## 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-lifeyears (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

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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.

Kidney International (2018) ■, ■-■; https://doi.org/10.1016/ j.kint.2018.04.011

KEYWORDS: age; CKD burden; chronic kidney disease; DALYs; diabetes; death; epidemiology; global health; glomerulonephritis; hypertension; incidence; prevalence; population

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he 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 noncommunicable diseases.<sup>1,2</sup> 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.<sup>3</sup> The number of adults with elevated blood pressure increased from 594 million in 1975 to 1.13 billion in 2015. 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.<sup>3–6</sup>

The global forces of demographic expansion and epidemiologic transition have shaped the epidemiology of noncommunicable 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); agestandardized 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

#### 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.

(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

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