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Epidemiological status, development trends, and risk factors of disability-adjusted life years due to diabetic kidney disease: A systematic analysis of Global Burden of Disease Study 2021

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Abstract

Background: Approximately 40% of individuals with diabetes worldwide are at risk of developing diabetic kidney disease (DKD), which is not only the leading cause of kidney failure, but also significantly increases the risk of cardiovascular disease, causing significant societal health and financial burdens. This study aimed to describe the burden of DKD and explore its cross-country epidemiological status, predict development trends, and assess its risk factors and sociodemographic transitions.

Methods: Based on the Global Burden of Diseases (GBD) Study 2021, data on DKD due to type 1 diabetes (DKD-T1DM) and type 2 diabetes (DKD-T2DM) were analyzed by sex, age, year, and location. Numbers and age-standardized rates were used to compare the disease burden between DKD-T1DM and DKD-T2DM among locations. Decomposition analysis was used to assess the potential drivers. Locally weighted scatter plot smoothing and Frontier analysis were used to estimate sociodemographic transitions of DKD disability-adjusted life years (DALYs).

Results: The DALYs due to DKD increased markedly from 1990 to 2021, with a 74.0% (from 2,227,518 to 3,875,628) and 173.6% (from 4,122,919 to 11,278,935) increase for DKD-T1DM and DKD-T2DM, respectively. In 2030, the estimated DALYs for DKD-T1DM surpassed 4.4 million, with that of DKD-T2DM exceeding 14.6 million. Notably, middle-sociodemographic index (SDI) quintile was responsible for the most significant DALYs. Decomposition analysis revealed that population growth and aging were major drivers for the increased DKD DALYs in most regions. Interestingly, the most pronounced effect of positive DALYs change from 1990 to 2021 was presented in high-SDI quintile, while in low-SDI quintile, DALYs for DKD-T1DM and DKD-T2DM presented a decreasing trend over the past years. Frontiers analysis revealed that there was a negative association between SDI quintiles and age-standardized DALY rates (ASDRs) in DKD-T1DM and DKD-T2DM. Countries with middle-SDI shouldered disproportionately high DKD burden. Kidney dysfunction (nearly 100.0% for DKD-T1DM and DKD-T2DM), high fasting plasma glucose (70.8% for DKD-T1DM and 87.4% for DKD-T2DM), and non-optimal temperatures (low and high, 5.0% for DKD-T1DM and 5.1% for DKD-T2DM) were common risk factors for age-standardized DALYs in T1DM-DKD and T2DM-DKD. There were other specific risk factors for DKD-T2DM such as high body mass index (38.2%), high systolic blood pressure (10.2%), dietary risks (17.8%), low physical activity (6.2%), lead exposure (1.2%), and other environmental risks.

Conclusions: DKD markedly increased and varied significantly across regions, contributing to a substantial disease burden, especially in middle-SDI countries. The rise in DKD is primarily driven by population growth, aging, and key risk factors such as high fasting plasma glucose and kidney dysfunction, with projections suggesting continued escalation of the burden by 2030.

Keywords: Diabetic kidney disease; Type 1 diabetes; Type 2 diabetes; Disability-adjusted life years; Disease burden

Introduction

Diabetes is the major cause of chronic kidney disease (CKD) worldwide, and nearly 40% of individuals with diabetes may develop CKD.[1–4] Diabetic kidney disease (DKD) can be diagnosed clinically by either persistent albuminuria or sustained reduction in the estimated glomerular filtration rate (eGFR) for at least three months among patients with diabetes.[5,6] DKD is not only the leading cause of kidney failure and end-stage renal disease (ESRD), accounting for about 50% of cases, but also an important contributor to cardiovascular disease and

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overall mortality in patients with diabetes. DKD care is associated with substantial expenditures, and the related cost among a primarily elderly cohort in the Medicare population was about $25 billion in 2011.[7] These data indicate that DKD causes a substantial burden worldwide, and the overall burden could continue to rise.[8]

To our knowledge, the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study is the significant comprehensive study to date to quantify the disease burden attributed to a wide range of modifiable risk factors. This study covers every GBD round, encompassing all countries worldwide, various age groups, genders, and evolving over time. The GBD 2021, the latest iteration of this study, offers a unique opportunity to assess the GBD attributable to these risk factors.[9] Although there have been several studies regarding the global or national burden of DKD using data from the GBD, it is essential to emphasize that the pathogenesis, disease process, epidemiological characteristics, and comprehensive management of type 1 diabetes (T1DM) and type 2 diabetes (T2DM) are different. DKD is usually confirmed in T1DM patients after five years of diagnosis, while it can be identified at the time of diagnosis of T2DM. Additionally, CKD is more common in T1DM, and the cardiovascular and renal disease burden in patients with T1DM is at least as high as in patients with T2DM.[8,10,11] Correspondingly, they pose distinct public health challenges. Therefore, when formulating management plans, decision-makers should comprehensively consider the epidemiological differences between DKD caused by T1DM and T2DM to devise more effective preventive and management strategies.

Disability-adjusted life years (DALYs) are of great significance in GBD research. They serve as a comprehensive and standardized measure to evaluate the burden of disease, enabling policymakers and researchers to prioritize interventions, allocate resources, and track progress in improving population health.[12] CKD is among the top 10 causes of reduced life expectancy or DALYs,[13] which is a comprehensive measure of the quantity and quality of life in time. With the increase in incidence and prevalence of T1DM and T2DM, DKD would become an important prevalent disease affecting DALYs.

Therefore, it is imperative to understand the current situation and development trends, drivers of DKD, and risk factors of DALYs in DKD across regions. It is crucial to understand the relationship between the health income level of different regions worldwide and DALYs in DKD. These insights will guide policymakers in developing appropriate intervention measures. Based on the GBD 2021, we conducted this study to describe the burden of DKD and explore its cross-country epidemiological status, development trends, risk factors, and sociodemographic transitions.

Methods

Data sources and definition

In this study, data were obtained from the GBD 2021 (http://ghdx.healthdata.org/gbd-results-tool), which is a comprehensive and comparative assessment of 369 diseases and injuries and 87 risk factors among 204 countries and territories between 1990 and 2021. We extracted the detailed information on measures of disease burden including the number and the rate of incidence, prevalence, death and DALYs attribute to DKD, and attributable risk factors for DKD. The definitions of these measurements along with the metrics were described elsewhere.[14]

All measures were presented as raw values and age-standardized rates (ASRs) per 100,000 population. Age standardization was performed using the World Health Organization's world population standard age structure. Sociodemographic index (SDI) is a measure used to assess the development level of countries/territories based on several socioeconomic indicators. The SDI accounts for three main components: Income per capita, educational attainment, and fertility rate (under the age of 25 years), ranging from 0 to 1, with higher values indicating a higher level of development. Further elaboration on the techniques used in developing and calculating the SDI can be found elsewhere.[15] Based on SDI from the year 2021, 204 countries and territories were classified into five categories: High, high-middle, middle, low-middle, and low SDI groups.

Disease model and statistical analysis

Based on data from 1999 to 2021, the nordpred R package (https://rdrr.io/github/haraldwf/nordpred/man/nordpred) was used to predict the numbers and age-standardized rates of the prevalence and DALYs of DKD in the next 10 years.[16] To assess the additive contribution of explanatory factors that drove the change in prevalence and DALYs from1990 to 2021, we conducted a decomposition analysis based on the population growth, aging, and age- and population-standardized rates (which is referred to herein as epidemiologic changes),[17,18] respectively. Linear, locally weighted scatter plot smoothing was used to explore the age-standardized DALY rates (per 100,000) (ASDRs) for DKD for countries and territories by SDI. To ascertain the projected correlation between SDI and rates of DALYs, a Gaussian process regression was applied to estimates from 1990 to 2021 across various global locations. Frontier analysis aimed to determine the lowest attainable burden of DKD, considering the development status of countries or territories as determined by the SDI. The frontier represented the countries or territories with exemplary performance, achieving the lowest DKD burden relative to their SDI. The term "effective difference" refers to the gap between the observed burden and the potential burden of disease that could be achieved in a country or territory given their SDI.[15] This gap can potentially be reduced or eliminated by leveraging the sociodemographic resources available in the respective country or territory.

For risk factors estimation, 84 factors were evaluated across four categories, including behavioral, environmental, occupational, and metabolic. The attributable number and ASR of DALYs related to these selected risk factors were determined through a comparative risk assessment method; the specific steps are described elsewhere.[19,20]

Data were visualized using packages, including ggplot2 (https://github.com/tidyverse/ggplot2), and ggsci (https://github.com/nanxstats/ggsci). Data cleaning was conducted with the tidyverse package (https://github.com/tidyverse/tidyverse). All data analysis and visualization were conducted using the R 4.1.0 software (The R Foundation for Statistical Computing, Vienna, Austria). In this study, we calculated 95% uncertainty intervals (UIs) of the burden of DKD using the 2.5th and 97.5th percentiles from a 1000-draw distribution for each metric for each variable, with all rates reported per 100,000 population. All tests were two-sided, and *P*-values less than 0.05 were considered statistically significant.

Results

Regional burden of DKD due to T1DM and T2DM from 1990 to 2021

Overall, the global burden of DKD increased significantly in the past 32 years [Table 1]. For DKD due to type 1 diabetes (DKD-T1DM), the global number of incident patients increased by 49.6%, from 63,601 (95% UI, 52,476–76,375) in 1990 to 95,140 (95% UI, 82,237–111,471) in 2021. The age-standardized incidence rate (per 100,000) (ASIR) showing a 19.3% (95% UI, 8.4–30.7%) increase, from 1.1 (95% UI, 0.9–1.3) in 1990 to 1.3 (95% UI, 1.1–1.5) in 2021. For DKD due to type 2 diabetes (DKD-T2DM), the global number of new cases increased from 753,106 (95% UI, 680,930–826,928) in 1990 to 2,012,025 (95% UI, 1,857,800–2,154,288) in 2021, with a 167.2% (95% UI, 153.5–182.6%) increase. The ASIR increased from 19.1 (95% UI, 17.3–20.8) to 23.1 (95% UI, 21.4–24.7), a 21.0% increase in the same period.

The number of global prevalent patients with DKD-T1DM increased by 112.1%, rising from 2,967,857 (95% UI, 2,607,069–3,328,285) in 1990 to 6,295,711 (95% UI, 5,459,693–7,114,345) in 2021. Meanwhile the age-standardized prevalence rate (per 100,000) (ASPR) increased from 57.5 (95% UI, 50.9–64.1) to 77.3 (95% UI, 66.9–87.6) (a 34.4% [95% UI, 25.4–43.2%] increase). Similarly, over the period from 1990 to 2021, the prevalence of DKD-T2DM increased from 58,105,268 (95% UI, 53,056,992–63,286,818) to 107,559,955 (95% UI, 99,170,797–115,994,732), marking an 85.1% (95% UI, 78.1–91.4%) increase. In contrast, the ASPR of DKD-T2DM showed a modest decrease of –5.1% in both sexes.

For DKD-T1DM, the number of DALYs worldwide was 2,227,518 (95% UI, 1,835,373–2,679,208) in 1990, increasing by 74.0% to reach 3,875,628 (95% UI, 3,062,396–4,845,503). However, the ASDR showed a downward trend, decreasing by 3.9%, from 47.0 (95% UI, 38.4–57.3) in 2019 to 45.2 (95% UI, 36.0–56.3) in 2021. The global DALYs of DKD-T2DM increased to 11,278,935 (95% UI, 9,682,785–13,103,871) in 2021, representing a 173.6% increase in DALYs over the last 32 years. The ASDR increased from 105.7 (95% UI, 90.7–122.7) in 1990 to 131.1 (95% UI, 112.8–152.5) in 2021, reflecting a 24.0% increase over the period.

In 1990, the overall global years of life lost (YLLs) number of DKD-T1DM was 2,097,154 (95% UI, 1,699,743–2,551,170) and reached 3,580,692 (95% UI, 2,826,228–4,518,921) in 2021, indicating a 70.7% increase. However,

Table 1: Numbers for all ages and ASRs (per 100,000) of the DKD burden indicators in the global regions (1990–2021).

Cause of DKD	Measure	Metrics	1990(*n* [95% UIs])	2021 (*n* [95% UIs])	% Change (95% UIs)
T1DM	Incidence	All ages number	63,601 (52,476, 76,375)	95,140 (82,237, 111,471)	49.6 (33.7, 66.0)
		ASR	1.1 (0.9, 1.3)	1.3 (1.1, 1.5)	19.3 (8.4, 30.7)
	Prevalence	All ages number	2,967,857 (2,607,069, 3,328,285)	6,295,711 (5,459,693, 7,114,345)	112.1 (97.4, 127.6)
		ASR	57.5 (50.9, 64.1)	77.3 (66.9, 87.6)	34.4 (25.4, 43.2)
	DALYs	All ages number	2,227,518 (1,835,373, 2,679,208)	3,875,628 (3,062,396, 4,845,503)	74.0 (50.1, 95.6)
		ASR	47.0 (38.4, 57.3)	45.2 (36.0, 56.3)	–3.9 (–17.1, 6.8)
	YLLs	All ages number	2,097,154 (1,699,743, 2,551,170)	3,580,692 (2,826,228, 4,518,921)	70.7 (45.6, 93.1)
		ASR	44.2 (35.7, 54.3)	41.8 (33.3, 52.6)	–5.4 (–19.4, 5.7)
	YLDs	All-ages number	130,365 (92,665, 172,844)	294,936 (206,539, 393,036)	126.2 (115.6, 138.3)
		ASR	2.9 (2.0, 3.8)	3.4 (2.4, 4.5)	18.7 (14.3, 24.1)
	Deaths	All ages number	49,300 (39,088, 61,208)	94,020 (71,457, 119,984)	90.7 (63.0, 114.0)
		ASR	1.0 (0.8, 1.4)	1.1 (0.8, 1.4)	0.4 (–14.0, 11.4)
T2DM	Incidence	All ages number	753,106 (680,930, 826,928)	2,012,025 (1,857,800, 2,154,288)	167.2 (153.5, 182.6)
		ASR	19.1 (17.3, 20.8)	23.1 (21.4, 24.7)	21.0 (15.0, 27.5)
	Prevalence	All ages number	58,105,268 (53,056,992, 63,286,818)	107,559,955 (99,170,797, 115,994,732)	85.1 (78.1, 91.4)
		ASR	1327.2 (1223.8, 1439.4)	1259.6 (1162.0, 1359.9)	–5.1 (–7.5, 3.0)
	DALYs	All ages number	4,122,919 (3,498,980, 4,818,958)	11,278,935 (9,682,785, 13,103,871)	173.6 (140.5, 194.3)
		ASR	105.7 (90.7, 122.7)	131.1 (112.8, 152.5)	24.0 (9.3, 33.0)
	YLLs	All ages number	3,280,717 (2,734,676, 3,948,590)	9,330,429 (7,888,759, 11,065,789)	184.4 (142.5, 212.9)
		ASR	84.4 (70.9, 100.8)	108.6 (91.7, 128.4)	28.6 (10.3, 40.2)
	YLDs	All ages number	842,202 (584,047, 1,093,224)	1,948,506 (1,358,645, 2,516,109)	131.4 (121.6, 142.6)
		ASR	21.3 (14.8, 27.5)	22.5 (15.7, 29.0)	5.7 (1.4, 10.5)
	Deaths	All ages number	147,970 (124,179, 176,413)	477,273 (401,541, 565,951)	222.5 (177.4, 253.8)
		ASR	4.1 (3.5, 4.9)	5.7 (4.8, 6.8)	37.8 (19.2, 49.6)

ASR: Age-standardized rate; DALYs: Disability-adjusted life years; DKD: Diabetic kidney disease; T1DM: Type 1 diabetes mellitu; T2DM: Type 2 diabetes; UIs: Uncertainty intervals; YLDs: Years lived with disability; YLLs: Years of life lost.

the age-standardized YLLs rate (per 100,000) showed a slight downward trend, decreasing by –5.4% (95% UI, –19.4% to 5.7%), from 44.2 (95% UI, 35.7–54.3) in 1990 to 41.8 (95% UI, 33.3–52.6) in 2021. The overall global YLLs to DKD-T2DM increased from 3,280,717 (95% UI, 2,734,676–3,948,590) to 9,330,429 (95% UI, 7,888,759–11,065,789) in 2021, representing a 184.4% increase in YLLs over the last 32 years. Age-standardized YLLs rate (per 100,000) increased by 28.6% to 108.6 (95% UI, 91.7–128.4).

In 1990, the global years lived with disability (YLDs) from DKD-T1DM was 130,365 (95% UI, 92,665–172,844) and reached 294,936 (95% UI, 206,539–393,036) in 2021, indicating an 126.2% increase in the YLDs in both sexes. The age-standardized YLDs rate (per 100,000) increased by 18.7% to 3.4 (95% UI, 2.4–4.5). For the DKD-T2DM, the number of global YLDs and age-standardized YLDs rates also showed increasing trends over the past 32 years, increasing of 131.4% (from 842,202 [95% UI, 584,047–1,093,224] to 1,948,506 [95% UI, 1,358,645–2,516,109]) and 5.7% (from 21.3 [95% UI, 14.8–27.5] to 22.5 [95% UI, 15.7–29.0]), respectively.

Global deaths due to DKD-T1DM increased to 49,300 (95% UI, 39,088–61,208) in 2021, representing a 90.7% increase over the last 32 years. From 1990 to 2021, the age-standardized death rate (per 100,000) changed slightly from 1.0 (95% UI, 0.8–1.4) to 1.1 (95% UI, 0.8–1.4), indicating a 0.4% change. The global mortality in DKD-T2DM across all ages increased from 147,970 (95% UI, 124,179–176,413) in 1990 to 477,273 (95% UI, 401,541–565,951) in 2021, indicating a significant 222.5% increase; the age-standardized death rate increased by 37.8% (from 4.1 [95% UI, 3.5– 4.9] to 5.7 [95% UI, 4.8–6.8]) in 2021.

Time trend of global DKD prevalence and DALYs from 1990 to 2030

Over the past years, the global prevalence and DALYs of DKD increased markedly. The global prevalence of DKD-T1DM has increased consistently since 1990, with males and females demonstrating a similar upward trend, although females exhibited a higher prevalence compared with males. The most notable increase was observed between 2010 and 2019. However, from 2019 to 2021, there was a temporary decline in global prevalence, dropping from approximately 6.5 million people in 2019 to around 6.3 million people in 2021. The trend is predicted to resume its upward trajectory, showing a smooth increase in prevalence from 2020 to 2030 and surpassing 7.5 million cases worldwide by 2030 [Figure 1A]. By contrast, the prevalence of DKD-T2DM has been increasing significantly since 1990, and the number of prevalent cases is expected to exceed 130 million by 2030. Further analysis indicated that the prevalence of males and females have increased almost equally over the past 32 years, with slightly more male patients than female patients [Figure 1B]. The detailed prevalent number and ASPR of people with DKD-T1DM and DKD-T2DM in different age groups and genders are shown in the Supplementary Table 1, http://links.lww.com/CM9/C255.

The time trend of global DALYs from 1990 to 2030 showed a steady upward trend for DKD-T1DM: It can be roughly divided into four growth trends from 1990 to 2030, with a 10-year boundary and by 2030, the number of DALYs is predicted to surpass 4.4 million. Notably the global growth rate of ADSR gradually decreased from 2000 to 2018 and the number of DALYs was greater in males than in females across all years [Figure 1C]. The number of DALYs in DKD-T2DM increased sharply from 1990 to 2020: A steeper slope trend will continue until 2030, with the DALYs predicted to exceed 14.6 million by 2030 [Figure 1D]. The detailed date is shown in the Supplementary Table 2, http://links.lww.com/CM9/C255.

Decomposition analysis of changes in DALYs and prevalence

Figure 2 presents the results of the decomposition analysis globally and within the five SDI quintiles, revealing changes in DALYs of DKD attributed to three population-level factors over the past 32 years, including population aging, population growth, and epidemiologic changes. For DKD-T1DM, there are varying degrees of increase in DLAYs for each SDI quintile [Figure 2A]. Aging and population growth were major drivers of change in DALYs in most GBD regions, contributing to 25.9% and 80.5% of the increased burden of DALYs in 2021, respectively. However, epidemiological changes showed negative growth, accounting for –6.4% of the total DALYs. Notably, the middle-SDI quintile had the most significant increase, with a growth amount of 720,020, experiencing the largest increase in DALYs in the past 32 years. The contribution of aging to the overall DALYs was most pronounced in the high-middle-SDI quintile (76.5%) and decreased to 44.7% in the middle-SDI, 21.3% in the high-SDI, 17.4% in the low-middle-SDI, and diminished substantially in the low-SDI quintile (–1.7%). It is worth noting that the increase in DALYs driven by population growth is predominantly observed in high-middle-SDI (117.7%) and low-SDI (124.5%) quintiles, with females showing higher DALYs than in males in both groups. In contrast, the relative contribution of population growth to the increase in DALYs is relatively small in high-SDI countries (44.3%). During the previous 32 years, epidemiological changes adjusted for age and population have varied globally: There was a 34.4% increase in the high-SDI quintile, a decelerating trend in the low-middle-SDI quintile (11.3%), and a decline in the low-SDI (–22.8%), middle-SDI (–28.4%) quintiles. Among them, the decrease was most pronounced in the high-middle-SDI quintile (–94.2%), and the rate of decrease was as high as 160.8% in females in this SDI quintile [Supplementary Table 3, http://links.lww.com/CM9/C255].

The increase in DKD-T2DM DALYs worldwide and across SDI quintiles was greater than that in the increases in DKD-T1DM DALYs. The major drivers of this increase globally were population growth and aging, contributing 48.3% and 31.2% of the increase in DALYs in 2021, respectively. Among SDI quintiles, the middle SDI quintile was the largest (nearly 1,359,000) in overall DALYs, with

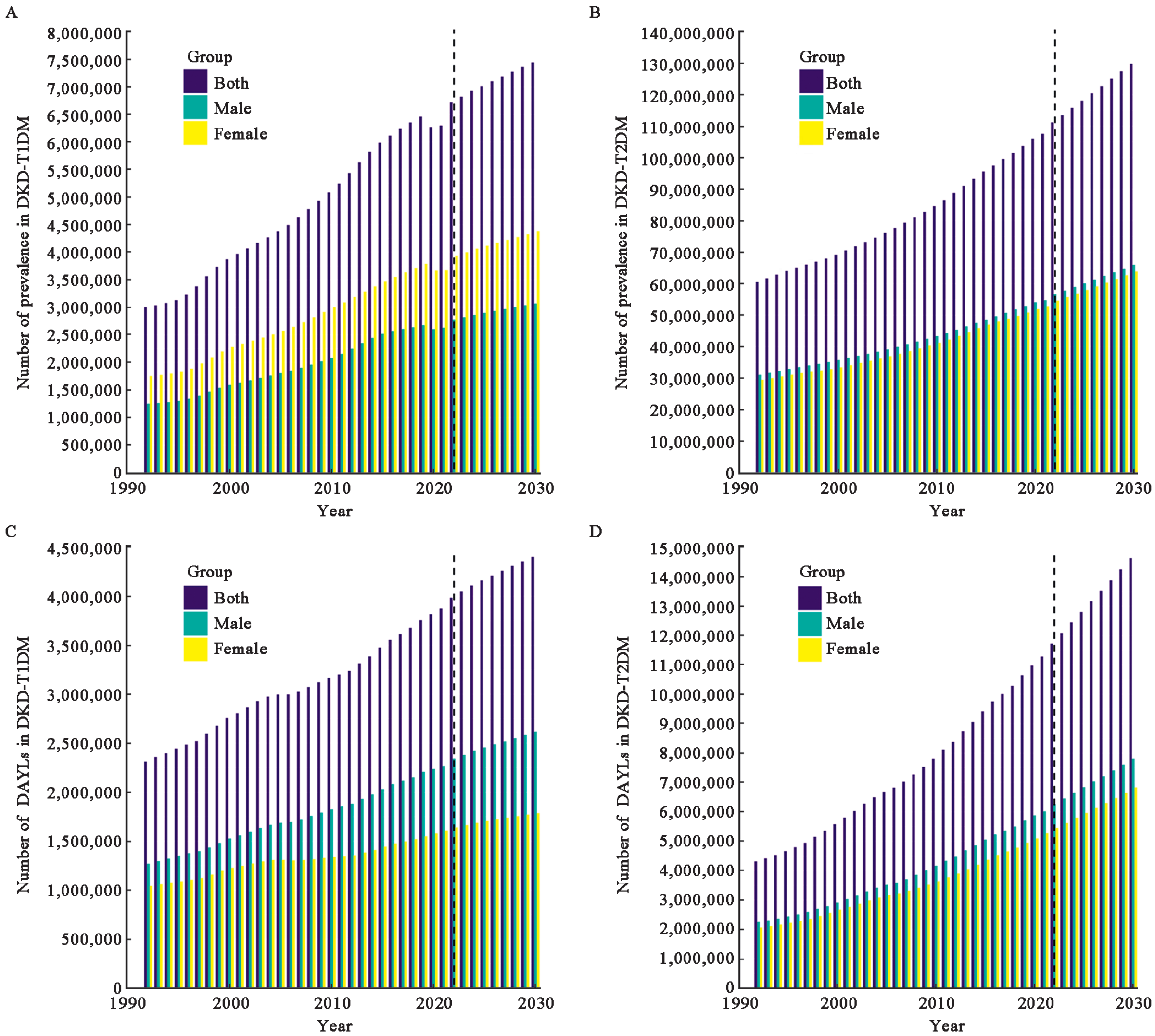

Figure 1: Time trend of global DKD prevalence and DALYs from 1990 to 2030. (A) The global prevalence of DKD-T1DM; (B) The global prevalence of DKD-T2DM; (C) The number of DALYs of DKD-T1DM; (D) The number of DALYs of DKD-T2DM. The dashed line indicates the year 2021. The data prior to the dashed line represent the actual statistics from GBD, while the data following the dashed line correspond to the predicted values for the period 2021–2030 (excluding 2021), derived using the nordpred R package (https://rdrr.io/github/haraldwf/nordpred/man/nordpred). DALYs: Disability-adjusted life years; DKD: Diabetic kidney disease; DKD-T1DM: DKD due to type 1 diabetes; DKD-T2DM: DKD due to type 2 diabetes.

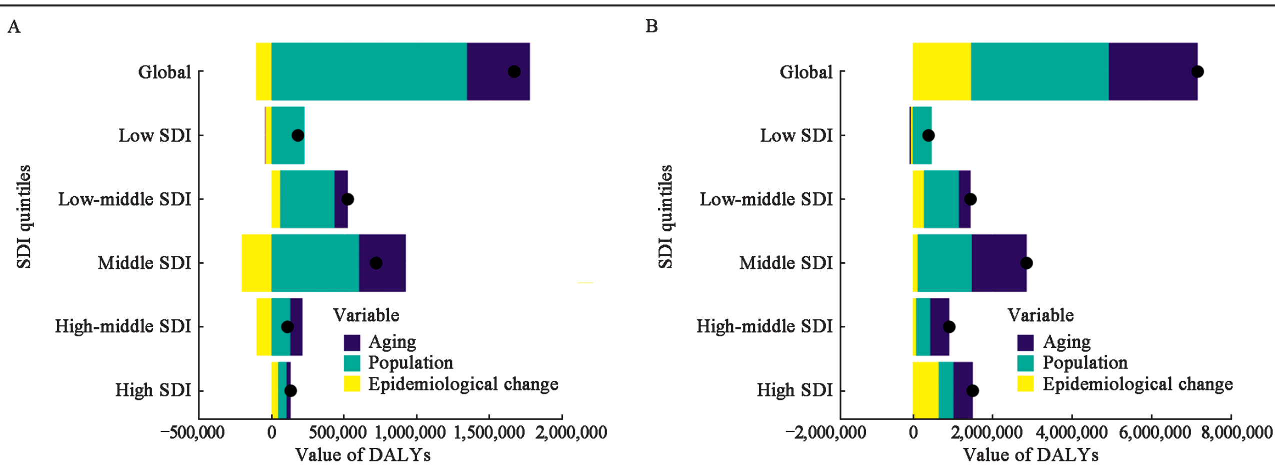

Figure 2: Changes in DKD DALYs according to population-level determinants of population growth, aging, and epidemiological change from 1990 to 2021 at the global level and by quintiles of SDI. (A) Changes in DKD-T1DM DALYs; (B) Changes in DKD-T2DM DALYs. The black dot represents the overall value of change contributed by all three components. For each component, the magnitude of a positive value indicates a corresponding increase in DKD DALYs attributed to the component; The magnitude of a negative value indicates a corresponding decrease in DKD DALYs attributed to the related component. DALYs: Disability-adjusted life years; DKD: Diabetic kidney disease; DKD-T1DM: DKD due to type 1 diabetes; DKD-T2DM: DKD due to type 2 diabetes; SDI: Sociodemographic index.

the contributions of age structure, population dynamics, and epidemiologic changes contributing to 48.1%, 47.5%, and 4.4% of the overall burden of DKD-T2DM, respectively. Population growth was the leading contributor to the increase in DALYs in the low-SDI quintiles (119.0%), and males accounted for a higher percentage of increased DALYs than females (125.7% *vs*. 110.7%). Furthermore, our results showed that the percent of epidemiological changes in DKD-T2DM worldwide varied from 1990 to 2021. Among the SDI quintiles, the high SDI quintile showed the most significant increase, reaching 43.1%, and the low-middle-SDI, high-middle-SDI, and middle-SDI quintiles showed a relative decelerating trend of 19.4%, 9.5%, and 4.4%, respectively. In contrast, there was a decreasing trend in the low-SDI quintile (–10.5%) [Figure 2B]. The detailed date is shown in Supplementary Table 4, http://links.lww.com/CM9/C255. Additionally, we performed a decomposition analysis of the prevalence change in DKD-T1DM/T2DM from 1990 to 2021 and the detailed finding are shown in Supplementary Figure 1, http://links.lww.com/CM9/C255.

Frontier analysis

In 2021, there was an inverse association between ASDR for DKD and SDI quintiles in most countries and territories: Due to T1DM (R = –0.13, P = 0.058) and due to T2DM (R = –0.17, P = 0.018). To better understand the potential improvement in DKD DALY rates that are potentially achievable by a country's development status, we employed a frontier analysis based on ASDR and SDI using data from 1990 to 2021 [Figure 3]. The frontier line helped to demarcate the countries and territories with the lowest DALY rates, indicating optimal performance for their corresponding SDI. The effective difference was then calculated as the distance from the frontier, representing the gap between the country's observed and potentially achievable DALYs. We computed the effective difference for each country and territory using the 2021 DALYs and SDI [Figure 3]. Generally, a smaller effective difference from the frontier was observed as SDI increased, with less variance in the results. The top 10 countries with the highest effective difference from the frontier (range of effective difference: 522.8–296.5) for DKD-T1DM were: American Samoa, Nauru, Marshall Islands, the Federated States of Micronesia, Niue, Mauritius, Northern Mariana Islands, Palau, Kiribati, and Fiji; these countries have disproportionally higher DALY rates than those with comparable sociodemographic resources. The top 10 countries with the lowest DALY rates given their level of development spectrum and thus the lowest effective difference (range: 0.5–3.9) included Tajikistan, Niger, Yemen, Slovenia, Iceland, Switzerland, Somalia, Australia, Czechia, and San Marino.

According to our findings, approximately 76.8% of countries and regions experienced an increase in the burden of DKD-T2DM disease from 1990 to 2021 [Figure 3]. We identified the top 10 countries with the highest DALY rates due to DKD-T2DM from the frontier and the range of effective difference between these countries was 1031.9–576.7. These countries were American Samoa, Nauru, Northern Mariana Islands, the Federated States of Micronesia, Marshall Islands, Niue, Mauritius, Palau, Fiji, and Kiribati. We also identified the top 10 countries with the lowest DALY rates based on their level of development. These countries had the lowest effective difference, ranging from 2.1 to 10.0, and included Tajikistan, Niger, Iceland, Belarus, Australia, Ukraine, Slovenia, Norway, Czechia, and San Marino. Notably, we observed that the ASDR decreased in Niger and Czechia between 1990 and 2021. In contrast, the other 4 countries among the top 10 countries with the lowest effective difference: Tajikistan, Belarus, Australia, and Ukraine, showed an increase in this rate over the same period.

Furthermore, in line with global and regional trends, most countries and territories experienced an increase in ASDR in DKD-T1DM between 1990 and 2021, especially for countries and regions situated in the high-middle SDI quintile. For instance, Ukraine witnessed a surge of 560.2%, rising from 1.9 in 1990 to 12.4 in 2021, while Armenia (209.8% increase from 3.2 to 9.8) and Belarus (161.2% increase from 3.9 to 10.3) also experienced great increase. Additionally, similar upward trends were observed in EI Salvador (184.3% increase from 47.1 to 133.9) and Lesotho (148.3% increase from 16.2 to 40.3). Furthermore, although certain high-income countries displayed a substantial decrease in the overall trend of ASDR between 1990 and 2021, their persistently high ASDR did not align with their level of development. For instance, Kuwait and Poland demonstrated a 57.4% (from 20.9 to 8.9) and 53.8% (from 14.8 to 6.9) decrease, respectively. The Republic of Korea exhibited a 49.1% (from 30.6 to 15.6) decrease and Singapore experienced a 44.1% (from 31.4 to 17.5) decrease. However, more than two-thirds of countries and regions situated in high-middle SDI quintile witnessed an increase in ASDR over the past 32 years. Conversely, low-SDI quintile countries like Ethiopia and Rwanda demonstrated a significantly decrease in ASDR, with a decline of 53.5% (from 215.9 to 100.4) and 39.5% (from 77.8 to 47.1), respectively.

For DKD-T2DM, nearly three-fourths of countries and regions showed a trend of increasing ASDR. Notably, significant increases and decreases in ASDR were observed among high-SDI quintile countries and region. As an example, significant increases were observed in the United States of America, Estonia, Saudi Arabia, Latvia, and Denmark, and declines were observed in Kuwait, Cyprus, Poland, Republic of Korea, and Singapore. The magnitude of change in ASDR was approximately equal for high-SDI countries and regions. Although the majority of countries and territories across different quintiles showed an increasing trend of ASDR between 1990 and 2021, there are still some countries and regions that experienced a significant decline, such as Ethiopia (–42.1% decrease from 563.3 to 326.0) situated in the low-SDI quintile, Bangladesh (–14.1% decrease from 105.6 to 90.7) in the low-middle-SDI quintile, Maldives (–43.6% decrease from 407.4 to 229.6) in the middle-SDI quintile, Spain (–25.5% decrease from 52.6 to 39.2) in the middle-high-SDI quintile, and Kuwait (48.6% decrease from 152.5 to 78.3) in the high-middle-SDI quintile.

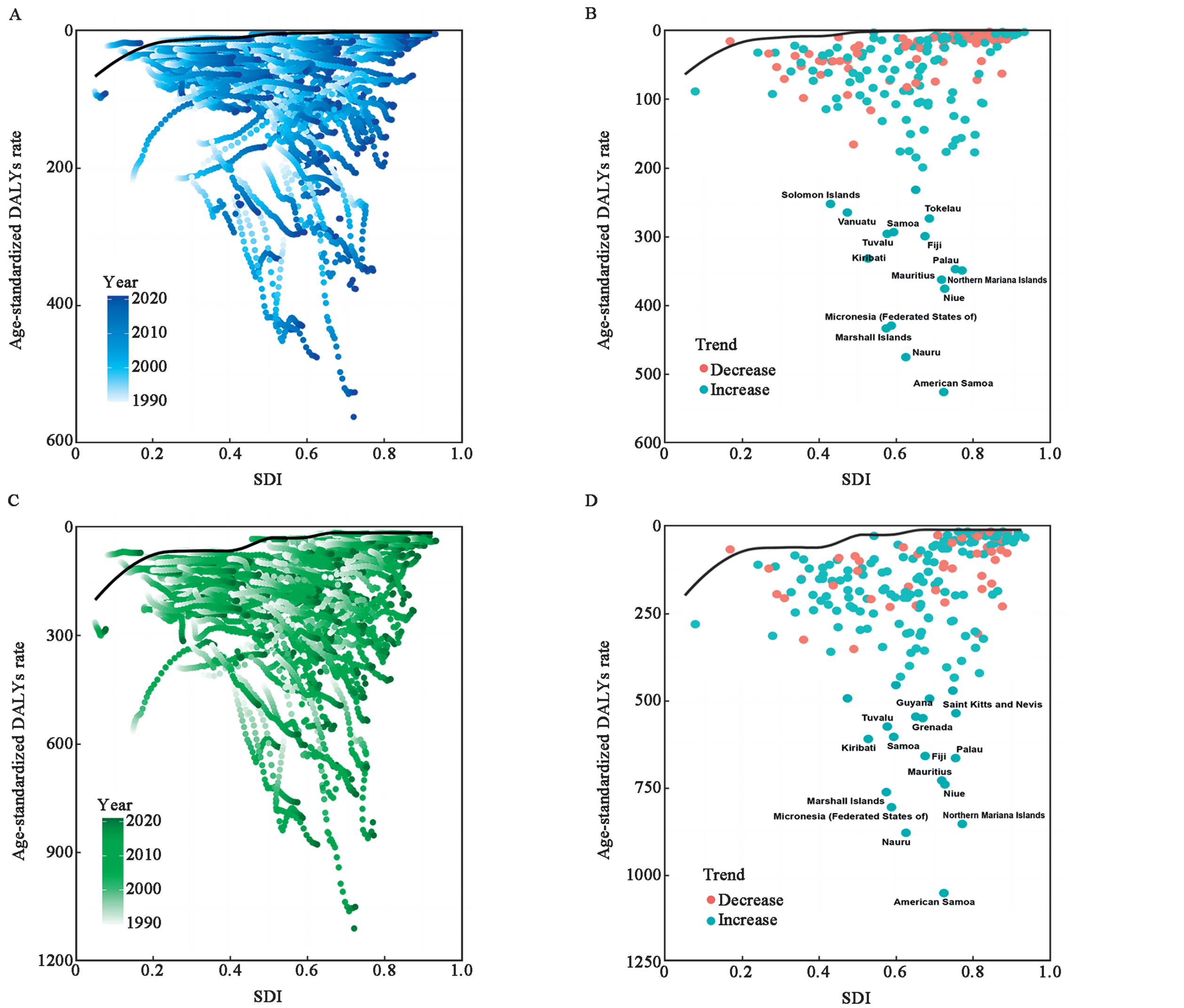

Figure 3: Frontier analysis exploring the relationship between SDI and age-standardized DALYs rate (ASDR) for DKD-T1DM (A and B) and DKD-T2DM (C and D). The frontier line is shown in solid black, which represented the countries or territories with exemplary performance, achieving the lowest DKD burden relative to their SDI. Each point represents a specific country or region in 2021. In (A) and (C), the color scale represents the years from 1990 (depicted in light blue/green) to 2021 (depicted in deep blue/green). In (B) and (D), the top 15 countries and territories with the largest effective difference (largest DKD DALYs gap from the frontier) are labeled in black. The direction of ASDR change from 1990 to 2021 is indicated by the color of the dots, with red dots indicate a decrease and blue dots indicate an increase. DALYs: Disability-adjusted life years; DKD: Diabetic kidney disease; DKD-T1DM: DKD due to type 1 diabetes; DKD-T2DM: DKD due to type 2 diabetes; SDI: Sociodemographic index.

Risk factors analysis

GBD DKD-DM estimates for 1990–2021 are available to download from the GBD Results Tool. During this period, the total number of DALYs for DKD-T1DM attributed to risk factors increased from 2.2 (95% UI, 1.8–2.7) million to 3.9 (95% UI, 3.1–4.8) million. Similarly, the total number of DKD-T2DM DALYs due to risk factors increased from 4.1 (95% UI, 3.5–4.8) million to 11.3 (95% UI, 9.7–13.1) million. In addition, the ASDR for DKD-T1DM in 2021 is 45.2, while for DKD-T2DM, it is 131.1 (95% UI, 112.8–152.5) in 2021.

We used percentages to represent the proportion of these risk factors in the overall ASDR in 2021. The analysis indicates that metabolic risks and environmental/occupational risks accounted for 100.0% and 5.0% of these DALYs for DKD-T1DM, respectively, as quantified in GBD 2021. Specifically, key metabolic risks factors include high fasting plasma glucose (70.8%) and kidney dysfunction (100.0%). Environmental/occupational risks are notably influenced by low temperature (3.9%) and high temperature (1.1%). A significant risk factor with an increasing ASDR from 1990 to 2019 is high fasting plasma glucose (from 26.8 [95% UI, 16.9–38.2] to 32.1 [95% UI, 21.6–43.4], a 19.8% increase). The relative contribution and trend of this risk factors varied as per the region's development status, with the high-SDI quintile showing the most significant increase, reaching 45.3% (from 11.8 [95% UI, 7.8–16.0] to 17.2 [95% UI, 12.8–21.9]) [Supplementary Table 5, http://links.lww.com/CM9/C255].

Compared with DKD-T1DM, DKD-T2DM had three significant risk factors quantified in GBD 2021: Metabolic risks, behavioral risks, and environmental/occupational risks, which accounted for 100.0%, 22.8%, and 6.3%

of the ASDR for DKD-T2DM, respectively. Metabolic risks can be further subdivided into kidney dysfunction (100.0%), high fasting plasma glucose (87.4%), high body mass index (BMI) (38.2%), and high systolic blood pressure (10.2%). Over the past 32 years, all these metabolic risks factors have shown an increasing trend in their contribution to ASDR in both sexes, with BMI showing the largest increase, reaching 62.6% (from 30.8 [95% UI, 13.9–49.5] to 50.1 [95% UI, 22.6–79.2]). Among the behavioral risk factors, dietary risks (17.8%) and low physical activity (6.2%) were the main contributors to DKD-T2DM DALYs. Dietary risks included low intake of fruits, whole grains, and vegetables, and high consumption of processed meats, red meats, sodium, and sugar-sweetened beverages. Environmental/occupational risks included high temperature (0.9%), low temperature (4.2%), lead exposure (1.2%), and other environmental risks (1.2%). Among them, BMI had a higher contribution to the age-standardized DALYs in females than males (42.9% *vs*. 34.1%). Other risk factors showed a similar contribution to age-standardized DALYs between males and females, without significant differences [Supplementary Table 6, http://links.lww.com/CM9/C255].

Discussion

The global prevalence and incidence of diabetes have increased considerably, significantly influencing the development of DKD—one of the most common complications of diabetes. Our study reported the number, ASR, and trend of the DKD burden. It also explored its cross-country epidemiological status, predicted development trends, and assessed several major risk factors of DALYs in 204 countries and territories over the past 32 years.

In 2019, there were 2.6 million incident cases of DKD, 135 million patients living with DKD, 0.5 million deaths due to DKD, and 13 million DALYs due to DKD globally; these figures increased considerably with the rising global population and improved sensitivity in the diagnosis of diabetes.[21] A previous study has shown a global increase in the ASIR and ASPR of DKD-T1DM overall and in males and females. This increase was higher in males, possibly due to a higher prevalence of risk factors of diabetes among males.[22,23] However, it was reported that in Saudi Arabia, this increasing trend was higher among females. This discrepancy might be due to the higher prevalence of auto-antibodies in females compared with males in Saudi Arabia, and the differences in T1DM-associated genes between Arabs and Caucasians.[24] Additionally, females in Saudi Arabia have a higher prevalence of obesity and physical inactivity: these are risk factors for insulin resistance, which accelerates β-cell dysfunction and cellular apoptosis, triggering autoimmune responses and β-cell loss in genetically predisposed individuals.[25,26]

Previous studies highlighted the significant role of T2DM in the progression of DKD, and it accounted for 95.3%, 96.3%, 83.2%, and 75.4% of total DKD incident cases, patients, deaths, and DALYs, respectively.[27] Our study revealed a greatly increased disease burden of DKD-T2DM from 1990 to 2021, the age-standardized prevalence, incidence and DALYs were significantly higher among males compared with females. This gender disparity may be attributed to a higher likelihood of exposure to T2DM risk factors in males. Factors such as reduced physical activity, higher rates of alcohol consumption, and increased daily energy intake contribute to this observed difference.[28] These findings are consistent with recent cross-sectional and prospective studies, which indicated that males in Europe and North America are more likely to have diabetes and impaired fasting blood sugar levels.[29] In contrast, data specific to the correlation between the prevalence of T2DM and gender in Asian populations is an important unmet need. Genetic and lifestyle factors can account for differences within similar populations.[28,30] Furthermore, it has been identified that racial disparities in diabetes prevalence between females and males and revealed that the association between life course factors and diabetes exhibited unique characteristics primarily among females.[31] On the other hand, the absolute counts of global prevalent and incident cases of DKD-T2DM increased substantially across all ages, but the ASIR and ASDR increased slightly from 1990 to 2021, and the ASPR showed a decreasing trend over the past 32 years—probably due to higher detection rates of new DKD cases among individuals with T2DM.

Furthermore, our study found a substantial increase in the number of global DKD deaths due to T1DM and T2DM over the past 32 years, while the age-standardized death rate showed only minor fluctuations, especially in DKD-T1DM. This disparity highlights the critical influence of demographic changes on DKD mortality. Despite significant advancements in DKD diagnosis, treatment, and management, coupled with an increased number and improved quality of healthcare professionals, the impact of these developments has been counterbalanced by the shifting demographics and population dynamics. In addition, the greater age-standardized death rate due to DKD-T2DM compared with DKD-T1DM from 2021 to 2030 is likely because T2DM patients experience a longer exposure duration to elevated blood glucose levels, resulting in more severe DKD progression than T1DM patients. Additionally, the challenges in managing blood glucose levels are greater in T2DM due to insulin resistance and lifestyle factors, leading to poorer DKD outcomes and higher mortality rates. The complications of T2DM, such as hypertension and cardiovascular diseases, will further exacerbate DKD and increase mortality risk. Moreover, unhealthy lifestyles, including poor diet and sedentary behavior, are more prevalent among T2DM patients, leading to a higher risk of DKD progression and mortality. Lastly, differences in treatment strategies between T2DM and T1DM, such as the use of insulin or oral medications, may impact DKD outcomes, with T2DM patients potentially facing greater challenges in achieving optimal disease management. It is important to consider potential individual variations and healthcare disparities as additional contributors to the observed disparity.

We assessed changes in DALYs of DKD-T1DM and DKD-T2DM to explore potential factors that influencing the variations in DALYs and ASDR in different countries and regions. We found that global DKD DALYs show a growing trend. By 2021, DALYs due to DKD-T1DM and DKD-T2DM had increase considerably by 74.0% and 173.6%, respectively. relative to 1990. And this growth trend is estimated to continue until 2030. The decomposition analysis of DALYs revealed that the increase in DKD burden was primarily driven by population growth and aging. However, the composition of factors differed between the two types of diabetes. For DKD-T1DM, the decline in epidemiological changes, except for the high- and low-middle-SDI quintiles, partially alleviated the burden in most GBD regions (far from offsetting the burden). Conversely, for DKD-T2DM, epidemiological changes increased in other SDI quintiles, except for countries with low-SDI quintile. Overall, The tide of diabetes prevalence and the resulting burden of DKD exceeded the expected impact of population growth and aging. These results demonstrate that the burden is disproportionately borne by countries with limited capacity to manage it. However, opportunities to reduce the burden of DKD exist at all stages of development. We also note that effective and increasingly common measures to control blood glucose and large-scale screening for CKD may alleviate the burden of diabetes to some extent and further reduce the burden of DKD. Although population growth itself cannot be intervened upon, the healthcare system can focus on modifiable risk factors associated with DKD, such as promoting diabetes prevention programs, encouraging early detection through regular screenings, and implementing comprehensive diabetes management strategies. By addressing these modifiable risk factors, the impact of DKD on the growing population can be mitigated, leading to improved health outcomes.

Although the overall trend is skewed more severely toward countries with less well-developed economies for the burden of DKD, our frontier analysis showed that relatively large DALYs are more concentrated in low-middle-SDI and middle-SDI quintiles, and even for T2DM-DKD, it is observed that a large portion of DALYs are mainly concentrated in high-SDI quintile countries and regions. The analysis provides a more optimistic assessment as there are several countries at all levels of development with DKD DALYs that are distant from the frontier (with relatively large effective differences from the frontier), suggesting missed opportunities to close the gap in DALYs. While frontier countries exist at all SDI levels, the most notable are those with low-SDI, which exhibited leading performance despite constrained resources; these countries might serve as exemplars of optimizing health outcomes in low-resource settings. Conversely, several countries or territories with high-SDI delivered lagging performance, suggesting that health progress enabled by sociodemographic prosperity may be overwhelmed by other forces. Future work should be undertaken to identify drivers of success in countries that serve as examples and factors hampering progress in countries that are lagging. Addressing this knowledge gap will be useful in forming efforts to alleviate the burden of DKD.[18] Overall, epidemiological studies of diabetes are challenging, especially for individuals with T1DM, which is relatively uncommon and estimated to account for only about 5% of all diabetes cases[32]: Traditional community-based epidemiologic cohorts are not large enough to provide accurate estimates. The present study contributes to the existing literature by incorporating information from a contemporary diabetes population to explore real-world kidney disease: Describe its burden, explore cross-country epidemiological status and development trends, and assess the risk factors and sociodemographic transitions for DKD.

Our study further found that kidney dysfunction, high fasting plasma glucose and non-optimal temperature exposure were common risk factors for T1DM-DKD and T2DM-DKD in GBD, with the first two being absolute risk factors, accounting for nearly all proportions. Besides these factors, there were other specific risk factors for DKD-T2DM such as high BMI, high systolic blood pressure, dietary risks, low physical activity, lead exposure and other environmental risks. Moreover, many DKD risk factors are also important risk factors for other major chronic diseases, such as cardiovascular diseases, obesity and metabolic syndrome, and other CKDs. Given the poor quality of life and increasing disease burden of patients with DKD, it is vital to make major efforts to reduce risk factors, such as blood glucose control and blood pressure management. Adopting a healthy lifestyle and reducing exposure to environmental toxins are also important.

Previous studies have provided descriptive analyses of the epidemiological changes in diabetes mellitus-related CKD. Building on this foundation, we conducted a comprehensive analysis by integrating additional data from the GBD study. We established a predictive model to forecast epidemiological changes in DKD until 2030. Through decomposition analysis and the assessment of risk factors, we identified potential driving factors and variables under control. Additionally, We analyzed the relationship between DALYs due to DKD and SDI and further used frontier analysis to explore countries or territories demonstrating outstanding performance, achieving the lowest DKD burden relative to their SDI levels. Our study offers valuable insights for formulating corresponding strategies to improve this future trend.

The present study had some limitations. First, data collected by various regions and countries may vary in quality, comparability, accuracy, and degree of omission. Some deviations inevitably occur in the estimated values, even with many statistical methods. Second, the availability of data for YLL and YLD estimations influences DALY estimates. Recent changes in health states might not have been captured in our estimates because of time lags in the reporting of health data by nations and the subsequent incorporation of these data into the GBD estimate. Wider intervals of uncertainty reflect the data scarcity for a specific location. Third, there may be some uncertainty in the projections of the size and distribution of the populations of countries and territories, which could affect the population-based analysis, including decomposition and projection.

In conclusion, over the past 32 years, the global burden of DKD has increased significantly, and there are inequalities in disease burden across countries. The growth trend of burden for DKD-T1DM is expected to decelerate from

2021 to 2030, while for DKD-T2DM, the trend of a steeper slope will continue until 2030. Our findings show a high contribution of potential drivers, risk factors, and sociodemographic transitions to the disease burden of DKD. In addition to glycemic control, there is a need to strengthen the evaluation and optimize comprehensive management strategies of DKD when developing appropriate healthcare policies based on each country's condition, both for patients with T1DM and T2DM.

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Conflicts of interest

None.

Data availability

If readers require access to the data, they may refer to the GBD 2021 (http://ghdx.healthdata.org/gbd-results-tool). Permission to access more results would be permitted if a reasonable request is recognized by the corresponding authors.

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