



# The Global Burden of Diabetic Kidney Disease: Time Trends and Gender Gaps

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## Abstract

**Purpose of Review** Diabetes mellitus prevalence is increasing throughout the world as a consequence of growing rates of obesity, metabolic syndrome, and westernization of lifestyle. It is currently unknown to what extent these trends affect the global burden of diabetic kidney disease (DKD). This review seeks to describe the global burden of DKD and how it has changed throughout time using recently released results of the Global Burden of Disease 2017 Study.

**Recent Findings** DKD prevalence has remained fairly stable at the global level and among many world regions since 1990. At the global level, the proportion of DKD deaths relative to other types of CKD is increasing.

**Summary** Certain world regions still have very high rates of DKD, whereas other world regions have decreasing prevalence and mortality. Screening will likely play an important role in mitigating the growing burden within high-risk regions.

**Keywords** Diabetic nephropathy · Global burden of diabetic kidney disease · Gender and diabetic kidney disease

## Introduction

### Diabetic Kidney Disease

Diabetic Kidney Disease (DKD) is a known microvascular complication of both type I and type II diabetes mellitus. Though early detection and adequate treatment of diabetes mellitus can slow DKD progression, DKD often advances to end-stage renal disease (ESRD) [1, 2]. Patients with DKD-ESRD experience a high rate of mortality in comparison to non-DKD ESRD patients [3].

Throughout the world, during the past three decades there has been an increase in the burden of non-communicable diseases such as diabetes mellitus [4••]. Reasons for the increase

are twofold. First, decreasing mortality from communicable diseases, especially within low-income world regions, has led to increased survival to older age [5••]. Second, causative processes of diabetes, such as obesity, metabolic syndrome, and westernization of diet have been increasing among low-income world regions [6–8]. Though these trends have been well-described within the literature, what has received little systematic attention is how such trends have affected the global burden of DKD. Studying the burden of DKD is important because of the relatively high mortality rate associated with DKD [9]. Further, identifying world regions with particularly high disease rates can serve as evidence for prioritization of efforts to detect and manage DKD across the disease spectrum.

This article describes the global burden of DKD and global mortality to this condition. Special focus is given to DKD prevalence between 1990 and 2017, as well as differences in disease burden between genders. To accomplish this, this review makes use of the Global Burden of Disease 2017 Study, which has recently published an update of the leading causes of morbidity and mortality throughout the world, and whose methods are published in detail elsewhere [5••, 10]. Finally, this article explores how the results of this study fit into what is known regarding gender trends and relative successes within certain world regions in detecting and addressing the burden of DKD.

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## Global Burden of DKD: Results from the Global Burden of Disease 2017 Study

### Prevalence

In 2017, at the global level, the age-standardized prevalence of DKD in men and women was 15.48/1000, and 16.50/1000, respectively (Fig. 1).

In 2017, among men, the world region with highest DKD prevalence was Oceania, followed by Southeast Asia. The region with lowest prevalence was Western Europe, followed by Australasia (world region composed of Australia and New Zealand). Among women, the region with highest prevalence was Oceania, followed by Eastern Europe. The region with lowest prevalence was Western Europe, followed by Andean Latin America.

In 2017, 16 of 21 world regions demonstrated higher DKD prevalence in women when compared with men (Fig. 1). The five world regions with higher rates in men include Andean

Latin America, Central Latin America, South Asia, Southeast Asia, and Caribbean.

### Prevalence by Gender Across Time

Compared with 1990, age-standardized-prevalence has remained fairly stable at the global level, though it has decreased slightly in men (Fig. 1). The only region indicating a rise in prevalence in men when comparing 1990 and 2017 is Southern Sub-Saharan Africa. The largest decrease among men is found in Tropical Latin America.

At the regional level, findings are more nuanced among women. Prevalence among women tended to increase over time (Fig. 1), with the greatest rise estimated in Southern Sub-Saharan Africa. Regions where prevalence in women decreased include Central Europe, Central Sub-Saharan Africa, East Asia, High-income Asia Pacific, and Western Europe, with high-income Asia Pacific demonstrating the greatest decline.

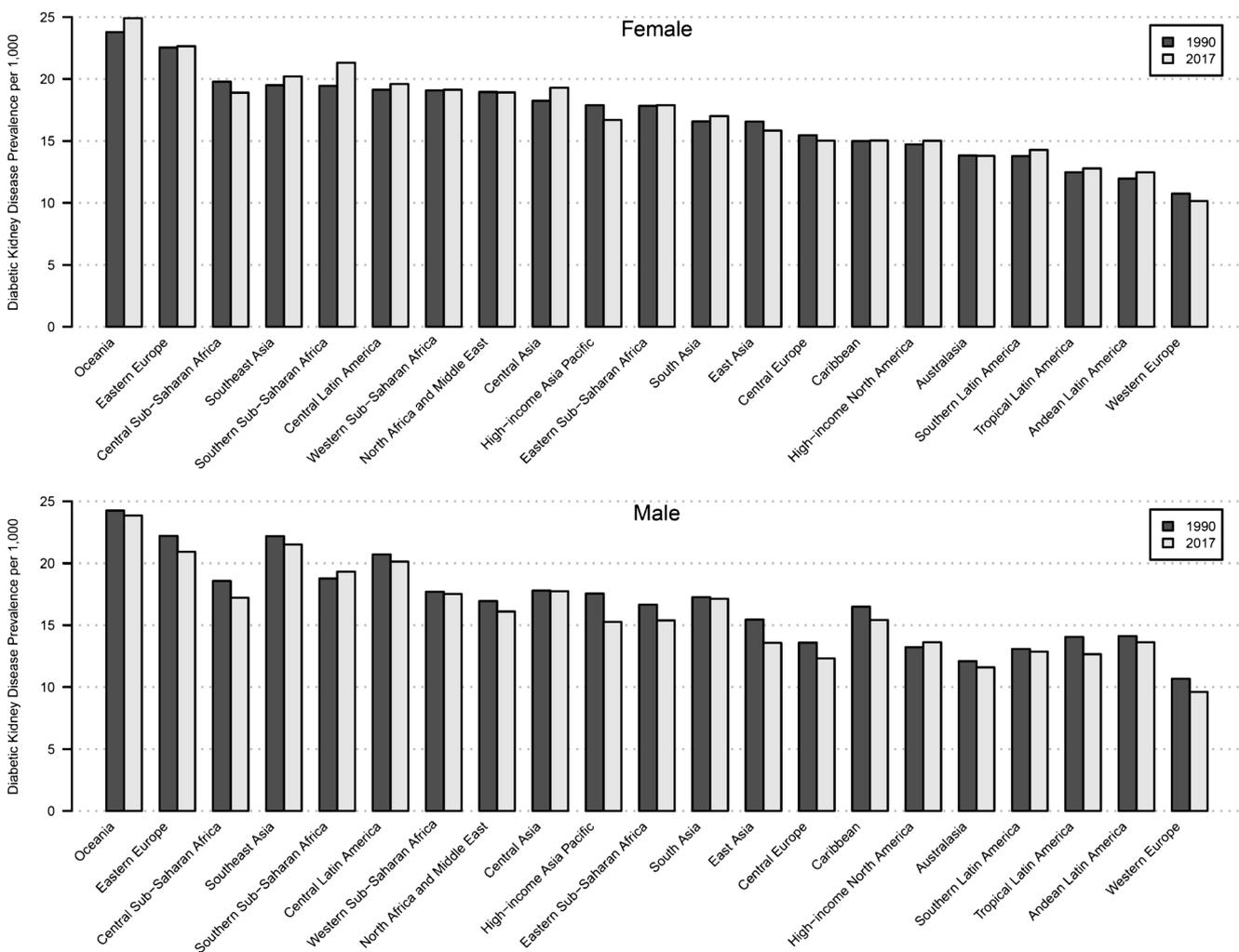


Fig. 1 Prevalence of diabetic kidney disease in 21 geographic regions and overall stratified by sex in 1990 and 2017 per 1000 capita

### Mortality by Gender

In 2017, at the global level, there were an estimated 219,451 deaths that were attributed to DKD among men and women, respectively (Table 1, Fig. 2). These deaths accounted for about 34% of all CKD deaths among men in 2017, and 36% in women (Appendix Fig. 1). These proportions have increased since 1990, where DKD deaths were 29% of all CKD deaths in men, and 32% of all CKD deaths in women (Appendix Fig. 1).

Not all world regions experienced an increase in the proportion of DKD mortality relative to other types of CKD since 1990. Of the 21 world regions, the proportion of DKD mortality rose since 1990 in 14 regions, most notably in Australasia, high-income North America, South Asia, and in women in Tropical Latin America (Table 1). The proportion of deaths remained relatively stable within Central Europe, Eastern Europe, Eastern Sub-Saharan Africa, Southern Latin

America, and Oceania. Two world regions experienced a decrease in the proportion of DKD deaths: Western Europe and high-income Asia Pacific (Table 1).

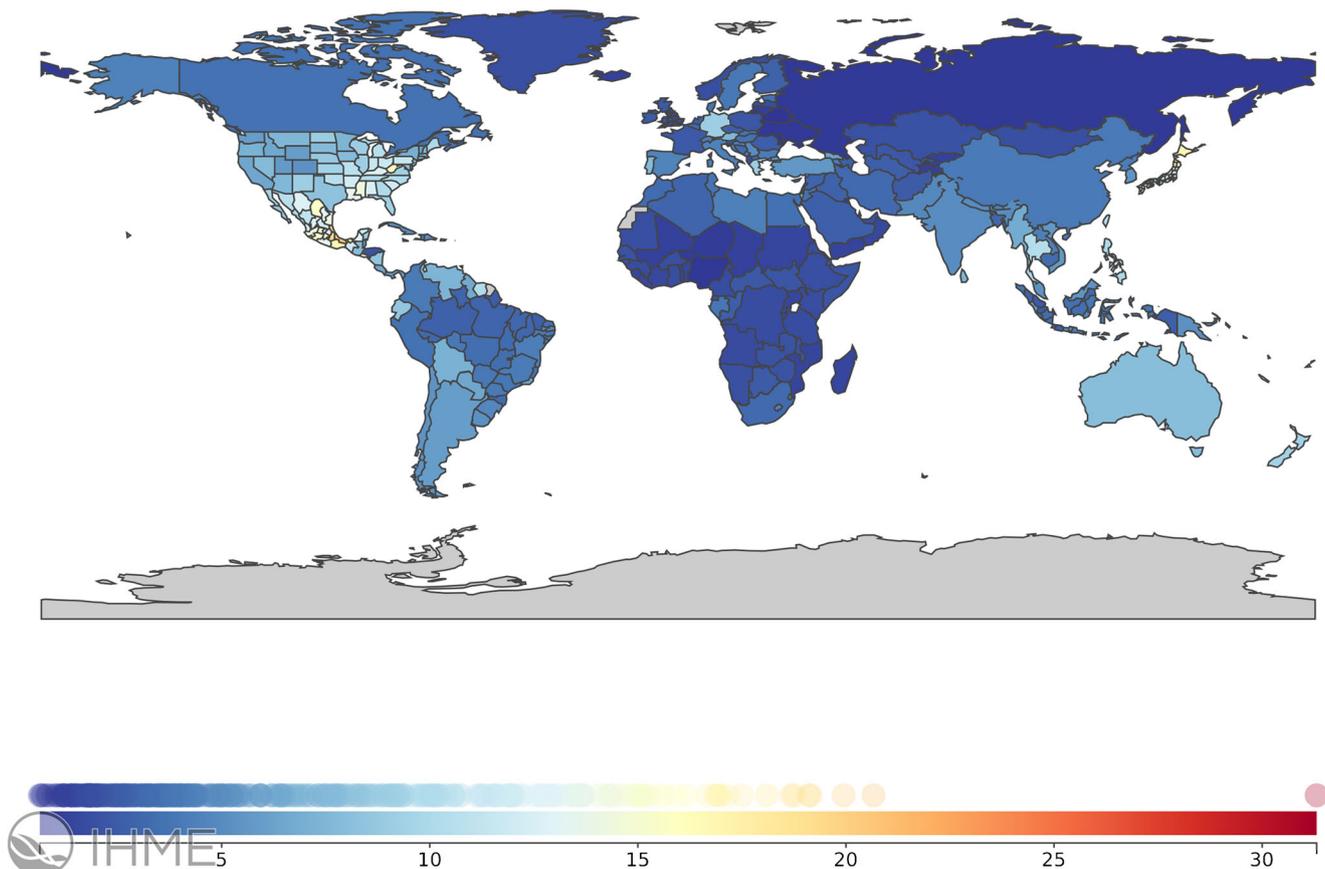
### Making Sense of the Data

The Global Burden of Disease Study makes possible the evaluation of trends in DKD burden at several geographic levels across time and between genders. The finding that the prevalent burden of DKD has not appreciably changed over the past two decades at the global level needs to be interpreted relative to regional patterns. Regional prevalence remained fairly stable across the past two decades; thus, regions with very high rates of DKD in 1990 remained high in 2017 (such as Western Sub-Saharan Africa), and likewise for regions with very low prevalent burden in 1990 (such as Western Europe). The two questions that arise from this observation are (1) Why have

**Table 1** Mortality due to diabetic kidney disease in 21 geographic regions and overall stratified by sex in 2017 and 1990

|                              | 1990      |                       |           |                       | 2017      |                        |           |                        |
|------------------------------|-----------|-----------------------|-----------|-----------------------|-----------|------------------------|-----------|------------------------|
|                              | Male      |                       | Female    |                       | Male      |                        | Female    |                        |
|                              | Mortality | (95% UI)              | Mortality | (95% UI)              | Mortality | (95% UI)               | Mortality | (95% UI)               |
| Global                       | 93,136.1  | (79,972.6, 109,472.3) | 94,013.5  | (83,297.6, 106,717.3) | 219,450.7 | (190,943.4, 249,974.1) | 206,848.9 | (184,396.5, 231,411.1) |
| Andean Latin America         | 603.9     | (506.0, 735.9)        | 670.8     | (573.9, 794.6)        | 1880.9    | (1531.1, 2286.3)       | 2193.6    | (1812.6, 2641.9)       |
| Australasia                  | 230.2     | (210.6, 249.9)        | 305.4     | (280.2, 330.7)        | 1242.6    | (1095.0, 1396.3)       | 1291.5    | (1140.3, 1458.5)       |
| Caribbean                    | 797.3     | (677.9, 943.5)        | 697.6     | (607.5, 800.2)        | 1782.2    | (1510.1, 2097.9)       | 1744.9    | (1495.3, 2021.8)       |
| Central Asia                 | 529.3     | (453.0, 620.7)        | 585.7     | (513.3, 670.9)        | 1529.1    | (1314.3, 1779.2)       | 1421.6    | (1240.2, 1634.5)       |
| Central Europe               | 1690.8    | (1430.8, 2047.2)      | 1753.3    | (1483.9, 2105.5)      | 1945.9    | (1642.7, 2290.9)       | 2105.2    | (1796.7, 2475.9)       |
| Central Latin America        | 3139.0    | (2734.2, 3625.8)      | 3563.0    | (3177.6, 4004.3)      | 16,369.9  | (14,138.2, 18,831.6)   | 16,445.8  | (14,594.7, 18,421.8)   |
| Central Sub-Saharan Africa   | 810.3     | (625.2, 1032.9)       | 790.9     | (631.4, 986.9)        | 1449.7    | (1127.9, 1827.0)       | 1503.3    | (1184.3, 1880.0)       |
| East Asia                    | 17,833.1  | (15,525.7, 21,687.3)  | 19,645.3  | (17,492.6, 22,373.8)  | 37,370.4  | (31,037.4, 42,627.2)   | 35,510.3  | (31,433.9, 39,991.4)   |
| Eastern Europe               | 1031.5    | (856.2, 1260.2)       | 1382.0    | (1159.6, 1668.2)      | 1106.2    | (917.7, 1357.0)        | 1644.2    | (1381.9, 1993.6)       |
| Eastern Sub-Saharan Africa   | 3044.8    | (2433.5, 3840.4)      | 3246.1    | (2695.0, 3825.0)      | 4494.2    | (3723.1, 5598.7)       | 4502.9    | (3826.3, 5244.0)       |
| High-income Asia Pacific     | 5194.9    | (4601.2, 5828.6)      | 6251.9    | (5557.2, 6896.5)      | 9026.1    | (7735.2, 10,611.1)     | 11,063.9  | (9559.0, 12,623.3)     |
| High-income North America    | 3156.2    | (2609.5, 3778.0)      | 4412.4    | (3688.0, 5207.2)      | 15,525.7  | (13,327.0, 17,909.4)   | 17,088.3  | (14,766.1, 19,614.6)   |
| North Africa and Middle East | 5119.1    | (4187.0, 6181.2)      | 5945.0    | (5013.0, 7004.4)      | 11,210.1  | (9319.3, 13,250.6)     | 11,256.5  | (9743.6, 13,024.4)     |
| Oceania                      | 216.3     | (172.1, 298.9)        | 230.3     | (191.4, 274.1)        | 640.5     | (490.6, 787.6)         | 560.6     | (460.4, 674.4)         |
| South Asia                   | 26,845.3  | (22,136.2, 33,798.9)  | 18,469.2  | (15,584.8, 21,756.2)  | 63,472.3  | (53,958.3, 73,810.0)   | 46,401.4  | (40,072.1, 53,265.2)   |
| Southeast Asia               | 11,376.8  | (9768.6, 13,122.9)    | 12,792.2  | (11,256.9, 14,579.0)  | 27,967.4  | (24,115.2, 31,707.8)   | 26,410.5  | (23,365.4, 29,872.4)   |
| Southern Latin America       | 1222.1    | (1025.3, 1474.0)      | 1292.8    | (1087.9, 1543.6)      | 2010.9    | (1648.4, 2468.4)       | 2343.8    | (1921.6, 2803.9)       |
| Southern Sub-Saharan Africa  | 545.1     | (437.9, 689.8)        | 501.1     | (411.9, 610.5)        | 1516.2    | (1214.6, 1872.7)       | 1414.9    | (1188.1, 1692.0)       |
| Tropical Latin America       | 2171.3    | (1877.7, 2549.1)      | 1769.7    | (1538.5, 2054.2)      | 5283.8    | (4527.9, 6228.2)       | 5298.2    | (4569.6, 6140.2)       |
| Western Europe               | 5496.1    | (4549.1, 6686.1)      | 7603.1    | (6270.8, 9107.7)      | 9735.7    | (7999.4, 11,776.1)     | 13,707.4  | (11,129.3, 16,417.9)   |
| Western Sub-Saharan Africa   | 2082.5    | (1646.8, 2668.6)      | 2105.7    | (1720.8, 2584.3)      | 3891.1    | (3166.3, 5057.1)       | 2940.1    | (2406.6, 3632.9)       |

UI uncertainty interval



**Fig. 2** Diabetic kidney disease mortality per 100,000 among all ages and both sexes in 2017

not the rates gone up? and (2) Why are the DKD rates different in different regions?

### Diabetes Mellitus Over Time

Diabetes mellitus prevalence has been increasing over time, especially among low- and middle-income countries [11, 12]. The literature describes how the prevalence of diabetes complications among people with diabetes have appreciably decreased over the past few decades but that the overall burden of these complications has remained relatively constant [13]. Thus, the relative stability of estimated DKD burden tells the story of success in reducing complications of diabetes mellitus, but little success in preventing incident DM cases. This pattern is relatively constant in all world regions except in the high-income Asia Pacific region, where DKD prevalence for both men and women has measurably decreased over time. Recent literature supporting this finding includes a study from Japan indicating a decrease in early-stage DKD in Japanese people with diabetes over the past two decades [14, 15]. On the other hand, in Brunei, the first published report from the national renal replacement therapy registry cites a very high obesity rate for the country as a contribution to high diabetes rates, and consequent DKD rates. As the country has only recently started

collecting registry data, there is little evidence of trends in disease activity over time at present. [16] The most recent edition of the Singapore Renal Registry cites that population aging largely contributes to observed increases in rates of CKD and diabetes, whereas the age-standardized rates of diabetes and advanced CKD have remained fairly stable since 1990. [17]

### Disease Screening in Western Europe

These data indicate that the prevalence of DKD within Western Europe was low compared with other world regions and has declined slightly between 1990 and 2017. These findings are consistent with data published by Stel et al. comparing trends in incidence of renal replacement therapy initiation by causative disease among nations [18]. This study also showed that Europe has not demonstrated an increase in rates of dialysis initiation among individuals with diabetes in recent years [18]. Though reasons for this are likely multifactorial, some attention must be paid to the emphasis many Western European countries place on diabetes screening within general and at-risk populations [19–22]. Further, availability of national healthcare systems may increase the likelihood of detection, as well as systematic and timely treatment of earlier stage diabetes.

## Obesity in Oceania

The world region Oceania is composed of countries with some of the highest rates of diabetes mellitus in the world [23–26]. These rates are largely driven by obesity, and complicated by lack of national health systems and screening campaigns [27, 28].

## Gender and Prevalence

One of the most notable aspects of these data is the tendency for CKD-DKD rates to be not only higher in women, but also to increase in women over time though this was not universal in all countries and time-period. However, age-standardized prevalence of DKD was higher among women than men in 16/21 world regions and this prevalence rose between 1990 and 2017 in 12/21 world regions for women vs. 1/21 in men (Fig. 1), suggesting a widespread rise in age-adjusted prevalence of DKD in women over time.

The role of gender in DKD-CKD as well as CKD in general is under-examined [29]. Cobo et al. explored the role of gender in CKD, considering the different factors by which gender may alter CKD progression rates [29, 30]. They note that gender is commonly an adjustment variable, or if a study notes a difference between sexes, it is thought to be incidental [29].

Researchers who have explored the relationship between gender and CKD have proposed several factors explaining a possible relationship between gender and disease progression. First, glomerular filtration rate-estimating equations may perform better in men than women and overestimate disease presence in women. Second, due to hormonal differences, women may be protected from kidney disease earlier in life, a protection that may wane with age. Third, social factors often play a role, such as women being more likely to present for screening or symptom diagnosis in comparison with men. Also, in societies that are more traditionally hierarchical, women may not have equal access health care for disease screening or management [31].

The United States Renal Data System publishes summary data on international comparisons of patients with end-stage renal disease [32]. Their report indicates that for all-cause ESRD, men tended to have higher incidence rates than women for almost all countries on which they report [33]. Thus, these results for DKD are in contrast to the above data which shows higher disease burden in women, compared to men. Of note, the above data is also consistent with a recent international study showing higher deaths from type II diabetes mellitus in women, vs. men, across several countries [34].

## DKD Mortality

There are several explanations for why the proportion of DKD deaths could change over time. (1) DKD deaths are increasing while other CKD causes are remaining relatively stable. (2)

Deaths due to other CKD causes are decreasing while DKD deaths are stable or even decreasing but at a slower rate. (3) DKD deaths are increasing and other CKD types are decreasing.

The patterns, and their underlying causes, are likely to be country-specific. As an example, GBD 2017 Study data indicate that within the USA, in both men and women, the proportion of DKD-CKD deaths increased from 1990 to 2017 (Appendix Fig. 1). According to the United States Renal Data System, 10-year survival has been increasing uniformly among those with DKD-CKD, hypertension-CKD, and glomerulonephritis-CKD from 1996 to 2006 [35]. So, the increase in DKD-CKD deaths likely reflects the increase in prevalence of DKD-CKD, which is outpacing other forms of CKD, within the USA (USRDS 2018).

## Challenges to Quantifying Burden and Progression

Quantifying the burden of a chronic disease has innate challenges. Specific to DKD, lack of national screening programs and pre-ESRD renal registries limits data availability. Second, absence of standardized terms across different regions makes it a logistically challenging task to compile, reconcile, and catalog all available data sources with as high a degree of accuracy as possible. The Global Burden of Disease Study invests great effort on addressing these limitations. Yet, world regions with persistent paucity of data will continue to challenge derivation of robust estimates.

## Where to Go From Here

DKD burden has decreased in very few regions over time. There are steps that can be taken at the national level to address this burden, and these are steps that can be carried out in both low- and high-income settings.

- 1) Establish screening programs for diabetes mellitus and DKD. The most effective way to reduce the downstream health effects of diabetes mellitus is early diagnosis and effective management of diabetes and its complications [1]. Cost-effectiveness studies tend to recommend screening in high-risk populations (those with diabetes family history, obesity, older than a specific age, etc.) [36–38]. Whether screening for a disease is cost-effective depends on the disease prevalence and costs to the healthcare system, which is country-specific. The higher the disease burdens or the fraction of health care expenditure and cost to the country, the more cost-effective screening and early diagnosis and treatment may be. Where a country with a lower disease burden may choose to screen only its high-risk subpopulations, one with a high disease prevalence may find screening of the entire population more cost-effective. Thus, national screening campaigns are best

informed by high-quality cost effectiveness studies relevant to their population's disease patterns.

- 2) Establish CKD registries. Tracking disease burden and activity is critical to determining what portion of a population is most affected by a disease, and thus guide how best to target efforts. Such baseline data can also help initiate research that is appropriately inclusive and targeted to the subpopulations at highest risk. As an example, the data presented here suggests there may be a greater need for research into gender differences in DKD.
- 3) Availability of Renal Replacement Therapy. As the burden of DKD grows within low-income countries, it will be crucial for such societies to be prepared to ensure that ESRD does not equal a death sentence [39]. No country can sustain the financial burden of maintenance dialysis programs without governmental support [39]. The modality best suited to a population's needs is also country-specific. For example, Thailand enacted a PD-First policy, and several Asian countries have found PD to be a more cost-effective and achievable way of building a dialysis program than hemodialysis [40]. Regardless of the approach, a national strategy coupled with development of a renal registry are important steps for low-income nations dealing with changes in population structure and shifting healthcare needs as non-communicable diseases play a greater role in quality of life and life expectancy.

## Conclusions

Newly released results from the Global Burden of Disease 2017 Study highlight important gender and regional differences in DKD prevalence and mortality. Understanding the country-specific variables contributing to national results can help guide country-tailored efforts to tackle the marked burden of DKD. Efforts to address DKD within populations need to combine screening and treatment programs, as well creation of disease registries. Certain world regions have an impressively low burden of disease that has been decreasing. Such areas should be studied with a focus on biological, environmental, and behavioral factors that can in turn inform world regions where the DKD burden is growing.

## Compliance with Ethical Standards

**Conflict of Interest** The author declares that she has no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by the author.

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