart Disease
AAMRs Age-Adjusted Mortality Rate
APCs Annual Percent Changes

CDC WONDER Centers for Disease Control and Prevention's Wide-Ranging

Online Data for Epidemiologic Research

### Supplementary Information

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Supplementary Material 1.

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# Authors' contributions

Y.A.: Project development, Data Collection, Manuscript writing A.R.: Project development, Data Collection, Manuscript writing S.R.: Project development, Data Collection, Manuscript writing S.M.E.A.: Data analysis, Manuscript writing F.A.: Data analysis, Manuscript writing I.N.: Data analysis, Manuscript writing A.S.: Data analysis, Manuscript writing S.S.: Figures, Manuscript writing A.: Data analysis, Manuscript Writing and Revision M.A.K.: Figures, Manuscript writing B.Z.: Figures, Manuscript writing M.F.: Tables, Manuscript writing N.E.: Tables, Manuscript writing M.S.K.: Tables, Manuscript writing M.H.S.: Manuscript Revision and Writing B.D.A.: Manuscript Revision and Writing All Authors reviewed the manuscript.

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# Data availability

The dataset supporting the conclusions of this article is included in this article. Datasets are publicly available for this study and can be accessed on the CDC WONDER website: https://wonder.cdc.gov/

### **Declarations**

### Ethics approval and consent to participate

This study was exempted from the institutional review board's approval because it uses publicly available data that is de-identified.

### Consent for publication

Not Applicable.

### **Competing interests**

The authors declare no competing interests.

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