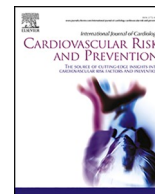




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Demographic trends and disparities in mortality related to coexisting heart failure and diabetes mellitus among older adults in the United States between 1999 and 2020: A retrospective population-based cohort study from the CDC WONDER database

Humza Saeed^a, M.B.B.S. Abdullah^a, Irum Naeem^b, Anna Zafar^b, Bilal Ahmad^c, Taimur ul Islam^d, Syed Saaid Rizvi^e, Nikita Kumari^e, Syed Ghazi Ali Kirmani^f, Fatima Mansoor^g, Amir Hassan^h, Adarsh Rajaⁱ, Mohamed Daoud^{j,1,*}, Aman Goyal^{k,1}

^a Rawalpindi Medical University, Rawalpindi, Punjab, Pakistan

^b King Edward Medical University, Lahore, Punjab, Pakistan

^c DG Khan Medical College, Dera Ghazi Khan, Punjab, Pakistan

^d Shifa college of medicine, Shifa Tameer e Millat University, Islamabad, Pakistan

^e Sindh Medical College, Jinnah Sindh Medical University, Karachi, Pakistan

^f Allama Iqbal Medical College, Lahore, Punjab, Pakistan

^g Karachi Medical and Dental College, Karachi, Pakistan

^h Bronglais General Hospital, Aberystwyth, UK

ⁱ Department of Internal Medicine, Shaheed Mohtarma Benazir Bhutto Medical College Lyari, Karachi, Pakistan

^j Bogomolets Medical University, Kyiv, Ukraine

^k Department of Internal Medicine, Seth GS Medical College and KEM Hospital, Mumbai, India

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ABSTRACT

Background: Heart Failure (HF) and Diabetes Mellitus (DM) often coexist, and each condition independently increases the likelihood of developing the other. While there has been concern regarding the increasing burden of disease for both conditions individually over the last decade, a comprehensive examination of mortality trends and demographic and regional disparities needs to be thoroughly explored in the United States (US).

Methods: This study analyzed death certificates from the CDC WONDER database, focusing on mortality caused by the co-occurrence of HF and DM in adults aged 75 and older from 1999 to 2020. Age-adjusted mortality rates (AAMRs) and annual percent changes (APCs) were computed and categorized by year, gender, race, census region, state, and metropolitan status.

Results: A total of 663,016 deaths were reported in patients with coexisting HF and DM. Overall, AAMR increased from 154.1 to 186.1 per 100,000 population between 1999 and 2020, with a notable significant increase from 2018 to 2020 (APC: 11.30). Older men had consistently higher AAMRs than older women (185 vs. 135.4). Furthermore, we found that AAMRs were highest among non-Hispanic (NH) American Indian or Alaskan natives and lowest in NH Asian or Pacific Islanders (214.4 vs. 104.1). Similarly, AAMRs were highest in the Midwestern region and among those dwelling in non-metropolitan areas.

Conclusions: Mortality from HF and DM has risen significantly in recent years, especially among older men, NH American Indian or Alaska Natives, and those in non-metropolitan areas. Urgent policies need to be developed to address these disparities and promote equitable healthcare access.

* Corresponding author. Bogomolets Medical University, Kyiv, UK.

E-mail addresses: hamzasaeed309@gmail.com (H. Saeed), Abdulahid6@gmail.com (M.B.B.S. Abdullah), irumnaeem7979@gmail.com (I. Naeem), amnazafar258@gmail.com (A. Zafar), ba03733@gmail.com (B. Ahmad), khantaimur179@gmail.com (T. Islam), rizvi.saaid@gmail.com (S.S. Rizvi), nikitakumari0282@gmail.com (N. Kumari), Ghazikirmani993@gmail.com (S.G.A. Kirmani), doctor.fatima.mansoor@gmail.com (F. Mansoor), amirhassanmahmood@gmail.com (A. Hassan), Adarshbudhwani01@gmail.com (A. Raja), drmohameddaoudmd@gmail.com (M. Daoud), amanmgv@gmail.com (A. Goyal).

¹ Last 2 are senior authors and contributed equally.

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Abbreviations:

Heart Failure (HF)
 Diabetes Mellitus (DM)
 Non-Hispanic (NH)
 Age-adjusted mortality rate (AAMR)
 Annual percent change (APC)
 United States (US)
 Heart failure with preserved ejection fraction (HFpEF)
 Heart failure with reduced ejection fraction (HFrEF)

1. Introduction

Heart diseases, including HF, remain the leading cause of death in the United States [1]. Heart failure (HF) affects approximately 6.7 million people in the United States (US), with a prevalence rate ranging from 1.9 % to 2.6 % in the general population and up to 8.5 % in older adults [2]. Similarly, more than 38 million people have diabetes mellitus (DM) in the US, although a considerable amount remains undiagnosed [3]. Among patients with HF, the prevalence of DM varies from 10 % to 47 %, including those with heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). Notably, the prevalence of DM is higher among hospitalized and older HF patients, exceeding 40 % [4]. Similarly, HF is four times more common among people with DM than in the general population, with prevalence rates ranging from 9 % to 22 %, and even higher percentages in older patients [5–7].

Previous studies have shown a significant increase in HF-related mortality among both young and older adults in the US between 2012 and 2019, likely due to the rising prevalence of cardiometabolic risk factors, such as DM [8,9]. Another major contributing factor is the rapid growth of the elderly population, particularly those aged 65 years or older, who contribute significantly to these fatalities [10]. Like HF, studies have also revealed an increasing trend in DM-related mortality. Specifically, mortality rates due to DM among patients aged 75 years and older are increasing, particularly in rural counties of the US, with a higher prevalence of deaths occurring at home and in hospice care [11, 12].

Despite the high prevalence of coexisting HF and DM, no prior study has specifically examined the mortality rates of individuals with both conditions. Understanding the impact of coexisting HF and DM on mortality is essential for enhancing patient care and treatment strategies. Identifying demographic, racial, gender, and regional mortality trends can also aid targeted interventions for high-risk populations. Therefore, we aimed to assess the mortality trends due to coexisting HF and DM among elderly patients in the United States between 1999 and 2020.

2. Materials and methodology**2.1. Patient eligibility and screening**

Deaths occurring in the US related to both HF and DM were sourced from the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) database. The Multiple Cause-of-Death Public Use record death certificates were studied to identify records in which both DM and HF were mentioned as either contributing or underlying cause of death on nationwide death certificates [13]. DM patients were identified with International Classification of Diseases 10th Revision Clinical Modification (ICD-10-CM) codes E10-E14, and HF patients were identified with ICD-10-CM code I50. Previously published studies have used the same ICD-10 codes [12, 14,15]. Those aged 75 years or older at the time of death were

considered as older adults. Previous studies have used a similar age cutoff to define older adults [9,16,17]. This study did not require approval from the Institutional Review Board because it was based on data from a de-identified database provided by the government for public use. The STROBE guidelines were followed in this observational study.

2.2. Data Abstraction

Data on deaths due to coexisting HF and DM, including population size and location, were gathered between January 1999 and December 2020. Demographic information, including sex and race/ethnicity, as well as regional data, encompassing urban-rural classification and state, were collected from 1999 to 2020. Race/ethnicity categories included non-Hispanic (NH) White, NH Black or African American, Hispanic or Latino, NH American Indian or Alaskan Native, and NH Asian or Pacific Islander. These classifications align with those previously used in analyses from the CDC WONDER database and are based on data reported on death certificates in compliance with the US Office of Budget and Management Guidelines [13]. The National Center for Health Statistics Urban-Rural Classification Scheme was used to classify the population into two categories based on the 2013 US census: Metropolitan (large metropolitan area [population, ≥ 1 million], medium/small metropolitan area [population, 50,000–999,999]), and non-metropolitan (population, $< 50,000$). U.S. Census Bureau definitions divided the regions into Northeast, Midwest, South, and West categories.

2.3. Data synthesis

The age-adjusted mortality rates (AAMR) per 100,000 people for HF and DM were calculated by normalizing the HF and DM-related deaths to the US population in 2000 [18]. The AAMRs were calculated by considering factors such as year, sex, race/ethnicity, state, census region, and metropolitan status. This is because the CDC WONDER has population sizes for every demographic, regional factors and age group for a specific year [13]. The 95 % confidence interval for AAMRs was also derived from the database. The annual percent change (APC) of the Joint Point Regression Program (version 5.0; National Cancer Institute) was utilized to determine trends in AAMR [19]. This method corresponds to log-linear regression models in which temporal variation occurs and can be used to find significant changes in AAMR over time. Using the Monte Carlo permutation test, APCs with 95 % CIs for AAMR were found at the identified line segments connecting the join points. Considering the 2-tailed *t*-test results, APCs were either increasing or decreasing if the slope representing the change in mortality deviated significantly from 0. The significance level was set at $p < 0.05$.

3. Results

Between 1999 and 2020, 663,016 deaths among the older population, where both HF and DM were either underlying or contributing causes, were recorded (Supplemental Table 1). Data on the place of death was found for 637,252 cases, with the highest in Medical Facilities (35 %), followed by nursing home/long-term care (31.9 %), decedents' homes (25.8 %), and hospices (3.4 %) (Supplemental Table 2).

3.1. Demographic trends in mortality

Older adults with both HF and DM had an overall AAMR of 154.1 (95 % CI: 152.1 to 156) in 1999, which increased to 186.1 (95 % CI: 184.3 to 187.8) in 2020. The overall AAMR increased from 1999 to 2005 (APC: 0.80; 95 % CI: 0.17 to 2.94), followed by a significant decrease from 2005 to 2011 (APC: 2.82; 95 % CI: 5.48 to -1.72). It increased from 2011 to 2018 (APC: 0.61; 95 % CI: 0.59 to 2.18) and then steeply increased from 2018 to 2020 (APC: 11.30; 95 % CI: 6.98 to 14.11) (Fig. 1, Supplemental Tables 4 and 5). In contrast to the older adults, the

AAMR in young and middle-aged adults changed from 8.4 (95 % CI: 8.3 to 8.6) in 1999 to 11 (95 % CI: 10.8 to 11.1) in 2020 (Supplemental Table 3).

3.2. Gender stratification

Over the course of the study period, older men’s AAMRs were consistently higher than those of older women (Men: 185; 95 % CI: 184.3 to 185.6 vs. Women: 135.4; 95 % CI: 135 to 135.8). In 1999, the AAMR for older men was 173.8 (95 % CI: 170.3 to 177.2). It grew dramatically to 191 (95 % CI: 187.6 to 194.4) in 2004 (APC: 1.83; 95 % CI: 0.37 to 5.66) and then decreased significantly to 170.6 (95 % CI: 167.7 to 173.6) in 2012 (APC: 1.74; 95 % CI: 4.70 to -0.98). The AAMR increased slightly to 189.1 (95 % CI: 186.3 to 191.9) in 2018 (APC: 1.58; 95 % CI: 0.34 to 3.71), followed by a sharp increase to 235.5 (95 % CI: 232.5 to 238.6) in 2020 (APC: 11.30; 95 % CI: 6.65 to 14.32). Similarly, the AAMR for older women was 142.9 (95 % CI: 140.7 to 145.2) in 1999. It remained stable until 2005 (APC: 0.44; 95 % CI: 0.52 to 2.29), then decreased significantly to 127.7 (95 % CI: 125.6 to 129.7) in 2010 (APC: 3.73; 95 % CI: 6.06 to -2.38). There was a period of stability until 2018 (APC: 0.53; 95 % CI: 1.43 to 0.90), followed by a large increase from 2018 to 2020 (APC: 11.34; 95 % CI: 6.98 to 14.12) (Fig. 1, Supplemental Tables 4 and 5).

3.3. Racial stratification

When stratified by race or ethnicity, AAMRs were highest among NH American Indian or Alaska Native patients (214.4; 95 % CI: 207.5 to 221.4), followed by NH African American (179.9; 95 % CI: 178.5 to 181.4), Hispanic (159.5; 95 % CI: 158 to 161.1), NH White (152.9; 95 % CI: 152.5 to 153.3), and NH Asian or Pacific Islander populations (104.1; 95 % CI: 102.4 to 105.8). The AAMR values of NH American or Alaska Natives remained stable throughout the study period (APC: 0.15; 95 % CI: 0.79 to 0.63). From 1999 to 2018, there was a significant decrease in AAMRs for NH African Americans (APC: 0.74; 95 % CI: 1.40 to -0.24) and Hispanics (APC: 1.56; 95 % CI: 2.08 to -1.08). However, from 2018 to 2020, there was a very steep increase in AAMRs for both NH African Americans (APC: 16.13; 95 % CI: 5.57 to 21.44) and Hispanics (APC: 15.95; 95 % CI: 7.26 to 20.82). From 1999 to 2005, the AAMR values of NH Whites were quite stable, followed by a significant decrease from 2005 to 2012 (APC: 2.45; 95 % CI: 5.08 to -1.64). From 2012 to 2018,

the AAMR values in NH Whites were increasing (APC: 1.14; 95 % CI: 0.57 to 2.92), followed by a steep increase from 2018 to 2020 (APC: 10.53; 95 % CI: 6.14 to 13.36). From 1999 to 2016, there was a significant decrease in AAMR values in NH Asian/Pacific Islanders (APC: 1.35; 95 % CI: 2.76 to -0.63), followed by a significant increase in AAMRs from 2016 to 2020 (APC: 4.63; 95 % CI: 0.77 to 12.54). (Fig. 2, Supplemental Tables 4 and 6).

3.4. State-wise distribution

AAMR values ranged from 76.2 (95 % CI: 73 to 79.4) in Nevada to 255.5 (95 % CI: 250.4 to 260.6) in Mississippi, with noticeable differences across states. States in the top 90th percentile, including North Dakota, Vermont, West Virginia, Oklahoma, Oregon, and Mississippi, had AAMRs approximately two to three times higher than those in the bottom 10th percentile, which included Massachusetts, Hawaii, District of Columbia, Arizona, Florida, and Nevada (Fig. 3, Supplemental Table 7).

3.5. Census region

Over the study period, the highest AAMR was observed in the Mid-western region at 177.4 (95 % CI: 176.6 to 178.3), followed by the Western region at 163.8 (95 % CI: 163 to 164.7), the Southern region at 147.3 (95 % CI: 146.7 to 147.9), and the Northeastern region at 130.2 (95 % CI: 129.4 to 130.9). In the Northeastern region, AAMRs remained stable from 1999 to 2005, followed by a significant decline from 2005 to 2008 (APC: 5.04; 95 % CI: 6.40 to -2.23). Stability continued from 2008 to 2018, then a steep upward trend was observed from 2018 to 2020 (APC: 13.42; 95 % CI: 8.37 to 16.46). In the Midwestern region, AAMRs were stable until 2005, followed by a significant decline until 2013 (APC: 2.56; 95 % CI: 5.54 to -1.44). Stability was observed until 2018, followed by a steep increase from 2018 to 2020 (APC: 12.25; 95 % CI: 6.44 to 16.11). In the Southern region, AAMRs significantly increased from 1999 to 2001 (APC: 7.13; 95 % CI: 0.89 to 13.33), followed by a significant decline until 2014 (APC: 1.67; 95 % CI: 4.25 to -1.23). Slight increases were observed from 2014 to 2018 (APC: 1.99; 95 % CI: 2.33 to 4.12), followed by a steep increase from 2018 to 2020 (APC: 11.04; 95 % CI: 5.46 to 15.11). In the Western region, AAMRs significantly increased from 1999 to 2005 (APC: 1.81; 95 % CI: 0.50 to 4.88), followed by a significant decline until 2014 (APC: 1.62; 95 % CI: 3.99 to -0.87), and

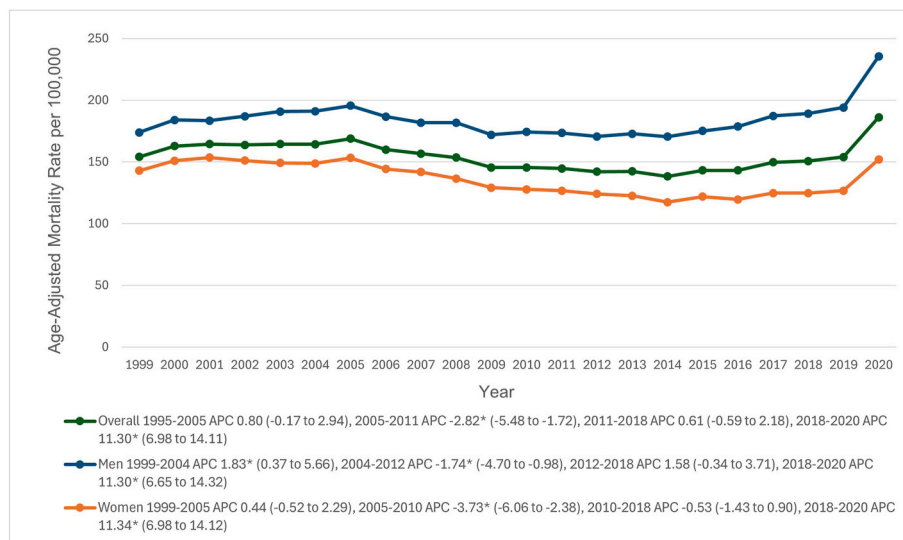


Fig. 1. Overall and Sex-Stratified Heart Failure and Diabetes Mellitus-related Age-Adjusted Mortality Rates per 100,000 in Older Adults in the United States, 1999 to 2020. * Indicates that the annual percentage change (APC) is significantly different from zero at $\alpha = 0.05$. AAMR = age-adjusted mortality rate; APC = annual percent change; CI = confidence interval.

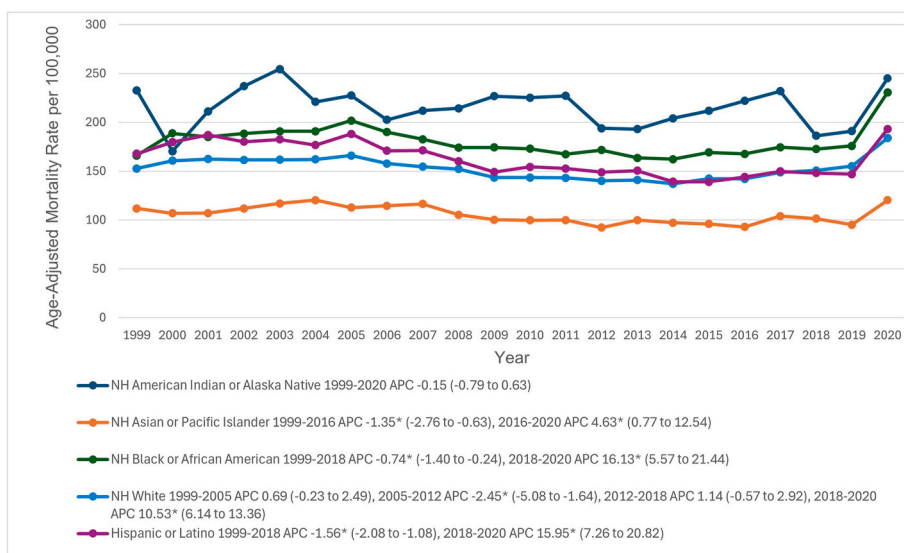


Fig. 2. Heart Failure and Diabetes Mellitus-related Age-Adjusted Mortality Rates per 100,000, Stratified by Race in Older Adults in the United States, 1999 to 2020 * Indicates that the APC is significantly different from zero at $\alpha = 0.05$. Abbreviations as in Fig. 1.

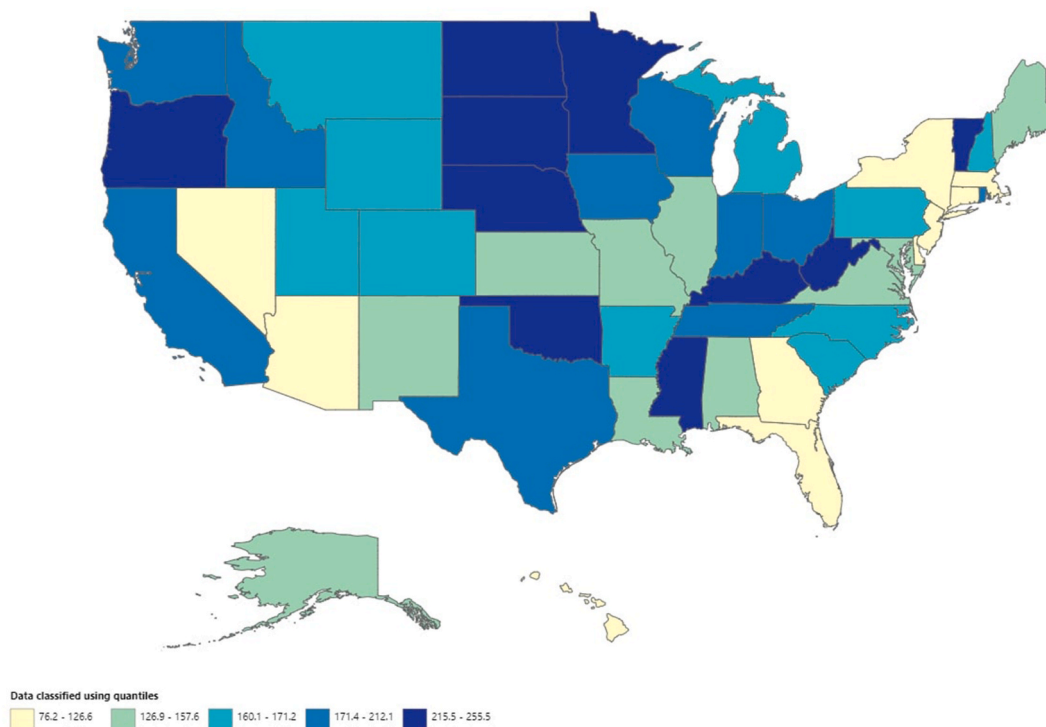


Fig. 3. Heart failure and diabetes mellitus-related age-adjusted mortality rates per 100,000, stratified by State in older adults in the United States, 1999 to 2020.

then an upward trend from 2014 to 2020 (APC: 3.50; 95 % CI: 2.29 to 5.47) (Fig. 4, Supplemental Tables 4 and 8).

3.6. Urbanization

Throughout the study period, non-metropolitan areas exhibited AAMRs attributable to both HF and DM that were consistently higher than those of metropolitan areas; the overall AAMRs were 202.5 (95 % CI: 201.5 to 203.5) and 143.7 (95 % CI: 143.3 to 144.1), respectively. There was an increase in the AAMR values between 1999 and 2005 (non-metropolitan APC: 1.28; 95 % CI: 0.80 to 4.36; metropolitan APC: 0.83; 95 % CI: 0.09 to 3.08). From 2005 to 2010, there was a significant

decrease in metropolitan areas' AAMRs (APC: 3.11; 95 % CI: 5.66 to -1.70) while in non-metropolitan areas, the AAMR values decreased from 2005 to 2013 (APC: 2.42; 95 % CI: 6.13 to 2.61). Between 2010 and 2018, there was a slight increase in the AAMRs of metropolitan areas (APC: 0.26; 95 % CI: 0.72 to 1.89), and a similar trend was observed in non-metropolitan areas between 2013 and 2018 (APC: 2.11; 95 % CI: 2.44 to 4.60). Finally, a significant upward trend was observed in AAMR values between 2018 and 2020 (non-metropolitan APC: 11.29; 95 % CI: 5.03 to 15.24; metropolitan APC: 11.70; 95 % CI: 7.26 to 14.50) (Fig. 5, Supplemental Tables 4 and 9).

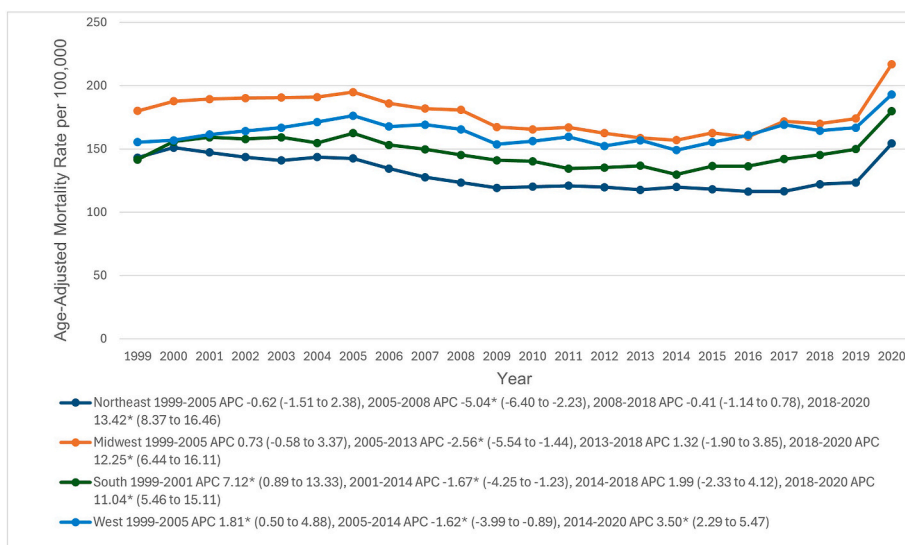


Fig. 4. Heart Failure and Diabetes Mellitus-related Age-Adjusted Mortality Rates per 100,000, Stratified by Census Regions in Older Adults in the United States, 1999 to 2020 * Indicates that the APC is significantly different from zero at $\alpha = 0.05$. Abbreviations as in Fig. 1.

3.7. Trends in mortality rates by individual disease type

3.7.1. Overall trends in heart failure alone

The AAMR for HF among older adults was 1367.2 in 1999, which decreased to 1233.2 in 2020. The AAMRs initially decreased significantly from 1999 to 2012 (APC: 2.10; 95 % CI: 2.36 to -1.86), followed by a significant increase till 2020 (APC: 1.58; 95 % CI: 1.12 to 2.16) (Fig. 6A, Supplemental Tables 4 and 10).

3.7.2. Overall trends in diabetes mellitus alone

The AAMR for DM among older adults was 693.1, which increased to 820 in 2020. The AAMRs initially decreased significantly from 1999 to 2018 (APC: 0.99; 95 % CI: 1.41 to -0.64), followed by a steep rise from 2018 to 2020 (APC: 13.88; 95 % CI: 5.93 to 17.46) (Fig. 6B–Supplemental Tables 4 and 10).

3.8. Gender trends in heart failure alone

The AAMR for HF was higher in older men compared to older women (1360.7 vs. 1080.4). Between 1999 and 2012, AAMR values decreased

for both genders. From 2012 to 2020, there was a significant increase in AAMR among older men (APC: 1.79; 95 % CI: 1.34 to 2.35), while older women experienced a non-significant rise in AAMR during the same period (APC: 1.26; 95 % CI: 0.24 to 2.92) (Supplementary Fig. 1, Supplemental Tables 4 and 10).

3.9. Gender trends in diabetes mellitus alone

Like HF, the AAMR for DM was higher in older men compared to older women (812.1 vs. 584.8). After a decline from 1999 to 2018, the AAMR values increased sharply from 2018 to 2020 in both older men (APC: 14.75; 95 % CI: 7.34 to 18.34) and older women (APC: 14.23; 95 % CI: 6.13 to 19.52) (Supplementary Fig. 2, Supplemental Tables 4 and 10).

3.10. Racial trends in heart failure alone

Racial analysis of HF showed that NH whites had the highest AAMR at 1251.6, while NH Asian or Pacific Islanders had the lowest at 557.2. After a decline from 1999 to 2012, NH Whites experienced a significant

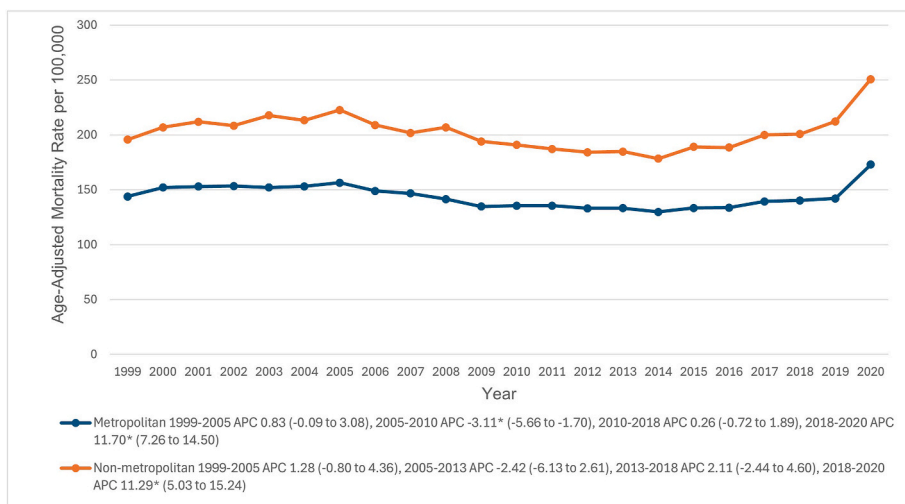


Fig. 5. Heart Failure and Diabetes Mellitus-related Age-Adjusted Mortality Rates per 100,000 in Older Adults in the Metropolitan and Non-metropolitan areas in the United States, 1999 to 2020 * Indicates that the APC is significantly different from zero at $\alpha = 0.05$. Abbreviations as in Fig. 1.

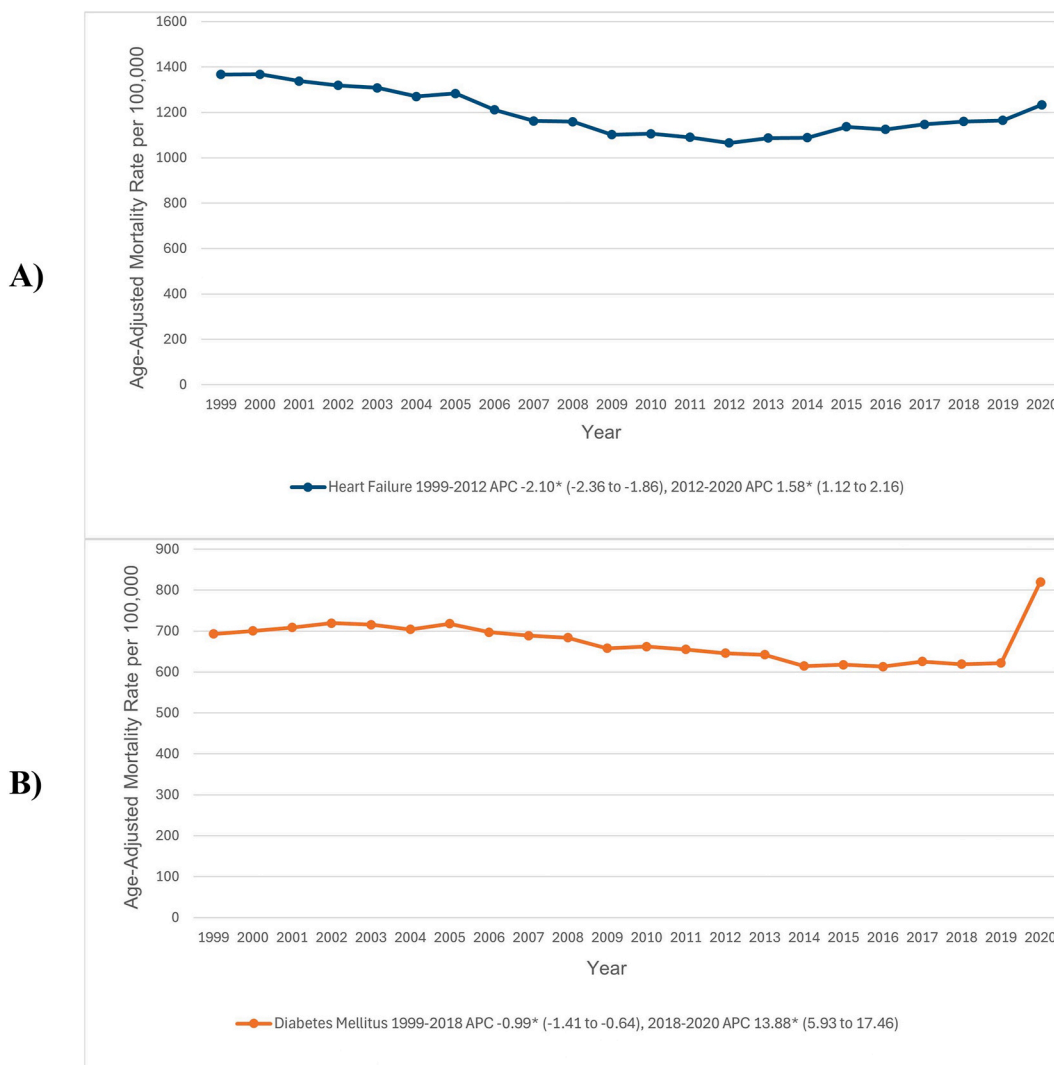


Fig. 6. (A) Heart Failure and (B) Diabetes Mellitus-related Age-Adjusted Mortality Rates per 100,000 in the United States among older adults, 1999–2020 * Indicates that the APC is significantly different from zero at $\alpha = 0.05$. Abbreviations as in Fig. 1.

increase in AAMR from 2012 to 2020 (APC: 1.89; 95 % CI: 1.44 to 2.42). Similarly, NH Asian or Pacific Islanders also saw a significant increase from 2014 to 2020 (APC: 1.99; 95 % CI: 1.05 to 3.35), following a decline from 1999 to 2014 (Supplementary Fig. 3, Supplementary Tables 4 and 11).

3.11. Racial trends in diabetes mellitus alone

Racial analysis of DM revealed that NH Black or African Americans recorded the highest AAMR at 999.7, while NH Asian or Pacific Islanders had the lowest at 598. Following a decrease from 1999 to 2018, there was a sharp increase in AAMR values for both NH Black or African Americans (APC: 20.47; 95 % CI: 9.34 to 27.30) and NH Asian or Pacific Islanders (APC: 15.62; 95 % CI: 5.98 to 20.13) (Supplementary Fig. 4, Supplementary Tables 4 and 12).

3.12. Trends in the heart failure and diabetes mellitus-related mortality rates in 2021 and 2022

Based on the mortality data of 2018–2022 in the CDC WONDER, the AAMR for HF-related deaths among older adults increased from 1233.2 in 2020 to 1312.4 in 2021, before decreasing to 1240.1 in 2022. Similarly, the AAMR for DM-related deaths rose from 820 in 2020 to 847.8 in 2021, then dropped to 778.3 in 2022. For combined HF and DM-related

deaths, the AAMR climbed from 186.1 in 2020 to 198.5 in 2021, and then fell back to 186.4 in 2022.

4. Discussion

The prevalence of HF and DM has increased over the past two decades. Our analysis of mortality rates among older adults (≥ 75 years) from 1999 to 2020 indicated a significant increase in mortality across various demographic groups, including sex, race/ethnicity, geographical region, and urbanization status. Older men had consistently higher AAMRs than older women, and NH American Indians and Alaskan Natives had the highest AAMRs among all races. Significant differences were also observed between metropolitan and non-metropolitan areas, with non-metropolitan areas having six-fold higher mortality rates than metropolitan areas.

The two important risk factors for the increment and progression of HF are advancing age and DM [20]. DM not only increases the risk of HF onset but also worsens outcomes for those already affected by the condition. The concurrent presence of these two ailments is on the rise, particularly among the elderly, with a decrease in the percentage of five-year survival [20,21]. The initial trends are consistent with those of previous studies, which show a decrease in HF mortality from 2000 onwards [22]. This decrease is attributed to the reduced overall mortality rates of cardiovascular diseases in the latter part of the 20th

century and early 2000s, driven by advancements in evidence-based medical and surgical treatments, as well as global prevention strategies for reducing cardiovascular risk factors [23].

However, the significant increase in trends from 2018 to 2020 is concerning, as indicated by our analysis. Our analysis also indicates that this increasing trend was more significantly influenced by DM as compared to HF. The reasons for this are multiple factors. First, with the ongoing expansion of the elderly population aged ≥ 75 years over time in economically advanced countries, there is a corresponding increase in the burden of chronic illnesses and morbidity (especially DM), higher rates of hospitalization, and documentation of deaths due to HF in this age group [24,25]. Second, our analysis shows that this sharp rise coincides with the COVID-19 era. During this pandemic, due to increased patient burden and limited emergency capacity, resources in the medical field were reallocated, and COVID-19 patients were prioritized, leading to a decrease in hospital admissions for cardiovascular conditions and access to acute cardiovascular care for patients around the globe [26]. Third, it has been reported that patients with comorbid diseases such as HF and DM can develop an acute form of COVID-19 and are at increased risk of developing complications requiring rigorous, intensive care, advanced hemodynamic monitoring, skilled nursing, and rehabilitation services; all of which were overwhelmed during this period, resulting in increased mortality, with approximately one in four individuals dying during hospitalization [27,28]. Fourth, HF patients, aware of their increased vulnerability, might have been reluctant to visit hospitals out of fear of contracting COVID-19 [29,30]. Lastly, patients with chronic conditions such as DM have encountered substantial obstacles during the pandemic. The burden on healthcare systems and scarcity of medical resources have led to suboptimal health service provision. This, coupled with potential difficulties in accessing essential medications and supplies such as anti-hyperglycemic drugs, insulin, and glucose strips, results in metabolic decompensation and inadequate control of comorbidities [27]. In addition, studies have shown that COVID-19 can also lead to HF and impact DM through several interconnected mechanisms. The virus causes direct myocardial injury, systemic inflammation, microvascular damage, and increased cardiac workload, which can exacerbate pre-existing HF or lead to its development [31]. Additionally, COVID-19 impairs pancreatic beta-cell function and exacerbates insulin resistance, worsening glycemic control, especially with glucocorticoid use [32]. This complex interplay necessitates comprehensive management strategies for both HF and DM in COVID-19 patients.

It is noteworthy that different COVID-19 variants had varying mortality rates, with the Delta variant being the most severe, leading to worse outcomes and higher mortality. However, as the Omicron BA.5 variant became dominant toward the end of the pandemic, disease-related outcomes significantly improved, and death rates became more comparable to those seen in severe flu cases [33,34]. This trend is particularly evident in the observed decrease in AAMR values for both HF and DM-related deaths following the peak of the pandemic.

As shown in Supplemental Table 4, there was a visible difference in AAMR between males and females. The general trends over the years were similar for both. Men suffer more from various risk factors for HF, as studies have shown that men have higher mortality for HF despite having lower hospitalization rates than females [35]. This could be hypothesized to be because men, in general, have shown a higher prevalence of various comorbidities, including hypertension, smoking, ventricular arrhythmias, atrial fibrillation, and chronic kidney disease, to name a few [35,36]. In general, women appear to have better survival rates, but the outcome is limited, as fewer women are included in trials conducted to study HF-related mortality trends. Our study also indicated a disparity in mortality rates among different races over the years, with American Indians having the highest AAMR followed by African Americans, while Asians have the lowest. Hispanics and whites had comparable mortality rates. This is consistent with other studies that reported HF mortality [9]. Social determinants of health, such as education, improved living standards, and access to standard healthcare

without prejudice, can improve these health disparities. Racial inequality is one of the major reasons for this difference, as several studies have reported that hospitals serving major African American and American Indian populations receive lower funding than other hospitals and offer poor health quality [37,38]. Disparity in health can be due to poverty, unemployment, and low ratios of Health Insurance among these populations [39,40]. Despite increasing mortality, a recent review of various clinical trials showed racial bias, with only 4.0 % of trial participants being African Americans, contributing to an incompetent reflection of the HF population [41]. Lewsey SC et al. reported racial disparity that existed in preference for advanced HF therapies and interventions as White populations were more likely to be older and had fewer procedure-related benefits. However, they were preferred for younger African American patients [41]. Recent studies on advanced HF management have shown a greater risk of cardiac transplant failure in the African American population by 1.4-fold over the White population [42]. African Americans have also been found to have multiple etiologies linked to HF, including hypertension, DM, and coronary artery disease [43]. These observations can justify the differences between AAMR trends in various races and the need for several steps to ensure equality in health standards.

Previous analyses also reported increased rates of HF mortality in non-metropolitan areas compared with metropolitan areas, which is in line with our findings [44]. This discrepancy is influenced by socio-economic factors and healthcare disparities [45]. Limited tertiary care setups in remote areas [46], along with the scarcity of primary care physicians and cardiac specialists in rural regions [47,48], could exacerbate the challenges faced by patients in accessing post-acute care and cardiac rehabilitation services [49,50]. One of the main hindrances is the increased travel distance that rural residents must cover to access health care. Moreover, transportation challenges, limited communication access, and the closure of an increasing number of hospitals contribute to lower healthcare utilization in non-metropolitan areas [44, 51]. It has also been reported that higher rates of individuals are uninsured in rural areas, which further exacerbates disparities [51]. Moreover, delays in the adoption of strategies to prevent and manage risk factors in rural areas could be another potential reason for the higher AAMRs observed in this group [52–54]. Moreover, it has been reported that over the past decade, the percentage of the elderly population in rural areas has been higher (as high as 18 % in some non-metropolitan counties) than in urban areas (12 %) due to the outward migration of young adults and inward migration of elderly retirees [45].

We also observed substantial disparities in the mortality rates associated with HF among elderly individuals across diverse geographic regions in the United States. The Midwest zone bears the greatest mortality load compared to the other zones, while the Northeast bears the least. The mortality rates in the West and South were comparable. These significant regional discrepancies may stem from many factors, including differences in ambulatory cardiology practices, varying levels of evidence-based medication, challenges in accessing quality healthcare, the impact of state Medicaid regulations, and increasing comorbidities [55]. These findings shed light on the complex interplay between regional factors that contribute to divergent health outcomes. Addressing these challenges and promoting equitable healthcare access are crucial steps towards mitigating these disparities and fostering healthier communities.

4.1. Future prospects

Our study highlights the combined effect of HF and DM on mortality trends, emphasizing the need for further research and comprehensive management strategies. Adopting contemporary guidelines and stringent post-discharge protocols, especially for older adults, is crucial [56, 57]. Implementing transitional care through regular home visits by trained nurses has shown effectiveness [58]. The COVID-19 pandemic has stressed the importance of crisis management, such as developing

robust telemedicine platforms and training healthcare professionals in underserved areas. Bridging racial and regional disparities is essential to ensure equitable healthcare delivery and to improve survival rates. In addition, high-quality trials and meta-analyses have demonstrated that the early use of SGLT2 inhibitors significantly benefits patients with coexisting HF and DM by improving clinical outcomes, reducing hospitalizations and mortality rates, and providing effective glycemic control. These medications offer cardioprotective benefits and lower healthcare costs, highlighting the importance of proactive disease management. Incorporating SGLT2 inhibitors into standard treatment protocols and continued research will further optimize their use and enhance patient outcomes and quality of life [59,60].

5. Limitations

This study had several limitations. First, reliance on death certificates and ICD codes may result in the unintentional reporting of both DM and HF as causes of death. Second, the increased reporting of HF diagnoses in electronic health records may not accurately reflect actual mortality trends. Third, the database lacks detailed information on HF parameters, such as vital signs, laboratory results, echocardiographic data, and genetic testing. Furthermore, a significant limitation is the lack of differentiation between types of heart failure, specifically HFpEF and HFrEF, as this information is typically not included in death certificates, and the CDC WONDER database does not report these separately under different ICD-10 codes. In addition, baseline characteristics such as atherosclerosis, atrial fibrillation, or a history of ischemic cardiomyopathy, which could contribute to mortality in heart failure patients, could not be calculated using this database. This limitation applies to all similar studies using this database. Lastly, from our analysis, we were unable to calculate the exact effect size of COVID-19's impact on mortality related to HF or DM alone or their coexistence.

6. Conclusion

The mortality rates among elderly individuals with coexisting HF and DM vary. There was a noticeable decline from 2005 to 2011 following an initial spike between 1999 and 2005. However, there was a subsequent surge beginning in 2011 that significantly increased between 2018 and 2020. Selecting an elderly cohort aged 75 and above as our subjects, we observed elevated rates predominantly among NH American Indians or Alaska Natives, males, individuals residing in the Midwest region of the United States, and those dwelling in non-urban areas. These findings underscore the pressing need for systemic reforms in healthcare practices and protocols.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical considerations

No ethical approval was required for this study design, as all data were obtained from publicly available sources.

CRedit authorship contribution statement

Humza Saeed: Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **M.B.B.S. Abdullah:** Writing

– review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Formal analysis. **Irum Naem:** Writing – original draft, Software, Resources, Data curation. **Amna Zafar:** Writing – original draft, Software, Resources, Methodology, Data curation. **Bilal Ahmad:** Writing – original draft, Validation, Formal analysis. **Taimur ul Islam:** Writing – original draft, Methodology, Formal analysis, Data curation. **Syed Saaid Rizvi:** Writing – original draft, Formal analysis, Data curation. **Nikita Kumari:** Writing – original draft, Methodology, Formal analysis, Data curation. **Syed Ghazi Ali Kirmani:** Writing – original draft, Formal analysis, Data curation. **Fatima Mansoor:** Software, Formal analysis, Conceptualization. **Amir Hassan:** Writing – original draft, Supervision, Investigation. **Adarsh Raja:** Writing – review & editing, Writing – original draft, Formal analysis. **Mohamed Daoud:** Writing – review & editing, Writing – original draft. **Aman Goyal:** Writing – review & editing, Validation, Project administration, Methodology, Data curation, Conceptualization.

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Appendix A. Supplementary data

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References

- [1] S.C. Curtin, B. Tejada-Vera, B.A. Bastian, Deaths: leading causes for 2020, *Natl. Vital Stat. Rep.* 72 (13) (2023 Dec 1) 1–115.
- [2] B. Bozkurt, T. Ahmad, K.M. Alexander, W.L. Baker, K. Bosak, K. Breathett, et al., Heart failure epidemiology and outcomes Statistics: a report of the heart failure society of America, *J. Card. Fail.* 29 (10) (2023 Oct 1) 1412–1451.
- [3] National Institute of Diabetes and Digestive and Kidney Diseases [Internet]. [cited 2024 Jul 10]. Diabetes Statistics - NIDDK. Available from: <https://www.niddk.nih.gov/health-information/health-statistics/diabetes-statistics>.
- [4] B.H. Greenberg, W.T. Abraham, N.M. Albert, K. Chiswell, R. Clare, W.G. Stough, et al., Influence of diabetes on characteristics and outcomes in patients hospitalized with heart failure: a report from the organized Program to initiate lifesaving treatment in hospitalized patients with heart failure (OPTIMIZE-HF), *Am. Heart J.* 154 (2) (2007 Aug 1) 277.e1–277.e8.
- [5] G.A. Nichols, C.M. Gullion, C.E. Koro, S.A. Ephross, J.B. Brown, The incidence of congestive heart failure in type 2 diabetes: an update, *Diabetes Care* 27 (8) (2004 Aug) 1879–1884.
- [6] A.G. Bertoni, W.G. Hundley, M.W. Massing, D.E. Bonds, G.L. Burke, D.C. Goff, Heart failure prevalence, incidence, and mortality in the elderly with diabetes, *Diabetes Care* 27 (3) (2004 Mar) 699–703.
- [7] L.J.M. Boonman-de Winter, F.H. Rutten, M.J.M. Cramer, M.J. Landman, A.H. Liem, G.E.H.M. Rutten, et al., High prevalence of previously unknown heart failure and left ventricular dysfunction in patients with type 2 diabetes, *Diabetologia* 55 (8) (2012 Aug 1) 2154–2162.
- [8] V. Jain, A.M.K. Minhas, A.A. Morris, S.J. Greene, A. Pandey, S.S. Khan, et al., Demographic and regional trends of heart failure-related mortality in young adults in the US, 1999–2019, *JAMA Cardiol* 7 (9) (2022 Sep 1) 900–904.
- [9] T.J. Siddiqi, A.M. Khan Minhas, S.J. Greene, H.G.C. Van Spall, S.S. Khan, A. Pandey, et al., Trends in heart failure-related mortality among older adults in the United States from 1999–2019, *JACC (J. Am. Coll. Cardiol.): Heart Fail.* 10 (11) (2022 Nov 1) 851–859.
- [10] S. Sidney, A.S. Go, M.G. Jaffe, M.D. Solomon, A.P. Ambrosy, J.S. Rana, Association between aging of the US population and heart disease mortality from 2011 to 2017, *JAMA Cardiol* 4 (12) (2019 Dec 1) 1280–1286.
- [11] Z.S. Siddiqui, Y. Xiao, P.O. Ansong, S.S. Muthu, A. Sony, S. Doghouz, et al., A 22-year study to assess disparities in place of death among patients with diabetes, *Cureus [Internet]* (2023 Dec 4) [cited 2024 Jul 10];15. Available from: <https://www.cureus.com/articles/200783-a-22-year-study-to-assess-disparities-in-place-of-death-among-patients-with-diabetes#!/>.
- [12] S.B. Dugani, C.M. Wood-Wentz, M.M. Mielke, K.R. Bailey, A. Vella, Assessment of disparities in diabetes mortality in adults in US rural vs nonrural counties, 1999–2018, *JAMA Netw. Open* 5 (9) (2022 Sep 20) e2232318.
- [13] Multiple Cause of Death Data on CDC WONDER [Internet]. [cited 2024 Jul 10]. Available from: <https://wonder.cdc.gov/mcd.html>.
- [14] V. Jain, A.M.K. Minhas, R.W. Ariss, S. Nazir, S.U. Khan, M.S. Khan, et al., Demographic and regional trends of cardiovascular diseases and diabetes mellitus-related mortality in the United States from 1999 to 2019, *Am. J. Med.* 136 (7) (2023 Jul 1) 659–668.e7.

- [15] A.M. Rashid, A. Jamil, Z. Khan, M. Shakoob, U.H. Kamal, I.I. Khan, et al., Trends in mortality related to kidney failure and diabetes mellitus in the United States: a 1999–2020 analysis, *J Nephrol* [Internet] (2024 Jun 25), <https://doi.org/10.1007/s40620-024-01990-z> [cited 2024 Jul 10].
- [16] Members Writing Group, D. Mozaffarian, E.J. Benjamin, A.S. Go, D.K. Arnett, M. J. Blaha, et al., Heart disease and stroke statistics–2016 update: a report from the American heart association, *Circulation* 133 (4) (2016 Jan 26) e38–e360.
- [17] J. Tromp, S.M.A. Paniagua, E.S. Lau, N.B. Allen, M.J. Blaha, R.T. Gansevoort, et al., Age dependent associations of risk factors with heart failure: pooled population based cohort study, *BMJ* 372 (2021 Mar 23) n461.
- [18] R.N. Anderson, H.M. Rosenberg, Age standardization of death rates: implementation of the year 2000 standard, *Natl. Vital Stat. Rep.* 47 (3) (1998 Oct 7) 1–16, 20.
- [19] Jointpoint Regression Program [Internet]. [cited 2024 Jul 10]. Available from: <https://surveillance.cancer.gov/jointpoint/>.
- [20] B.I. Jugdutt, Aging and heart failure: changing demographics and implications for therapy in the elderly, *Heart Fail. Rev.* 15 (5) (2010 Sep 1) 401–405.
- [21] A.M. From, C.L. Leibson, F. Bursi, M.M. Redfield, S.A. Weston, S.J. Jacobsen, et al., Diabetes in heart failure: prevalence and impact on outcome in the population, *Am. J. Med.* 119 (7) (2006 Jul 1) 591–599.
- [22] T.T. Win, H.T. Davis, W.K. Laskey, Mortality among patients hospitalized with heart failure and diabetes mellitus, *Circulation* 133 (5) (2016 May) e030323.
- [23] G.A. Mensah, G.S. Wei, P.D. Sorlie, L.J. Fine, Y. Rosenberg, P.G. Kaufmann, et al., Decline in cardiovascular mortality, *Circ. Res.* 120 (2) (2017 Jan 20) 366–380.
- [24] M.J. Goldacre, D. Mant, M. Duncan, M. Griffith, Mortality from heart failure in an English population, 1979–2003: study of death certification, *Journal of Epidemiology & Community Health* 59 (9) (2005 Sep 1) 782–784.
- [25] C. Shaw, Interim 2001-based national population projections for the United Kingdom and constituent countries, *Popul. Trends* 111 (2003) 7–17.
- [26] T. Morishita, D. Takada, J. ho Shin, T. Higuchi, S. Kunisawa, K. Fushimi, et al., Effects of the COVID-19 pandemic on heart failure hospitalizations in Japan: interrupted time series analysis, *ESC Heart Failure* 9 (1) (2022) 31–38.
- [27] C. Koliaki, A. Tentolouris, I. Eleftheriadou, A. Melidonis, G. Dimitriadis, N. Tentolouris, Clinical management of diabetes mellitus in the era of COVID-19: practical issues, peculiarities and concerns, *J. Clin. Med.* 9 (7) (2020 Jul 18) 2288.
- [28] R.C.W. Ma, R.I.G. Holt, COVID-19 and diabetes, *Diabet. Med.* 37 (5) (2020) 723–725.
- [29] A.S. Bhatt, A. Moscone, E.E. McElrath, A.S. Varshney, B.L. Claggett, D.L. Bhatt, et al., Fewer hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic, *J. Am. Coll. Cardiol.* 76 (3) (2020 Jul 21) 280–288.
- [30] G.C. Fonarow, B. Ziaeian, Hospital readmission reduction Program for heart failure: the spread of intended and unintended consequences, *J. Am. Coll. Cardiol.* 73 (9) (2019 Mar 12) 1013–1015.
- [31] H. Bashir, M. Yildiz, J. Cafardi, A. Bhatia, S. Garcia, T.D. Henry, et al., A review of heart failure in patients with COVID-19, *Heart Fail. Clin.* 19 (2) (2023 Apr) e1–e8.
- [32] R. Wong, E. Lam, C.T. Bramante, S.G. Johnson, J. Reusch, K.J. Wilkins, et al., Does COVID-19 infection increase the risk of diabetes? Current evidence, *Curr Diab Rep* 23 (8) (2023) 207–216.
- [33] CDC. Centers for Disease Control and Prevention, Hospital outcomes for flu and COVID-19 have become more similar [cited 2024 Aug 2]. <https://www.cdc.gov/flu/spotlights/2023-2024/hospital-outcomes.htm>, 2024.
- [34] Xie Y, Choi T, Al-Aly Z. Mortality in Patients Hospitalized for COVID-19 vs Influenza in Fall-Winter 2023-2024. [cited 2024 Aug 2]; Available from: <https://jamanetwork.com/journals/jama/fullarticle/2818660>.
- [35] A. de P. Mansur, C.H. Del Carlo, G.H.F. Gonçalves, S.D. Avakian, L.C. Ribeiro, B. M. Ianni, et al., Sex differences in heart failure mortality with preserved, mildly reduced and reduced ejection fraction: a retrospective, single-center, large-cohort study, *Int. J. Environ. Res. Publ. Health* 19 (23) (2022 Dec 2) 16171.
- [36] A. Pandey, W. Omar, C. Ayers, M. LaMonte, L. Klein, N.B. Allen, et al., Sex and race differences in lifetime risk of heart failure with preserved ejection fraction and heart failure with reduced ejection fraction, *Circulation* 137 (17) (2018 Apr 24) 1814–1823.
- [37] G. Himmelstein, J.N. Ceasar, K.E. Himmelstein, Hospitals that serve many Black patients have lower revenues and profits: structural racism in hospital financing, *J. Gen. Intern. Med.* 38 (3) (2023 Feb 1) 586–591.
- [38] Ballard Brief [Internet]. [cited 2024 Jul 10]. Inadequate Healthcare for American Indians in the United States. Available from: <https://ballardbrief.byu.edu/issue-briefs/inadequate-healthcare-for-american-indians-in-the-united-states>.
- [39] Center for American Indian Resilience [Internet]. [cited 2024 Jul 10]. American Indian Health Equity/Disparities. Available from: <https://in.nau.edu/cair/ai-health-equity-and-disparities/>.
- [40] D.S. Jones, The persistence of American Indian health disparities, *Am. J. Publ. Health* 96 (12) (2006 Dec) 2122–2134.
- [41] S.C. Lewsey, K. Breathett, Racial and ethnic disparities in heart failure: current state and future directions, *Curr. Opin. Cardiol.* 36 (3) (2021 May) 320.
- [42] B.A. Young, Health disparities in advanced heart failure treatment: the intersection of race and sex, *JAMA Netw. Open* 3 (7) (2020 Jul 21) e2011034.
- [43] A.L. Bui, T.B. Horwich, G.C. Fonarow, Epidemiology and risk profile of heart failure, *Nat. Rev. Cardiol.* 8 (1) (2011 Jan) 30–41.
- [44] J.B. Pierce, N.S. Shah, L.C. Petito, L. Pool, D.M. Lloyd-Jones, J. Feinglass, et al., Trends in heart failure-related cardiovascular mortality in rural versus urban United States counties, 2011–2018: a cross-sectional study, *PLoS One* 16 (3) (2021 Mar 3) e0246813.
- [45] J.N. Bolin, G.R. Bellamy, A.O. Ferdinand, A.M. Vuong, B.A. Kash, A. Schulze, et al., Rural healthy people 2020: new decade, same challenges, *J. Rural Health* 31 (3) (2015) 326–333.
- [46] E. Merwin, A. Snyder, E. Katz, Differential access to quality rural healthcare: professional and policy challenges, *Fam. Community Health* 29 (3) (2006 Sep) 186.
- [47] S. Basu, S.A. Berkowitz, R.L. Phillips, A. Bitton, B.E. Landon, R.S. Phillips, Association of primary care physician supply with population mortality in the United States, 2005–2015, *JAMA Intern. Med.* 179 (4) (2019 Apr 1) 506–514.
- [48] K.J. Johnston, H. Wen, K.E. Joynt Maddox, Lack of access to specialists associated with mortality and preventable hospitalizations of rural medicare beneficiaries, *Health Aff.* 38 (12) (2019 Dec) 1993–2002.
- [49] C.M. Kosar, L. Loomer, N.B. Ferdows, A.N. Trivedi, O.A. Panagiotou, M. Rahman, Assessment of rural-urban differences in postacute care utilization and outcomes among older US adults, *JAMA Netw. Open* 3 (1) (2020 Jan 8) e1918738.
- [50] H.E. Valencia, P.D. Savage, P.A. Ades, Cardiac rehabilitation participation in underserved populations, *J. Cardpulm. Rehabil. Prev.* 31 (4) (2011 Aug) 203.
- [51] J.C. Probst, S.B. Ladtka, J.Y. Wang, A.O. Johnson, Effects of residence and race on burden of travel for care: cross sectional analysis of the 2001 US National Household Travel Survey, *BMC Health Serv. Res.* 7 (1) (2007 Mar 9) 40.
- [52] S. Kotit, Rurality and race in heart failure risk: insights from the southern community cohort study, *Global Cardiology Science and Practice* [Internet] (2024) [cited 2024 Jul 10];2024(1), <https://globalcardiologyscienceandpractice.com/index.php/gcsp/article/view/686>.
- [53] R.T. Goins, U. Kategile, K.C. Dudley, Telemedicine, rural elderly, and policy issues, *J. Aging Soc. Pol.* 13 (4) (2002 Sep 20) 53–71.
- [54] C. Scott Kruse, P. Karem, K. Shifflett, L. Vegi, K. Ravi, M. Brooks, Evaluating barriers to adopting telemedicine worldwide: a systematic review, *J. Telemed. Telecare* 24 (1) (2018 Jan 1) 4–12.
- [55] P.A. Glynn, R. Molsberry, K. Harrington, N.S. Shah, L.C. Petito, C.W. Yancy, et al., Geographic variation in trends and disparities in heart failure mortality in the United States, 1999 to 2017, *J. Am. Heart Assoc.* 10 (9) (2021 May 4) e020541.
- [56] I.P. Popa, M. Haba, C. Ștefan, M.A. Mărănducă, D.M. Tănase, D.N. Șerban, L. I. Șerban, et al., Modern approaches for the treatment of heart failure: recent advances and future perspectives, *Pharmaceutics* 14 (9) (2022 Sep) 1964.
- [57] M. Gabler, N. Picker, S. Geier, L. Ley, J. Aberle, M. Lehrke, et al., Guideline adherence and associated outcomes in the treatment of type 2 diabetes mellitus patients with an incident cardiovascular comorbidity: an analysis based on a large German claims dataset, *Diabetes Ther* 12 (4) (2021 Apr 1) 1209–1226.
- [58] H.G.C. Van Spall, T. Rahman, O. Mytton, C. Ramasundarathettege, Q. Ibrahim, C. Kabali, et al., Comparative effectiveness of transitional care services in patients discharged from the hospital with heart failure: a systematic review and network meta-analysis, *Eur. J. Heart Fail.* 19 (11) (2017) 1427–1443.
- [59] R. Aldafas, T. Crabtree, M. Alkharajji, Y. Vinogradova, I. Idris, Sodium-glucose cotransporter-2 inhibitors (SGLT2) in frail or older people with type 2 diabetes and heart failure: a systematic review and meta-analysis, *Age Ageing* 53 (1) (2024 Jan 1) afad254.
- [60] H. Akasaka, K. Sugimoto, A. Shintani, S. Taniuchi, K. Yamamoto, K. Iwakura, et al., Effects of ipragliflozin on left ventricular diastolic function in patients with type 2 diabetes and heart failure with preserved ejection fraction: the EXCEED randomized controlled multicenter study, *Geriatr. Gerontol. Int.* 22 (4) (2022) 298–304.