Analysis of the Global Burden of Disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016

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The last quarter century witnessed significant population growth, aging, and major changes in epidemiologic trends, which may have shaped the state of chronic kidney disease (CKD) epidemiology. Here, we used the Global Burden of Disease study data and methodologies to describe the change in burden of CKD from 1990 to 2016 involving incidence, prevalence, death, and disability-adjusted-life-years (DALYs). Globally, the incidence of CKD increased by 89% to 21,328,972 (uncertainty interval 19,100,079–23,599,380), prevalence increased by 87% to 275,929,799 (uncertainty interval 252,442,316–300,414,224), death due to CKD increased by 98% to 1,186,561 (uncertainty interval 1,150,743–1,236,564), and DALYs increased by 62% to 35,032,384 (uncertainty interval 32,622,073–37,954,350). Measures of burden varied substantially by level of development and geography. Decomposition analyses showed that the increase in CKD DALYs was driven by population growth and aging. Globally and in most Global Burden of Disease study regions, age-standardized DALY rates decreased, except in High-income North America, Central Latin America, Oceania, Southern Sub-Saharan Africa, and Central Asia, where the increased burden of CKD due to diabetes and to a lesser extent CKD due to hypertension and other causes outpaced burden expected by demographic expansion. More of the CKD burden (63%) was in low and lower-middle-income countries. There was an inverse relationship between age-standardized CKD DALY rate and health care access and quality of care. Frontier analyses showed significant opportunities for improvement at all levels of the development spectrum. Thus, the global toll of CKD is significant, rising, and unevenly distributed; it is primarily driven by demographic expansion and in some regions a significant tide of diabetes. Opportunities exist to reduce CKD burden at all levels of development.

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The last quarter century witnessed significant global population growth, aging, and an accelerated pace of epidemiologic transition, with reduced mortality from communicable diseases and increased burden of non-communicable diseases.[1,2] Globally, the burden of diabetes and hypertension considered as the 2 leading drivers of chronic kidney disease (CKD) has increased significantly over the past several decades. The number of adults living with diabetes quadrupled between 1980 and 2014, increasing from 108 million in 1980 to 422 million adults in 2014.[3] The number of adults with elevated blood pressure increased from 594 million in 1975 to 1.13 billion in 2015.[4] The increase in burden of diabetes and elevated blood pressure occurred at a much faster rate in low- and middle-income countries than in high-income countries.[3–6]

The global forces of demographic expansion and epidemiologic transition have shaped the epidemiology of non-communicable diseases including diabetes and hypertension and very likely has shaped the state of CKD epidemiology. However, a detailed quantitative analysis of the global, regional, and national burden of CKD over the past 25 years is not available. In this work, we used the Global Burden of Disease (GBD) data from 1990 to 2016 to (i) describe the state of CKD

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epidemiology at the global, regional, and national level; (ii) examine how demographic and epidemiologic drivers shaped the change in burden of CKD over this period; and (iii) characterize the relationship between burden of CKD and measures of health and economic prosperity in any given country.

RESULTS

GBD terms and definitions used in this work are provided in Table 1. Demographics, Sociodemographic Index (SDI), and Healthcare Access and Quality (HAQ) parameters at the global level and by SDI quintile are presented in Table 2. The global incidence of CKD was 11,299,557.27 (95% uncertainty interval [UI] = 10,220,333.36–12,357,374.38) in 1990, and increased to 21,328,971.86 (UI = 19,100,079.20–23,599,380.24) in 2016—representing an 88.76% increase in incidence over the last 27 years. CKD incidence rate per 100,000 population increased from 214.63 (UI = 194.13–234.72) in 1990 to 288.53 (UI = 258.38–319.24) in 2016. Age-standardized incident rate per 100,000 population increased from 299.06 (UI = 269.36–329.00) to 310.13 (UI = 275.51–343.70) (Table 3 and Supplementary Figure S1A). Age-standardized incident rate increased for CKD due to diabetes, glomerulonephritis, and CKD due to other causes; it decreased for CKD due to hypertension (Table 3 and Supplementary Figure S1B).

The overall global prevalence of CKD increased from 147,598,152.80 (UI = 135,827,679.51–160,280,895.47) in 1990 to 275,929,799.20 (UI = 252,442,315.84–300,414,224.26) in 2016; representing an 86.95% increase in prevalence over the last 27 years. Prevalence rate per 100,000 population increased from 2803.54 (UI = 2579.97–3044.44) to 3732.67 (UI = 3414.94–4063.89). Age-standardized prevalence rate increased from 4040.95 (UI = 3710.83–4382.80) to 4056.54 (UI = 3706.70–4414.26) (Table 4 and Supplementary Figure S2A). Age-standardized prevalence rate increased for CKD due to diabetes, and decreased for CKD due to hypertension, glomerulonephritis, and other causes (Table 4 and Supplementary Figure S2B).

Global death due to CKD increased from 599,200.30 (UI = 577,653.17–650,084.02) in 1990 to 1,186,560.90 (UI = 1,150,743.14–1,236,564.41) in 2016, representing a 98.02% increase in death due to CKD over the last 27 years. From 1990 to 2016, CKD death per 100,000 population increased from 11.38 (UI = 10.97–12.35) to 16.05 (UI = 15.57–16.73); age-standardized death rate increased from 17.48 (UI = 16.89–18.98) to 18.25 (UI = 17.73–18.97) (Table 5 and Supplementary Figure S3A). Age-standardized death rate increased for CKD due to diabetes and hypertension, decreased for CKD due to glomerulonephritis, and remained relatively unchanged for CKD due to other causes (Table 5 and Supplementary Figure S3B).

Global disability-adjusted life-years (DALYs) were 21,597,163.60 (UI = 20,093,986.99–23,354864.85) in 1990, and increased to 35,032,384.43 (UI = 32,622,072.69–37,954,350.03) in 2016; representing a 62.21% increase in DALYs over the last 27 years. DALY rates per 100,000 population increased from 410.23 (UI = 381.67–443.61) to 473.90 (UI = 441.30–513.43). Age-standardized DALY rates decreased from 521.44 (UI = 484.58–565.29) to 500.12 (UI = 465.54–541.43) in 2016 (Table 6 and Supplementary Figure S4A). Age-standardized DALY rates by cause revealed an increase in CKD DALYs attributable to diabetes and to a lesser extent hypertension, and decrease in CKD DALYs

Table 1 | Terms and definitions

Age-standardized rate: Rate per 100,000 population following standardization to the global age structure. The difference between age-standardized rates across geographies and over time is independent of population size and age structure.

Decomposition: The analytic approach to identify the additive contribution of the effect of the differences in factors in 2 populations to the difference in their overall value. Decomposition of chronic kidney disease (CKD) DALYs by age structure, population growth, and epidemiologic changes allows the quantification of contribution of each of these factors to the overall effect. Similarly, decomposition of CKD DALYs by the 4 causes of CKD allows the quantification of the contribution of each cause to the overall CKD DALYs.

Disability-adjusted life-years (DALYs): A measure that quantitates the overall burden of disease in terms of years of healthy life lost due to the disease. It represents the sum of years lost due to premature death and years living with disability due to the disease. The years of living with disability are weighted in proportion to the severity of the underlying disease.

Frontier analysis: The analytic approach used to identify the lowest potentially achievable burden of CKD on the basis of development status, as measured by the Sociodemographic Index (SDI). The frontier delineates the countries or territories with leading performance (at the frontier pushing the envelope) that have the lowest CKD burden for their SDI. Distance from the frontier is termed "effective difference" and represents the gap between the observed burden and the potentially achievable burden of disease in a country or territory given their SDI; this gap could be potentially reduced or eliminated based on the country or territory's sociodemographic resources. For example, if a country or territory falls well below the frontier value given its SDI, this observation suggests unrealized opportunity for reduction (or improvement) in CKD DALYs that should be possible based on the country or territory's place on the development spectrum.

Global Burden of Diseases, Injuries, and Risk Factors Study (GBD): A global research study group headquartered at the Institute of Health Metrics and Evaluation at the University of Washington in Seattle. It comprises more than 3000 international collaborators from more than 130 countries and aims to quantitate the burden of disease, disability, and death from 333 diseases and injuries, and 88 risk factors in 195 countries and territories, by age and sex, from 1990 to the present, allowing comparisons over time, across age groups, and among populations. The GBD study is funded by the Bill and Melinda Gates Foundation.

Healthcare Quality and Access (HAQ) index: A novel summary measure on a scale of 0 (worst) to 100 (best) that was recently developed by the GBD study. It is based on risk standardized death rates of 32 GBD causes that are considered amenable to personal health care. It provides a single interpretable measure that facilitates comparable assessment of personal health care access and quality across 195 countries and territories, over time, and along the development spectrum.

Sociodemographic Index (SDI): A summary measure that quantitates a country or territory's level of a sociodemographic development. It is interpretable across geographies and over time. SDI is expressed on a scale of 0 to 1 and is the composite average of the rankings of the incomes per capita, average educational attainment, and total fertility rates of all areas in the GBD study. Zero represents the lowest income per capita, lowest educational attainment, and highest total fertility rate observed across all GBD geographies from 1970 to 2016, and 1 represents the highest income per capita, highest educational attainment, and lowest total fertility rate.

Table 2 | Demographics, SDI, and HAQ parameters at the global level and by SDI quintile

	Global	High SDI[a]	High-middle SDI[a]	Middle SDI[a]	Low-middle SDI[a]	Low SDI[a]
Population[b]	7392.28	1025.59	1164.63	2299.84	2129.75	767.91
Sex (%)[b]						
Male	3725.91 (50.40)	503.28 (49.07)	584.75 (50.21)	1165.24 (50.67)	1084.60 (50.93)	385.80 (50.24)
Female	3666.38 (49.60)	522.32 (50.93)	579.88 (49.79)	1134.60 (49.33)	1045.14 (49.07)	382.11 (49.76)
Age category (%)[b]						
< 5	631.97 (8.55)	53.79 (5.24)	72.83 (6.25)	159.01 (6.91)	223.08 (10.47)	122.92 (16.01)
5-14	1253.20 (16.95)	111.60 (10.88)	138.94 (11.93)	347.71 (15.12)	446.00 (20.94)	208.25 (27.12)
15-49	3819.18 (51.66)	467.59 (45.59)	627.67 (53.89)	1240.26 (53.93)	1122.24 (52.69)	359.22 (46.78)
50-69	1283.64 (17.36)	262.81 (25.63)	246.62 (21.18)	438.71 (19.08)	271.38 (12.74)	63.13 (8.22)
>69	404.29 (5.47)	129.80 (12.66)	78.58 (6.75)	114.16 (4.96)	67.04 (3.15)	14.39 (1.87)
SDI (IQR)[c]	0.70 (0.51–0.82)	0.88 (0.87–0.90)	0.79 (0.76–0.82)	0.70 (0.67–0.73)	0.56 (0.51–0.59)	0.35 (0.31–0.43)
HAQ (IQR)[c]	63.40 (49.60–76.60)	86.40 (81.40–89.00)	71.80 (65.70–79.00)	63.15 (58.10–2.80)	51.85 (48.70–60.10)	43.00 (38.80–45.60)

GBD, Global Burden of Disease study; HAQ, Healthcare Access and Quality index; IQR, interquartile range; SDI, Sociodemographic Index.
All values were estimated based on GBD 2016 except for HAQ, which was estimated using GBD 2015.
[a]Low SDI: SDI < 0.46; low-middle SDI: 0.46–0.64; middle SDI: 0.65–0.74; high-middle SDI: 0.75–0.85; high SDI: SDI > 0.85.
[b]Number presented in millions.
[c]Median and IQR at country and territory level.

attributable to glomerulonephritis and other causes (Table 6 and Supplementary Figure S4B). Estimates for incidence, prevalence, death and DALYs due to CKD as absolute values, rates per 100,000 population, age-standardized rates per 100,000 population, and by causes at the regional and national level are presented in Supplementary Table S2A–D.

Prevalence of CKD by age and sociodemographic development in 2016

Worldwide raw prevalence and age-standardized prevalence rate of CKD in 2016 are shown in Figure 1a and b, respectively. The prevalence rate of CKD per 100,000 population by age group showed an earlier rise for low-SDI countries; countries in the highest SDI quintile exhibited a later and much steeper rise, with the prevalence rate exceeding that of any SDI quintile in age groups >90 (Figure 2). To gain a better understanding of the age distribution of people with CKD globally and by SDI quintile, an age profile of CKD was constructed. We observed differences in percent CKD by age group across the SDI spectrum; the differences appeared graded across the development spectrum and were most manifest between highest and lowest SDI quintile. There was a greater percentage of CKD earlier in life (in adolescent years and early adulthood), and an earlier peak (age group 60–64) in low-SDI countries than in high-SDI countries. In high-SDI countries, the increase started to manifest in third decade of life, and achieved a higher and later peak (age group 75–79). All SDI quintiles exhibited a sharp decline in percent CKD following the peak (Supplementary Figure S5A). The age distribution of death due to CKD exhibited a similar pattern in that more death due to CKD occurred in younger age groups in low-SDI countries than in high-SDI countries (Supplementary Figure S5B).

Drivers of CKD epidemiology: population growth, aging, and epidemiologic changes

To examine to what extent the forces of population growth, aging, and epidemiologic changes shaped CKD epidemiology over the past 27 years, we developed a decomposition analysis of raw DALYs by population, age structure, and age and population standardized morbidity and mortality rates (which we are referring to here as epidemiologic changes). Overall, there was a significant increase in CKD DALYs globally and in each SDI quintile, but it was most pronounced in middle and low-middle SDI quintiles, which exhibited the largest increase in overall DALYs in the past 27 years (Figure 3). Globally, population growth followed by aging of the world population contributed 69.80% and 42.86%, respectively, to the increased burden of CKD DALYs between 1990 and 2016 (Supplementary Figure S6A). The contribution of aging to overall DALYs was most pronounced in the high-SDI quintile (70.09%), and decreased where it was 64.00% in the high-middle–, 66.27% in the middle, 40.24% in the low-middle–, and nearly vanished in the low-SDI quintile (1.60%). Most of the increase in CKD DALYs was driven by population growth in low-middle– (100.42%) and low-SDI quintiles (112.32%); the relative contribution of population growth to increase in CKD DALYs was smaller (32.71%) in high-SDI countries. The epidemiologic changes that capture the underlying change in age and population-adjusted CKD morbidity and mortality rates over the past 27 years have decreased globally, and the decrease was least pronounced in high- and low-SDI quintiles, and was more evident in low-middle–, middle-, and high-middle– SDI quintiles (Figure 3, Supplementary Figure S6A, Table 7). Decomposition analysis in GBD regions revealed substantial heterogeneity in demographic and epidemiologic trends. Aging and population growth were major drivers of change in CKD DALYs in most GBD regions (Supplementary Table S3). Most notably, whereas most GBD regions exhibited a decrease in underlying age and population-adjusted CKD mortality and morbidity rates (epidemiologic changes)—a trend also seen at the global level and in each SDI level—there were several GBD regions that exhibited a remarkable deviation from this trend and showed an increase in epidemiologic changes, including Central Asia, High-income North America, Central Latin America, Southern Sub-Saharan Africa, and Oceania, which contributed 37.27%, 35.06%, 31.71%, 23.17%,

Table 3 | Number, rate, and age-standardized rate for overall CKD incidence and by cause of CKD in 2016 and percentage change from 1990 globally and by SDI quintile

Location	Incidence number		Incidence rate per 100,000 persons		Age-standardized incidence rate per 100,000 persons									
					Overall		Due to diabetes		Due to hypertension		Due to glomerulonephritis		Due to other causes	
	Number (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])
Global	21,328,971.86 (19,100,079.20–23,599,380.24)	88.76%	288.53 (258.38–319.24)	34.43%	310.13 (275.51–343.70)	3.70%	130.53 (112.32–151.09)	9.48% (42.09%)	51.27 (44.11–58.91)	−7.15% (16.53%)	58.84 (49.23– 68.09)	5.65% (18.97%)	69.49 (59.51–79.99)	0.84% (22.41%)
High SDI[c]	4,665,147.35 (4,052,923.51–5,249,329.08)	60.12%	454.87 (395.18–511.83)	38.38%	271.62 (237.61–302.92)	-2.73%	136.04 (115.53–155.84)	5.38% (50.08%)	33.80 (28.46–39.64)	−22.17% (12.44%)	44.74 (36.38–53.68)	−0.69% (16.47%)	57.04 (47.79–67.53)	−7.53% (21.00%)
High-middle SDI[c]	3,767,609.44 (3,341,457.26–4,184,136.78)	74.52%	323.50 (286.91–359.27)	32.24%	293.97 (260.18–326.45)	2.19%	114.35 (99.09–131.14)	16.86% (38.90%)	65.32 (57.07–73.32)	−19.17% (22.22%)	43.37 (36.08–50.13)	13.71% (14.75%)	70.93 (61.52–80.54)	0.09% (24.13%)
Middle SDI[c]	5,609,016.05 (4,988,815.28–6,212,407.51)	104.78%	243.89 (216.92–270.12)	58.65%	252.59 (223.86–280.08)	5.24%	112.84 (96.76–130.95)	7.23% (44.67%)	37.99 (32.16–44.27)	5.26% (15.04%)	56.38 (46.13–65.76)	2.33% (22.32%)	45.38 (38.10–52.87)	4.11% (17.97%)
Low-middle SDI[c]	5,325,626.64 (4,771,667.75–5,938,794.61)	105.38%	250.06 (224.05–278.85)	29.58%	349.76 (308.67–390.36)	6.04%	138.63 (116.26–163.71)	14.01% (39.63%)	51.30 (43.42–60.83)	0.10% (14.67%)	74.40 (61.51–87.30)	2.76% (21.27%)	85.43 (71.18–99.46)	0.98% (24.42%)
Low SDI[c]	2,029,763.19 (1,809,195.78–2,264,511.01)	123.67%	264.32 (235.60–294.89)	6.93%	505.54 (440.96–572.47)	6.62%	171.21 (141.66–205.18)	11.59% (33.87%)	102.52 (84.20–121.51)	2.95% (20.28%)	98.01 (78.16–117.62)	5.01% (19.39%)	133.80 (110.60–157.60)	4.67% (26.47%)

CKD, chronic kidney disease; SDI, Sociodemographic Index.
[a]UI is the uncertainty interval, which reflects the certainty of an estimate based on data availability, study size, and consistency across data sources.
[b]Percentage attributed to overall rate is the proportion of overall age-standardized rate change attributed by each of the following 4 causes: diabetes, hypertension, glomerulonephritis, and other causes.
[c]Low SDI: SDI < 0.46; low-middle SDI: 0.46–0.64; middle SDI: 0.65–0.74; high-middle SDI: 0.75–0.85; High SDI: SDI > 0.85.

and 14.31% to the increased DALYs in those GBD regions, respectively (Supplementary Figure S6B and Supplementary Table S3). Further analyses of those regions with increased age and population-adjusted CKD mortality and morbidity rates showed that the burden of CKD due to diabetes, and to a lesser extent CKD due to hypertension and to other causes, outpaced the burden that would be expected by demographic factors, including population growth and aging (Supplementary Figure S7A–E). In those GBD regions burden of CKD due to diabetes and hypertension manifested much earlier in life (in younger age groups), and was much higher than expected based on demographic factors in each age group (Supplementary Figure S7A–E). Decomposition analyses by population growth, aging, and epidemiologic changes are presented in Table 7 at the global and SDI level and in Supplementary Table S3 at the regional and national level.

Decomposition analysis by cause of CKD

We developed decomposition analyses by the 4 causes of CKD (diabetes, hypertension, glomerulonephritis, and other causes); these analyses were not age- and population-standardized. From 1990 to 2016, diabetes followed by hypertension were the leading drivers of increased DALYs globally and in each SDI quintile (Figure 4). Globally, CKD due to diabetes and CKD due to hypertension contributed 50.62% and 23.26% of the overall increase in CKD DALYs, respectively. The contribution of diabetes to the change of overall DALYs in each SDI quintile was lowest in the low-SDI group (33.80%) and increased in a graded fashion across the SDI spectrum, where it was highest in the high-SDI quintile (57.23%) (Supplementary Figure S8A and Table 7). A similar but less dramatic picture was evident for hypertension as a driver of change in overall CKD burden, contributing 15.31% and 23.71% of change in CKD DALYs in low- and high-SDI quintiles, respectively. In GBD regions, diabetes was the leading driver of change in CKD DALYs (Supplementary Figure S8B), but its relative contribution varied greatly among geographies: it was high and exceeded 50% in Central Europe (225.17%), Australasia (88.22%), East Asia (70.88%), Southeast Asia (66.32%), High-income North America (60.33%), High-income Asia Pacific (59.58%), and Oceania (57.14%), and it was least pronounced in the 4 corners of Sub-Saharan Africa (27.88%). There was also variability in the contribution of hypertension to change in CKD DALYs: it was high in Central Europe (213.19%), East Asia (58.01%), Western Europe (29.67%), and Southeast Asia (29.24%) and lowest in Eastern Europe (12.88%), Central Latin America (12.64%), and Central Asia (5.22%). Decomposition analyses by cause of CKD are provided in Table 7 at the global and SDI level and in Supplementary Table S3 at the regional and national level.

CKD DALYs and sociodemographic development

An analysis of population-weighted age-standardized DALY rates by World Bank Income classification showed that burden of CKD is much more pronounced in low- and lower-middle–income countries (Supplementary Figure S9). There

Table 4 | Number, rate, age-standardized rate for overall CKD prevalence and by cause of CKD in 2016 and percentage change from 1990 globally and by SDI quintile

	Prevalence number		Prevalence rate per 100,000 persons		Age-standardized prevalence rate per 100,000 persons									
					Overall		Due to diabetes		Due to hypertension		Due to glomerulonephritis		Due to other causes	
Location	Number (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990	Number (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])
Global	275,929,799.24 (252,442,315.84–300,414,224.26)	86.95%	3732.67 (3414.94–4063.89)	33.14%	4056.54 (3706.70–4414.26)	0.39%	1690.73 (1487.36–1911.57)	5.87% (41.68%)	744.10 (655.16–828.76)	−2.58% (18.34%)	735.69 (644.72–823.81)	−5.04% (18.14%)	886.03 (765.01–1,010.49)	−2.14% (21.84%)
High SDI[c]	54,401,342.48 (49,090,889.58–59,373,868.12)	57.10%	5304.38 (4786.58–5789.22)	35.78%	3130.33 (2838.65–3413.33)	−4.92%	1521.03 (1349.26–1707.14)	3.46% (48.59%)	448.42 (389.23–502.65)	−13.54% (14.33%)	490.48 (422.73–555.20)	−14.05% (15.67%)	670.40 (572.29–776.90)	−8.51% (21.42%)
High-middle SDI[c]	50,978,711.10 (46,566,021.84–55,646,977.83)	73.34%	4377.25 (3998.35–4778.08)	31.34%	3983.00 (3628.60–4347.50)	−1.51%	1527.36 (1363.04–1701.65)	12.60% (38.35%)	789.57 (701.97–874.35)	−10.27% (19.82%)	727.49 (649.01–807.93)	−13.16% (18.26%)	938.57 (827.40–1,049.47)	−3.25% (23.56%)
Middle SDI[c]	74,076,729.20 (67,564,941.57–81,133,648.25)	102.07%	3220.95 (2937.81–3527.80)	56.55%	3458.33 (3153.88–3771.98)	0.48%	1540.27 (1348.79–1748.90)	1.55% (44.54%)	690.17 (602.61–774.10)	0.81% (19.96%)	635.23 (551.86–716.98)	-2.03% (18.37%)	592.66 (501.79–683.37)	0.10% (17.14%)
Low-middle SDI[c]	71,084,491.91 (64,727,778.82 - 78,070,122.44)	102.82%	3337.70 (3039.23–3665.70)	27.97%	4994.12 (4533.83–5470.63)	0.80%	1970.47 (1692.55–2269.92)	6.84% (39.46%)	897.72 (785.61–1013.32)	−2.57% (17.98%)	941.33 (821.16–1063.35)	−2.81% (18.85%)	1184.59 (1004.46–1369.99)	−2.94% (23.72%)
Low SDI[c]	26,350,737.28 (23,767,164.74 - 29,106,098.64)	119.51%	3431.48 (3095.04–3790.29)	4.94%	7409.73 (6690.19–8173.08)	3.75%	2523.60 (2143.31–2947.70)	7.50% (34.06%)	1503.26 (1301.51–1709.51)	1.93% (20.29%)	1490.57 (1292.00–1687.99)	1.39% (20.12%)	1892.30 (1581.07–2203.11)	2.32% (25.54%)

CKD, chronic kidney disease; SDI, Sociodemographic Index.

[a]UI is the uncertainty interval, which reflects the certainty of an estimate based on data availability, study size, and consistency across data sources.

[b]Percentage attributed to overall rate is the proportion of overall age-standardized rate change attributed by each of the following 4 causes: diabetes, hypertension, glomerulonephritis, and other causes.

[c]Low SDI: SDI < 0.46; low-middle SDI: 0.46–0.64; middle SDI: 0.65–0.74; high-middle SDI: 0.75–0.85; high SDI: SDI > 0.85.

Table 5 | Number, rate, and age-standardized rate for overall CKD death and by cause of CKD in 2016 and percentage change from 1990 globally and by SDI quintile

	Death number		Death rate per 100,000 persons		Age-standardized death rate per 100,000 persons									
					Overall		Due to diabetes		Due to hypertension		Due to glomerulonephritis		Due to other causes	
Location	Number (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990	Number (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])
Global	1,186,560.90 (1,150,743.14–1,236,564.41)	98.02%	16.05 (15.57–16.73)	41.03%	18.25 (17.73–18.97)	4.39%	7.60 (6.88–8.27)	9.47% (41.66%)	4.81 (4.29–5.37)	7.33% (26.36%)	2.23 (1.97–2.52)	−7.46% (12.24%)	3.60 (3.17–4.08)	−1.08% (19.75%)
High SDI[c]	227,605.95 (221,469.92–233,472.20)	95.78%	22.19 (21.59–22.76)	69.21%	11.24 (10.95–11.52)	1.72%	5.06 (4.66–5.47)	9.16% (45.03%)	2.67 (2.33–3.04)	10.69% (23.72%)	1.19 (1.06–1.34)	−24.26% (10.64%)	2.32 (2.02– 2.63)	−4.51% (20.61%)
High-middle SDI[c]	143,537.36 (137,405.42–150,442.27)	78.56%	12.32 (11.80–12.92)	35.29%	11.68 (11.19–12.23)	-1.38%	4.49 (4.10–4.91)	6.63% (38.44%)	3.04 (2.74–3.37)	11.06% (26.03%)	1.67 (1.49–1.88)	−22.84% (14.31%)	2.48 (2.21–2.77)	−9.20% (21.21%)
Middle SDI[c]	456,587.39 (427,337.70–469,749.92)	111.97%	19.85 (18.58–20.43)	64.22%	23.64 (22.09–24.31)	-0.16%	10.20 (9.04–11.14)	1.92% (43.15%)	7.06 (6.25–7.87)	−5.16% (29.88%)	2.72 (2.36–3.13)	4.67% (11.50%)	3.66 (3.14–4.17)	0.93% (15.46%)
Low-middle SDI[c]	293,545.90 (276,884.41–332,196.76)	87.14%	13.78 (13.00–15.60)	18.08%	23.55 (22.17–26.68)	-2.37%	9.36 (8.20–10.77)	2.72% (39.73%)	6.30 (5.56–7.25)	−2.62% (26.76%)	2.57 (2.22–3.04)	−9.19% (10.93%)	5.32 (4.50–6.41)	−6.81% (22.58%)
Low SDI[c]	64,442.22 (59,084.54–70,450.52)	115.14%	8.39 (7.69–9.17)	2.85%	21.39 (19.52–23.59)	8.66%	7.48 (6.33–8.61)	17.90% (34.99%)	5.34 (4.57– 6.16)	9.16% (24.95%)	3.28 (2.76–3.93)	−3.76% (15.35%)	5.28 (4.48–6.26)	4.95% (24.71%)

CKD, chronic kidney disease; SDI, Sociodemographic Index.
[a]UI is the uncertainty interval, which reflects the certainty of an estimate based on data availability, study size, and consistency across data sources.
[b]Percentage attributed to overall rate is the proportion of overall age-standardized rate change attributed by each of the following 4 causes: diabetes, hypertension, glomerulonephritis, and other causes.
[c]Low SDI: SDI < 0.46; low-middle SDI: 0.46–0.64; middle SDI: 0.65–0.74; high-middle SDI: 0.75–0.85; high SDI: SDI > 0.85.

Table 6 | Number, rate, and age-standardized rate for overall CKD DALYs and by cause of CKD in 2016 and percentage change from 1990 globally and by SDI quintile

Location	DALYs number		DALY rate per 100,000 persons		Age-standardized DALY rate per 100,000 persons									
					Overall		Due to diabetes		Due to hypertension		Due to glomerulonephritis		Due to other causes	
	Number (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990	Number (UI[a])	Percentage change from 1990	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])	Rate (UI[a])	Percentage change from 1990 (% attributed to overall rate[b])
Global	35,032,384.43 (32,622,072.69–37,954,350.03)	62.21%	473.90 (441.30–513.43)	15.52%	500.12 (465.54–541.43)	–4.09%	209.19 (188.85–230.83)	3.12% (41.83%)	98.19 (85.54–111.11)	0.90% (19.63%)	82.18 (72.80–93.29)	–15.05% (16.43%)	110.56 (97.50–125.47)	–11.20% (22.11%)
High SDI[c]	4,556,608.40 (4,122,534.15–5,002,384.73)	56.34%	444.29 (401.97–487.76)	35.12%	276.47 (248.55–304.94)	–2.39%	139.84 (124.13–155.88)	8.68% (50.58%)	43.65 (37.38–50.23)	5.11% (15.79%)	35.80 (30.70–41.28)	–27.20% (12.95%)	57.18 (48.98–65.83)	–10.45% (20.68%)
High-middle SDI[c]	4,283,183.32 (3,878,763.42–4,734,449.11)	43.75%	367.77 (333.05–406.52)	8.92%	334.85 (303.34–370.51)	–13.04%	134.82 (119.94–150.05)	–0.73% (40.26%)	60.33 (52.27–68.34)	1.75% (18.02%)	63.11 (55.07–71.96)	–31.56% (18.85%)	76.58 (66.87–87.26)	–21.64% (22.87%)
Middle SDI[c]	13,192,113.48 (12,353,263.71–14,063,175.02)	69.03%	573.61 (537.14–611.49)	30.96%	590.95 (552.41–629.96)	–5.51%	264.61 (236.84–289.37)	–2.61% (44.78%)	132.73 (115.51–150.18)	–6.66% (22.46%)	89.33 (79.28–100.99)	–7.31% (15.12%)	104.29 (91.84–117.24)	–9.45% (17.65%)
Low-middle SDI[c]	10,170,560.30 (9,444,386.55–11,228,676.15)	58.18%	477.55 (443.45–527.23)	–0.20%	649.63 (600.30–718.96)	–11.64%	253.80 (223.09–289.54)	–3.30% (39.07%)	137.34 (119.97–158.31)	–10.70% (21.14%)	97.54 (84.35–113.43)	–19.50% (15.01%)	160.95 (138.22–189.59)	–18.64% (24.78%)
Low SDI[c]	2,819,808.48 (2,547,583.05–3,132,976.12)	93.45%	367.20 (331.75–407.99)	-7.52%	662.45 (598.73–738.77)	0.51%	225.71 (193.18–260.11)	11.04% (34.07%)	125.77 (104.80–146.18)	2.84% (18.99%)	131.96 (111.61–155.17)	–9.43% (19.92%)	179.01 (153.48–207.27)	–4.70% (27.02%)

CKD, chronic kidney disease; DALYs, disability-adjusted life-years; SDI, Sociodemographic Index.
[a]UI is the uncertainty interval, which reflects the certainty of an estimate based on data availability, study size, and consistency across data sources.
[b]Percentage attributed to overall rate is the proportion of overall age-standardized rate change attributed by each of the following 4 causes: diabetes, hypertension, glomerulonephritis, and other causes.
[c]Low SDI: SDI < 0.46; low-middle SDI: 0.46–0.64; middle SDI: 0.65–0.74; high-middle SDI: 0.75–0.85; high SDI: SDI > 0.85.

was a graded decrease of age-standardized DALY rates of CKD as SDI quintile increased, in that DALY rates were highest for the low-SDI quintile (662.45, UI = 738.77–598.73) and gradually decreased to lowest in the highest SDI quintile (276.47, UI = 304.94–248.55) (Supplementary Figure S9). To develop an understanding of the distribution of CKD burden in relation to countries' health system performance, we examined the relationship between age-standardized DALY rates and HAQ (Figure 5). Results revealed an inverse relationship, in that countries with high HAQ had relatively lower age-standardized CKD DALY rates, whereas countries with low HAQ had much higher CKD age-standardized DALY rates ($r = -0.52$). Spline analyses of the relationship between age-standardized DALY rates and HAQ, which also controlled for SDI, showed a near linear association (Supplementary Figure S10A). Because regional differences might confound the association of HAQ and DALYs, we developed analytic strategies to examine the relationship after accounting for GBD regions; the results were consistent in that there was a near linear inverse relationship between age-standardized DALY rates and HAQ within GBD regions (Supplementary Figure S10B). Taken together, the findings suggest that a disproportionally higher burden of CKD is borne by countries that are least equipped to handle it.

In order to gain a better understanding of the potential improvement in CKD DALY rates that are potentially achievable given a country's development status, we built a frontier analysis based on age-standardized DALY rates and SDI using data from 1990 to 2016 (Figure 6a). The frontier line delineates the countries and territories with lowest DALY rates (optimal performers) given their SDI. Distance from the frontier is termed effective difference and represents the gap between a country's observed and potentially achievable DALYs; this gap could be potentially reduced or eliminated based on the country or territory's sociodemographic resources (Table 1). The effective difference from the frontier for each country and territory was calculated using the 2016 DALYs and SDI (Figure 6b and Supplementary Table S4). Overall, the effective difference for a given SDI tended to be smaller and exhibited less variance as SDI increased. The top 10 countries with highest effective difference from the frontier (range of effective difference: 1829.83–1241.34) included the Solomon Islands, Fiji, the Federated States of Micronesia, the Marshall Islands, Afghanistan, El Salvador, Vanuatu, Mauritius, Mexico, and Nicaragua; these countries have disproportionally higher CKD DALY rates than other countries with comparable sociodemographic resources. The top 10 countries with the lowest DALY rates given their place on the development spectrum and thus the lowest effective difference (range: 24.01–51.65) included Finland, Andorra, United Kingdom, Iceland, Ukraine, Sweden, Norway, France, Moldova, and Slovenia.

DISCUSSION

In this work we show that from 1990 to 2016, the burden of CKD measured in incidence, prevalence, death due to CKD, and DALYs due to CKD increased substantially. Globally, in

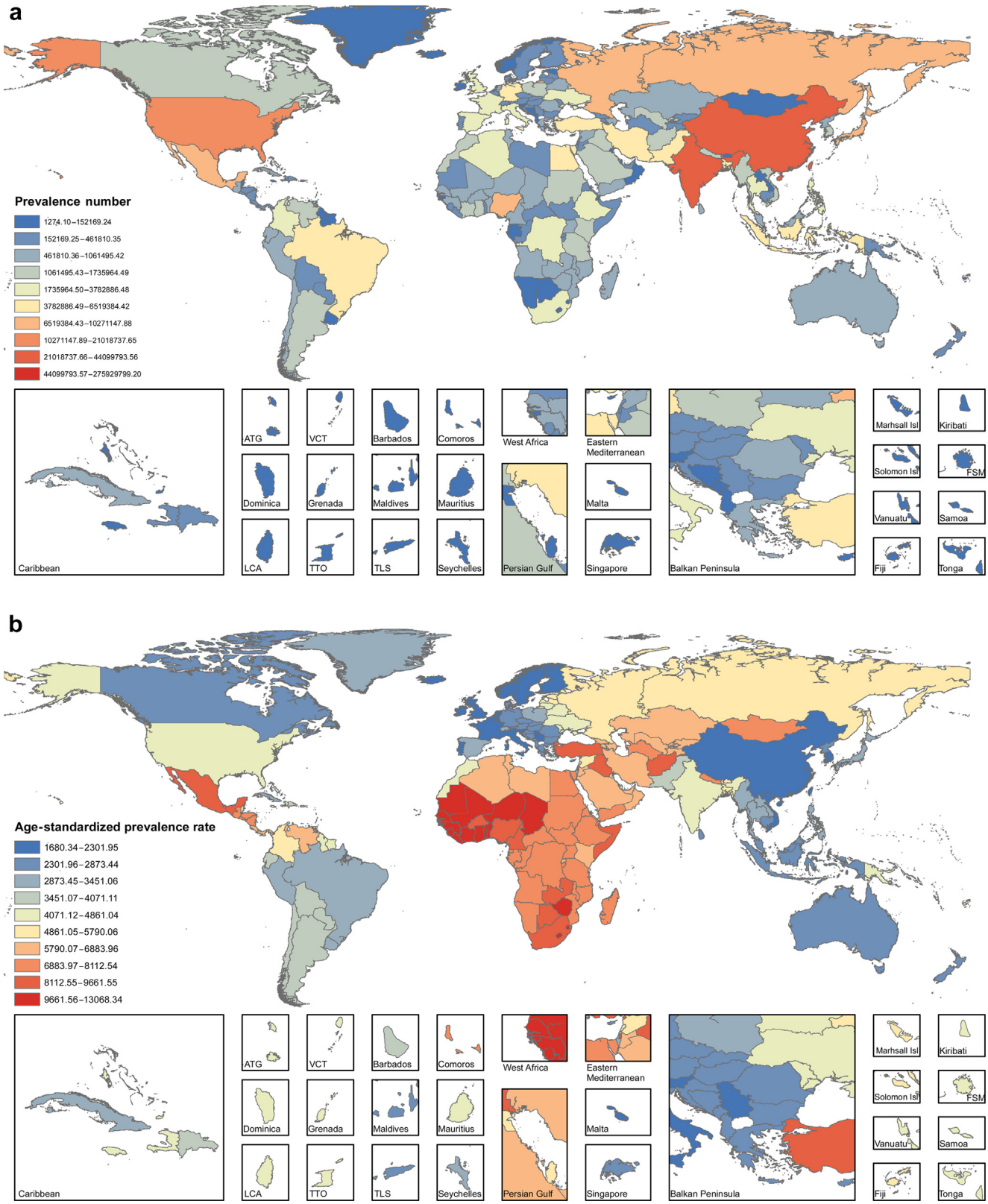

Figure 1 | (a) Worldwide prevalence of chronic kidney disease (CKD). (**b**) Worldwide age-standardized prevalence rate of CKD. Rate is per 100,000 population. ATG, Antigua and Barbuda; FSM, Federated States of Micronesia; Isl, Island; LCA, Saint Lucia; TLS, Timor-Leste; TTO, Trinidad and Tobago; VCT, Saint Vincent and the Grenadines. Heat gradient represents deciles from red (highest) to blue (lowest).

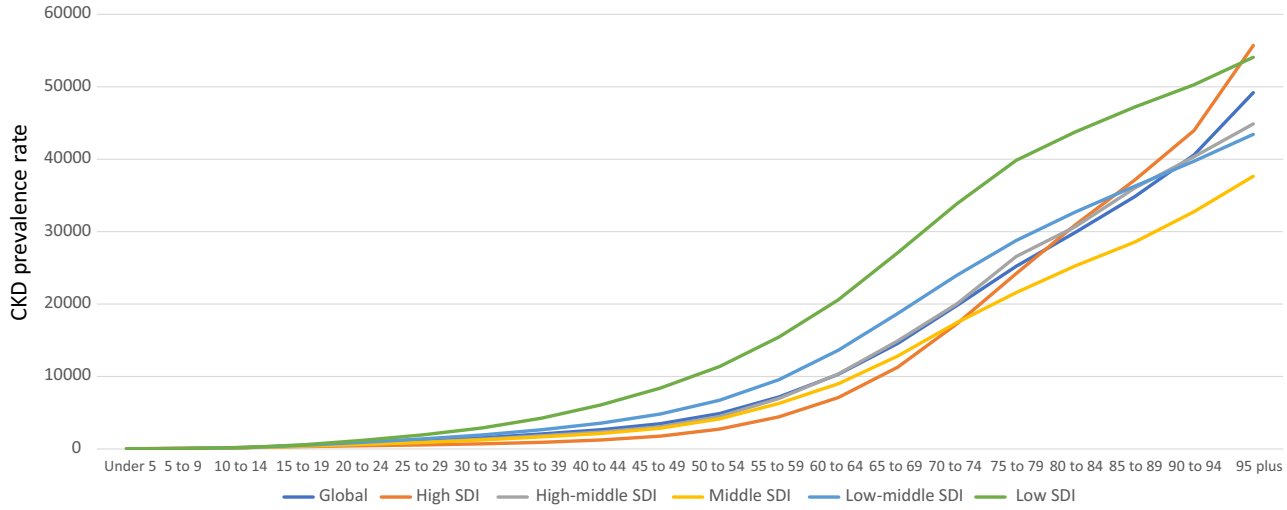

Figure 2 | Chronic kidney disease (CKD) prevalence rate across age groups at the global level and by Sociodemographic Index (SDI) quintiles. Rate is per 100,000 population.

2016 there were more than 21 million incident cases of CKD per year (an increase of 88.76%), 276 million prevalent cases (an increase of 86.95%), nearly 1.2 million deaths due to CKD (an increase of 98.02%), and 35 million years of healthy life lost due to CKD (an increase of 62.21%). Change in CKD burden varied by level of development and geography. Decomposition of CKD DALYs showed that the increase was primarily driven by population growth and aging, and was tempered (but far from offset) by decrease in age-standardized mortality and morbidity rates in most GBD regions except in High-income North America, Central Latin America, Oceania, Southern Sub-Saharan Africa, and Central Asia, where the tide of

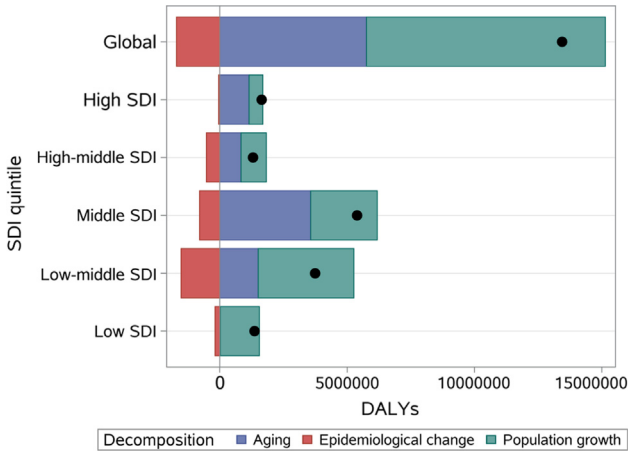

Figure 3 | Changes in chronic kidney disease (CKD) disability-adjusted life-years (DALYs) according to population-level determinants of population growth, aging, and epidemiological change from 1990 to 2016 at the global level and by Sociodemographic Index (SDI) quintile. The black dot represents the overall value of change contributed by all 3 components. For each component, the magnitude of a positive value indicates a corresponding increase in CKD DALYs attributed to the component; the magnitude of a negative value indicates a corresponding decrease in CKD DALYs attributed to the related component.

diabetes and the increased burden of CKD due to diabetes outpaced burden expected by demographic forces of population growth and aging. The results show that the burden is more disproportionally borne by countries that are least equipped to handle it, but opportunities for reduction in CKD burden exist at all levels of development.

There are several cross-cutting themes that are evident in this analysis. First, the forces of demographic expansion (population growth and aging) have dramatically influenced the change in burden of CKD in each SDI quintile. Second, the underlying epidemiologic trends (decreased underlying morbidity and mortality rates due to CKD) have softened (lessened) but far from offset the impact of population growth and aging. Third, although there was remarkable heterogeneity in demographic and epidemiologic trends across the development spectrum and across GBD regions, decomposition analyses of CKD burden by cause revealed substantial variation but a consistent theme of diabetes followed by hypertension as leading drivers of CKD. Fourth, the burden of CKD was more heavily tilted toward poorer and less well-developed economies, and countries with highest age-standardized CKD DALY rates had the lowest performance on health care access and quality measures. Fifth, our frontier analysis suggested that even at the low end of the development spectrum, there are several countries with leading performance in CKD DALYs; these countries may serve as exemplars to identify drivers of success, and echo a theme in many GBD studies that "development is not destiny," suggesting that a country or territory's place on the development spectrum should not preclude it from aligning policies and leveraging available resources to realize potential opportunities for reduction in burden of kidney disease.

In this analysis, and according to the GBD data and methodologies, the 2016 prevalence rate of CKD was 3.7%, and age-standardized prevalence was 4.1%. The estimates may not be immediately comparable to other studies that have

Table 7| Changes in DALYs number according to population-level determinants and causes from 1990 to 2016 globally and by SDI quintile

Location	Overall difference[a]	Change due to population-level determinants (% contribution to the total changes)				Change due to causes (% contribution to the total changes)			
		Aging[b]	Population growth[c]	Epidemiologic changes[d]	Diabetes	Hypertension	Glomerulonephritis	Other causes
Global	13,435,220.83	5,757,866.93 (42.86%)	9,377,469.73 (69.80%)	−1,700,115.83 (−12.65%)	6,800,415.24 (50.62%)	3,125,624.91 (23.26%)	1,323,760.84 (9.85%)	2,185,419.83 (16.27%)
High SDI[e]	1,642,018.44	1,150,885.97 (70.09%)	537,150.25 (32.71%)	−46,017.77 (−2.80%)	939,768.18 (57.23%)	389,308.38 (23.71%)	40,123.21 (2.44%)	272,818.68 (16.61%)
High-middle SDI[e]	1,303,536.18	834,270.59 (64.00%)	995,095.31 (76.34%)	−525,829.73 (−40.34%)	728,017.74 (55.85%)	347,282.99 (26.64%)	49,037.99 (3.76%)	179,197.47 (13.75%)
Middle SDI[e]	5,387,728.38	3,570,653.13 (66.27%)	2,610,131.57 (48.45%)	−793,056.31 (−14.72%)	2,873,896.37 (53.34%)	1,349,269.61 (25.04%)	511,717.01 (9.50%)	652,845.39 (12.12%)
Low-middle SDI[e]	3,740,819.21	1,505,422.42 (40.24%)	3,756,561.75 (100.42%)	−1,521,164.97 (−40.66%)	1,792,896.66 (47.93%)	829,003.46 (22.16%)	419,694.41 (11.22%)	699,224.67 (18.69%)
Low SDI[e]	1,362,166.62	21,823.44 (1.60%)	1,530,005.99 (112.32%)	−189,662.81 (−13.92%)	460,414.25 (33.80%)	208,569.48 (15.31%)	304,556.67 (22.36%)	388,626.23 (28.53%)

DALYs, disability-adjusted life-years; SDI, Sociodemographic Index.
[a]Change in DALYs number between 2016 and 1990.
[b]Change in DALYs number due to change in the age structure.
[c]Change in DALYs number due to change in population number.
[d]Change in DALYs number due to epidemiologic changes. Epidemiologic changes refer to the DALY number change when age structure and population hold constant.
[e]Low SDI: SDI < 0.46; low-middle SDI: 0.46–0.64; middle SDI: 0.65–0.74; high-middle SDI: 0.75–0.85; high SDI: SDI > 0.85.

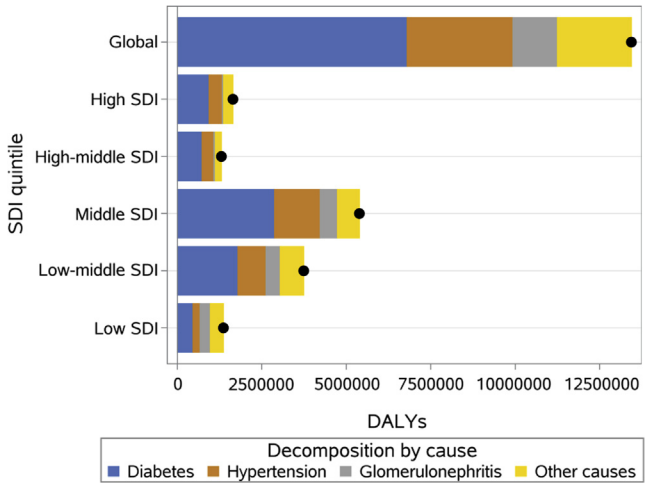

Figure 4| Changes in chronic kidney disease (CKD) disability-adjusted life-years (DALYs) according to the 4 causes from 1990 to 2016 at the global level and by Sociodemographic Index (SDI) quintile. The black dot represents the overall value of change contributed by all 4 causes. For each component, the magnitude of a positive value indicates a corresponding increase in CKD DALYs attributed to the component; the magnitude of a negative value indicates a corresponding decrease in CKD DALYs attributed to the related component.

exclusively reported prevalence in the adult population. However, these estimates are generally congruent with findings by Brück *et al.*, who reported an adjusted prevalence of CKD stage 3 to 5 of 1.0% to 5.9% in the European Union.[7] Estimates reported by Mills *et al.* and Hill *et al.*[8,9] were higher. And estimates in other studies exhibited substantial variability[10,11]; the variability in estimates by these studies is likely the reflection of several factors, including the methodology of measuring creatinine, issues related to calibration and estimating equations, the representativeness of the population

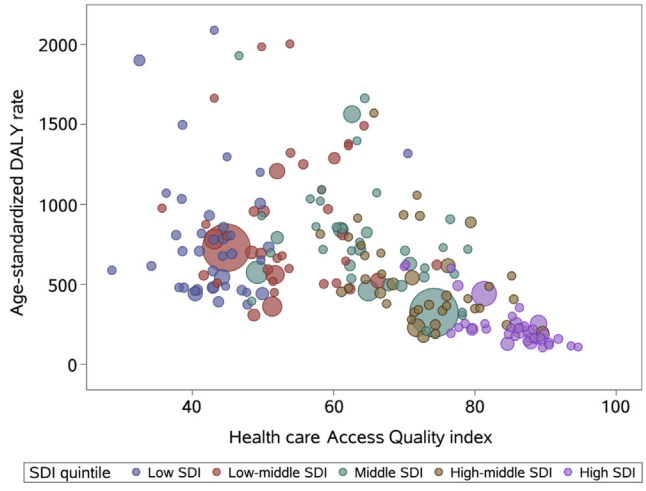

Figure 5| Association between age-standardized chronic kidney disease (CKD) disability-adjusted life-years (DALY) rate and Healthcare Access and Quality index. Each circle represents a country; circles are colored according to Sociodemographic Index (SDI) quintile; circle size corresponds to population number.

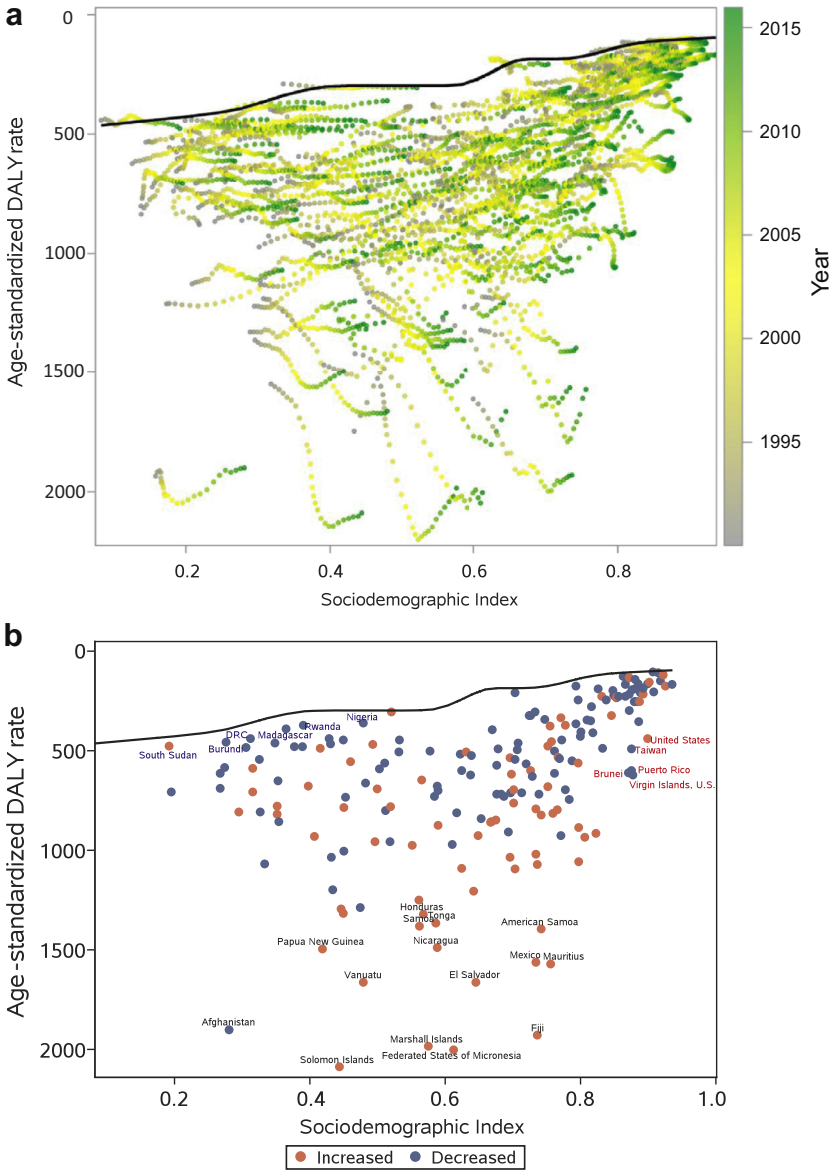

Figure 6 | (a) Frontier analysis based on Sociodemographic Index (SDI) and age-standardized chronic kidney disease (CKD) disability-adjusted life-years (DALY) rate from 1990 to 2016. Color scale represents the years from 1990 depicted in gray to 2016 depicted in green. The frontier is delineated in solid black color. (**b**) Frontier analysis based on SDI and age-standardized CKD DALY rate in 2016. The frontier is delineated in solid black color; countries and territories are represented as dots. The top 15 countries with the largest effective difference (largest CKD DALYs gap from the frontier) are labeled in black; examples of frontier countries with low SDI (<0.5) and low effective difference are labeled in blue (e.g., South Sudan, Burundi, Democratic Republic of Congo, Madagascar, Rwanda, and Nigeria), and examples of countries and territories with high SDI (>0.85) and relatively high effective difference for their level of development are labeled in red (e.g., United States, Puerto Rico, US Virgin Islands, Brunei, and Taiwan). Red dots indicate an increase in age-standardized CKD DALY rate from 1990 to 2016; blue dots indicate a decrease in age-standardized CKD DALY rate between 1990 and 2016. DRC, Democratic Republic of Congo.

examined, the age and gender structure of the population studied, and possibly other explanatory factors.[10–26] The GBD integrative meta-regression approach comprehensively incorporates all dimensions of health data from different sources, considers the underlying demographic parameters of populations, corrects for inconsistencies, and fills in gaps when data are incomplete, ultimately producing the GBD estimates.[27] Furthermore, GBD also provides a measure of uncertainty (uncertainty intervals) to show how much is known, but perhaps more importantly, how much we do not know about the burden of a specific disease in each country. As such, the estimates provided in this report have integrated data from all epidemiologic reports and might more closely approximate the true burden of CKD in any given country.

While the world's health is improving, as global DALYs from all diseases fell from 2,448,430,506.75 (UI = 2,305,218,240.22–2,608,339,531.40) in 1990 to 2,391,258,032.63 (UI = 2,184,254,133.63–2,631,699,016.86) in 2016, CKD DALYs have increased from 21,597,163.60 (UI = 20,093,986.99–23,354,864.85) in 1990 accounting for 0.88% of all DALYs to

35,032,384.43 (UI = 32,622,072.69–37,954,350.03) in 2016, accounting for 1.47% of all DALYs.[28] The increase in burden of CKD does not only reflect a shift from communicable to noncommunicable diseases, but also an increasing share of CKD DALYs within the noncommunicable disease group, from 2.01% in 1990 to 2.39% in 2016.[28,29] Compared with other disease entities, the magnitude of health loss from CKD is substantial; for example, CKD DALYs in 2016 (35,032,384.43) were higher than DALYs for all digestive diseases (34,368,942.12) and nearly 61% of DALYs for diabetes (57,233,688.58).[28]

The number of deaths caused by CKD has nearly doubled, from 0.6 million deaths in 1990 to 1.2 million deaths in 2016; CKD was the 18th leading cause of death in 1990 and ascended to the 11th leading cause of death in 2016.[28] From 1990 to 2016, the all-cause age-standardized death rate decreased, in which death rates decreased for communicable and noncommunicable diseases.[28] However, within the noncommunicable diseases category, rates decreased for cardiovascular diseases, cancer, and digestive diseases and increased for CKD, diabetes, neurologic disorders, and drug use disorders.[28] This dramatic divergence in mortality trends is most likely a reflection of progress made in the management of cardiovascular diseases, cancer, and digestive diseases, and lack of progress in CKD, diabetes, and neurologic diseases, and is a manifestation of our overwhelming failure of stemming the tide of death from substance use disorders. Interestingly, and although age-standardized death rates from CKD due to diabetes and hypertension have increased, death rates of CKD due to glomerulonephritis have decreased between 1990 and 2016, which represents a bright spot and illustrates some progress made in the treatment of glomerulonephritis globally.

The overall increase in burden of CKD is in large part driven by aging and population growth. The raw incidence, prevalence, death, and DALYs of CKD have increased; however, age-standardized incidence and prevalence rates have not changed appreciably, and the age-standardized death rate exhibited a tempered increase of 4.39% while its share of overall death increased significantly from 1.45% in 1990 (ranking 14th) to 2.19% in 2016 (ranking 10th). Between 1990 and 2016, age-standardized DALY rates decreased by 4.09%, which represents some progress; however, its share of all age-standardized DALYs increased from 1.08% in 1990 (ranking 25th) to 1.49% (ranking 21st) in 2016.[28]

In our analyses, we observed that the increased burden of CKD is driven in large part by the increased global epidemic of diabetes and to a lesser extent hypertension.[3,4,30] Over the past 27 years, the increased burden of CKD due to diabetes and CKD due to hypertension contributed 50.62% and 23.26% of the increased burden of overall CKD, respectively. The relative contribution of diabetes as a driver varied by SDI and by GBD region; overall, the relative contributions of diabetes and hypertension as drivers of change in DALYs have decreased as SDI decreased. Diabetes was responsible for much of the change in DALYs in Australasia, East Asia, Southeast Asia, High-income North America, High-income Asia Pacific, and Oceania (Supplementary Table S3 and Figure 8b). Whereas globally and in many GBD regions the underlying morbidity and mortality rates of CKD have declined, there are several GBD regions that diverged from this trend and exhibited an increase in these rates, namely Oceania, Southern Sub-Saharan Africa, Central Latin America, High-income North America, and Central Asia. Our decomposition analyses suggest that in these regions particularly, the epidemic of diabetes and subsequently CKD due to diabetes not only outpaced the increased burden that would be expected by population growth and aging and but also overwhelmed progress made to reduce the burden; CKD due to diabetes is affecting younger members of the population, and for each age group the rates were higher than expected based on demographic expansion in several geographic regions.

In this study, we found that the burden of CKD is more heavily tilted toward countries with less well-developed economies; there was also an inverse relationship between age-standardized DALY rates and measures of health care access and quality. While this analysis highlights a significant challenge, our frontier analysis provides a more optimistic assessment in that there are several countries at all levels of the development spectrum with CKD DALYs that are distant from the frontier (with relatively large effective difference from the frontier), which suggests unrealized opportunities to close the DALYs gap. While frontier countries exist at all SDI levels, most notable are those with low SDI, which exhibited leading performance despite constrained resources; these countries might serve as exemplars on optimization of health outcomes in low-resource settings. Conversely, several countries with high SDI delivered lagging performance (e.g., United States and Taiwan), an observation 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 exemplar countries[31] and forces hampering progress in laggard countries; addressing this knowledge gap will likely be useful in informing effort to alleviate the burden of CKD.[32,33]

As in any assessment of this scope, this study has limitations. First, this is a macro-level assessment of global, regional, and national epidemiologic trends of CKD over the span of more than a quarter century, and as such it may not have captured micro level trends.[31] This may be especially relevant in large geographies (e.g., China, India, and the United States), which may exhibit significant subnational variation in burden of CKD not reflected in our analyses.[7–10,15] We relied on the GBD data to produce the estimates provided in this report, and while GBD methodologies and results are considered state-of-the-art, robust, and reliable, they are necessarily limited by the quality of the available data.[27] For many countries with limited data, GBD estimates were derived by mathematical modeling.[27] Furthermore, variability and inconsistency of data collection methods and tools across the countries and over time could influence geographic variations and temporal trends.[34] In this analysis, we did not report burden of CKD by gender, and we

did not restrict the analyses to the adult population. Our decomposition analyses considered major demographic factors and the 4 causes of CKD as defined by the GBD framework; other potential drivers likely exist but are beyond the scope of this analysis. While we outlined several limitations, we, however, note that because the GBD estimates will be updated annually, we anticipate that data collection systems and GBD methodologies will continue to evolve to address some of these limitations (e.g., provision of subnational estimates). Key strengths include leveraging the availability of the GBD data spanning the years 1990 to 2016; the GBD data is the most comprehensive compilation and analysis of global health information available. We developed decomposition analyses to elucidate the influence of demographic trends and cause of disease as drivers of change in burden of CKD over the past 27 years, and finally, we developed a frontier analysis to enable comparative evaluation among countries with similar SDI.

In conclusion, the global toll of CKD is substantial and has risen dramatically over the past 27 years; death and disability due to CKD have increased, largely driven by population growth and aging. Diabetes followed by hypertension were the leading drivers of CKD globally. There was a significant variation in demographic and epidemiologic trends among geographic regions, and the burden of CKD is more heavily tilted toward less well-developed economies with suboptimal health system performance. While health loss due to CKD exhibited a relationship with measures of economic and sociodemographic prosperity, our frontier analysis showed that "development is not destiny," as several countries with constrained resources have a leading performance for CKD DALYs and may serve as exemplars to others to help reduce suffering from kidney disease. The rising burden of CKD should be reflected in the global and national health agendas.

MATERIALS AND METHODS

Data sources

The GBD study provides a detailed epidemiologic assessment of 333 diseases and injuries and 84 risk factors by age and sex on a global scale and for 195 countries and territories spanning the years from 1990 to 2016.[37–44] An integrative Bayesian meta-regression method that estimates a generalized negative binomial model for all epidemiological data was used through DisMod-MR 2.1 in the computation of GBD estimates of disease burden[27]; detailed descriptions of overall GBD 2016 methodologies and specific CKD methodology have been provided elsewhere.[27,35–39] Data on CKD incidence, prevalence, death due to CKD, and DALYs and their uncertainty intervals were curated from GBD data sources. All GBD data used in this study were obtained from the Global Burden of Disease Collaborative Network; results were provided by the Institute for Health Metrics and Evaluation (Seattle, WA).[28]

In the GBD study, CKD was considered both as a disease and a metabolic risk factor. In this analysis, we approached CKD as a disease. CKD was defined as estimated glomerular filtration rate of less than 60 ml/min per 1.73 m^2.[36]

Measures of burden

Measures of burden at the global, regional, and national levels included incidence, prevalence, death due to CKD, and DALYs due to CKD (Table 1). Death due to CKD was estimated by the GBD using cause of death ensemble model.[38,43] DALYs were calculated through summation of years lived with disability and years of life lost. The years lived with disability is a measure of disease burden that represents the years lived with CKD; it considers the duration of time living with the disease and related disability weights to reflect the underlying severity of CKD. The years of life lost represented the years lost due to premature mortality caused by CKD. Both years lived with disability and years of life lost were estimated for each age, gender, and location in a specific year (Table 1). All measures are reported as raw values, rates per 100,000 population, and age-standardized rates per 100,000 population, where age standardization was based on the World Health Organization world population standard age structure.

Country classification

In our analyses we classified countries according to the 2016 SDI in quintiles (Table 1). SDI is a standardized composite summary measure on a scale of 0 to 1 that is comparable by geography and over time[44]; it includes (i) average income per person, (ii) educational attainment, and (iii) total fertility rate of the country. We also classified countries according to GBD region, and according to World Bank Income Group in fiscal year 2018 (Supplementary Table S1).

Decomposition analysis

To gain a better understanding of explanatory factors that drove change in CKD DALYs between 1990 and 2016, we conducted decomposition analyses by (i) population size, age structure, and epidemiologic changes, and (ii) CKD cause. The decomposition analyses (further defined in Table 1 and described in detail in Supplementary Methods) show the change in CKD DALYs contributed by each component.

Health Care Access and Quality

The HAQ index provides a summary measure on a scale of 0 to 100 to facilitate comparison of personal health care access and quality by geography and over time[44] (Table 1). To gain a better understanding of the distribution of CKD burden in relation to countries' health system performance, we examined the relationship between age-standardized DALY rates in 2016 and HAQ in 2015 by Pearson correlation coefficient. Further details are provided in Supplementary Methods.

Frontier Analysis

To evaluate the relationship between burden of CKD and sociodemographic development, we applied a frontier analysis as a quantitative methodology to identify the lowest potentially achievable age-standardized DALY rate on the basis of development status as measured by the SDI (Table 1). The methodology of the frontier analysis is further described in Supplementary Methods.

Statistical software SAS Enterprise Guide 7.1 was used for the analyses. Maps were generated using ArcGIS 10.5.1 developed by ESRI (Redlands, CA).

DISCLOSURE

All the authors declared no competing interests.

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In this report, we used the Global Burden of Disease (GBD) studies data and methodologies. The Global Burden of Disease Collaborator Network comprises more than 3000 collaborators worldwide and is headquartered at the Institute for Health Metrics and Evaluation (IHME) in Seattle, Washington. The estimates used in generating this manuscript relied on the GBD data and methodologies, and we acknowledge the

visionary global health leadership of IHME, and the contribution of all collaborators, without whom this report would not be possible.

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SUPPLEMENTARY MATERIAL

Supplementary Methods.

Table S1. Classification of countries according to Global Burden of Disease (GBD) region, Sociodemographic Index (SDI) quintile, and World Bank income.

Table S2A. Number, rate, and age-standardized rate for overall chronic kidney disease (CKD) incidence and by cause of CKD in 2016 and percentage change from 1990.

Table S2B. Number, rate, and age-standardized rate for overall chronic kidney disease (CKD) prevalence and by cause of CKD in 2016 and percentage change from 1990.

Table S2C. Number, rate, and age-standardized rate for overall chronic kidney disease (CKD) death and by cause of CKD in 2016 and percentage change from 1990.

Table S2D. Number, rate, and age-standardized rate for overall chronic kidney disease (CKD) disability-adjusted life-years (DALYs) and by cause of CKD in 2016 and percentage change from 1990.

Table S3. Changes in disability-adjusted life-years (DALYs) according to population-level determinants and causes from 1990 to 2016.

Table S4. Frontier disability-adjusted life-years (DALYs) and effective difference by country or territory.

Figure S1. (**A**) Global chronic kidney disease (CKD) incident number, rate, and age-standardized rate from 1990 to 2016. (**B**) Global age-standardized incident rate of CKD by 4 causes from 1990 to 2016. Rate per 100,000 population.

Figure S2. (**A**) Global chronic kidney disease (CKD) prevalence number, rate, and age-standardized rate from 1990 to 2016. (**B**) Global age-standardized prevalence rate of CKD by 4 causes from 1990 to 2016. Rate per 100,000 population.

Figure S3. (**A**) Global death number, rate, and age-standardized rate due to chronic kidney disease (CKD) from 1990 to 2016. (**B**) Global age-standardized death rate due to CKD by 4 causes from 1990 to 2016. Rate per 100,000 population.

Figure S4. (**A**) Global chronic kidney disease (CKD) disability-adjusted life-years (DALYs) number, rate, and age-standardized rate from 1990 to 2016. (**B**) Global age-standardized CKD DALY rate by 4 causes from 1990 to 2016. Rate per 100,000 population.

Figure S5. (**A**) Proportion of chronic kidney disease (CKD) prevalence in each age group at the global level and by Sociodemographic Index (SDI) quintile. (**B**) Proportion of death due to CKD in each age group at the global level and by SDI quintile.

Figure S6. (**A**) Population-level determinants attributed to changes in chronic kidney disease (CKD) disability-adjusted life-years (DALYs) from 1990 to 2016 at the global level and by Sociodemographic Index (SDI) quintile. (**B**) Changes in CKD DALYs according to population-level determinants from 1990 to 2016 by Global Burden of Disease (GBD) region.

Figure S7. Changes in chronic kidney disease (CKD) disability-adjusted life-years (DALYs) number by CKD cause and age group from 1990 to 2016 after accounting for contribution of population growth and aging. Causes included diabetes, hypertension, glomerulonephritis, and other causes from 1990 to 2016. Analyses were performed in Global Burden of Disease (GBD) regions that exhibited an increase in age- and population-standardized CKD DALY rates, including high-income North America, Oceania, Central Latin America, Central Asia, and Southern Sub-Saharan Africa.

Figure S8. (**A**) Four causes attributed to changes in chronic kidney disease (CKD) disability-adjusted life-years (DALYs) from 1990 to 2016 by Sociodemographic Index (SDI) quintile. (**B**) Changes in CKD DALYs according to 4 causes from 1990 to 2016 by Global Burden of Disease (GBD) region.

Figure S9. Age-standardized chronic kidney disease (CKD) disability-adjusted life-years (DALY) rate by World Bank Income classification and Sociodemographic Index (SDI) quintile.

Figure S10. (**A**) Spline analysis for association between Healthcare Access and Quality (HAQ) and age-standardized chronic kidney disease (CKD) disability-adjusted life-years (DALY) rate. (**B**) Spline analysis for within-region association between Healthcare Access and Quality (HAQ) and age-standardized CKD DALY rate. Rate per 100,000 population.

Supplementary material is linked to the online version of the paper at www.kidney-international.org.

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