RENAL FAILURE
2025, VOL. 47, NO. 1, 2472039
https://doi.org/10.1080/0886022X.2025.2472039

Taylor & Francis
Taylor & Francis Group

CLINICAL STUDY

Global, regional, and national burden of cardiovascular disease attributable to kidney dysfunction (1990–2021) with projections to 2050: analysis of the 2021 Global Burden of Disease study

Tian Zhang, Ting Li and Pengfei Jin

Department of Pharmacy, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Key Laboratory of Assessment of Clinical Drugs Risk and Individual Application, (Beijing Hospital), Beijing, P.R. China

ABSTRACT

Aims: This study examines global trends in cardiovascular disease (CVD) associated with kidney dysfunction (KD) from 1990 to 2021 and projects future trends through 2050.

Methods: This study analyzed the 2021 Global Burden of Disease (GBD) database, focusing on age-standardized mortality rate (ASMR), age-standardized disability-adjusted life years rate (ASDR), absolute numbers, estimated annual percentage change, and average annual percent change. A Bayesian age-period-cohort model was employed to project global trends from 2022 to 2050. Variables included age, gender, national levels, and Socio-demographic Index (SDI) regions.

Results: From 1990 to 2021, the CVD burden from KD increased, with deaths rising from 1,312,393 to 2,095,800 and DALYs from 27,382,767 to 41,589,861. However, the ASMR decreased from 40.58 per 100,000 in 1990 to 25.55 in 2021, while ASDR fell from 742.17 to 489.81 during the same period. The burden was higher in men, peaking at ages 70–74 and in women at ages 85–89. Regions with lower-middle and low SDI recorded the highest CVD burden, inversely related to SDI levels. Geographically, Central Asia and Eastern Europe recorded the highest rates, while high-income Asia Pacific and Southern Latin America had the lowest. Projections suggest a sustained decline in global CVD burden due to KD from 2022 to 2050, although disparities between sexes are expected to persist, with men bearing a heavier burden.

Conclusion: CVD attributable to KD remains a major global public health challenge, especially for men, the elderly, and low SDI regions. These spatial and temporal variations highlight the need for region-specific healthcare strategies.

ARTICLE HISTORY
Received 18 December 2024
Revised 6 February 2025
Accepted 19 February 2025

KEYWORDS
Cardiovascular disease; kidney dysfunction; global burden of disease; prediction

Introduction

Cardiovascular disease (CVD) is the leading cause of global morbidity and mortality, posing significant economic challenges both regionally and worldwide [1]. Between 1990 and 2019, CVD cases nearly doubled, increasing from 271 million to 523 million, while deaths rose from 12.1 million to 18.6 million [2]. CVD includes conditions such as ischemic heart disease, coronary artery disease, stroke, myocardial infarction, and congestive heart failure. Notably, nearly 80% of CVD cases occur in low- and middle-income countries, where aging populations and rapid urbanization exacerbate the incidence and impact of these diseases [3]. To effectively address the CVD epidemic, urgent actions are required. Therefore, developing prevention strategies at both population and individual levels is essential to alleviate the overall burden of CVD [4].

CVD is associated with several modifiable risk factors, most notably kidney dysfunction (KD) [5]. KD increases the risk of CVD and acts as a risk multiplier, particularly for individuals with hypertension or diabetes [6]. Defined by reduced kidney function, KD is characterized by metabolite retention, water, and electrolyte imbalances, and systemic symptoms. If left untreated, KD can progress to end-stage renal disease (ESRD), requiring dialysis or kidney transplantation [7]. Globally, nearly 10% of adults are affected by various kidney diseases [8]. Over the past three decades, deaths from KD have increased from 1,571,720 to 3,161,552, while disability-adjusted life years (DALYs) have risen from 42,090,331 to 76,486,945. Although age-standardized rates (ASR) for deaths and DALYs have decreased, their total counts are projected to increase [9]. KD is often difficult to detect in its early stages but can lead to fatal outcomes in advanced stages,

CONTACT Pengfei Jin j790101@163.com Beijing Hospital, No. 1 Da Hua Road, Dong Dan, Beijing 100730, P.R. China
Supplemental data for this article can be accessed online at https://doi.org/10.1080/0886022X.2025.2472039.

with many patients unaware of their condition, especially in regions with limited economic development and healthcare infrastructure [10]. Thus, the CVD burden linked to KD remains a critical public health issue.

Previous studies have identified KD as a significant risk factor for non-communicable diseases [11]. However, no comprehensive analysis has yet quantified the CVD burden attributable to KD. Our findings build upon earlier research, offering policymakers valuable insights into the long-term impact of prevention strategies.

In this study, we analyzed the CVD burden linked to KD, considering various factors such as global trends, age, gender, national levels, and Socio-demographic Index (SDI) regions. We utilized mortality and DALYs data from the 2021 Global Burden of Disease (GBD) study. To assess temporal trends from 1990 to 2021, we applied a joinpoint regression model. Additionally, the Bayesian age-period-cohort (BAPC) model was used to project trends from 2022 to 2050.

Methods

Data sources

Mortality, DALYs, and their age-standardized rates, including age-standardized mortality rate (ASMR) and age-standardized disability-adjusted life years rate (ASDR), associated with KD-related CVD and specific CVDs, were obtained from the Global Health Data Exchange (GHDx) query tool (https://ghdx.healthdata.org/gbd-2021). This dataset covers the period from 1990 to 2021 and spans global demographics, including age, gender, and national levels, as well as SDI regions across 204 countries and territories. This study was approved by the University of Washington in Seattle, WA, which waived informed consent because only de-identified and aggregated data were utilized.

Definitions

KD is characterized by impaired kidney function, which leads the retention of metabolites and imbalances in water, electrolytes, and acid-base metabolism. Over time, these changes cause systemic symptoms and may progress to ESRD, necessitating dialysis or kidney transplantation [12]. Over the past four decades, nephrologists have identified two main syndromes within KD: acute kidney injury and chronic kidney disease (CKD). These syndromes are defined by serum creatinine levels or glomerular filtration rate (GFR), with KD specifically defined as GFR < 60 mL/min/1.73 m^2 or an albumin to creatinine ratio (ACR) > 30 mg/g, which are levels that minimize risk at the population level. Both GFR and ACR significantly contribute to the increased disability and mortality associated with non-communicable diseases [11,13]. Furthermore, KD is a major risk factor for cardiovascular disease and exacerbates risks for patients with hypertension or diabetes [14].

According to GBD 2021, KD-related cardiovascular diseases mainly include ischemic heart disease, stroke, and lower extremity peripheral arterial disease.

DALYs provide an integrative measure of the burden imposed by CVD related to KD. DALYs combine years lived with disability (YLDs) and years of life lost (YLLs) from premature deaths attributable to KD-related CVD. YLDs are calculated by the multiplying the number of individuals affected by KD-related CVD and the disability weight, which ranges from 0 (perfect health) to 1 (death). Conversely, YLLs are derived by multiplying the number of deaths in each age group by the standard life expectancy for that cohort [7].

The SDI is a comprehensive measure of a country's socioeconomic status. It is calculated by averaging the rankings of three key indicators: per capital income, average educational attainment, and fertility rates of women under 25 years old [15]. Subsequently, the world is divided into 21 GBD regions, based on socioeconomic factors and geographic location.

Statistical analyses

This research involved a secondary analysis of the GBD database. We used multiple metrics to quantify the burden of CVD attributable to KD. These metrics included the ASR, absolute numbers, percent change, estimated annual percentage change (EAPC), and average annual percent change (AAPC). Additionally, we forecasted global burden trends by sex from 2022 to 2050 using a BAPC model. Understanding these trends is essential for developing targeted interventions.

First, this study utilized data from the GBD database, encompassing all age groups. Absolute numbers, percentage changes, ASMR, and ASDR were directly sourced from the GBD 2021 data. Each came with 95% uncertainty intervals (UIs). To calculate the EAPC and its 95% confidence intervals (CIs), a linear regression was applied to the natural logarithm of the ASRs. An ASR is considered to trend downward if both the EAPC estimate and its 95% CI upper bound are below 0. Conversely, an upward trend is noted if the EAPC estimate and its 95% CI lower bound exceed 0. If neither condition is met, the ASR is considered stable over time [16].

Second, we used a joinpoint regression model to assess temporal trends in the CVD burden due to KD. Specifically, we employed the log-linear model ($\ln(y) = xb$), which is well-suited for analyzing relative changes in disease burden over time. Model optimization was conducted using permutation tests with a significance level (alpha) set at 0.05 and 4499 permutations. The significance of joinpoints was tested using this threshold. The number of joinpoints was set to range from a minimum of 0 to a maximum of 6, and the program determined the optimal number of joinpoints for the model. This model was implemented using Joinpoint software from the National Cancer Institute (Rockville, MD, USA). We calculated the AAPC and its 95% CI to evaluate the trends. When the CI of the AAPC estimate is greater than 0, the indicator trends upward; it trends downward if less than 0, and is stable when the interval includes 0 [17].

Third, we utilized the BAPC model to project global disease burden trends by sex from 2022 to 2050. The model relies on three key assumptions: First, age, period, and cohort effects are additive and can be separated temporally; Second,

smoothness priors ensure that adjacent time periods and birth cohorts have similar effect sizes; Third, historical age-period-cohort interaction patterns continue during the projection period. We chose the BAPC model for the following reasons: First, its Bayesian framework with penalized complexity priors minimizes overfitting in small-population regions, such as low-SDI countries; Second, the use of Integrated Nested Laplace Approximations (INLA) addresses the convergence issues often encountered with Markov chain Monte Carlo methods in high-dimensional parameter spaces [13]; Third, the model's wide application in analyzing chronic disease trends and forecasting future disease burdens ensures comparability with previous studies [11]. The BAPC model employs Bayesian inference and a second-order stochastic excursion to smooth prior values and predict posterior rates. It uses INLA to estimate marginal posterior distributions [13], a method extensively used in chronic disease trend analysis and burden forecasting.

Additionally, we explored the relationships between age-standardized DALYs, death rates and the SDI across 21 GBD regions and 204 countries. This analysis was conducted using locally estimated scatterplot smoothing regression. For statistical analysis and data visualization, we utilized R statistical software (version 4.2.3) and Joinpoint software (version 5.1.0).

Results

Global burden of cardiovascular disease attributable to kidney dysfunction

Deaths worldwide attributed to CVD linked to KD rose from 1,312,393 (95% UI 1,032,996 to 1,571,479) in 1990 to 2,095,800 (95% UI 1,638,359 to 2,562,746) in 2021, marking a 59.59% increase. However, the global burden declined after adjusting for temporal and age-related influences. The ASMR for KD-related CVD decreased from 40.58 (95% UI 31.93 to 49.24) per 100,000 persons in 1990 to 25.55 (95% UI 19.84 to 31.36) per 100,000 persons in 2021. This decline corresponds to an EAPC of −1.57 (95% CI −1.62 to −1.52) (Tables 1 and 2). Over the period from 1990 to 2021, the AAPC was −1.49 (95% CI −1.71 to −1.27), showing statistical significance. Joinpoint regression identified four significant shifts in ASMR, occurring in 1995, 1998, 2004, and 2007 (Figure 1; Supplementary Table S1).

Similarly, the DALYs associated with KD-related CVD increased from 27,382,767 (95% UI 22,234,707 to 32,604,562) in 1990 to 41,589,861 (95% UI 33,250,168 to 50,391,379) in 2021, reflecting a 51.88% rise. Despite this increase in absolute numbers, the ASDR decreased from 742.17 (95% UI 597.93 to 879.88) per 100,000 in 1990 to 489.81 (95% UI 391.39 to 593.21) per 100,000 in 2021. This decline was accompanied by an EAPC of −1.44 (95% CI −1.49 to −1.38) annually (Tables 1 and 2). Over the entire period (from 1990 to 2021), the AAPC was found to be −1.31 (95% CI −1.52 to −1.11), indicating statistical significance. Joinpoint regression analysis further identified significant shifts in ASDR in 1995, 1998, 2004, 2007, and 2019 (Figure 1; Supplementary material, Table S1).

In 2021, ischemic heart disease ranked as the primary cause of CVD deaths associated with KD, with an ASMR of 17.18 (95% UI 11.94 to 21.83) per 100,000 population. Stroke followed, with an ASMR of 8.10 (95% UI 5.58 to 10.73), and lower extremity peripheral arterial disease, with an ASMR of 0.27 (95% UI 0.18 to 0.36). From 1990 to 2021, all CVD subcategories showed a declining trend in mortality burden. The variations in ASDR across CVD subcategories were consistent with those observed in ASMR (Tables 1 and 2).

Global burden of cardiovascular disease attributable to kidney dysfunction by sex and age

Throughout the past three decades, it has been observed that men have borne a heavier KD-related CVD burden compared to women globally. In 2021, mortality peaked for men aged 70–74 years and women aged 85–89 years. The DALYs were highest for men aged 65–69 and for women aged 70–74 years. Before the age of 80, both mortality and DALYs were higher in males than females. Beyond age 80, these numbers were lower in males than in females. In addition, age-specific mortality and DALYs rates increased with age, with higher rates observed in the elderly. Consistently, these rates were higher in males than females across all age groups (Figure 2).

From 1990 to 2021, both mortality and DALYs due to KD-attributed CVD more than doubled for both genders. Males were consistently more affected than females during this period. In contrast, the global ASMR and ASDR for KD-related CVD slightly decreased for both sexes during the same period. Specifically, the ASMR in men fell from 44.65 (95% UI 35.01 to 53.89) per 100,000 persons in 1990 to 30.25 (95% UI 23.76 to 37.38) per 100,000 persons in 2021, with an EAPC of −1.29 (95% CI −1.34 to −1.25) and an AAPC of −1.23 (95% CI −1.42 to −1.04). In women, the ASMR decreased from 37.02 (95% UI 28.84 to 45.52) per 100,000 persons in 1990 to 21.67 (95% UI 16.77 to 26.76) per 100,000 persons in 2021, with an EAPC of −1.82 (95% CI −1.88 to −1.76) and an AAPC of −1.71 (95% CI −1.90 to −1.52) (Table 1, Figures 1 and 3; Supplementary material, Table S1). Similarly, the ASDR in men decreased from 851.58 (95% UI 686.58 to 1023.05) per 100,000 persons in 1990 to 598.14 (95% UI 479.64 to 722.15) per 100,000 persons in 2021, with an EAPC of −1.21 (95% CI −1.26 to −1.16) and an AAPC of −1.12 (95% CI −1.33 to −0.91). The ASDR in women decreased from 642.58 (95% UI 519.51 to 765.26) per 100,000 persons in 1990 to 392.51 (95% UI 312.52 to 473.79) per 100,000 persons in 2021, with an EAPC of −1.70 (95% CI −1.77 to −1.64) and an AAPC of −1.58 (95% CI −1.75 to −1.41)] (Table 2, Figures 1 and 3; Supplementary material, Table S1).

Global burden of cardiovascular disease attributable to kidney dysfunction by SDI

In 2021, the highest ASMR and ASDR for KD-related CVD were observed in regions with low-middle SDI (ASMR 34.76/100,000; ASDR 709.62/100,000) and low SDI (ASMR

Table 1. The death burden of cardiovascular disease attributable to kidney dysfunction in 1990 and 2021 and the temporal trends from 1990 to 2021.

	1990		2021		1990–2021	
	Death cases	ASR per 100,000	Death cases	ASR per 100,000	Percentage change in absolute number	EAPC of ASMR
	No. (95% UI)	ASMR (95% UI)	No. (95% UI)	ASMR (95% UI)	(95% UI)	(95% CI)
Global	1,312,393 (1,032,996 to 1,571,479)	40.58 (31.93 to 49.24)	2,095,800 (1,638,359 to 2,562,746)	25.55 (19.84 to 31.36)	59.69% (49.92 to 69.41)	−1.57 (−1.62 to −1.52)
Sex						
Male	623,346 (495,620 to 750,360)	44.65 (35.01 to 53.89)	1,077,455 (851,106 to 1,324,784)	30.25 (23.76 to 37.38)	72.85% (59.14 to 87.52)	−1.29 (−1.34 to −1.25)
Female	689,047 (537,316 to 841,782)	37.02 (28.84 to 45.52)	1,018,345 (788,247 to 1,258,057)	21.67 (16.77 to 26.76)	47.79% (36.36 to 58.83)	−1.82 (−1.88 to −1.76)
SDI						
High SDI	366,107 (278,223 to 457,738)	33.81 (25.77 to 42.08)	328,619 (247,541 to 409,647)	12.84 (9.77 to 15.96)	−10.24% (−17.13 to −4.64)	−3.38 (−3.5 to −3.26)
High-middle SDI	392,561 (310,481 to 477,797)	49.85 (39.13 to 61.27)	537,847 (407,993 to 673,922)	28.2 (21.4 to 35.3)	37.01% (25.56 to 49.58)	−2.03 (−2.23 to −1.83)
Middle SDI	302,980 (245,232 to 367,916)	38.61 (30.71 to 47.53)	680,645 (536,161 to 838,371)	29.21 (22.75 to 36.21)	124.65% (101.59 to 149.88)	−0.75 (−0.86 to −0.65)
Low-middle SDI	187,564 (150,599 to 226,585)	37.44 (29.37 to 45.42)	427,796 (332,730 to 520,208)	34.76 (26.94 to 42.79)	128.08% (108.22 to 151.61)	−0.16 (−0.22 to −0.11)
Low SDI	61,387 (48,784 to 74,878)	33.84 (26.63 to 41.62)	118,821 (92,144 to 146,124)	29.8 (22.84 to 37.03)	93.56% (75.42 to 113.55)	−0.35 (−0.46 to −0.24)
GBD region						
Andean Latin America	2,871 (2,209 to 3,582)	16.18 (12.43 to 20.27)	5,464 (3,969 to 7,020)	9.74 (7.06 to 12.53)	90.33% (59.06 to 124.09)	−1.86 (−2.18 to −1.53)
Australasia	7,265 (5,340 to 9,140)	33.14 (24.52 to 41.62)	6,323 (4,645 to 7,991)	9.64 (7.11 to 12.14)	−12.97% (−22.61 to −3.86)	−4.2 (−4.28 to −4.11)
Caribbean	7,874 (6,023 to 9,655)	34.54 (26.53 to 42.39)	11,783 (8,990 to 14,777)	21.3 (16.22 to 26.74)	49.65% (33.56 to 66.81)	−1.58 (−1.74 to −1.42)
Central Asia	34,057 (26,816 to 41,175)	85.58 (66.8 to 103.97)	45,058 (34,894 to 56,076)	70.71 (54.25 to 88.09)	32.30% (20.72 to 43.49)	−1.01 (−1.28 to −0.75)
Central Europe	69,877 (54,037 to 86,251)	55.29 (42.59 to 68.59)	67,185 (51,256 to 84,731)	27.99 (21.45 to 35.18)	−3.85% (−11.74 to 3.94)	−2.55 (−2.67 to −2.44)
Central Latin America	20,628 (16,038 to 24,930)	30.84 (23.86 to 37.39)	55,065 (41,823 to 68,866)	23.25 (17.66 to 29.15)	166.94% (140.18 to 197.59)	−1.04 (−1.28 to −0.81)
Central Sub-Saharan Africa	7,755 (5,865 to 10,002)	46.57 (35.11 to 60.01)	16,073 (11,950 to 20,868)	40.69 (30.29 to 53.63)	107.25% (68.37 to 154.56)	−0.64 (−0.71 to −0.58)
East Asia	208,131 (158,555 to 264,597)	34.23 (26.12 to 43.72)	456,662 (342,646 to 608,496)	24.81 (18.24 to 33.08)	119.41% (76.53 to 176.8)	−0.52 (−0.86 to −0.19)
Eastern Europe	184,427 (141,205 to 225,770)	79.68 (61.62 to 96.98)	201,059 (151,980 to 247,537)	56.48 (42.62 to 69.32)	9.02% (0.73 to 19.58)	−1.63 (−2.06 to −1.19)
Eastern Sub-Saharan Africa	13,435 (10,380 to 17,072)	21.65 (16.56 to 27.8)	24,404 (18,419 to 31,611)	18.07 (13.51 to 23.42)	81.64% (53.34 to 108.61)	−0.71 (−0.76 to −0.66)
High-income Asia Pacific	36,929 (27,387 to 46,797)	21.48 (15.73 to 27.24)	45,350 (31,975 to 58,485)	6.89 (5.03 to 8.75)	22.80% (6.87 to 35.43)	−3.67 (−3.85 to −3.49)
High-income North America	132,514 (97,593 to 166,697)	36 (26.57 to 45.14)	130,631 (98,786 to 162,461)	17.56 (13.32 to 21.69)	−1.42% (−7.78 to 4.92)	−2.68 (−2.86 to −2.51)
North Africa and Middle East	77,874 (59,290 to 96,193)	58.28 (43.84 to 72.71)	149,470 (109,093 to 190,829)	41.15 (29.97 to 52.55)	91.94% (72.41 to 111.92)	−1.12 (−1.18 to −1.06)
Oceania	1,044 (813 to 1,355)	45.87 (35.2 to 59.08)	2,472 (1,898 to 3,212)	41.27 (31.19 to 53.58)	136.77% (97.98 to 188.73)	−0.34 (−0.37 to −0.31)
South Asia	159,964 (126,732 to 199,474)	33.86 (26.2 to 41.94)	418,778 (319,799 to 519,770)	33.5 (25.48 to 41.32)	161.79% (132.72 to 195.14)	0.07 (−0.06 to 0.19)
Southeast Asia	92,943 (75,978 to 112,701)	43.67 (35.15 to 53.11)	220,462 (174,132 to 272,295)	39.01 (30.51 to 48.59)	137.20% (110.33 to 167.23)	−0.35 (−0.46 to −0.25)
Southern Latin America	10,043 (7,481 to 12,670)	24.71 (18.13 to 31.35)	8,373 (6,291 to 10,445)	9.14 (6.88 to 11.39)	−16.63% (−22.94 to −10.78)	−2.84 (−2.99 to −2.7)
Southern Sub-Saharan Africa	6,187 (4,847 to 7,525)	27.37 (20.89 to 33.51)	14,611 (11,765 to 17,549)	31.92 (25.54 to 39.08)	136.17% (116.52 to 174.7)	0.51 (0.09 to 0.94)
Tropical Latin America	26,739 (21,860 to 32,053)	35.96 (28.91 to 43.47)	37,674 (30,030 to 45,703)	15.11 (12.01 to 18.38)	40.89% (32.73 to 47.85)	−2.67 (−2.77 to −2.57)
Western Europe	184,589 (141,640 to 229,608)	31.38 (24.12 to 38.87)	128,441 (96,544 to 160,126)	10.27 (7.86 to 12.75)	−30.42% (−37.28 to −25.24)	−3.8 (−3.9 to −3.69)
Western Sub-Saharan Africa	27,247 (21,934 to 33,542)	38.89 (31.25 to 48.03)	50,464 (40,456 to 62,381)	34.36 (27.25 to 42.42)	85.21% (59.14 to 115.76)	−0.4 (−0.49 to −0.31)
CVD subcategories						
Ischemic heart disease	828,212 (594,880 to 1,050,788)	26.53 (18.85 to 33.72)	1,398,574 (976,437 to 1,778,399)	17.18 (11.94 to 21.83)	68.87% (58.16 to 78.99)	−1.45 (−1.49 to −1.42)
Lower extremity peripheral arterial disease	11,514 (7,652 to 15,213)	0.41 (0.28 to 0.55)	21,127 (14,271 to 27,923)	0.27 (0.18 to 0.36)	83.48% (70.68 to 96.56)	−1.61 (−1.75 to −1.47)
Stroke	472,667 (330,423 to 619,504)	13.64 (9.25 to 18.25)	676,099 (467,784 to 896,743)	8.1 (5.58 to 10.73)	43.04% (29.34 to 56.49)	−1.79 (−1.89 to −1.69)

ASMR, age-standardized mortality rate; ASR, age-standardized rate; CVD, cardiovascular disease; EAPC, estimated annual percentage change; GBD, Global Burden of Disease Study; UI, uncertainty interval. CI, confidence interval.

Table 2. The DALYs burden of cardiovascular disease attributable to kidney dysfunction in 1990 and 2021 and the temporal trends from 1990 to 2021.

	1990		2021		1990–2021	
	DALYs cases	ASR per 100,000	DALYs cases	ASR per 100,000	Percentage change in absolute number	EAPC of ASDR
	No. (95% UI)	ASDR (95% UI)	No. (95% UI)	ASDR (95% UI)	(95% UI)	(95% CI)
Global	27,382,767 (22,234,707 to 32,604,562)	742.17 (597.93 to 879.88)	41,589,861 (33,250,168 to 50,391,379)	489.81 (391.39 to 593.21)	51.88% (42.63 to 61.16)	−1.44 (−1.49 to −1.38)
Sex						
Male	14,419,256 (11,776,217 to 17,390,240)	851.58 (686.58 to 1023.05)	23,400,725 (18,957,319 to 28,292,163)	598.14 (479.64 to 722.15)	62.29% (49.25 to 76.53)	−1.21 (−1.26 to −1.16)
Female	12,963,512 (10,512,759 to 15,397,189)	642.58 (519.51 to 765.26)	18,189,135 (14,493,872 to 21,991,644)	392.51 (312.52 to 473.79)	40.31% (29.62 to 50.8)	−1.70 (−1.77 to −1.64)
SDI						
High SDI	6,040,575 (4,734,655 to 7,346,794)	548.06 (430.57 to 664.63)	4,996,174 (3,868,939 to 6,101,128)	220.4 (173.92 to 266.1)	−17.29% (−22.01 to −13.42)	−3.19 (−3.33 to −3.05)
High-middle SDI	7,734,113 (6,278,656 to 9,257,305)	856.77 (690.3 to 1031.82)	9,374,066 (7,385,967 to 11,581,525)	482.12 (379.01 to 594.29)	21.20% (11.33 to 31.37)	−2.11 (−2.35 to −1.87)
Middle SDI	7,232,671 (5,913,868 to 8,807,282)	750.17 (611.72 to 916.52)	14,321,609 (11,374,183 to 17,448,551)	555.5 (440.55 to 679.88)	98.01% (80.16 to 118.83)	−0.86 (−0.95 to −0.78)
Low-middle SDI	4,761,329 (3,888,546 to 5,718,224)	794.83 (643.62 to 954.95)	9,962,155 (7,933,999 to 12,151,016)	709.62 (559.48 to 858.77)	109.23% (92.18 to 128.94)	−0.32 (−0.36 to −0.28)
Low SDI	1,578,887 (1,272,643 to 1,924,759)	719.83 (575.38 to 878.66)	2,897,404 (2,295,596 to 3,536,080)	597.97 (468.77 to 731.27)	83.51% (66.51 to 101.81)	−0.63 (−0.71 to −0.55)
GBD region						
Andean Latin America	60,076 (47,645 to 73,458)	303.16 (238.57 to 372.33)	103,362 (76,308 to 134,808)	177.54 (130.63 to 230.85)	72.05% (44.25 to 102.49)	−1.95 (−2.27 to −1.63)
Australasia	117,096 (88,488 to 145,807)	508.43 (383.46 to 631.96)	84,425 (64,278 to 104,475)	139.51 (107.13 to 171.93)	−27.90% (−34.37 to −21.55)	−4.41 (−4.53 to −4.29)
Caribbean	159,017 (126,463 to 192,458)	639.2 (505.32 to 776.75)	230,455 (179,859 to 284,647)	424.57 (332.08 to 524.68)	44.92% (28.08 to 62.71)	−1.32 (−1.49 to −1.15)
Central Asia	690,533 (562,160 to 816,067)	1574.74 (1267.28 to 1868.55)	907,358 (726,518 to 1,119,539)	1243.96 (979.87 to 1537.34)	31.40% (19.4 to 43.59)	−1.26 (−1.58 to −0.94)
Central Europe	1,297,312 (1,029,846 to 1,566,449)	934.23 (736.11 to 1129.34)	1,030,031 (802,461 to 1,262,421)	444.98 (348.9 to 543.68)	−20.60% (−26.34 to −14.9)	−2.81 (−2.94 to −2.68)
Central Latin America	425,515 (341,350 to 511,418)	552.5 (437.5 to 663.36)	1,026,820 (790,661 to 1,269,630)	417.92 (320.09 to 518.2)	141.31% (117.53 to 170.62)	−1.1 (−1.33 to −0.87)
Central Sub-Saharan Africa	199,404 (153,235 to 255,411)	957.08 (730.98 to 1235.06)	403,312 (299,366 to 525,070)	807.46 (606.17 to 1044.96)	102.26% (63.54 to 150.12)	−0.76 (−0.82 to −0.69)
East Asia	4,863,738 (3,828,226 to 6,103,356)	631.09 (487.49 to 794.25)	8,452,924 (6,472,391 to 11,082,001)	416.58 (317.97 to 550.67)	73.79% (41.65 to 115.68)	−0.89 (−1.17 to −0.61)
Eastern Europe	3,444,608 (2,700,444 to 4,164,344)	1341.94 (1052.31 to 1614.53)	3,405,204 (2,649,706 to 4,160,629)	968.69 (755.39 to 1183.22)	−1.14% (−8.93 to 7.89)	−1.65 (−2.13 to −1.17)
Eastern Sub-Saharan Africa	357,738 (276,997 to 452,183)	481.45 (374.63 to 608.71)	625,866 (474,235 to 804,065)	379.81 (288.86 to 492.14)	74.95% (47.16 to 101.4)	−0.93 (−0.99 to −0.87)
High-income Asia Pacific	689,395 (534,226 to 857,234)	366.11 (281.03 to 456.93)	678,440 (514,042 to 852,396)	128.42 (100.73 to 159.17)	−1.59% (−10.71 to 6.44)	−3.44 (−3.58 to −3.29)
High-income North America	2,095,464 (1,575,572 to 2,582,591)	578.69 (438.12 to 709.61)	2,019,126 (1,574,084 to 2,478,183)	291.42 (228.2 to 354.8)	−3.64% (−8.89 to 2.28)	−2.56 (−2.73 to −2.38)
North Africa and Middle East	1,845,717 (1,451,690 to 2,295,071)	1149.62 (884.03 to 1419.31)	3,308,381 (2,466,297 to 4,234,067)	770.51 (569.14 to 975.54)	79.25% (60.15 to 98.99)	−1.33 (−1.38 to −1.29)
Oceania	29,446 (22,897 to 38,523)	998.63 (782.43 to 1285.58)	67,692 (51,548 to 87,102)	891.76 (686.65 to 1156.78)	129.88% (91.24 to 182.9)	−0.35 (−0.38 to −0.31)
South Asia	4,233,740 (3,374,568 to 5,221,650)	736.91 (585.48 to 911.41)	9,760,123 (7,530,474 to 12,140,016)	678.71 (520.99 to 835.91)	130.53% (106.24 to 159.32)	−0.22 (−0.3 to −0.13)
Southeast Asia	2,387,972 (1,977,252 to 2,879,496)	943.06 (774.81 to 1144.82)	5,315,809 (4,198,644 to 6,494,351)	822.39 (651.11 to 1002.89)	122.61% (96.81 to 148.59)	−0.43 (−0.51 to −0.35)
Southern Latin America	190,069 (147,551 to 234,157)	432.65 (333.62 to 532.54)	146,957 (111,820 to 180,981)	165.45 (126.13 to 203.86)	−22.68% (−27.22 to −18.21)	−2.84 (−2.96 to −2.72)
Southern Sub-Saharan Africa	149,172 (121,861 to 179,488)	564.09 (453.13 to 678.12)	336,216 (279,990 to 399,826)	620.42 (504.67 to 742.66)	125.39% (106.71 to 154.66)	0.34 (−0.08 to 0.76)
Tropical Latin America	609,765 (509,809 to 721,905)	700.52 (576.95 to 824.96)	788,990 (646,046 to 932,498)	307.55 (250.01 to 364.38)	29.39% (23.25 to 35.45)	−2.66 (−2.73 to −2.58)
Western Europe	2,902,363 (2,256,439 to 3,552,432)	491.11 (385.72 to 598)	1,729,458 (1,336,210 to 2,124,726)	156.51 (123.02 to 191.55)	−40.41% (−45.49 to −36.62)	−3.90 (−4.03 to −3.78)
Western Sub-Saharan Africa	634,626 (516,306 to 777,621)	769.65 (623.31 to 940.52)	1,168,910 (928,608 to 1,434,804)	649.65 (523.69 to 798.64)	84.19% (57 to 117.64)	−0.57 (−0.66 to −0.47)
CVD subcategories						
Ischemic heart disease	16,229,802 (11,947,344 to 20,312,854)	450.95 (328.61 to 568.32)	26,134,286 (18,902,485 to 33,382,272)	309.84 (222.64 to 395.39)	61.03% (50.84 to 70.97)	−1.29 (−1.34 to −1.25)
Lower extremity peripheral arterial disease	251,094 (163,931 to 347,790)	7.66 (5.04 to 10.67)	445,921 (290,812 to 628,215)	5.38 (3.5 to 7.59)	77.59% (68.98 to 86.91)	−1.36 (−1.46 to −1.26)
Stroke	10,901,871 (8,143,322 to 13,924,641)	283.56 (207.22 to 361.93)	15,009,653 (10,939,085 to 19,133,717)	174.59 (127.03 to 222.85)	37.68% (26.56 to 50.17)	−1.68 (−1.77 to −1.59)

ASDR, age-standardized DALYs rate; ASR, age-standardized rate; CVD, cardiovascular disease; DALYs, disability-adjusted life years; EAPC, estimated annual percentage change; GBD, Global Burden of Disease Study; UI, uncertainty interval. CI, confidence interval.

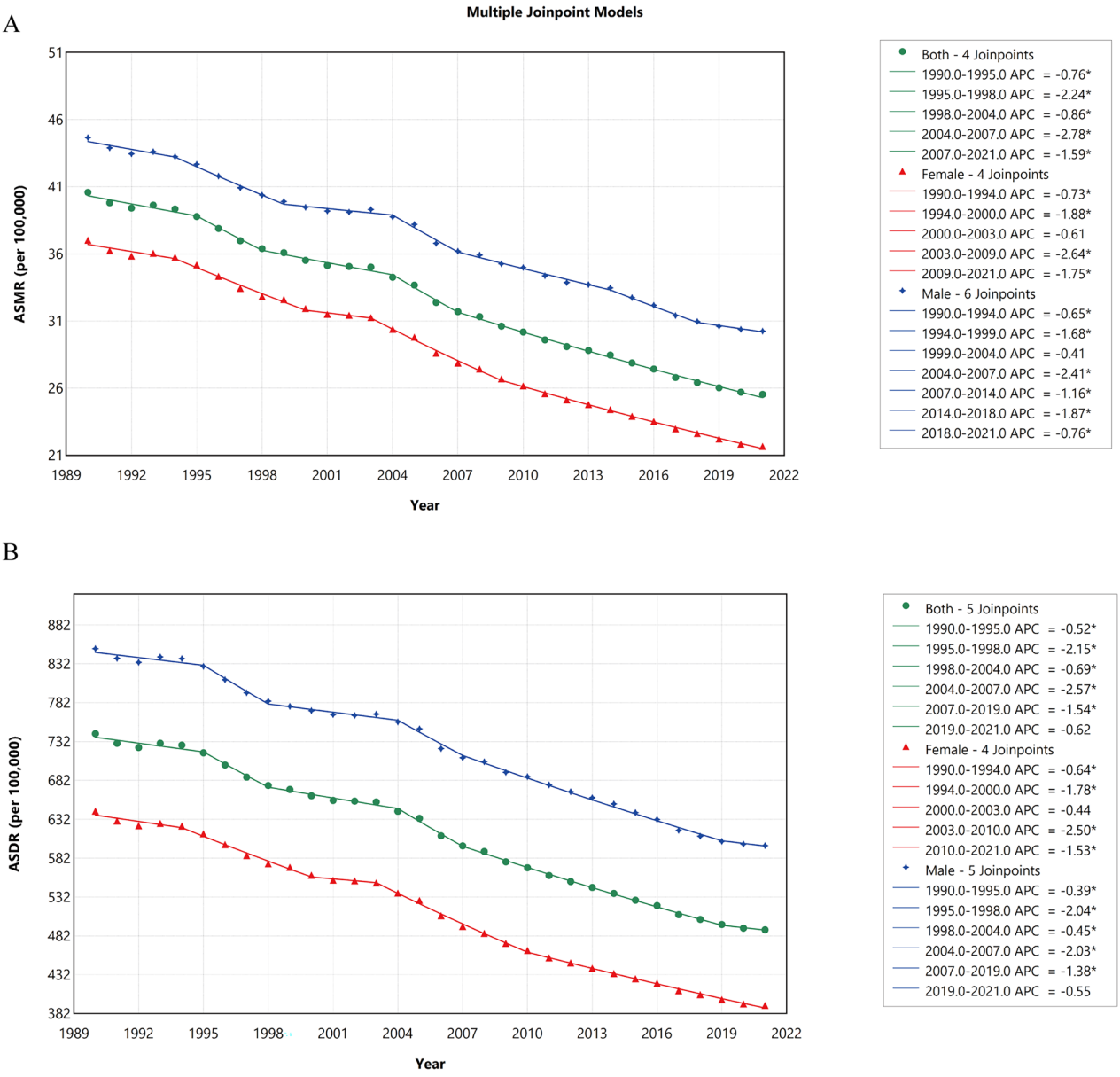

Figure 1. Joinpoint regression analysis of the sex-specific age-standardized mortality (A) and DALYs (B) rate (per 100,000 population) for cardiovascular disease attributable to kidney dysfunction from 1990 to 2021. ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; DALYs, disability-adjusted life years.

29.8/100,000; ASDR 597.97/100,000). In contrast, regions with high SDI exhibited the lowest ASMR and ASDR (ASMR 12.84/100,000; ASDR 220.4/100,000), and regions with high-middle SDI had even lower rates (ASMR 28.2/100,000; ASDR 482.12/100,000). From 1990 to 2021, ASMR and ASDR followed similar trends across the five SDI categories (Tables 1 and 2). Figure 4 illustrates a negative correlation between SDI and both ASMR ($\rho = -0.318$, $p < 0.001$) and ASDR ($\rho = -0.418$, $p < 0.001$) across 21 GBD regions. Notably, ASMR and ASDR trends showed an overall decrease as SDI exceeded 0.7.

However, discrepancies were observed where local trends did not align with SDI quintiles. For instance, in South Asia, ASMR and ASDR remained stable despite increasing SDI. Results in Figure 5 further supports the relationship between ASMR ($\rho = -0.436$, $p < 0.001$) or ASDR ($\rho = -0.505$, $p < 0.001$) and SDI across all countries in 2021. Generally, these rates initially increased with rising SDI up to approximately 0.59, after which they declined with further increases in SDI. Particularly, regions with low-middle to middle SDI (SDI: 0.5–0.7) had the highest KD-related CVD ASMR and ASDR. In countries like Nauru, Turkmenistan, and Uzbekistan, ASMR and ASDR were notably higher than predicted by SDI alone.

Global burden of cardiovascular disease attributable to kidney dysfunction by different geographic regions

In 2021, the regions with the lowest ASMR and ASDR for KD-attributed CVD were high-income Asia Pacific (ASMR

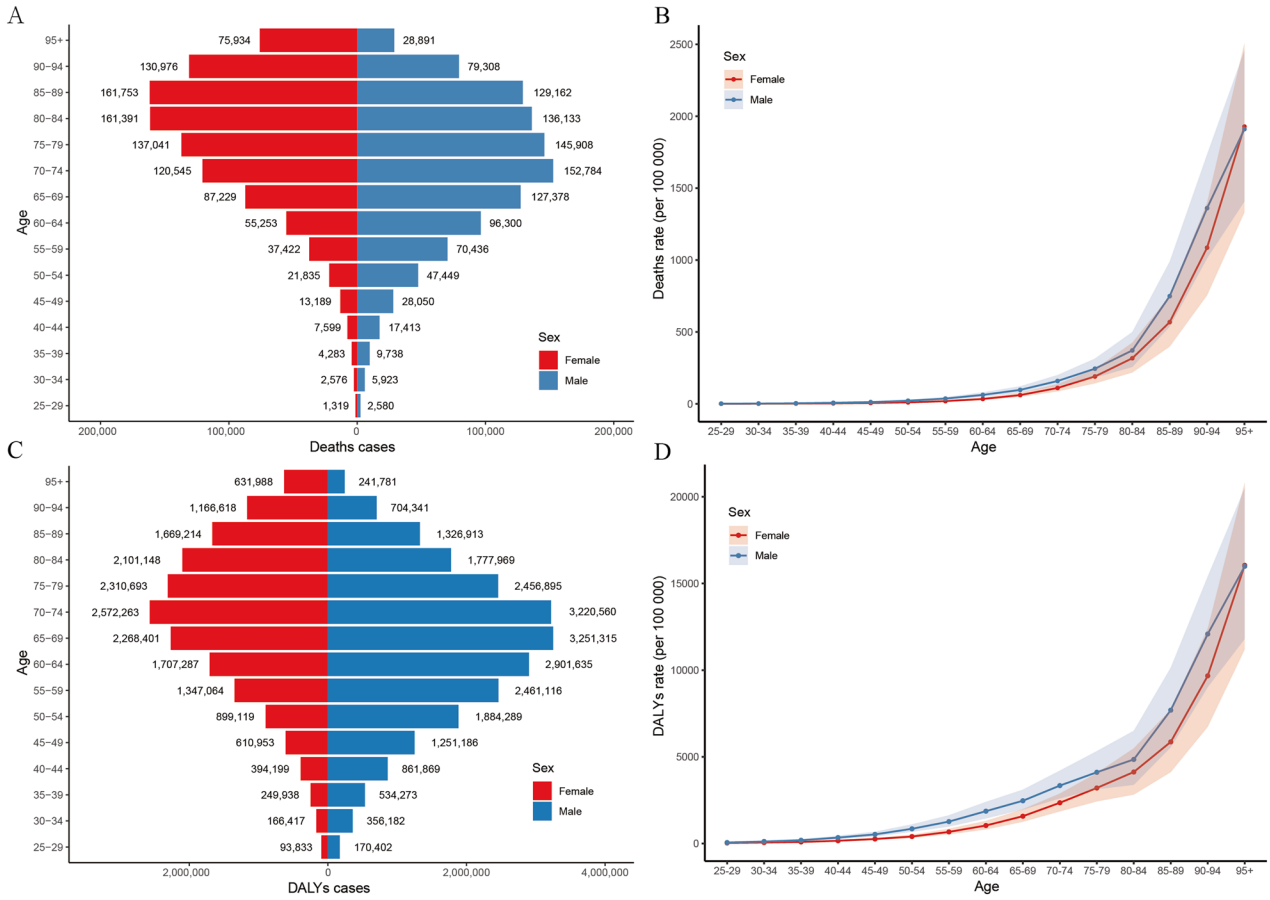

Figure 2. Age-specific numbers and rates of deaths and DALYs of cardiovascular disease attributable to kidney dysfunction by gender, 2021. (A) Age-specific deaths number; (B) Age-specific deaths rate; (C) Age-specific DALYs number; (D) Age-specific DALYs rate. DALYs, disability-adjusted life years.

6.89/100,000; ASDR 128.42/100,000), Southern Latin America (ASMR 9.14/100,000; ASDR 165.45/100,000), Australasia (ASMR 9.64/100,000; ASDR 139.51/100,000), and Western Europe (ASMR 10.27/100,000; ASDR 156.51/100,000). In contrast, regions such as Central Asia (ASMR 70.71/100,000; ASDR 1243.96/100,000), Eastern Europe (ASMR 56.48/100,000; ASDR 968.69/100,000), and Oceania (ASMR 41.27/100,000; ASDR 891.76/100,000) bored the highest burden for the same period (Tables 1 and 2). Notably, East Asia and South Asia reported the highest number of deaths and DALYs associated with KD-related CVD in 2021. Between 1990 and 2021, the largest increases in deaths and DALYs related to KD-attributed CVD were observed in South Asia and Central Latin America (Tables 1 and 2).

In 2021, among 204 countries or territories, San Marino (ASMR 5.67/100,000; ASDR 92.46/100,000) and France (ASMR 6.3/100,000; ASDR 97.37/100,000) displayed the lowest ASMR and ASDR for KD-related CVD and France. Conversely, the highest ASMR and ASDR were recorded in Nauru (ASMR 96.88/100,000; ASDR 2,268.19/100,000) and Turkmenistan (ASMR 91.46/100,000; ASDR 1,720.8/100,000) (Supplementary material, Tables S2 and S3; Figure 6). Significant reductions in ASMR and ASDR from 1990 to 2021 were observed in countries such as Israel, Denmark, Republic of Korea, Portugal, and Estonia. In contrast, Lesotho and Zimbabwe had the most significant increases (Supplementary material, Tables S2 and S3, Figure S1). Notably, China and India reported the highest numbers of deaths and DALYs due to KD-related CVD in 2021 (Supplementary material, Tables S2 and S3, Figure S2). Meanwhile, Djibouti and Honduras showed the most substantial increase in death cases and DALYs from 1990 to 2021 (Supplementary material, Tables S2 and S3).

Global trends of cardiovascular disease attributable to kidney dysfunction predicted by the BAPC model

Overall, the ASMR and ASDR of KD attributable to CVD are predicted to decline from 2022 to 2050 for both sexes. However, sex differences persist, with men experiencing a greater disease burden than women. Globally, ASMR is expected to decrease by approximately 26.8 per 100,000 population in men and 16.7 per 100,000 population in women. Similarly, ASDR is predicted to decline to 571.3 per 100,000 for men and 335.2 per 100,000 for women (Figure 7).

Discussion

Current study provides a comprehensive assessment of global CVD trends attributed to KD across various geographic regions and countries. It also projects trends from 2022 to 2050. While absolute deaths and DALYs from KD-related CVD

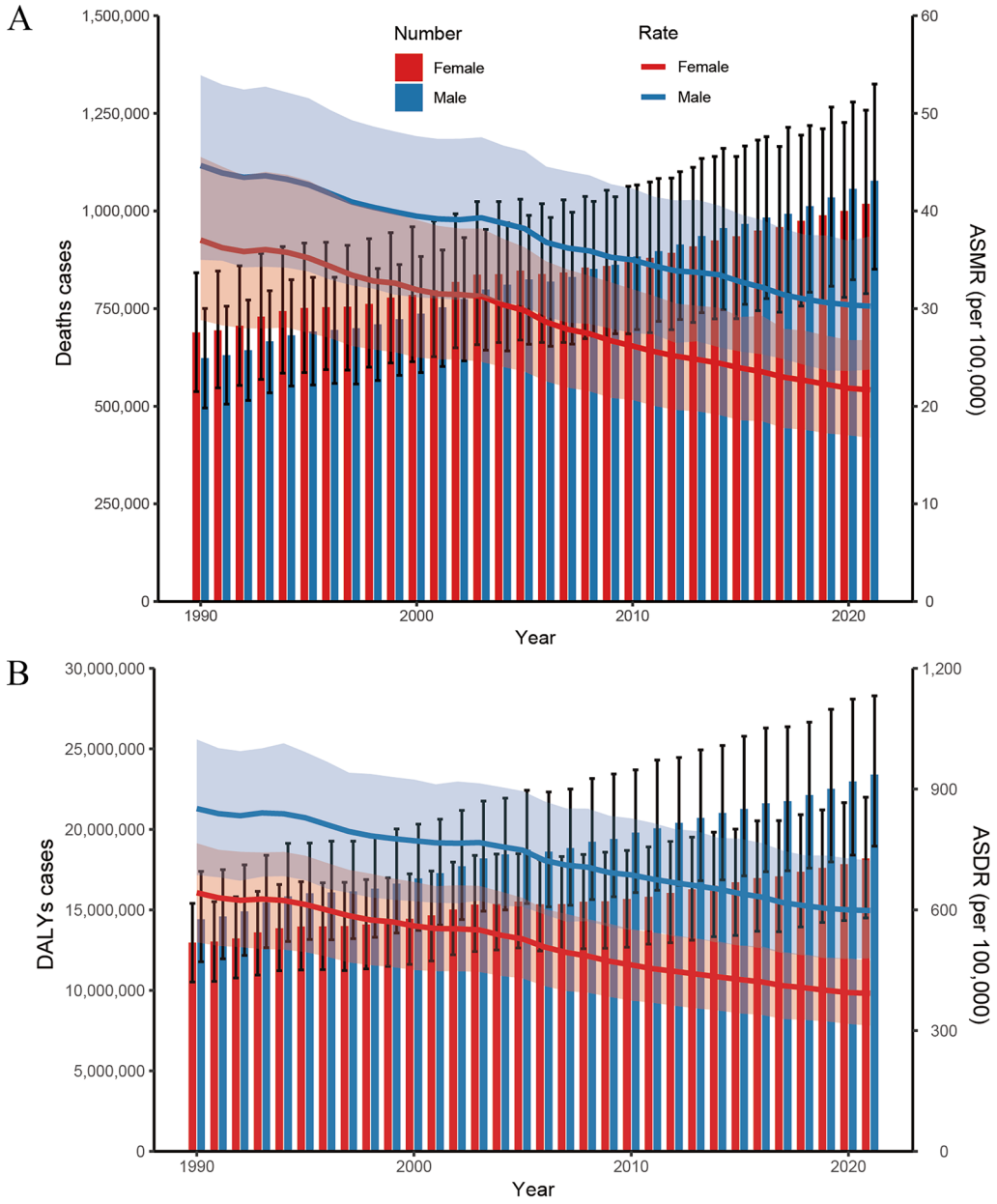

Figure 3. Temporal trends in deaths (A) and DALYs (B) number and age-standardized rate (per 100,000 population) for cardiovascular disease attributable to kidney dysfunction by sex from 1990 to 2021. ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; DALYs, disability-adjusted life years.

increased, the ASMR and ASDR decreased between 1990 and 2021. In 2021, ischemic heart disease and stroke were the leading contributors to the global CVD burden from KD. Males consistently experienced a higher burden of KD-related CVD than females. Furthermore, older populations have higher CVD burdens than younger populations. Across various SDI regions, the ASMR and ASDR exhibited similar trends, with notable changes in high SDI areas. In 2021, low SDI regions recorded the highest ASMR and ASDR, while high SDI regions had the lowest. From 1990 to 2021, high SDI regions saw declines in both mortality and DALYs, unlike the increases observed in other regions. Significant geographic disparities exist, with Central Asia exhibiting the highest ASMR and ASDR, while the High-income Asia Pacific region has the lowest. In 2021, San Marino and France reported the lowest ASMR and ASDR, while Nauru and Turkmenistan had the highest. Over the next thirty years, the incidence to KD-related CVD is expected to decline, though men will continue to experience a greater disease burden than women. To mitigate this burden, particularly among males, the elderly, and population in the lower SDI regions, targeted strategies are essential.

Extensive epidemiologic and clinical research has established a clear relationship between KD and the incidence and mortality of CVD [18,19]. As a vital excretory organ, kidney maintains homeostasis and contributes to drug metabolism. Globally, approximately 861 million individuals worldwide are affected by KD [20]. The estimated glomerular filtration rate

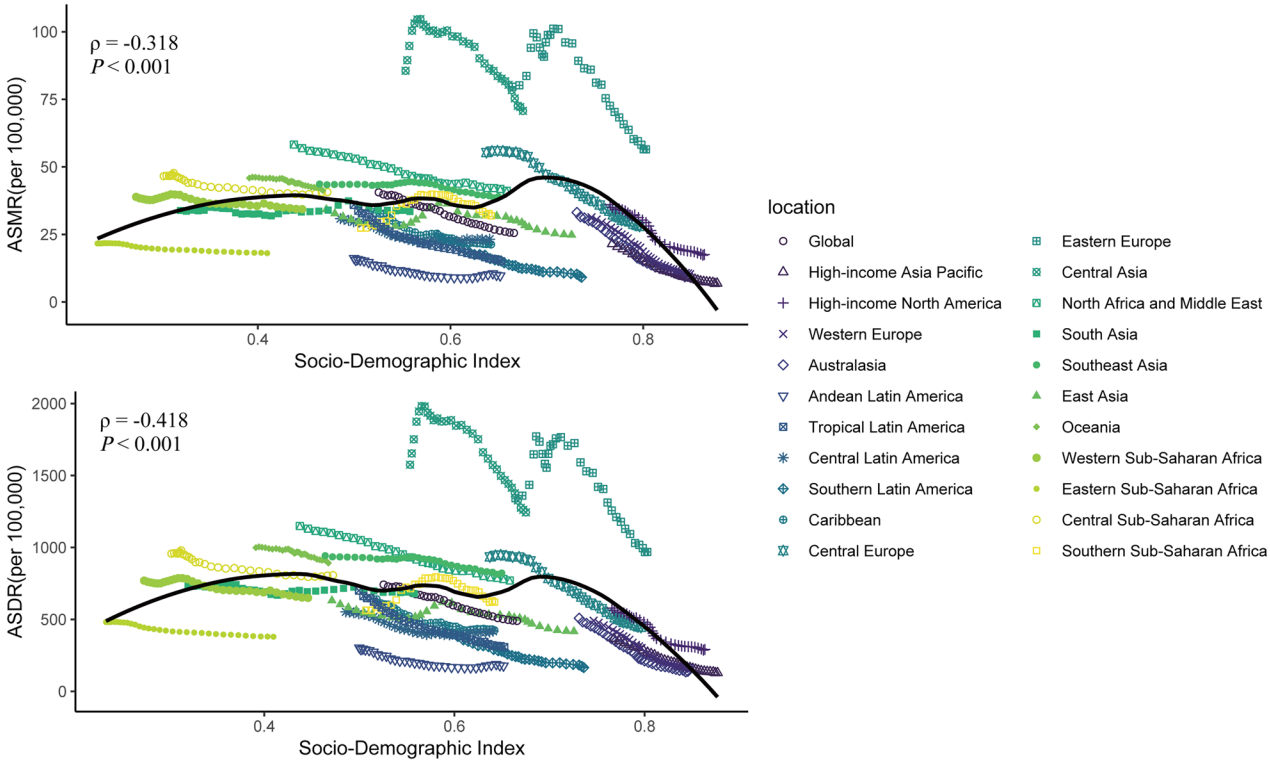

Figure 4. The global age-standardized mortality and DALYs rate (per 100,000 population) for cardiovascular disease attributable to kidney dysfunction by SDI across 21 GBD regions for both sexes from 1990 to 2021. The ρ indices and *P*-values were derived from Pearson's correlation analysis. The black line indicated the value for all areas based on estimates from 1990 to 2021. For each region, points from left to right depict estimates for each year from 1990 to 2021. ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; DALYs, disability-adjusted life years; SDI, Socio-Demographic index.

(eGFR) is a key metric for evaluating kidney function and is independently associated with CVD incidents and overall mortality. Notably, CVD incidence increases as eGFR decreases [19]. When eGFR falls below 60 mL/min/1.73 m^2, the age-adjusted rate of cardiovascular events increases with further eGFR reductions [21]. Analysis of data from the National Health and Nutrition Examination Survey (NHANES) II revealed that an initial eGFR of <70 mL/min/1.73 m^2 was associated with a 51% higher adjusted risk of cardiovascular mortality than an eGFR of ≥90 mL/min/1.73 m^2 [22].

Our recent study have revealed a significant increase in global mortality and DALYs associated with KD-related CVD between 1990 and 2021. This increase is primarily driven by rapid population expansion and an aging demographic. Conversely, there has been a slight decline in global age-standardized mortality and disability rates, likely due to age standardization reflecting demographic structure adjustments. This trend may also indicate advancements in healthcare provision, preventive strategies, and disease management.

Age-specific analysis shows that mortality and DALYs due to KD-related CVD rise with increasing age. Elderly individuals exhibit higher rates than younger populations, consistent with previous studies [23]. This pattern largely results from older patients experiencing multiple comorbidities. Over a lifetime, the accumulation of cardiovascular risk factors adversely impacts their health. These factors, both modifiable or non-modifiable, are diverse and often associated with metabolic comorbidities prevalent in older adults [24]. Age is inherently a non-modifiable risk factor [25]. Furthermore, older adults often use medications that might further worsen kidney function. Behavioral and metabolic factors, such as physical activity and dietary intake, are also crucial in aging populations [26]. Interestingly, although the absolute number of deaths and DALYs is lower in men over 80 compared to women, the rates are higher for men. This discrepancy may be due to women's longer life expectancy [27]. Cardiovascular disease remains a leading cause of disability and mortality among the elderly, highlighting the need for early disease detection and management of risk factors to delay disease onset or progression.

Our gender analysis reveals that male bear a greater burden of CVD attributable to KD than females. This disparity arises a mix of biological, behavioral, and sociocultural factors. Biologically, estrogen protects women by interacting with both the classic estrogen receptor and the G protein-coupled estrogen receptor [28]. Beyond hormonal influences, sex-specific regulation of cardiometabolic processes, particularly *via* SRY regulation, significantly impacts variations in cardiovascular disease risk [28]. Behaviorally, men tend to have higher levels of risk factors such as smoking, obesity, hypertension, and elevated blood sugar [29,30]. Despite variations in the burden of KD-related CVD among different age and sex groups, it remains a significant health issue among the older adults globally. Hence, implementing

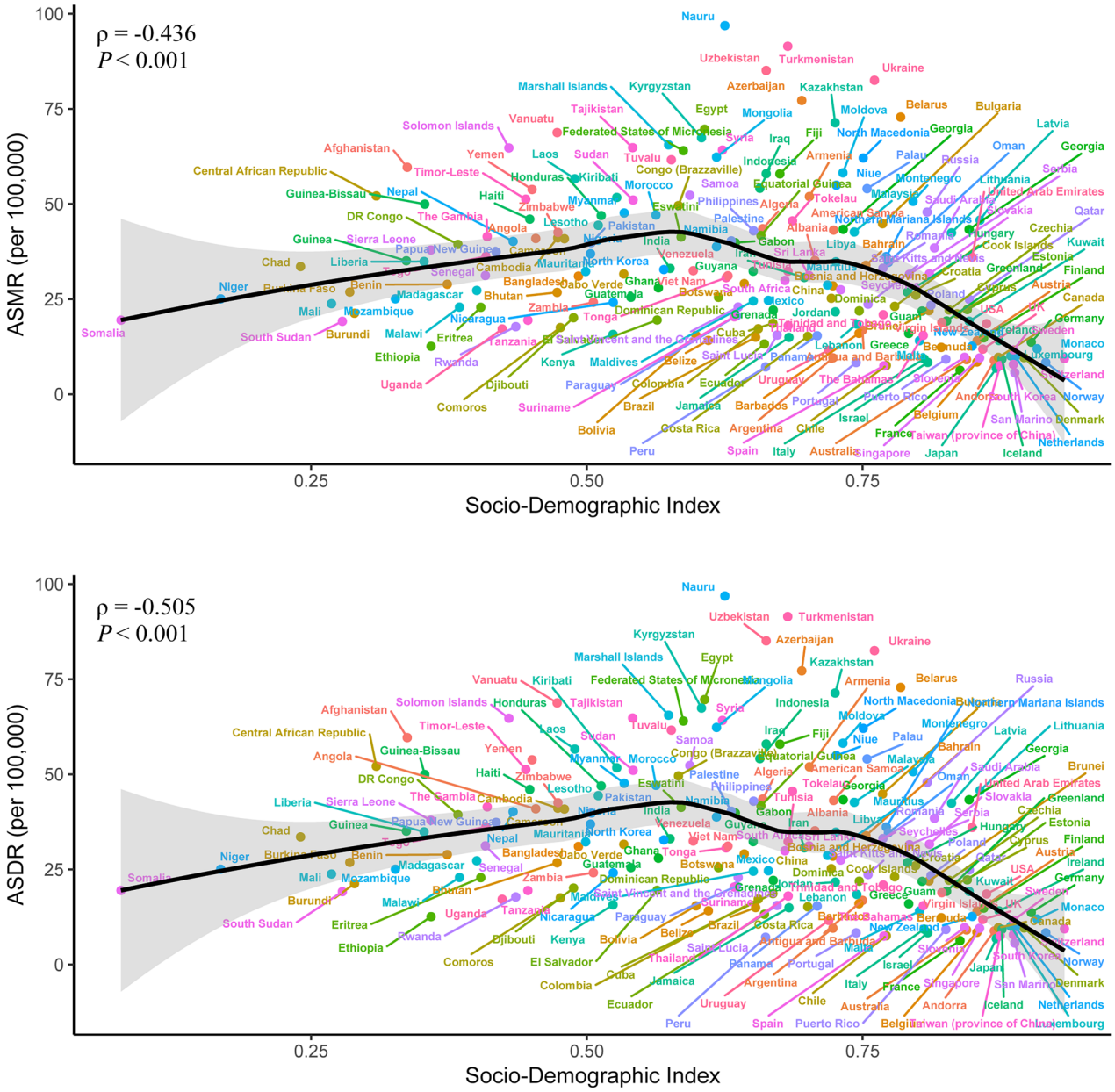

Figure 5. The global age-standardized mortality and DALYs rate (per 100,000 population) for cardiovascular disease attributable to kidney dysfunction by SDI across 204 countries and territories in 2021. The black line represents an adaptive association obtained by fitting adaptive Loess regression using all available data points. ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; DALYs, disability-adjusted life years; SDI, Socio-Demographic index.

sex-responsive programs to address KD-related CVD in older populations is essential.

Moreover, our analysis of geographic location and socio-economic status revealed significant variations in the burden and trends of KD-related CVD. These differences likely result from demographic disparities and variations in healthcare access and quality, which are influenced by socioeconomic development [31]. Over the past three decades, mortality and DALYs from KD-related CVD rose by 59.69% and 51.88%, respectively. Between 1990 and 2021, 47 countries, mainly in high SDI regions, showed substantial reductions in these metrics. Conversely, regions with lower SDI experienced rising mortality and DALYs. For example, countries like Djibouti and Honduras, located in Eastern Sub-Saharan Africa and Central Latin America, respectively, reported the largest increases. Since 1990, 30 countries have recorded significant increases in both ASMR and ASDR for KD-related CVD. In 2021, the highest ASMR and ASDR, alongside with notable increases since 1990, were found in low to middle SDI regions. Conversely, the lowest ASMR and ASDR in 2021 and their significant declines since 1990 were observed in high-middle and high SDI regions. A previous study revealed that regions in Europe and Central Asia have CVD death rates over twice as high as those in high-income countries [32].

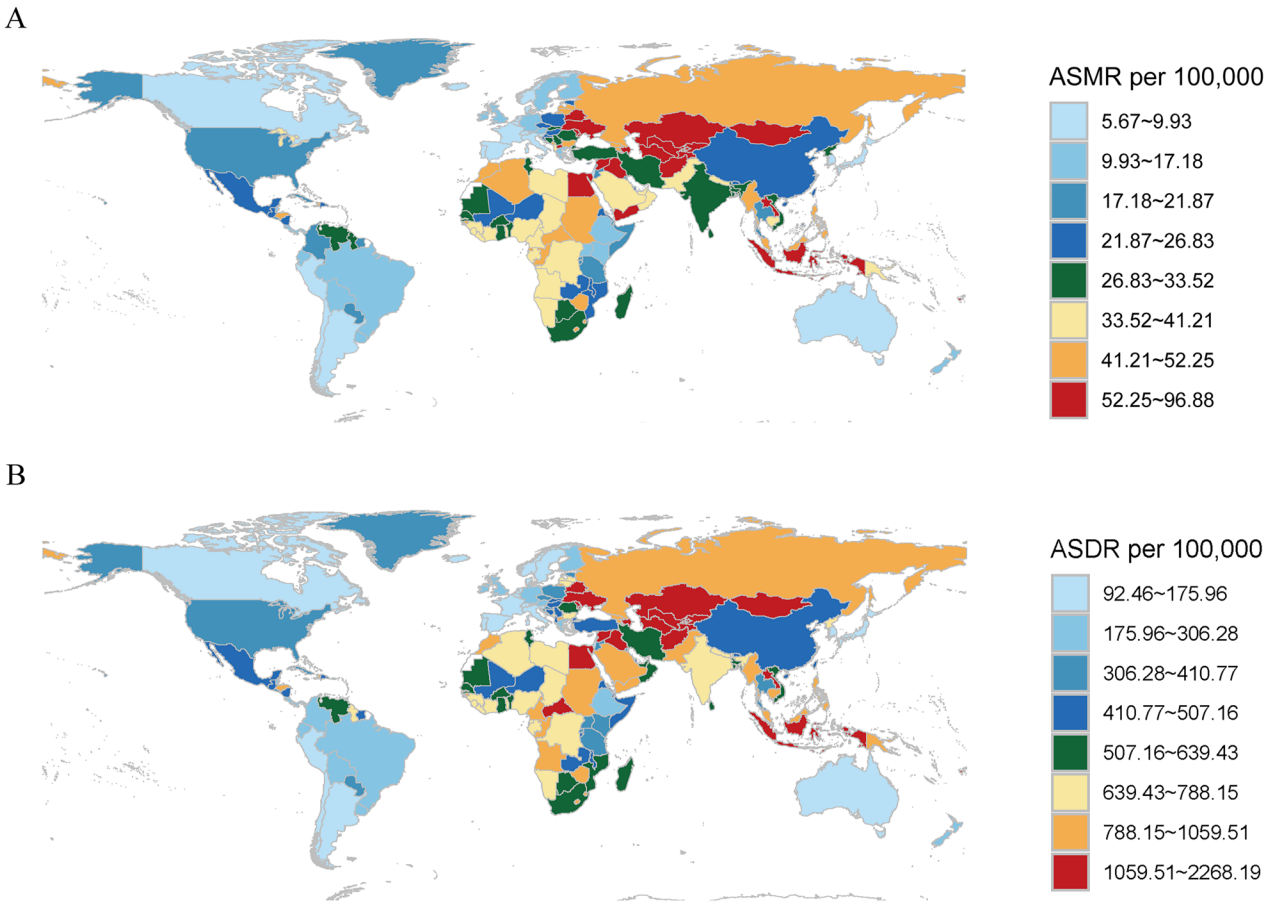

Figure 6. The global age-standardized mortality (A) and DALYs (B) rate (per 100,000 population) for cardiovascular disease attributable to kidney dysfunction in 204 countries and territories in 2021. ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; DALYs, disability-adjusted life years.

This emphasizes the ongoing health disparities across different socioeconomic settings. Patients in underdeveloped regions faced challenges due to insufficient diagnoses and limited treatment choices. Conversely, high SDI areas benefit from superior healthcare resources, effective health services, and robust social support, all of which are crucial protective factors against KD-related CVD. This results in a reduced burden of disease. Our study highlights that areas like Eastern Europe, East Asia, South Asia, Southeast Asia, and Central Asia continue to be significantly impacted by KD-related CVD. Given that half of the global population resides in Asia, addressing CVD in this region is a critical global health concern. Our research highlights a significant geosocioeconomic disparity in mortality and DALYs burden of KD-related CVD. Developing or lower-income nations are increasingly confronted with challenges from CVD and its associated risk factors. The Prospective Urban and Rural Epidemiological study, which examined data from over 150,000 participants in developing nations, revealed an intriguing pattern: individuals in low-income areas had the lowest cardiovascular risk yet exhibited the highest incidence and case-fatality rates of CVD. This finding] starkly contrast with trends observed in high-income countries [33]. This discrepancy can be attributed to several factors prevalent in low-income countries, including a lack of health awareness, infrequent medical checkups, and inadequate medical resources and skilled nephrologists [7]. These findings underscore the importance of implementing targeted, systematic, and effective interventions to manage CVD risk in low- to middle-income regions. Such measures include personal health education, regular kidney function screening, early initiation of renal protective therapies, and effective treatment of primary diseases affecting kidney function [34]. Furthermore, enhancing healthcare workers' knowledge of KD treatments, providing medical consultations, and educating the public about the risks of KD in underdeveloped nations are essential actions [35,36].

Limitations

A systemic and comprehensive assessment of the global CVD burden attributable to KD has been largely unexplored in previous studies. This research address this gap by providing a systematic and timely evaluation using the GBD2021 database. Notably, it is the first study to evaluate the CVD burden attributable to KD worldwide, analyzing variables such as age, gender, nation, and SDI regions quantified by deaths and DALYs, while also employing the BAPC model to forecast trends from 2022 to 2050. However, our study encounters

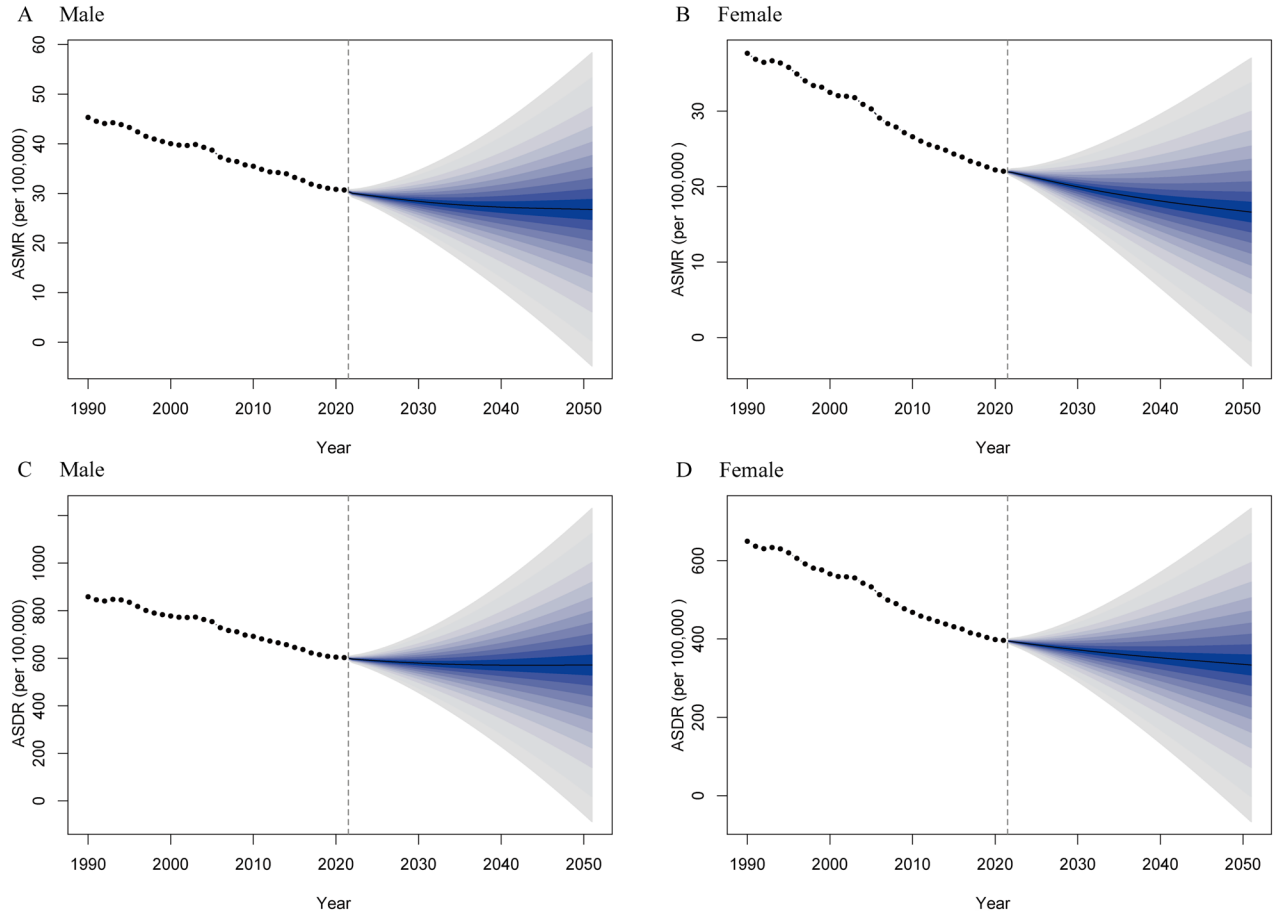

Figure 7. Global trends of cardiovascular disease attributable to kidney dysfunction in age-standardized mortality (A, B) and DALYs (C, D) rates (per 100,000 population) from 2021 to 2050 by sex predicted by BAPC models: observed (dashed lines) and predicted rates (solid lines). The blue region means the upper and lower limits of the 95% UIs. ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life years rate; BAPC: Bayesian age-period-cohort; DALYs, disability-adjusted life years; UIs: Uncertainty interval.

several limitations. First, similar to other GBD studies, the analysis is constrained by data availability in certain regions, particularly those with lower SDI [37]. Second, the GBD study does not differentiate between acute kidney injury and chronic kidney dysfunction, which limits our ability to assess their distinct impacts. Third, while the data obtained from the GBD database is robust and considered reliable, the absence of original, individual-level illness burden data remains a limitation. Fourth, the age-related data presentation is influenced by the characteristics of the GBD database. The database does not independently report data for age groups under 25 years and lacks granular details for further division. Consequently, our ability to provide a detailed age-specific analysis for the younger population is limited.

Conclusions

In conclusion, CVD attributable to KD remains a major global public health challenge, particularly affecting males, the elderly, and regions with lower SDI. The primary contributors to this burden are ischemic heart disease and stroke. The observed variations in the spatial and temporal trends of CVD burden attributable to KD highlight the necessity for tailored healthcare strategies in different regions. Our findings offer valuable insights for public health policymakers to formulate strategies to prevent and mitigate the CVD burden linked to KD.

Acknowledgments

We acknowledged the participants and investigators for making the GBD data available.

Author contributions

Tian Zhang: Data curation, Investigation, Methodology, Software, Formal analysis, and Writing – original draft. Ting Li: Investigation, Methodology, Software, Formal analysis. Pengfei Jin: Conceptualization, Methodology, Supervision, Validation, and Writing – review & editing.

Consent for publication

All authors read and approved the manuscript for publication.

Ethics approval and consent to participate

This study was based on publicly available data; therefore, further ethical review was not required.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was financially supported by the Capital Funds for Health Improvement and Research (CFH) (2024-1-4052) and, the National Health Commission Clinical Research Projects for Innovative Drugs (WKZX2023CX210007).

Data availability statement

The data used in this study were sourced from the Global Health Data Exchange (GHDx) query tool (https://ghdx.healthdata.org/gbd-2021). The data are available from the corresponding author (Dr. Pengfei Jin) on reasonable request.

References

[1] Li Y, Cao G, Jing W, et al. Global trends and regional differences in incidence and mortality of cardiovascular disease, 1990 – 2019: findings from 2019 global burden of disease study. Eur J Prev Cardiol. 2023;30(3):276–286. doi: 10.1093/eurjpc/zwac285.

[2] Roth GA, Mensah GA, Johnson CO, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019. J Am Coll Cardiol. 2020;76(25):2982–3021. doi: 10.1016/j.jacc.2020.11.010.

[3] Wadhera RK, Figueroa JF, Rodriguez F, et al. Racial and ethnic disparities in heart and cerebrovascular disease deaths during the COVID-19 pandemic in the United States. Circulation. 2021;143(24):2346–2354. doi: 10.1161/CIRCULATIONAHA.121.054378.

[4] Mangione CM, Barry MJ, Nicholson WK, et al. Behavioral counseling interventions to promote a healthy diet and physical activity for cardiovascular disease prevention in adults without cardiovascular disease risk factors. JAMA. 2022;328(4):367–374. doi: 10.1001/jama.2022.10951.

[5] Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular disease. Hypertension. 2003;42(5):1050–1065. doi: 10.1161/01.HYP.0000102971.85504.7c.

[6] van der Velde M, Matsushita K, Coresh J, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. Kidney Int. 2011;79(12):1341–1352. doi: 10.1038/ki.2010.536.

[7] Zhang S, Ren H-F, Du R-X, et al. Global, regional, and national burden of kidney dysfunction from 1990 to 2019: a systematic analysis from the global burden of disease study 2019. BMC Public Health. 2023;23(1):1218. doi: 10.1186/s12889-023-16130-8.

[8] Ene-Iordache B, Perico N, Bikbov B, et al. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. Lancet Glob Health. 2016;4(5):e307–e319. doi: 10.1016/S2214-109X(16)00071-1.

[9] Yu Y, Zhang M, Tang Y, et al. Global disease burden attributable to kidney dysfunction, 1990–2019: a health inequality and trend analysis based on the global burden of disease study. Diabetes Res Clin Pract. 2024;215:111801. doi: 10.1016/j.diabres.2024.111801.

[10] Braunwald E. Diabetes, heart failure, and renal dysfunction: the vicious circles. Prog Cardiovasc Dis. 2019;62(4):298–302. doi: 10.1016/j.pcad.2019.07.003.

[11] Chen J, Li C, Bu CLN, et al. Global burden of non-communicable diseases attributable to kidney dysfunction with projection into 2040. Chin Med J (Engl). 2024. Epub ahead of print. doi: 10.1097/CM9.0000000000003143.

[12] Augustine J. Kidney transplant: new opportunities and challenges. Cleve Clin J Med. 2018;85(2):138–144. doi: 10.3949/ccjm.85gr.18001.

[13] Chawla LS, Eggers PW, Star RA, et al. Acute kidney injury and chronic kidney disease as interconnected syndromes. N Engl J Med. 2014;371(1):58–66. doi: 10.1056/NEJMra1214243.

[14] Geng T, Xu W, Gao H, et al. Relationship between control of cardiovascular risk factors and chronic kidney disease progression, cardiovascular disease events, and mortality in Chinese adults. J Am Coll Cardiol. 2024;84(14):1313–1324. doi: 10.1016/j.jacc.2024.06.041.

[15] Bai J, Cui J, Shi F, et al. Global epidemiological patterns in the burden of main non-communicable diseases, 1990–2019: relationships with socio-demographic index. Int J Public Health. 2023;68:1605502. doi: 10.3389/ijph.2023.1605502.

[16] Khan Minhas AM, Sedhom R, Jean ED, et al. Global burden of cardiovascular disease attributable to smoking, 1990–2019: an analysis of the 2019 Global Burden of Disease Study. Eur J Prev Cardiol. 2024;31(9):1123–1131. doi: 10.1093/eurjpc/zwae040.

[17] Shi L, Bao C, Wen Y, et al. Analysis and comparison of the trends in burden of rheumatic heart disease in China and worldwide from 1990 to 2019. BMC Cardiovasc Disord. 2023;23(1):517. doi: 10.1186/s12872-023-03552-w.

[18] Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004;351(13):1296–1305. doi: 10.1056/NEJMoa041031.

[19] Matsushita K, Coresh J, Sang Y, et al. Estimated glomerular filtration rate and albuminuria for prediction of cardiovascular outcomes: a collaborative meta-analysis of individual participant data. Lancet Diabetes Endocrinol. 2015;3(7):514–525. doi: 10.1016/S2213-8587(15)00040-6.

[20] Jager KJ, Kovesdy C, Langham R, et al. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. Kidney Int. 2019;96(5):1048–1050. doi: 10.1016/j.kint.2019.07.012.

[21] Go AS. Cardiovascular disease consequences of CKD. Semin Nephrol. 2016;36(4):293–304. doi: 10.1016/j.semnephrol.2016.05.006.

[22] Muntner P, He J, Hamm L, et al. Renal insufficiency and subsequent death resulting from cardiovascular disease

in the United States. J Am Soc Nephrol. 2002;13(3):745–753. doi: 10.1681/ASN.V133745.

[23] Dong J, Zhang Z, Sun J, et al. The cardiovascular disease burden attributable to kidney dysfunction from 1990 to 2021: an age-period-cohort analysis of the Global Burden of Disease study. Eur Heart J Qual Care Clin Outcomes. 2024. Epub ahead of print. doi: 10.1093/ehjqcco/qcae088.

[24] Balakumar P, Maung-U K, Jagadeesh G. Prevalence and prevention of cardiovascular disease and diabetes mellitus. Pharmacol Res. 2016;113(Pt A):600–609. doi: 10.1016/j.phrs.2016.09.040.

[25] Marian AJ, Bhatnagar A, Bolli R, et al. Introduction to cardiovascular aging compendium. Circ Res. 2018;123(7):737–739. doi: 10.1161/CIRCRESAHA.118.313940.

[26] Wilkinson TJ, Miksza J, Zaccardi F, et al. Associations between frailty trajectories and cardiovascular, renal, and mortality outcomes in chronic kidney disease. J Cachexia Sarcopenia Muscle. 2022;13(5):2426–2435. doi: 10.1002/jcsm.13047.

[27] Li X-Y, Kong X-M, Yang C-H, et al. Global, regional, and national burden of ischemic stroke, 1990–2021: an analysis of data from the global burden of disease study 2021. EClinicalMedicine. 2024;75:102758. doi: 10.1016/j.eclinm.2024.102758.

[28] Ghaffari S, Naderi Nabi F, Sugiyama MG, et al. Estrogen inhibits LDL (low-density lipoprotein) transcytosis by human coronary artery endothelial cells via GPER (G-protein-coupled estrogen receptor) and SR-BI (scavenger receptor class B type 1). Arterioscler Thromb Vasc Biol. 2018;38(10):2283–2294. doi: 10.1161/ATVBAHA.118.310792.

[29] Briganti EM, Branley P, Chadban SJ, et al. Smoking is associated with renal impairment and proteinuria in the normal population: the AusDiab kidney study. Australian Diabetes, Obesity and Lifestyle Study. Am J Kidney Dis. 2002;40(4):704–712. doi: 10.1053/ajkd.2002.35677.

[30] Maric-Bilkan C. Sex differences in micro- and macro-vascular complications of diabetes mellitus. Clin Sci (Lond). 2017;131(9):833–846. doi: 10.1042/CS20160998.

[31] Jiang S, Yu T, Di D, et al. Worldwide burden and trends of diabetes among people aged 70 years and older, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Diabetes Metab Res Rev. 2024;40(3):e3745. doi: 10.1002/dmrr.3745.

[32] Lenfant C. Can we prevent cardiovascular diseases in low- and middle-income countries? Bull World Health Organ. 2001;79(10):980–982. discussion 983–7.

[33] Yusuf S, Rangarajan S, Teo K, et al. Cardiovascular risk and events in 17 low-, middle-, and high-income countries. N Engl J Med. 2014;371(9):818–827. doi: 10.1056/NEJMoa1311890.

[34] Tonelli M, Agarwal S, Cass A, et al. How to advocate for the inclusion of chronic kidney disease in a national noncommunicable chronic disease program. Kidney Int. 2014;85(6):1269–1274. doi: 10.1038/ki.2012.488.

[35] Bruno A, Galbraith K, McKinnon R. Global supply of health professionals. N Engl J Med. 2014;370(23):2246. doi: 10.1056/NEJMc1404326.

[36] Sayed S, Cherniak W, Lawler M, et al. Improving pathology and laboratory medicine in low-income and middle-income countries: roadmap to solutions. Lancet. 2018;391(10133):1939–1952. doi: 10.1016/S0140-6736(18)30459-8.

[37] Dong X-J, Zhang X-Q, Wang B-B, et al. The burden of cardiovascular disease attributable to high fasting plasma glucose: findings from the global burden of disease study 2019. Diabetes Metab Syndr. 2024;18(5):103025. doi: 10.1016/j.dsx.2024.103025.