

RESEARCH

Open Access



Global, regional, and national burden of chronic kidney disease and its underlying etiologies from 1990 to 2021: a systematic analysis for the Global Burden of Disease Study 2021

Ling Deng^{1†}, Shujin Guo¹, Yuping Liu¹, Yaojia Zhou², Youren Liu¹, Xiaoxia Zheng¹, Xijie Yu^{3*} and Ping Shuai^{1*}

Abstract

Background We aimed to investigate global, regional, and national burden of chronic kidney disease (CKD) and its underlying etiologies from 1990 to 2021.

Methods We summarized the results of the Global Burden of Disease (GBD) 2021 to derive the disease burden of CKD by considering four distinct types of epidemiological data, namely incidence, prevalence, mortality, and disability-adjusted life years (DALYs). The Joinpoint regression analysis, which is skilled in calculating annual percentage change (APC) and average annual percentage change (AAPC), was used to estimate global trends for CKD from 1990 to 2021.

Results The age-standardized mortality rate (ASMR) and age-standardized DALYs rate of CKD were more prominent in regions with Low and Low-middle socio-demographic index (SDI) quintiles. From 1990 to 2021, the countries with the largest increases in ASMR were Ukraine. Globally, the most common cause of death for CKD was type 2 diabetes mellitus (T2DM), while the most common cause of prevalence, incidence, and DALYs was the other and unspecified causes. The main causes of death and DALYs from CKD varied in different parts of the world. The disease burden of CKD increased with age. In most age groups, the global prevalence and incidence of CKD were higher in females than males. At all ages, the global mortality rate and DALYs rate of CKD were higher in males compared to females. Joint point regression analysis found that from 1990 to 2021 the global age-standardized prevalence rate (ASPR) revealed a downward trend, while age-standardized incidence rate (ASIR), ASMR, and age-standardized DALYs rate showed an upward trend, with the most notable increase in ASMR during the 1997–2000 period and in age-standardized DALYs rate during the 1996–2003 period.

Conclusions The study unveiled the uneven global distribution of the burden of CKD and its attributable causes. From 1990 to 2021, an increase in the burden of incidence, mortality, and DALYs due to CKD was observed. Population

[†]Ling Deng and Shujin Guo these authors share the first authorship.

*Correspondence:

Xijie Yu

xijieyu@hotmail.com

Ping Shuai

8369898@qq.com

Full list of author information is available at the end of the article



growth and aging will contribute to a further increase in the burden of CKD. Healthcare providers should develop health policies, and optimize the allocation of medical resources, based on age, sex, region, and disease type.

Keywords Chronic kidney disease, Global burden of disease study, Etiology, Age and gender distribution, Time trend

Introduction

Chronic kidney disease (CKD) is a progressive disease characterized by changes in the structure and function of the kidneys for various reasons [1]. CKD is generally defined as decreased estimated glomerular filtration rate (eGFR) (<60 mL/min/1.73 m²) or markers of kidney injury, such as proteinuria, hematuria, or abnormalities detected through renal biopsy or imaging that are present for at least 3 months [2]. The global burden of CKD is substantial and growing. In 2017, 697.5 million cases of all-stage CKD were recorded, with a global prevalence of 9.1%. Since 1990, the global all-age prevalence of CKD has increased by 29.3%. Globally, in 2017, 1.2 million people died from CKD. Between 1990 and 2017, the global all-age mortality for CKD increased by 41.5% [3]. CKD imposes a substantial financial burden on global healthcare systems. In 2021, the prevalence of CKD among American Medicare beneficiaries over the age of 65 is 13.5%, but this group accounts for a quarter (\$76.8 billion) of total Medicare spending. [4] Worryingly, the costs associated with CKD in the America increased by 40% between 2011 and 2021. [4] In China, with the expected rise in the prevalence of CKD, the total economic burden of CKD is projected to increase from \$179 billion in 2019 to \$198 billion in 2025 [5]. Globally, similar cost increases are expected. Furthermore, CKD leads to premature death, disability, lower quality of life, and other psychosocial harms, and imposes high costs on governments, patients, and their families [6]. The World Health Organization (WHO) has classified CKD as a major global health concern and included it in the assessment of the Global Burden of Disease (GBD) (<https://www.healthdata.org/>).

The primary causes of CKD vary by setting, with those that are common and well-studied, such as diabetes, hypertension, and glomerulonephritis. Still, the causes of CKD are not fully understood [7]. For instance, CKD of unknown etiology and no known treatment has been found in some farming communities in South Asia and Central America; Recurring volume losses are presumed to be a cause, particularly the increasing frequency of heat waves linked to climate change [8]. This possible reason for CKD highlights the potential role of adequate hydration as a renal protection strategy. In developing countries, factors such

as HIV infection [9], and exposure to toxins, or heavy metals [10] also play an additional role. In some parts of the world where the burden of CKD is particularly high, the cause remains unknown [11].

CKD is usually insidious and most patients are asymptomatic until the disease progresses (i.e. eGFR below 30 mL/min/1.73 m²). The rate at which kidney function is lost varies depending on the etiology, exposure, and intervention. Still, in most cases, it usually takes months to decades to progress to kidney failure. CKD is associated with an increased risk of death from cardiovascular disease and is a risk multiplier in patients with diabetes and hypertension [12, 13]. Importantly, early detection and the use of off-the-shelf, often inexpensive methods to treat diabetes, hypertension, and CKD are possible. These interventions may improve renal and cardiovascular outcomes and slow the progression of end-stage renal disease (ESRD) [14–16]. Despite the availability of these interventions, the burden of CKD and its associated risk factors remain understudied in many parts of the world. Even in countries where data are available, awareness of the disease among the general public and health authorities is relatively low, partly leading to its progression to ESRD [17]. After the 1960s, the cost of treating CKD rose, with the availability of renal replacement technology making it possible to apply long-term life-saving but expensive treatments for ESRD [18]. Nephrology workforces in many countries are mainly concerned with treating ESRD rather than preventing and treating early CKD.

With its extensive data sources and statistical modeling methods, the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) can provide the most comprehensive estimate of the burden of CKD to date (<https://vizhub.healthdata.org/gbd-results/>). The GBD also quantifies the disease burden of CKD due to different causes. In this study, we aimed to summarize the results of the GBD 2021 on CKD including prevalence, incidence, mortality, and disability-adjusted life years (DALYs), with a focus on etiology, age and gender distribution, and time trends, to estimate the patterns and trends of CKD. We hope this analysis will provide clinicians and epidemiologists with insights into prevention, screening, and treatment, and help health policymakers further optimize the allocation of medical resources and develop more effective public health strategies.

Methods

Data acquisition and download

The GBD 2021 study provides the latest estimates of epidemiological data on the burden of 371 diseases and injuries, as well as 88 risk factors across 21 GBD regions and 204 countries and territories from 1990 to 2021, using enhanced standardized methodologies (<https://ghdx.healthdata.org/gbd-2021/sources>) [19]. In this study, the determinations relating to CKD were drawn from the GBD 2021 data [20]. The GBD 2021 estimates the burden of CKD stages 1–5, excluding renal replacement therapy. There are many causes of CKD, such as diabetes, hypertension, glomerulonephritis, cystic kidney diseases, and air pollution, GBD 2021 provides estimates of the burden of CKD for each of five causes: diabetes mellitus type 1 (T1DM), diabetes mellitus type 2 (T2DM), hypertension, glomerulonephritis, and a residual category of other and unspecified causes. For each CKD patient, GBD 2021 groups primary kidney disease using International Classification of Diseases (ICD) codes, mapping individuals to GBD etiological groups. Individuals with CKD but without the ICD codes for primary kidney disease are grouped as having CKD of uncertain cause. The definition of the 9th and 10th editions of the GBD 2021 ICD codes for CKD and its attributable causes is shown in Supplementary Table S1.

Burden description

A comprehensive assessment was conducted to quantify the global, regional, and national burden of CKD and its attributable causes. DALYs, a standard measure for quantifying the years of healthy life lost from the onset of a disease to death, is the sum of years of life lost (YLLs) and years lived with disability (YLDs). In addition, the survey delved into the demographic variables that influence CKD, examining the distribution of the CKD burden across different age groups and genders.

Additionally, the study employed the socio-demographic index (SDI). This comprehensive indicator is designed to quantify the development of a country or region and exhibits a robust correlation with population health outcomes. In short, it is the geometric mean of 0 to 1 index of fertility rates among females under 25 years, mean years of education among individuals aged 15 years and above, and lag-distributed income per capita. For GBD 2021, final SDI values are multiplied by 100 for a scale of 0 to 100. An SDI of 0 signifies the highest fertility rates and the lowest years of schooling and income. At the same time, an SDI of 100 represents the lowest fertility rates and the highest years of education and income. The 204 countries and territories are assembled and

categorized into five SDI regions (low, low-middle, middle, high-middle, and high) in the GBD 2021 [21].

Joinpoint regression analysis

Annual percentage change (APC) is a measure of the percentage increase or decrease in a variable in a given year. Average annual percent change (AAPC) measures the average yearly change in a variable over the study period. Unlike APC, AAPC looks at general trends over time and eliminates short-term fluctuations, so it is more instructive when assessing long-term trends. In the present study, the APC and AAPC were calculated by Joinpoint [22]. The standard error data of indicators required by the Joinpoint model can be calculated by the following formula, i.e., standard error = (upper confidence interval (CI) - lower CI) / (1.96 * 2).

Time trend analysis is an important part of epidemiological research. Traditional regression models fit and evaluate the general trends of disease distribution during the study period from a global perspective, but fail to capture the local change characteristics. Kim et al. first proposed the Joinpoint regression model in 1998. This model's core idea is to establish piecewise regression based on the time characteristics of disease distribution. Several connecting points divided the study time into different intervals, and the trends in each interval were fitted and optimized to assess in more detail the characteristics of specific disease changes in different intervals throughout the time range. The Joinpoint regression model which was developed by the Division of Cancer Control and Population Sciences at the National Cancer Institute of the United States has been widely used to study disease incidence and mortality trends [23–25]. From a statistical standpoint, an APC or AAPC estimate exceeding zero denotes an upward trajectory in the specified interval. In contrast, an APC or AAPC estimate falling below zero signals a downward trend. The Joinpoint also gives 95% CI and *p* values to assess significance. If the *p* value is less than 0.05, it is considered statistically significant.

Statistics analysis

Taking into account uncertainties in the primary data sources, data manipulations, measurement errors, and model selection, 1000 estimates were performed for all entities quantified in the GBD in the ensemble and meta-regression models to produce final estimates with 95% uncertainty intervals (UIs), which include the 2.5th and 97.5th percentiles of the 1000 random draws [3].

Unless otherwise noted, the prevalence, incidence, mortality, and DALYs rate were expressed as predicted values per 100,000 population, including their 95% UIs.

Statistical computing software R (Version 4.4.1) was used for all analysis and graphical representation.

Results

Global level

In 2021, the worldwide number of CKD cases was 673,722,703 (95% UI: 629,095,119–722,364,096), with an age-standardized prevalence rate (ASPR) of 8006.00 per 100,000 persons (7482.12–8575.62). The global incidence of CKD involved 19,935,038 cases (18,702,793–21,170,794), with an age-standardized incidence rate (ASIR) of 233.56 per 100,000 persons (220.02–247.24). The number of deaths was 1,527,639 (1,389,377–1,638,914), with an age-standardized mortality rate (ASMR) of 18.50 per 100,000 persons (16.72–19.85). The global DALYs for CKD was 44,453,684 (40,840,762–48,508,462), with an age-standardized DALYs rate of 529.62 per 100,000 persons (486.25–577.42) (Table 1).

SDI level

In 2021, the ASPR of CKD was highest in regions with a Low-middle SDI, at 9,171.03 per 100,000 persons (95% UI: 8543.99–9848.15), and lowest in regions with a High SDI at 6733.55 per 100,000 (6322.09–7159.65). The ASIR of CKD was highest in regions with a High SDI, at 277.75 per 100,000 persons (260.70–295.01), and lowest in regions with a Low SDI at 155.00 per 100,000 (143.40–167.34). The ASMR of CKD was found to be highest in regions with a Low SDI, recorded at 29.43 per 100,000 persons (26.13–33.79), and lowest in High-middle SDI regions at 12.02 per 100,000 (10.68–13.38). The age-standardized DALYs rate for CKD was highest in regions with a Low SDI, at 791.80 per 100,000 persons (704.14–909.10), and lowest in regions with a High-middle SDI, at 324.64 per 100,000 (293.58–360.92) (Table 1).

During the period from 1990 to 2021, a slight downward trend of ASPR was observed in regions with a Middle SDI, at -0.02 per 100,000 persons (95% UI: -0.03 to -0.01) (Table 1, Supplementary Table S2, Fig. 1A). The highest increasing trend of ASIR was observed in regions with a Middle SDI, at 0.36 per 100,000 persons (0.29–0.44) (Table 1, Supplementary Table S3, Fig. 1B). The most significant increases in the ASMR and age-standardized DALYs rate were observed in High SDI regions, at 0.53 per 100,000 persons (0.46–0.60) (Table 1, Supplementary Table S4, Fig. 1C) and 0.29 per 100,000 persons (0.24–0.34) (Table 1, Supplementary Table S5, Fig. 1), respectively.

Regional level

In 2021, the ASPR was highest in Central Asia, at 10,698.24 per 100,000 persons (95% UI: 10,022.94–11,348.10). By contrast, the region with the lowest

ASPR was Western Europe at 5226.19 per 100,000 persons (4924.43–5544.20) (Table 2 and Fig. 2A). The ASIR was highest in Central Latin America, at 411.41 per 100,000 persons (390.17–431.32). The region with the lowest ASIR was Eastern Sub-Saharan Africa at 118.08 per 100,000 persons (108.97–127.55) (Table 2 and Fig. 2B). The region with the highest ASMR was Central Sub-Saharan Africa at 43.69 per 100,000 persons (33.26–56.29), the region with the lowest ASMR was Eastern Europe at 5.22 per 100,000 persons (4.73–5.82) (Table 2 and Fig. 2C). The age-standardized DALYs rate was highest in Central Latin America, at 1171.14 per 100,000 persons (1054.82–1316.26), lowest in Eastern Europe, at 204.68 per 100,000 persons (180.40–232.13) (Table 2 and Fig. 2D).

From 1990 to 2021, East Asia exhibited the most significant downward trend of ASPR, at -0.12 per 100,000 persons (95% UI: -0.13 to -0.10). Andean Latin America exhibited the most significant increasing trend of ASIR, at 0.85 per 100,000 persons (0.71–1.00). High-income North America experienced the most significant upward trends in ASMR and age-standardized DALYs rate, at 1.47 per 100,000 persons (1.39–1.55) and 0.91 per 100,000 persons (0.82–1.00), respectively (Table 2).

National level

In 2021, Republic of Mauritius (11,411.55 per 100,000 persons; 95% UI: 10,649.12–12,263.72) had the highest ASPR of CKD. Conversely, French Republic (4368.82 per 100,000 persons; 4085.59–4698.68) exhibited the lowest ASPR (Fig. 2A and Supplementary Table S6). From 1990 to 2021, the Republic of Guatemala (0.10 per 100,000 persons; 0.06–0.14) experienced the most substantial relative increase in ASPR (Supplementary Table S7). In 2021, the country with the highest ASIR was the Kingdom of Saudi Arabia at 495.83 per 100,000 persons (465.09–529.64). Republic of Uganda (106.71 per 100,000 persons; 97.77–116.52) exhibited the lowest ASIR (Fig. 2B and Supplementary Table S8). Significant changes of ASIR from 1990 to 2021 were particularly evident in Republic of Estonia (1.07 per 100,000 persons; 0.93–1.23) (Supplementary Table S9). In 2021, Republic of Mauritius (80.13 per 100,000 persons; 74.12–84.55) had the highest ASMR. Republic of Belarus (2.35 per 100,000 persons; 1.94–2.78) had the lowest ASMR (Fig. 2C and Supplementary Table S10). From 1990 to 2021, the country with the largest increase in ASMR was Ukraine (17.15 per 100,000 persons; 12.5–22.21) (Supplementary Table S11). For more information about DALYs of CKD, see Fig. 2D and Supplementary Tables S12 and S13.

Table 1 Disease burden in 2021 and rate change in age-standardized rates from 1990 to 2021 for chronic kidney disease globally and by SDI quintile

Characteristics	Prevalence (95% uncertainty interval)			Incidence (95% uncertainty interval)			Mortality (95% uncertainty interval)			DALYs (95% uncertainty interval)		
	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021
Global	673,722,703 (629,095,119–722,364,096)	8006.00 (7482.12–8575.62)	–0.01 (–0.02 to 0.00)	19,935,038 (18,702,793–21,170,794)	233.56 (220.02–247.24)	0.22 (0.17–0.27)	1,527,639 (1,389,377–1,638,914)	18.50 (16.72–19.85)	0.25 (0.10–0.34)	44,453,684 (40,840,762–48,508,462)	529.62 (486.25–577.42)	0.10 (0.01–0.18)
Low SDI	54,528,960 (50,362,040–59,039,888)	7984.37 (7449.39–8549.73)	–0.01 (–0.02 to 0.00)	950,557 (888,494–1,011,543)	155.00 (143.40–167.34)	0.27 (0.22–0.33)	1,367,977 (1,188,677–1,575,797)	29.43 (26.13–33.79)	–0.01 (–0.12 to 0.12)	5,042,405 (4,408,653–5,841,516)	791.80 (704.14–909.10)	–0.07 (–0.16 to 0.03)
Low-middle SDI	149,861,034 (139,108,422–161,539,154)	9171.03 (8543.99–9848.15)	–0.01 (–0.02 to 0.00)	3,130,960 (2,912,350–3,362,301)	204.97 (189.81–220.29)	0.34 (0.29–0.39)	309,509 (280,315–349,455)	23.08 (20.97–26.31)	0.24 (–0.02 to 0.43)	10,611,260 (9,599,821–11,771,755)	686.98 (622.50–765.20)	0.13 (–0.03 to 0.27)
Middle SDI	220,823,054 (205,500,731–237,345,634)	8280.06 (7728.02–8885.29)	–0.02 (–0.03 to –0.01)	6,251,147 (5,866,964–6,655,539)	232.96 (219.53–246.12)	0.36 (0.29–0.44)	513,051 (458,865–556,752)	20.89 (18.45–22.67)	0.10 (–0.09 to 0.20)	15,700,568 (14,206,921–17,147,169)	596.45 (540.33–650.48)	0.02 (–0.11 to 0.10)
High-middle SDI	127,111,061 (118,337,580–136,309,239)	7267.74 (6782.08–7816.70)	–0.01 (–0.02 to –0.00)	3,917,149 (3,653,537–4,175,391)	205.90 (194.10–218.61)	0.34 (0.29–0.39)	226,797 (201,672–252,703)	12.02 (10.68–13.38)	0.24 (–0.01 to 0.43)	5,944,277 (5,372,850–6,623,407)	324.64 (293.58–360.92)	0.13 (–0.04 to 0.27)
High SDI	120,879,407 (113,333,443–127,967,827)	6733.55 (6322.09–7159.65)	–0.02 (–0.03 to –0.01)	5,666,653 (5,273,251–6,033,381)	277.75 (260.70–295.01)	0.10 (0.05–0.16)	340,083 (289,016–369,665)	14.11 (12.30–15.21)	0.53 (0.46–0.60)	7,115,740 (6,464,112–7,759,250)	358.51 (324.74–390.20)	0.29 (0.24–0.34)

Data in parentheses represent the 95% uncertainty intervals. SDI, socio-demographic index. DALYs disability-adjusted life-years

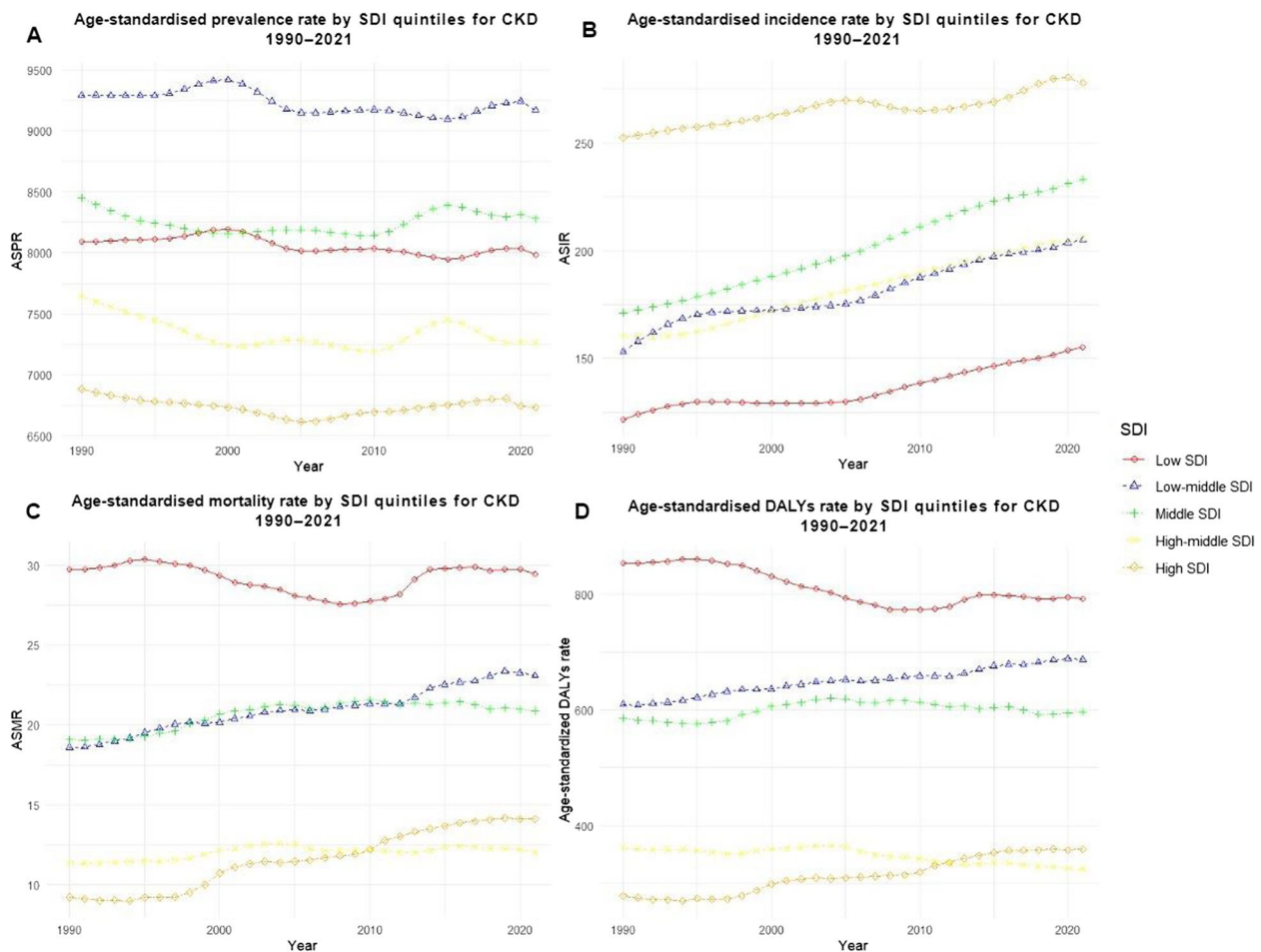


Fig. 1 Global chronic kidney disease burden by SDI quintiles from 1990 to 2021. **(A)** Age-standardized prevalence rate (ASPR); **(B)** Age-standardized incidence rate (ASIR); **(C)** Age-standardized mortality rate (ASMR); **(D)** Age-standardized disability-adjusted life years (DALYs) rate. SDI, Socio-demographic Index. CKD, chronic kidney disease

Burden of global CKD due to different causes

In 2021, the global ASPR of CKD due to T1DM, T2DM, hypertension, glomerulonephritis, other and unspecified causes were documented as 77.31 (95% UI: 66.91–87.58), 1259.63 (1161.99–1359.92), 291.19 (272.49–311.88), 129.94 (120.25–139.51), 6247.94 (5823.88– 6691.38), respectively. The global ASIR of CKD due to the above 5 causes were 1.31 (1.12–1.55), 23.07 (21.40–24.72), 14.97 (14.02–15.93), 4.84 (4.42–5.29), 189.36 (178.21–200.61), respectively. The global AMIR of CKD due to different causes were 1.08 (0.83–1.38), 5.72 (4.83–6.79), 5.54 (4.68–6.41), 2.34 (1.96–2.74), 3.81 (3.20–4.41), respectively, and the age-standardized DALYs rate due to different causes were 45.20 (36.01–56.35), 131.08 (112.75–152.49), 128.41 (109.14–145.64), 84.47 (73.20–96.13), 140.45 (122.56–159.28), respectively (Table 3). It can be seen that the number one cause of death for CKD was T2DM, with the highest absolute number of deaths due to T2DM in 2021 at 454,359 (381,290–524,688). In

addition to other and unspecified causes, the most common cause of prevalence, incidence, and DALYs for CKD was T2DM.

Regional disparities in the burden of CKD due to different causes

In 2021, throughout 21 GBD regions, the main reason for prevalent cases (Fig. 3A, Fig. 3E and Supplementary Table S14) and incident cases (Fig. 3B, Fig. 3F and Supplementary Table S15) of CKD was other and unspecified causes, followed by T2DM. The main causes of death and DALYs from CKD varied in different parts of the world. The leading cause of death in Andean Latin America, Caribbean, Tropical Latin America, South Asia, East Asia, and Oceania was T2DM; in High-income North America, Southeast Asia, Southern Sub-Saharan Africa, and Western Sub-Saharan Africa, it was hypertension; in Eastern Europe, Central Latin America, Central sub-Saharan Africa, and Eastern sub-Saharan Africa, it was

Table 2 Disease burden in 2021 and rate change in age-standardized rates from 1990 to 2021 by 21 Global Burden of Disease regions

Characteristics	Prevalence (95% uncertainty interval)			Incidence (95% uncertainty interval)			Mortality (95% uncertainty interval)			DALYs (95% uncertainty interval)		
	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021
Central Europe, eastern Europe, and central Asia												
Central Asia	9,356,434 (8,704,146–9,969,948)	10,698.24 (10,022.94–11,348.10)	0.005 (–0.01 to 0.02)	168,442 (154,020–183,300)	187.28 (173.80–201.56)	0.64 (0.57–0.72)	9,397 (8,278–10,515)	12.11 (10.72–13.53)	1.42 (1.01–1.87)	427,633 (377,524–490,696)	493.20 (435.99–565.47)	0.51 (0.37–0.68)
Central Europe	11,481,266 (10,766,159–12,145,281)	6205.18 (5841.05–6596.24)	–0.03 (–0.04 to –0.01)	458,516 (423,618–495,453)	218.39 (203.44–234.06)	0.65 (0.56–0.75)	21,635 (19,445–23,977)	9.39 (8.41–10.47)	–0.10 (–0.18 to –0.02)	539,982 (472,193–612,672)	266.92 (233.43–306.23)	–0.22 (–0.28 to –0.15)
Eastern Europe	27,312,843 (25,403,078–29,335,270)	9266.31 (8619.37–9989.49)	–0.01 (–0.01 to 0.002)	548,051 (501,351–595,626)	180.10 (167.54–193.25)	0.66 (0.59–0.73)	17,821 (16,126–19,853)	5.22 (4.73–5.82)	0.46 (0.3–0.60)	642,467 (562,943–726,952)	204.68 (180.40–232.13)	–0.01 (–0.08 to 0.07)
High-income												
Australasia	2,810,776 (2,637,789–2,995,329)	5910.04 (5548.15–6301.57)	–0.03 (–0.06 to 0.001)	160,661 (146,984–172,346)	297.30 (274.48–317.56)	0.15 (0.07–0.22)	5,968 (5,025–6,525)	9.63 (8.23–10.47)	0.14 (0.06–0.20)	113,693 (101,514–125,301)	216.61 (193.23–239.24)	0.03 (–0.02 to 0.07)
High-income Asia Pacific	29,276,226 (27,336,162–31,020,670)	7920.71 (7393.74–8457.44)	–0.08 (–0.09 to –0.07)	1,249,340 (1,151,298–1,346,531)	274.49 (255.82–293.59)	0.02 (–0.02 to 0.06)	63,459 (50,432–70,953)	9.74 (8.09–10.68)	–0.23 (–0.29 to –0.19)	1,146,613 (990,343–1,268,312)	235.57 (206.04–259.61)	–0.25 (–0.29 to –0.22)
High-income North America	42,488,578 (39,404,535–45,165,702)	7434.68 (6959.33–7911.44)	0.004 (–0.01 to 0.02)	2,026,546 (1,868,598–2,175,327)	316.15 (294.31–338.42)	0.06 (–0.00 to 0.12)	143,679 (124,827–154,757)	20.55 (18.10–22.00)	1.47 (1.39–1.55)	3,120,983 (2,864,207–3,351,576)	508.81 (467.04–545.39)	0.91 (0.82–1.00)
Southern Latin America	4,860,631 (4,530,777–5,214,539)	5970.43 (5543.08–6414.98)	0.03 (0.01–0.06)	244,517 (224,582–263,090)	281.73 (260.45–302.55)	0.32 (0.22–0.44)	21,583 (19,510–22,986)	23.85 (21.63–25.37)	–0.08 (–0.14 to –0.03)	441,138 (411,345–467,913)	515.22 (481.75–515.22)	–0.16 (–0.20 to –0.11)
Western Europe	41,591,466 (39,070,950–43,910,754)	5226.19 (4924.43–5544.20)	–0.04 (–0.06 to –0.03)	2,271,237 (2,122,275–2,425,621)	238.55 (223.94–254.27)	0.07 (0.01–0.13)	133,481 (109,637–148,166)	10.66 (8.90–11.81)	0.29 (0.18–0.38)	2,361,342 (2,067,098–2,638,163)	241.72 (209.82–271.06)	0.03 (–0.02 to 0.09)
Latin America and Caribbean												
Andean Latin America	3,743,589 (3,478,926–4,028,408)	5946.06 (5524.81–6371.54)	0.03 (0.01–0.05)	177,934 (165,435–192,798)	298.18 (276.18–322.60)	0.85 (0.71–1.00)	21,619 (17,903–25,800)	37.66 (31.27–44.93)	0.32 (0.08–0.63)	524,246 (434,446–625,013)	872.44 (723.54–1037.91)	0.16 (–0.04 to 0.41)
Caribbean	3,468,705 (3,235,452–3,720,720)	6632.98 (6181.25–7112.38)	0.02 (0.01–0.04)	145,322 (136,425–154,427)	274.22 (257.52–291.86)	0.62 (0.53–0.72)	13,888 (12,086–16,193)	25.78 (22.39–30.07)	0.38 (0.19–0.58)	385,286 (331,558–454,109)	735.85 (631.01–867.89)	0.30 (0.13–0.50)
Central Latin America	22,101,801 (20,701,763–23,422,153)	8642.90 (8089.33–9163.75)	0.02 (0.00–0.04)	1,056,443 (1,000,773–1,110,306)	411.41 (390.17–431.32)	0.49 (0.37–0.61)	104,444 (94,171–116,461)	42.35 (38.32–47.03)	0.52 (0.37–0.67)	2,993,750 (2,691,663–3,371,708)	1171.14 (1054.82–1316.26)	0.53 (0.38–0.69)
Tropical Latin America	19,295,702 (18,022,781–20,680,042)	7576.23 (7080.97–8107.55)	–0.02 (–0.03 to –0.01)	663,468 (620,124–707,786)	259.33 (242.85–275.61)	0.34 (0.26–0.45)	46,925 (42,508–49,437)	18.84 (17.00–19.87)	0.05 (–0.00 to 0.09)	1,311,915 (1,220,675–1,401,164)	516.97 (480.55–552.11)	–0.08 (–0.12 to –0.05)

Table 2 (continued)

Characteristics	Prevalence (95% uncertainty interval)			Incidence (95% uncertainty interval)			Mortality (95% uncertainty interval)			DALYs (95% uncertainty interval)		
	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021
North Africa and Middle East												
North Africa	49,668,756	9180.02	0.01 (−0.00 to 0.02)	1,988,922	411.19 (385.40–438.45)	0.61 (0.53–0.70)	144,687	37.71 (32.73–42.39)	0.21 (−0.24 to 0.51)	3,925,988	846.64 (747.17–948.02)	0.11 (−0.24 to 0.35)
and Middle East	(45,835,433–9830.12)	(8523.53–9830.12)		(1,863,403–2,127,840)			(126,153–162,699)			(3,427,227–4,413,622)		
South Asia												
South Asia	158,803,354	9565.26	−0.04 (−0.05 to −0.03)	2,755,183	177.65 (164.06–192.03)	0.21 (0.16–0.27)	226,043	16.45 (14.03–19.25)	0.18 (−0.08 to 0.41)	8,443,339	540.57 (473.83–620.42)	0.06 (−0.10 to 0.24)
	(147,190,732–171,556,959)	(8903.67–10,265.71)		(2,545,113–2,967,871)			(192,546–264,155)			(7,372,315–9,681,828)		
Southeast Asia, east Asia, and Ocean												
East Asia	122,849,231	6258.13	−0.12 (−0.13 to −0.10)	3,505,756	176.80 (156.01–176.80)	0.12 (0.05–0.20)	217,342	11.15 (9.20–13.21)	−0.22 (−0.39 to −0.05)	6,486,167	322.36 (275.35–377.34)	−0.30 (−0.42 to −0.18)
	(113,607,491–132,118,615)	(5823.13–6729.82)		(3,245,783–3,750,967)			(178,047–259,057)			(5,538,060–7,597,380)		
Oceania	776,661	7950.68	0.03 (0.01–0.04)	15,011	162.83 (151.06–174.45)	0.28 (0.19–0.36)	1,546	21.56 (17.98–26.37)	0.25 (−0.11 to 0.79)	65,815	699.04 (597.93–821.29)	0.20 (−0.09 to 0.60)
	(715,870–846,878)	(7408.82–8567.73)		(13,905–16,088)			(1,265–1,892)			(55,558–77,796)		
Southeast Asia	73,561,437	10,474.65	0.02 (0.02–0.03)	1,568,475	231.28 (215.53–247.34)	0.48 (0.40–0.56)	170,033	28.47 (24.79–31.87)	0.25 (0.02–0.43)	5,703,263	846.26 (753.05–940.53)	0.13 (−0.02 to 0.27)
	(67,779,796–79,733,436)	(9718.92–11,301.72)		(1,457,741–1,685,245)			(148,864–190,537)			(5,028,657–6,329,025)		
Sub-Saharan Africa												
Central Sub-Saharan Africa	6,811,951	9165.20	−0.01 (−0.03 to 0.02)	88,402	130.46 (120.30–142.08)	0.38 (0.30–0.47)	21,011	43.69 (33.26–56.29)	0.02 (−0.22 to 0.33)	783,700	1124.70 (899.03–1436.09)	−0.03 (−0.24 to 0.25)
	(6,363,747–7,313,187)	(8640.85–9709.73)		(82,071–94,885)			(16,114–27,467)			(622,595–996,532)		
Eastern Sub-Saharan Africa	15,017,845	5821.27	0.03 (0.02–0.03)	244,189	118.08 (108.97–127.55)	0.24 (0.18–0.31)	60,918	40.09 (35.57–46.03)	−0.05 (−0.19 to 0.08)	2,047,629	948.36 (838.71–1090.36)	−0.13 (−0.23 to −0.01)
	(13,741,759–16,422,384)	(5404.49–6293.60)		(228,098–260,057)			(53,817–69,935)			(1,792,019–2,374,164)		
Southern Sub-Saharan Africa	5,972,950	9037.91	0.01 (−0.00 to 0.02)	142,811	233.60 (216.73–248.74)	0.38 (0.32–0.45)	17,365	34.43 (31.05–38.29)	0.65 (0.27–0.90)	551,466	895.96 (807.34–996.98)	0.44 (0.20–0.62)
	(5,547,456–6,415,524)	(8440.60–9647.06)		(132,638–152,029)			(15,612–19,485)			(494,226–622,064)		
Western Sub-Saharan Africa	22,472,497	8324.27	0.002 (−0.01 to 0.01)	455,812	179.77 (165.43–194.20)	0.32 (0.26–0.38)	64,796	36.41 (31.14–42.75)	0.08 (−0.09 to 0.25)	2,437,269	930.73 (788.43–1081.08)	0.002 (−0.13 to 0.14)
	(20,882,526–24,191,820)	(7782.26–8871.02)		(426,702–486,021)			(53,512–76,124)			(1,992,652–2,893,649)		

Data in parentheses represent the 95% uncertainty intervals. DALYs disability-adjusted life-years

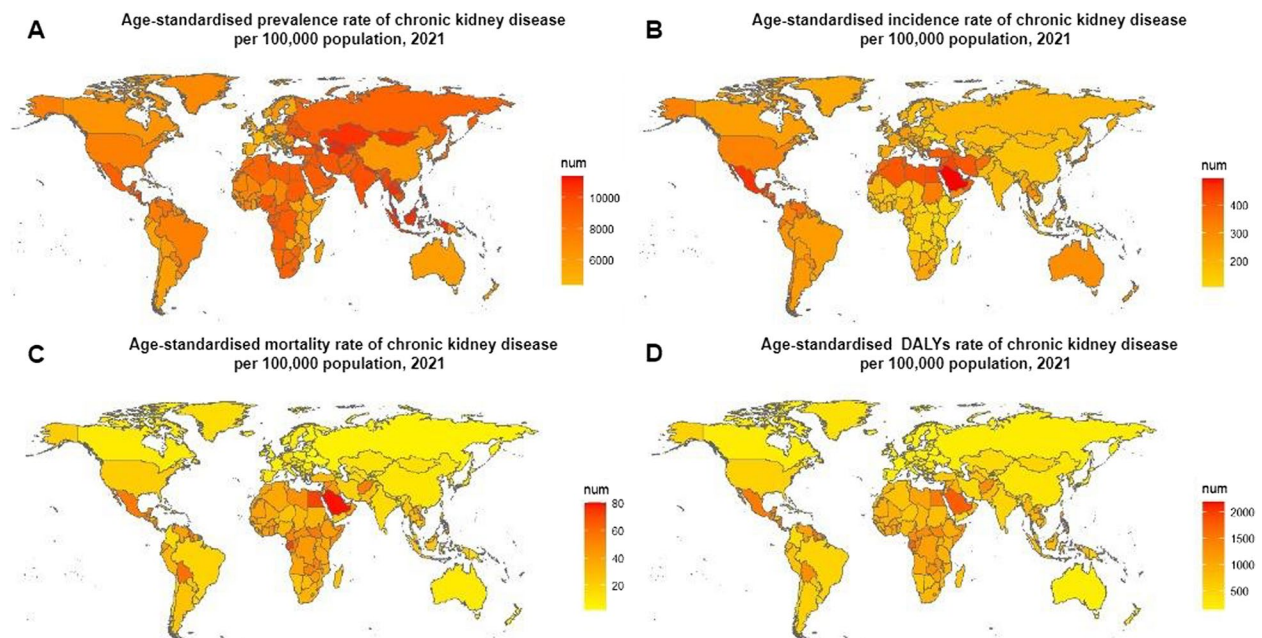


Fig. 2 Global distribution of chronic kidney disease burden in 2021. (A) Age-standardized prevalence rate; (B) Age-standardized incidence rate; (C) Age-standardized mortality rate; (D) Age-standardized DALYs rate. DALYs, disability-adjusted life-years

glomerulonephritis (Fig. 3C, Fig. 3G and Supplementary Table S16). The leading cause of DALYs in High-income North America, Andean Latin America, the Caribbean, Tropical Latin America, East Asia, and Oceania was T2DM; in Southeast Asia, and Southern Sub-Saharan Africa, it was hypertension; in Central Latin America, Central Sub-Saharan Africa, Eastern Sub-Saharan Africa, and Western Sub-Saharan Africa, it was glomerulonephritis (Fig. 3D, Fig. 3H and Supplementary Table S17).

Age and sex patterns

In 2021, the global prevalence of CKD increased with age (Fig. 4A and Supplementary Table S18). In most age groups, the prevalence was higher in females than in males (Fig. 4A and Supplementary Table S19). Overall, the global incidence of CKD increased with age. The incidence of new CKD cases was highest in older adults aged 80 to 84 years and lowest in the 5–9 age group children (Fig. 4B and Supplementary Table S20). Similarly, in most age groups, the incidence was higher in females than in males (Fig. 4B and Supplementary Table S21). The global mortality of CKD increased with age, except for those in the 5–9 and 10–14 age groups were lower than those under the age of 5 (Fig. 4C and Supplementary Table S22). The mortality of CKD was higher in males (21.91) compared to females (15.90). Likewise, the mortality was higher in males than females in all age groups (Fig. 4C and Supplementary Table S23). The DALYs rate analysis revealed a trend similar to that of mortality, with

DALYs rate increasing with age. (Fig. 4D and Supplementary Table S24). Both in the overall population and across age groups, the age-standardized DALYs rate of CKD was higher in males compared to females (Fig. 4D and Supplementary Table S25).

Temporal joinpoint analysis

From 1990 to 2021, Joinpoint regression analysis revealed that the ASPR exhibited a global downward trend (AAPC = -0.021% ; 95% CI: -0.025% to -0.016% ; $P < 0.001$). The trend for females was much the same as for the overall population (Fig. 5A and Supplementary Table S26). Global ASIR exhibited a steady upward trend (AAPC = 0.634% ; 0.629% to 0.639% ; $P < 0.001$). The ASIR was on the rise globally for both males and females (Fig. 5B and Supplementary Table S27). Similarly, the ASMR followed an upward trend (AAPC = 0.745% ; 0.723% to 0.765% ; $P < 0.001$), with the most notable increase during the 1997–2000 period (APC = 2.269% ; 1.837% to 2.479% ; $P < 0.001$) and females contributing largely to this change (Fig. 5C and Supplementary Table S28). The trend of age-standardized DALYs rate mirrored the ASMR, with an overall increase (AAPC = 0.322% ; 0.299% to 0.342% ; $P < 0.001$). The most notable increase in age-standardized DALYs rate was observed from 1996 to 2003 (APC = 0.982% ; 0.870% to 1.126% ; $P < 0.001$) (Fig. 5D and Supplementary Table S29).

Table 3 Disease burden in 2021 and rate change in age-standardized rates from 1990 to 2021 by cause of CKD

Characteristics	Prevalence (95% uncertainty interval)			Incidence (95% uncertainty interval)			Mortality (95% uncertainty interval)			DALYs (95% uncertainty interval)		
	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021	Counts (2021)	Age-standardized rates per 100,000 (2021)	Rate change in age-standardized rates, 1990–2021
CKD due to T1DM	6,295,710 (5,459,693–7,114,345)	77.31 (66.91–87.58)	0.34 (0.25–0.43)	95,140 (82,237–111,471)	1.31 (1.12–1.55)	0.19 (0.08–0.31)	94,020 (71,457–119,984)	1.08 (0.83–1.38)	0.003 (–0.14 to 0.11)	3,875,628 (3,062,396–4,845,503)	45.20 (36.01–56.35)	–0.04 (–0.17 to 0.17)
CKD due to T2DM	107,559,955 (99,170,797–115,994,732)	1259.63 (1161.99–1359.92)	–0.05 (–0.07 to –0.03)	2,012,025 (1,857,800–2,154,288)	23.07 (21.40–24.72)	0.21 (0.15–0.27)	477,273 (401,541–565,951)	5.72 (4.83–6.79)	0.38 (0.19–0.50)	11,278,935 (9,682,785–13,103,871)	131.08 (112.75–152.49)	0.24 (0.09–0.33)
CKD due to hypertension	24,467,653 (22,861,634–26,230,869)	291.19 (311.88)	–0.06 (–0.08 to –0.05)	1,282,205 (1,195,230–1,366,296)	14.97 (14.02–15.93)	0.22 (0.17–0.28)	454,359 (381,290–524,688)	5.54 (4.68–6.41)	0.29 (0.12–0.40)	10,850,728 (9,207,080–12,320,650)	128.41 (109.14–145.64)	0.19 (0.04–0.28)
CKD due to glomerulonephritis	10,735,809 (9,925,500–11,520,171)	129.94 (139.51)	0.01 (–0.01 to 0.03)	357,288 (329,226–388,483)	4.84 (4.42–5.29)	0.13 (0.08–0.18)	193,997 (162,332–226,569)	2.34 (1.96–2.74)	0.16 (0.07–0.25)	6,959,758 (6,018,414–7,961,673)	84.47 (73.20–96.13)	0.09 (0.00–0.17)
CKD due to other and unspecified causes	524,663,971 (488,899,870–562,780,408)	6247.94 (582,388–6691.38)	–0.00 (–0.01 to 0.01)	16,188,381 (15,192,359–17,180,106)	189.36 (200.61)	0.22 (0.17–0.27)	307,990 (357,326–259,417)	3.81 (3.20–4.41)	0.15 (0.03–0.24)	11,488,636 (10,007,838–13,046,210)	140.45 (122.56–159.28)	–0.01 (–0.07 to 0.06)

Data in parentheses represent the 95% uncertainty intervals. CKD chronic kidney disease. T1DM diabetes mellitus type 1. T2DM, diabetes mellitus type 2

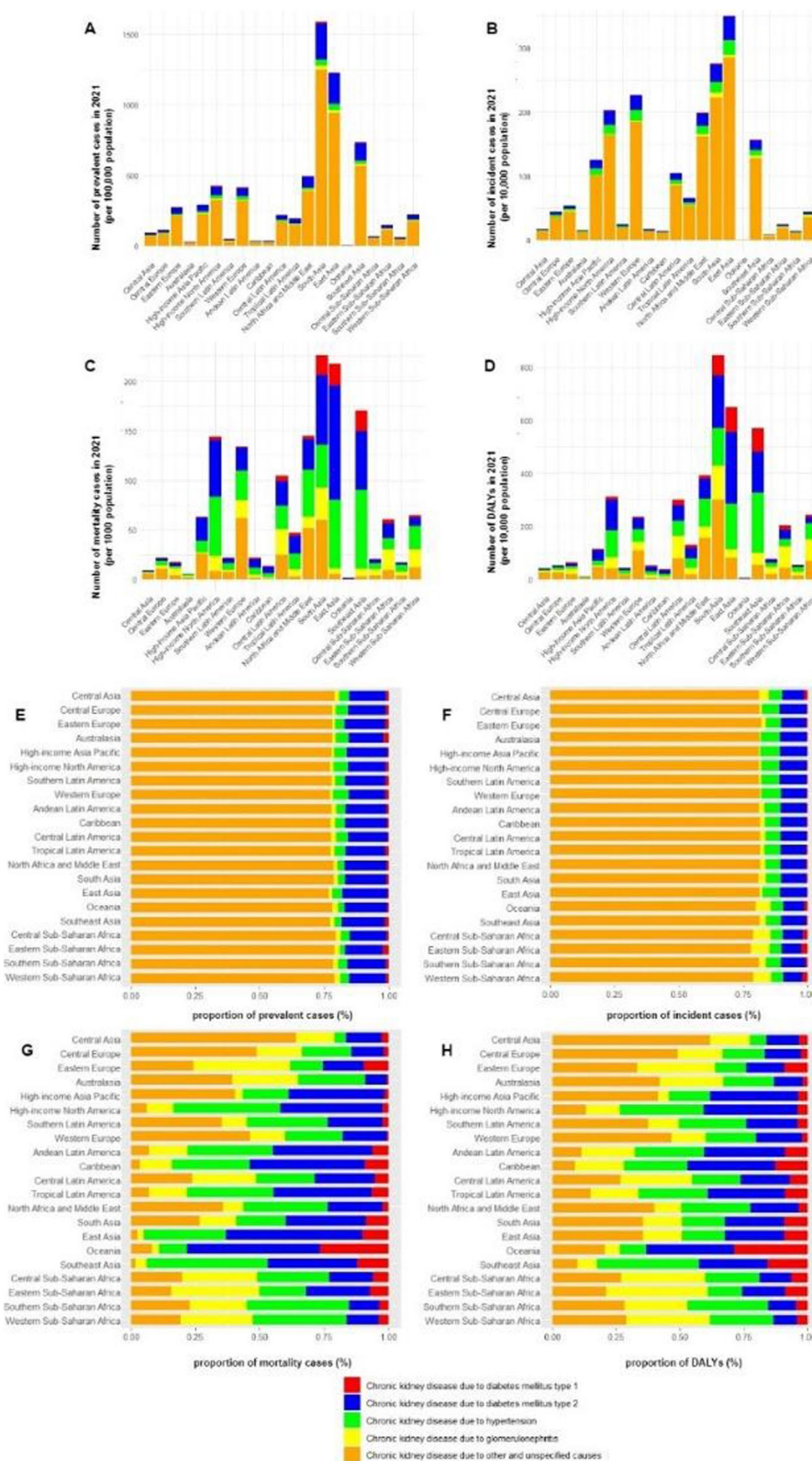


Fig. 3 Number and proportion of chronic kidney disease contributed by 21 GBD regions, in 2021. (A) Number of prevalent cases; (B) Number of incident cases; (C) Number of mortality cases; (D) Number of DALYs; (E) Proportion of prevalent cases; (F) Proportion of incident cases; (G) Proportion of mortality cases; (H) Proportion of DALYs. DALYs, disability-adjusted life-years

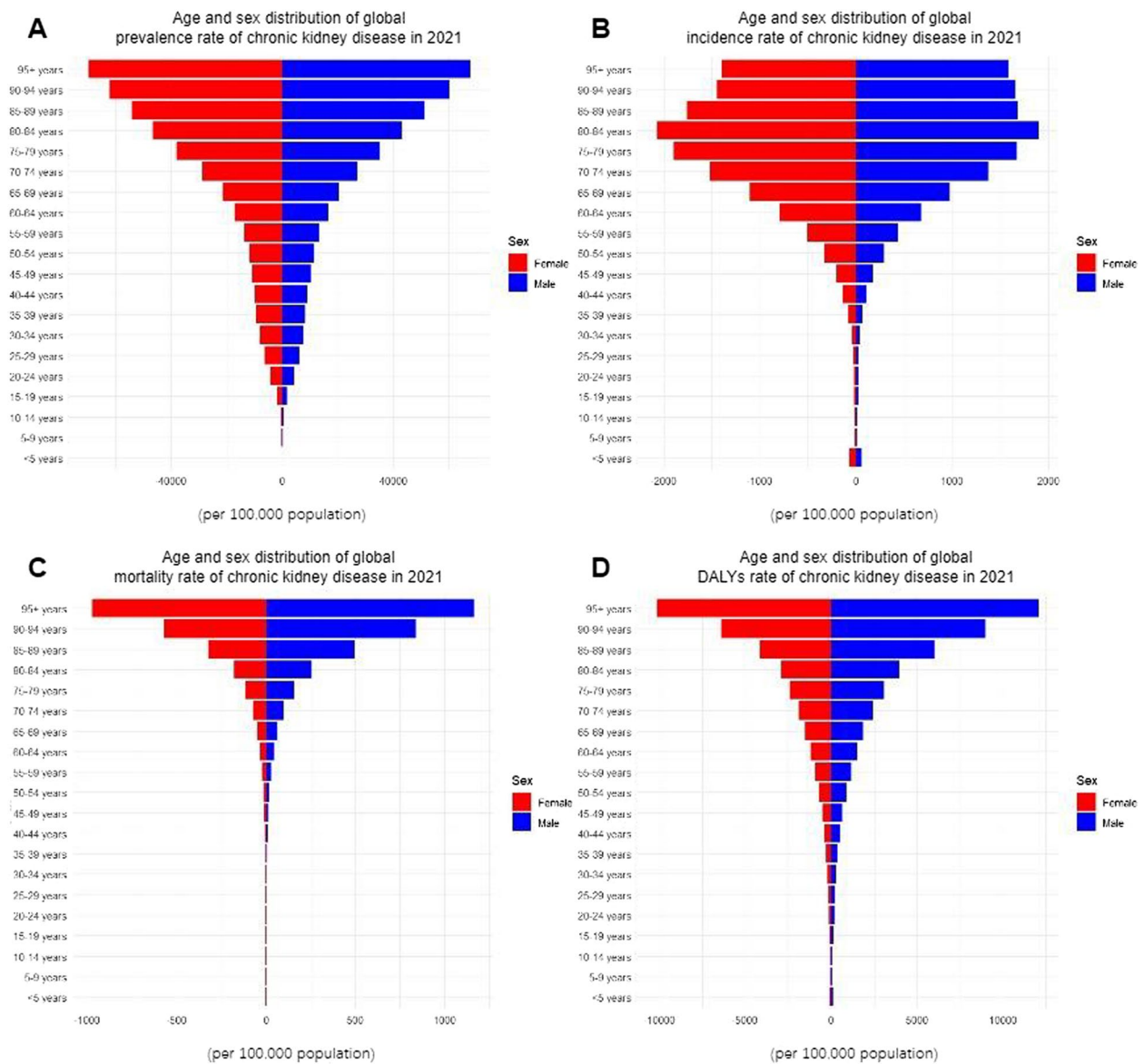


Fig. 4 Sex- and age-structured analysis of chronic kidney disease burden in 2021. (A) Prevalence rate; (B) Incidence rate; (C) Mortality rate; (D) DALYs rate. DALYs, disability-adjusted life-years

Discussion

CKD represents a major public health challenge worldwide, with its impact on morbidity and mortality has attracted considerable research attention. GBD 2017 CKD Collaborators reported the global, regional, and national burden of CKD based on the 2017 GBD study and also the cardiovascular disease and gout attributable CKD burden [3]. Moreover, Dong et al. reported the burden and trends of CKD from 1990 to 2019 and predictions to 2030 by Bayesian age-period-cohort analysis [26]. In addition, a number of other epidemiological studies have been conducted at the national level to

assess the burden of CKD [27–31]. Our study used GBD findings to explore the burden of CKD and its underlying etiologies, and updated the previous articles on this topic. Notably, this study introduced an innovative evaluation of temporal trends in the burden of CKD, identifying pivotal moments or critical years, when significant changes occurred in disease indicators.

The number of individuals with CKD reached almost 674 million in 2021, involving more people than many common chronic diseases such as diabetes, chronic respiratory disease, cardiovascular disease, and osteoarthritis [19]. To this must be added the global burden of

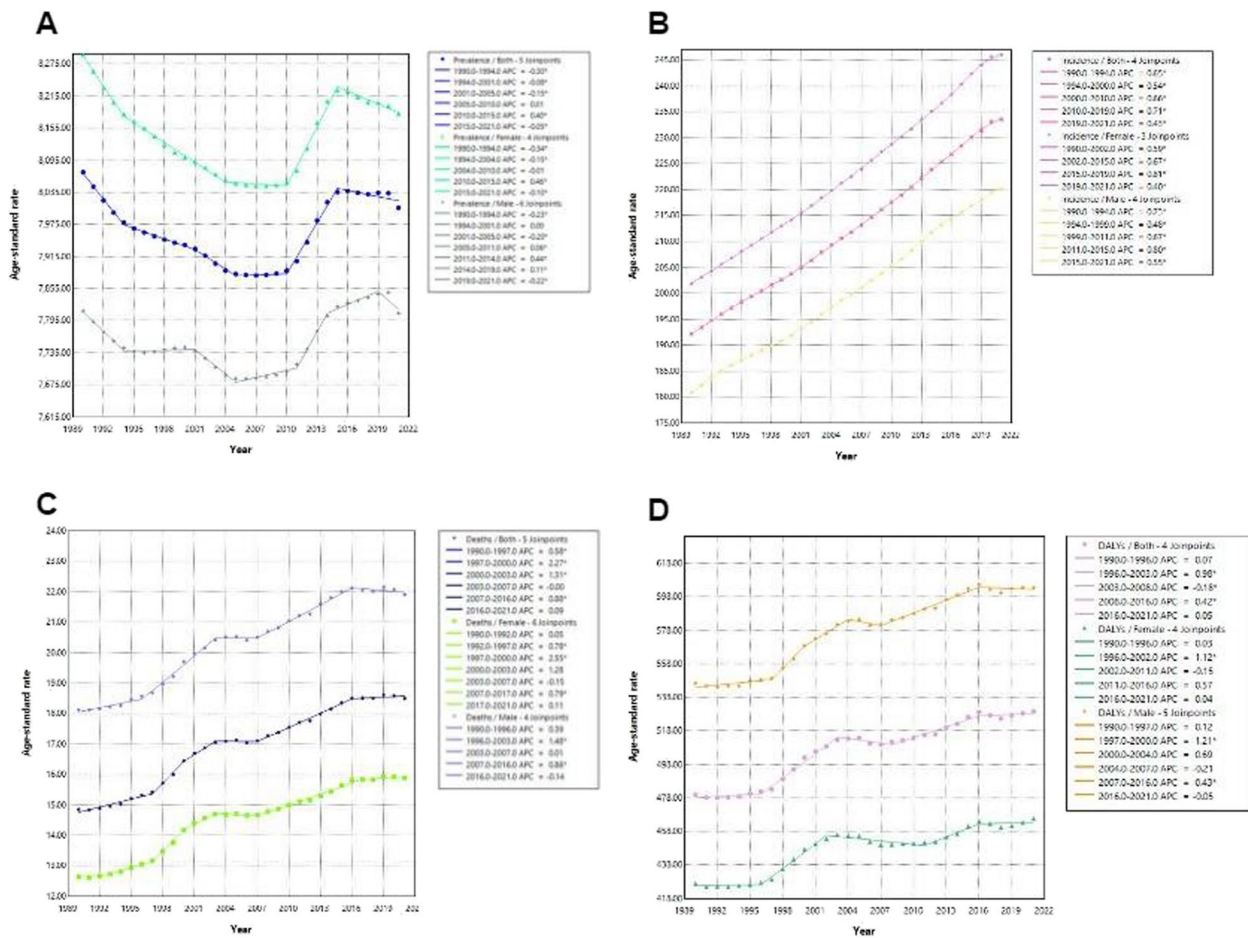


Fig. 5 Joinpoint regression analysis of the chronic kidney disease burden temporal trends, 1990–2021. **(A)** Age-standardized prevalence rate; **(B)** Age-standardized incidence rate; **(C)** Age-standardized mortality rate; **(D)** Age-standardized disability-adjusted life years (DALYs) rate

acute kidney injury and kidney failure (including patients receiving dialysis and kidney transplantation), which increased the global prevalence of kidney disease to approximately 850 million, translating into a worldwide prevalence of >10% [3, 32]. It is important to note that this prevalence may be underestimated due to the lack of early kidney disease detection and screening programs in many parts of the world [33]. In our study, regions with Low SDI had the lowest ASIR. Such low ASIR was unexpected and reflected the underestimation of CKD in Low SDI regions due to a lack of early detection and screening programs. In 2021, CKD diagnoses resulted in 1.5 million deaths, and this number is expected to rise to 2.2 million in the best-case scenario and 4 million in the worst-case scenario by 2040. [34] The ASMR and age-standardized DALYs rate of CKD were more prominent in regions with Low and Low-middle SDI quintiles, where there is a large gap between the burden of CKD and the provision of adequate healthcare [3]. In these regions, a large proportion of individuals do not have access to effective

treatment for kidney disease [34]. In resource-poor settings with weak primary care infrastructure, up to 90% of people with CKD are unaware they have the disease and therefore do not seek treatment [33, 35, 36].

In our study, in terms of prevalent cases and incident cases, the etiological composition of CKD was significantly dominated by other and unspecified causes. However, the picture was different when assessing the burden of mortality and DALYs from CKD. T2DM, hypertension, and glomerulonephritis were identified as the leading causes, respectively, in some regions. This indicates a global situation: in the diagnosis and initial treatment phase of CKD, the cause of the disease is often not accurately determined, and the treatment is merely targeted at CKD. The exact cause of CKD is not well documented until it has progressed to a severe stage leading to death or severe disability. It is worth noting that the treatment strategies of CKD due to different etiologies vary greatly. Taking diabetes and hypertension as an example, effective control of blood glucose levels and blood pressure

is a key measure to delay the progression and prevent the deterioration of CKD. Therefore, only treating CKD itself and ignoring the management of the primary cause is undoubtedly a palliative treatment, it is difficult to achieve the best therapeutic effect. To optimize the treatment strategy, we should focus on the precise diagnosis and targeted treatment of the cause, to comprehensively improve the health status of patients with CKD. The increasing burdens of diabetes and hypertension are the best-recognized drivers of CKD, especially in economically developed regions. In high-income countries, up to one-third of people with diabetes and one-fifth of people with hypertension have CKD, leading to the belief that focusing on diabetes and hypertension will reduce the increasing burden of CKD [37]. However, in addition to diabetes and hypertension, multiple causes, mediators, and risk factors, such as glomerular disease, infectious diseases, environmental factors, nephrotoxins, and smoking, contribute to kidney disease, especially in Low- and Low-middle-income countries, which account for two-thirds of the global burden of kidney disease [38]. The GBD team estimated that in 2019, up to 8% of CKD deaths could be attributed to non-optimal (high or low) ambient temperatures [39]. For example, constant exposure to high temperatures, especially in agricultural and outdoor workers who lack access to adaptive interventions, may increase heat stress and thus exacerbate the risk of kidney disease [6, 40–42]. Heat stress is a potential risk factor for unexplained CKD in agricultural regions, and it is increasingly recognized as a major global cause of CKD. This unexplained CKD is mainly observed in the global South, including India, Sri Lanka, Central and South America, and parts of Africa [43–45]. Although kidney disease is often classified as a noncommunicable disease, infection is also an important cause of kidney disease in Low- and Low-middle-income countries, either directly involving the kidneys (for instance, in the case of leptospirosis or HIV infection) or indirectly through infection-associated glomerulonephritis, hemodynamic mechanisms, or systemic inflammatory responses [46–48]. Studies have shown that leptospirosis may contribute to the development of unexplained CKD or an increased susceptibility to risk factors such as heat stress [49, 50]. Climate change and global biodiversity loss are making it more favorable for parasites (e.g., those that cause malaria or schistosomiasis) or their vectors (e.g., mosquitoes or ticks) to survive, increasing the risk of AKI and CKD-related infectious diseases outside the tropics [51]. It is important to note that although the association between certain infections and kidney disease is well known, the role of infections in the onset or progression of CKD has not been well-studied. Our study showed that in some regions, the leading cause of death

and DALYs from CKD was not diabetes, or hypertension, but other and unspecified causes. Even if a person has diabetes or hypertension, the cause of their CKD is not necessarily diabetes or hypertension. A biopsy is the gold standard method for determining the underlying etiologies of CKD. If contraindications for renal biopsy are ruled out, renal biopsy should be expanded to understand the cause of CKD, especially in regions where other and unspecified causes are the leading cause of CKD death and DALYs.

It is estimated that in November 2022, the global population has reached 8 billion [52], and by 2050, the global population will reach 9.7 billion [53]. On average, the world's population is aging much faster than in the past. In 2019, global life expectancy reached 72.8 years, an increase of nearly nine years from 64.0 years in 1990, and it is expected to reach an average of around 77.2 years by 2050 [54]. In 2024, just over 10% of the world's population was over 65; by 2050, this age group is expected to account for more than 16% of the global population [55]. Population growth and aging are associated with an increased burden of many non-communicable diseases, including CKD and its risk factors such as diabetes and hypertension. In our study, it can be observed that the burden of CKD continues to rise with age. Even in healthy people, kidney function declines with age, so age is considered a risk factor for CKD. Renal aging is manifested by macroscopic and microscopic changes and functional changes. Renal function changes include decreased GFR, impaired renal tubular function, and decreased endocrine function [55–57]. As people age, even without a specific cause of kidney disease, a complex interplay between the number of nephrons at birth, genetic predisposition, and environmental factors can lead to a decline in kidney function [58]. This suggests that in the absence of traditional CKD risk factors in healthy individuals, population aging will coincide with an increase in the burden of CKD. Studies showed that the prevalence of CKD is 29 percent higher in women than in men, but men are more likely to die of CKD than women, which is consistent with our findings [3, 59]. Notably, despite the increased risk of death for men, men are 47 percent more likely than women to receive dialysis or a kidney transplant. [3]. In older adults, women have a lower baseline GFR, while men's GFR declines more rapidly with age [60, 61]. The complex interactions between age and gender ought to be better understood to develop appropriate health policies.

Our study showed that the ASIR, ASMR, and age-standardized DALYs rate of CKD continued to increase from 1990 to 2021. Mortality from CKD have been rising compared to cardiovascular disease, stroke, and respiratory disease. Kidney disease is currently the

third fastest-growing cause of death globally and the only noncommunicable disease for which ASMR continues to rise [62]. Based on current trends, the burden of CKD will continue to increase in the coming decades, especially in the context of population growth and aging. This underscores the urgency of addressing CKD as a major public health problem.

This study, like other GBD estimation work, has several limitations. First, high-quality population-based studies of CKD prevalence are lacking in many countries. In some countries, due to limited medical resources, many people do not have access to kidney disease detection and screening at an early stage, so the incidence and prevalence of CKD may be underestimated. Additionally, some low-income regions have little to no available data on the incidence or prevalence of CKD in the population; therefore, GBD relies on statistical methods and predictive covariate values to estimate the CKD burden in these regions. Second, although the KDIGO guidelines propose a standardized definition of CKD, sources of information on CKD differ in terms of sampling, laboratory methods, and equations used to calculate eGFR. To account for these differences and standardize the data across studies, GBD adjusted the data sources to represent incidence or prevalence as calculated according to the reference definition of eGFR, estimated using the CKD-EPI equation. This correction increases the uncertainty of the input data and comes from a limited number of sources, which may not accurately characterize biases in different demographic subgroups of the population. Third, most data sources reporting CKD incidence or prevalence are cross-sectional and do not repeat serum creatinine or urine ACR measurement over 3 months to confirm the chronicity of abnormalities, as the KDIGO guidelines recommended. Studies have shown that using a measure of reduced eGFR to characterize CKD may overestimate prevalence by 25–50%. Therefore, the results of our analysis may overestimate the incidence or prevalence of CKD. Finally, the etiological distribution of CKD was provided by GBD using data from renal replacement therapy registries, the prevalence and incidence were estimated using the etiologic distribution of CKD.

In summary, this study used data from GBD 2021 to describe the global, regional, and national burden of CKD and its attributable causes, delineate differences in age and sex, and analyze trends between 1990 and 2021. The findings indicated a continued increase in the disease burden. Healthcare providers should recognize that population growth and social aging will result in an increasing number of people at risk for CKD. Targeted primary prevention, secondary prevention, and care strategies should be optimized according to age, sex, region, and type of disease.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12889-025-21851-z>.

Supplementary Material 1.

Acknowledgements

We acknowledge the exceptional contributions made by the collaborators of the Global Burden of Diseases, Injuries, and Risk Factors Study 2021. We sincerely appreciate the IHME institution for providing the GBD data.

Clinical trial

Not applicable.

Authors' contributions

LD conceived the study. PS designed the protocol. LD, SJG, YJZ, and YRL analysed the GBD data. PS, and XXZ contributed to the statistical analysis and interpretation of data. LD drafted the manuscript, YPL, and XJY critically revised the manuscript. PS and SJG accessed and verified the underlying data. All authors have read and approved the final version of the manuscript.

Funding

This study was supported by the Science and Technology Department of Sichuan Province > Key Research and Development Program of Sichuan Province (2022YFS0600); Medical and Engineer Cross Joint Fund of University of Electronic Science and Technology of China (ZYGX2021YGLH208); Subject Funds of Health Care for Cadres of Sichuan Province (No. 2024–208).

Data availability

The data from this study can be accessed openly through the GBD 2021 online database, as outlined in the Methods section.

Declarations

Ethics approval and consent to participate

The GBD study used de-identified data; both the waiver of informed consent and experimental protocols were reviewed and approved by the University of Washington Institutional Review Board (application number 46665). All methods were performed in accordance with the relevant guidelines and regulations. The GBD study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement. Further information can be found here: <http://gather-statement.org/>

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Health Management and Institute of Health Management, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, China. ²Animal Experimental Center of West China Hospital, Sichuan University, Chengdu, China. ³Laboratory of Endocrinology and Metabolism, West China Hospital, Sichuan University, Chengdu, China.

Received: 8 November 2024 Accepted: 7 February 2025

Published online: 17 February 2025

References

- Kalantar-Zadeh K, Jafar TH, Nitsch D, Neuen BL, Perkovic V. Chronic kidney disease. *Lancet*. 2021;398(10302):786–802.
- Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. *Lancet*. 2017;389:1238–52.
- GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990–2017: a

- systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2020;395(10225):709–33.
4. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). United States Renal Data System (USRDS). 2023 Annual Data Report: Epidemiology of kidney disease in the United States. Available from: <https://usrds-adr.niddk.nih.gov/2023>.
 5. Jian Y, Zhu D, Zhou D, et al. ARIMA model for predicting chronic kidney disease and estimating its economic burden in China. *BMC Public Health*. 2022;22(1):2456.
 6. Francis A, Harhay MN, Ong ACM, et al. Chronic kidney disease and the global public health agenda: an international consensus. *Nat Rev Nephrol*. 2024;20(7):473–85.
 7. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. *Kidney Int*. 2011;80:1258–70.
 8. Pearce N, Caplin B. Let's take the heat out of the CKDu debate: more evidence is needed. *Occup Environ Med*. 2019;76:357–9.
 9. Ekrikpo UE, Kengne AP, Bello AK, et al. Chronic kidney disease in the global adult HIV-infected population: a systematic review and meta-analysis. *PLoS One*. 2018; 13:e0195443.
 10. Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. *Lancet*. 2013;382:260–72.
 11. Correa-Rotter R, Wesseling C, Johnson RJ. CKD of unknown origin in Central America: the case for a Mesoamerican nephropathy. *Am J Kidney Dis*. 2014;63:506–20.
 12. 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;3:514–25.
 13. Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet*. 2010;375:2073–81.
 14. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO. Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kid Int Suppl*. 2012;2013(3):1–150.
 15. Maione A, Navaneethan SD, Graziano G, et al. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and combined therapy in patients with micro- and macroalbuminuria and other cardiovascular risk factors: a systematic review of randomized controlled trials. *Nephrol Dial Transplant*. 2011;26:2827–47.
 16. Ruggenenti P, Cravedi P, Remuzzi G. Mechanisms and treatment of CKD. *J Am Soc Nephrol*. 2012;23:1917–28.
 17. Tuot DS, Zhu Y, Velasquez A, et al. Variation in patients' awareness of CKD according to how they are asked. *Clin J Am Soc Nephrol*. 2016;11:1566–73.
 18. Himmelfarb J, Ikizler TA. Hemodialysis. *N Engl J Med*. 2010;363:1833–45.
 19. GBD 2021 Diseases and Injuries Collaborators. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024;403(10440):2133–61.
 20. GBD 2021 Causes of Death Collaborators. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet*. 2024; 403(10440):2100–2132.
 21. Global Burden of Disease Study 2019. (GBD 2019) sociodemographic Index (SDI) 1950–2019. Available from: <https://ghdx.healthdata.org/record/hme-data/gbd-2019-socio-demographic-index-sdi-1950-2019>.
 22. Joinpoint Trend Analysis Software. Version 4.9.1.0-April 2022; surveillance research program, division of cancer control & population sciences, National Cancer Institute. Available from: <https://surveillance.cancer.gov/joinpoint/>.
 23. Tuo Y, Li Y, Li Y, et al. Global, regional, and national burden of thalassemia, 1990–2021: a systematic analysis for the global burden of disease study 2021. *EClinicalMedicine*. 2024;7(2): 102619.
 24. Zhan Z, Chen B, Lin W, et al. Rising Burden of Colon and Rectum Cancer in China: An Analysis of Trends, Gender Disparities, and Projections to 2030. *Ann Surg Oncol*. <https://doi.org/10.1245/s10434-025-16905-w>. Published online January 21, 2025.
 25. Zhu Y, Shen T, Guo R, et al. Global, regional, and national burden of young COPD, 1990–2021, with forecasts to 2050: a systematic analysis for the global burden of disease study 2021. *BMC Public Health*. 2025;25(1):276.
 26. Dong B, Zhao Y, Wang J, et al. Epidemiological analysis of chronic kidney disease from 1990 to 2019 and predictions to 2030 by Bayesian age-period-cohort analysis. *Ren Fail*. 2024;46(2):2403645.
 27. Dávila-Cervantes CA, Agudelo-Botero M. Young-onset chronic kidney disease in Mexico: Secondary analysis of global burden of disease study, 1990–2019. *Prev Med*. 2024;181: 107901.
 28. Khashayar P, Sharifnejad Tehrani Y, Tabatabaei-Malazy O, et al. The national trend of the burden of Chronic Kidney Disease (CKD) in Iran from 1990 to 2019. *J Diabetes Metab Disord*. 2023;22(2):1657–71.
 29. Pandey AR, Poudyal A, Adhikari B, Shrestha N. Burden of chronic kidney disease in Nepal: An analysis of the burden of disease from 1990 to 2019. *PLOS Glob Public Health*. 2023;3(7): e0001727.
 30. Shahbazi F, Doosti-Irani A, Soltanian A, Poorolajal J. National trends and projection of chronic kidney disease incidence according to etiology from 1990 to 2030 in Iran: a Bayesian age-period-cohort modeling study. *Epidemiol Health*. 2023;45: e2023027.
 31. Li Y, Ning Y, Shen B, et al. Temporal trends in prevalence and mortality for chronic kidney disease in China from 1990 to 2019: an analysis of the Global Burden of Disease Study 2019. *Clin Kidney J*. 2022;16(2):312–21.
 32. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication—worldwide more than 850 million individuals have kidney diseases. *Kidney Int*. 2019;96(5):1048–50.
 33. Chronic kidney disease in the United States. Centers for Disease Control and Prevention; 2023. Available from: <https://www.cdc.gov/kidney-disease/php/data-research/>.
 34. Foreman KJ, Marquez N, Dolgert A, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. *Lancet*. 2018;392:2052–90.
 35. Bosi A, Xu Y, Gasparini A, et al. Use of nephrotoxic medications in adults with chronic kidney disease in Swedish and US routine care. *Clin Kidney J*. 2021;15(3):442–51.
 36. Gummidi B, John O, Ghosh A, et al. A Systematic Study of the Prevalence and Risk Factors of CKD in Uddanam. *India Kidney Int Rep*. 2020;5(12):2246–55.
 37. US National Institute of Diabetes and Digestive and Kidney Diseases. Kidney disease statistics for the United States. <https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease> (2023).
 38. Stanifer JW, Muir A, Jafar TH, Patel UD. Chronic kidney disease in low- and middle-income countries. *Nephrol Dial Transplant*. 2016;31(6):868–74.
 39. Ebi KL, Capon A, Berry P, et al. Hot weather and heat extremes: health risks. *Lancet*. 2021;398(10301):698–708.
 40. Rosinger AY, Bethancourt H, Swanson ZS, et al. Drinking water salinity is associated with hypertension and hyperdilute urine among Daasanach pastoralists in Northern Kenya. *Sci Total Environ*. 2021;770: 144667.
 41. Wan ET, Darssan D, Karatela S, Reid SA, Osborne NJ. Association of Pesticides and Kidney Function among Adults in the US Population 2001–2010. *Int J Environ Res Public Health*. 2021;18(19):10249.
 42. Gao Z, Wu N, Du X, Li H, Mei X, Song Y. Toxic Nephropathy Secondary to Chronic Mercury Poisoning: Clinical Characteristics and Outcomes. *Kidney Int Rep*. 2022;7(6):1189–97.
 43. Parameswaran S, Rinu PK, Kar SS, et al. A Newly Recognized Endemic Region of CKD of Undetermined Etiology (CKDu) in South India—"Tondaimandalam Nephropathy". *Kidney Int Rep*. 2020;5(11):2066–73.
 44. Wijewickrama ES, Thakshila WAG, Ekanayake EMD, et al. Prevalence of CKD of Unknown Etiology and its Potential Risk Factors in a Rural Population in Sri Lanka. *Kidney Int Rep*. 2022;7(10):2303–7.
 45. Cabrera JWE, Vervaeke BA, Schreurs G, Nast CC, Santa-Cruz F, De Broe ME. Chronic Interstitial Nephritis in Agricultural Communities: A Patient in Paraguay. *Kidney Int Rep*. 2022;7(5):1131–5.
 46. Wearne N, Okpechi IG. HIV-associated renal disease - an overview. *Clin Nephrol*. 2016;86 (2016)(13):41–47.
 47. Guo Q, Wu S, Xu C, Wang J, Chen J. Global Disease Burden From Acute Glomerulonephritis 1990–2019. *Kidney Int Rep*. 2021;6(8):2212–7.

48. Olowu WA, Niang A, Osafo C, et al. Outcomes of acute kidney injury in children and adults in sub-Saharan Africa: a systematic review. *Lancet Glob Health*. 2016;4(4):e242–50.
49. Yang CW. Leptospirosis Renal Disease: Emerging Culprit of Chronic Kidney Disease Unknown Etiology. *Nephron*. 2018;138(2):129–36.
50. Riefkohl A, Ramírez-Rubio O, Laws RL, et al. Leptospira seropositivity as a risk factor for Mesoamerican Nephropathy. *Int J Occup Environ Health*. 2017;23(1):1–10.
51. Barraclough KA, Blashki GA, Holt SG, Agar JWM. Climate change and kidney disease-threats and opportunities. *Kidney Int*. 2017;92(3):526–30.
52. United Nations. Day of 8 billion. un.org <https://www.un.org/en/dayof8billion> (2022).
53. United Nations, Department of Economic and Social Affairs. World population prospects 2022. un.org <https://population.un.org/wpp/> (2022).
54. World Health Organization. Ageing and health. who.int <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health> (2024).
55. Zhou XJ, Rakheja D, Yu X, Saxena R, Vaziri ND, Silva FG. The aging kidney. *Kidney Int*. 2008;74(6):710–20.
56. Denic A, Lieske JC, Chakkera HA, et al. The Substantial Loss of Nephrons in Healthy Human Kidneys with Aging. *J Am Soc Nephrol*. 2017;28(1):313–20.
57. Denic A, Glasscock RJ, Rule AD. Structural and Functional Changes With the Aging Kidney. *Adv Chronic Kidney Dis*. 2016;23(1):19–28.
58. Chesnaye NC, Ortiz A, Zoccali C, Stel VS, Jager KJ. The impact of population ageing on the burden of chronic kidney disease. *Nat Rev Nephrol*. 2024;20(9):569–85.
59. Chesnaye NC, Carrero JJ, Hecking M, Jager KJ. Differences in the epidemiology, management and outcomes of kidney disease in men and women. *Nat Rev Nephrol*. 2024;20(1):7–20.
60. Melsom T, Norvik JV, Enoksen IT, et al. Sex Differences in Age-Related Loss of Kidney Function. *J Am Soc Nephrol*. 2022;33(10):1891–902.
61. van der Burgh AC, Rizopoulos D, Ikram MA, Hoorn EJ, Chaker L. Determinants of the Evolution of Kidney Function With Age. *Kidney Int Rep*. 2021;6(12):3054–63.
62. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016;388(10053):1459–1544.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.