Getting to know the enemy better – The global burden of chronic kidney disease

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Abstract

A good understanding of disease burden is the first step in formulating a response to it. Analysis of GBD 2016 dataset shows 87% rise in the global burden of CKD and a doubling of CKD deaths between 1990 and 2016. Countries with lower level of socio-economic development and poorer access to quality healthcare experience a higher CKD burden. Reduction in age-standardized mortality and global DALYs over time indicate progress, but deviations from this trend in some geographies present a call to action.

Non-communicable diseases (NCD) are now responsible for almost three-fourth of all deaths globally, up from 57% in 1990. About 80% of all premature NCD deaths are in low and middle-income countries. (1)

A relative newcomer to the NCD arena, kidney disease has struggled to receive visibility. Effort to change the narrative were spurred by development of a universally accepted definition of chronic kidney disease (CKD), and meta-analyses of large cohorts showing the range of adverse health consequences of CKD. (2) The evidence is now overwhelming that CKD is vastly more common than was appreciated just 20 years ago, and that its adverse health impact is not limited to end-stage kidney failure. The Global Burden of Disease (GBD) 2013 report for the first time documented that CKD had rapidly moved up the ranks of causes of global deaths, with the increase being second only to HIV and AIDS. In 2016, CKD was 11th on the list. (3) In contrast, the age-standardized cardiovascular and cancer related mortality fell during the same period.

Sound health policymaking relies heavily on accurate and regularly updated disease burden estimates, so that public policy alternatives can be objectively analyzed. Absence of a good sense of the kidney disease burden has prevented the public health community from mounting appropriate health systems response to CKD in the face of competing demands for conditions with better defined estimates e.g. diabetes, hypertension, cardiovascular disease and cancers.

Since 1991, the GBD reports have documented health loss from death or disability at global and country levels. (1) Raw data are collected from multiple sources, benchmarked for quality and analyzed using complex techniques including mathematical modeling, extrapolations, adjustments and integrative Bayesian meta-regression analyses. Increasingly, countries are using on GBD estimates to shape future of NCD control.

GBD uses mortality and disability-adjusted life years (DALY) to measures the impact of diseases. DALY is a sum of the years of life lost due to mortality (benchmark life expectancy 86 years) with years lived with disability. Disability weights are determined by household surveys using pairwise comparison of health states with lay descriptions and trade-off questions and assigned to individual conditions on a scale ranging from 0 (perfect health) to 1 (death). For example, 2 years lived with a disease that carries a disability weight of 0.3 equals 0.6 DALY. Development status of countries is indicated by socio-demographic index (SDI, scale 0 – 1), based on average income per person, educational attainment and total fertility rate. The health access and quality (HAQ) index measures personal access to healthcare and its quality. It is expressed on a scale of 0 to 100 and is derived from outcomes of 32 diseases that can be avoided or effectively treated with proper medical care.

In this issue of KI, Xie et al present estimates and trends of global and country specific prevalence, incidence, death and DALYs for CKD over the years 1900-2016; examine the impact of population growth, aging and causes of CKD (diabetes, hypertension, glomerulonephritis and other causes) on the evolution of CKD burden; and relationship of country-level CKD burden with SDI and HAQ using the GBD data and methodology (4).

The estimated global crude prevalence of CKD was 147.6 (95% CI 135.8-160.2) million in 1990, which increased by 87% to 276 (252.4-300.4) million cases in 2016. The age-standardized prevalence showed a smaller increase (from 4,040 to 4,056 per 100,000 population). The global incidence of CKD increased by 89% from 11.3 million in 1990 to 21.3 million in 2016, and the age standardized values increased from 299 to 310 per 100,000 population. The crude mortality doubled, from 0.59 to 1.2 million. The global DALYs rose by 62%, from 21 to 35 million, but the age-adjusted values decreased from 521 to 500 per 100,000 population.

Decomposition analyses showed population growth and aging to be the main drivers of the increase in DALYs. Aging was the more prominent driver in high SDI nations with higher life expectancies and population growth was the main force in low SDI nations known for high fertility and lower life expectancy. Diabetes and hypertension contributed 50.6% and 23.3% of the increased CKD DALYs. The impact of these two conditions was most marked in high SDI countries and gradually decreased as the SDI status came down, hinting at existence of other causes in countries with lower SDI. The relative contribution of diabetes to CKD DALYs across the globe varied from 27-88%.

The study shows large inequities in global CKD care – the per 100,000 CKD DALY rates were 276 in the highest SDI quintile and 662 in the lowest SDI quintile. CKD developed and caused deaths at an earlier age amongst individuals in low SDI nations. A graded increase in DALYs was noted as the HAQ scores declined, even after controlling for SDI.

Using the SDI and HAQ, the authors conducted the Frontier analysis, an econometric technique that uses regression modeling to estimate "inefficiency", implying suboptimal decision-making or execution to achieve an output (minimization of DALYs). Countries with the minimum DALYs given their level of development are considered least inefficient and define the frontier. The further a country is from the frontier, the greater is the potential of improving efficiency within the limitation of its resources. The range of effective distance from frontier was 24-51 DALYs for the 10 best performers to 1,241-1,829 DALYs for the 10 worst performers.

How do these comprehensive global and country level estimates for CKD burden provided in this important study compare with past estimates? A systematic analysis of 33 studies (5) estimated the number of adults with CKD in the world in 2010 at 497.5 (95% CI 463.7-551.1) million. Another meta-analysis (6) estimated the global prevalence of CKD stage 3-5, comparable to the present study, at 10·6% (9·2–12·2%). The global crude and age-standardized prevalence of CKD at 3.7% and 4.4% respectively in the present report are almost half of these estimates, raising the possibility that perhaps early stages of CKD are not uniformly captured in the routine databases, and persistence of fallacies in CKD prevalence studies pertaining to creatinine estimation, calibration and the diagnosis being made on one-time testing. (7) The current study did not have albuminuria as its case definition, which might underestimate the burden.

This study estimated the global number of CKD deaths in 2016 at 1.2 million, which contrasts with the estimates of Liyanage et al, who estimated that at least 2.3 million cases with ESRD died without access to renal replacement therapy in 2010, suggesting the possibility that not all ESRD deaths are counted, especially in the poor countries. (8)

Despite an overall increase in contribution of CKD DALYs to the global all cause DALYs from 0.88% to 1.47%, the age adjusted mortality and DALYs have actually come down in most of the world, suggesting the success of public health interventions. There were notable exceptions, however, where the DALYs rose, driven primarily by increased burden of CKD due to diabetes. CKD appeared at an earlier age in these regions, a mix of high and low SDI countries. This is a call to action for health care providers to implement the methods that have worked elsewhere to reduce this burden.

Notable by its absence in this report is sex-disaggregated analysis, increasingly requested by governments, UN agencies, non-governmental organizations, funding bodies, universities and medical journals. Other limitations of this study are inherent to GBD source data and modeling techniques. GBD captures only some etiologies, clubs acute glomerulonephritis with diabetes and does not identify acute kidney injury, a major public health problem throughout the emerging world. There could be some caveats in the interpretation of Frontier analysis. One way to move closer to the efficiency frontier is to simply not count the number of subjects with CKD. For example, the rating of Taiwan as inefficient amongst high SDI countries seems anomalous, given the existence of one of the most effective CKD screening and management programs. (9) It appears a laggard because it counts and provides care including dialysis to all its subjects with CKD who therefore live longer and increase the DALYs. Similar caveats, but in the opposite direction, might be working to show Burundi, South Sudan, DRC, etc on the frontier envelope and thus gives them exemplar status amongst the low SDI countries.

Notwithstanding the limitations, the GBD approach is evolving constantly and future refinements will allow greater clarification of the risk factors. The decision to bring out annual estimates provides a great opportunity to measure the impact of public health interventions on the evolution of disease burden.

Looking ahead, a key task for global nephrology community is to improve the evidence that goes into GBD database and work with the GBD collaboration to refine the methodology for CKD-specific analyses. These include identifying the missing disease drivers, especially in low SDI nations, and refinement of disability weighting for different stages of CKD. Data is emerging on the relationship of ambient pollution and heat stress with kidney disease burden in different parts of the world. The effect of climate change on kidney health needs to be examined. Addressing these challenges might require developing kidney disease-specific program verticals, the effect of which should be examined in future GBD iterations to optimize strategies for improving global kidney health. Therein lies the opportunity for us to break out of the narrative that managing kidney disease burden just requires addressing diabetes and hypertension.

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Table 1: Global burden of chronic kidney disease

	Global number 1990	Global number 2016	Percent Increase	Age Adjusted rate /100,000 (1990)	Age Adjusted rate /100,000 (2016)
CKD prevalence	147.6 million	275.9 million	86.9	4040.9	4056.5
CKD incidence	11.3 million	21.3 million	88.8	299.0	310.1
Death due to CKD	0.59 million	1.18 million	98	17.48	18.25
Global DALYs	21.6 million	35.0 million	62.2	521.4	500.1

CKD: chronic kidney disease; DALYs: Disability adjusted life years