Published in final edited form as:
Adv Chronic Kidney Dis. 2018 March ; 25(2): 121–132. doi:10.1053/j.ackd.2017.10.011.

The Global Epidemiology of Diabetes and Kidney Disease

Digsu N. Koye,
Dianna J. Magliano,
Robert G. Nelson,
Meda E. Pavkov

Department of Clinical Diabetes and Epidemiology, Baker Heart and Diabetes Institute, Melbourne, Australia; Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia; Department of Epidemiology and Biostatistics, Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia; Chronic Kidney Disease Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, AZ; and Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, GA.

Abstract

The prevalence of diabetes is increasing worldwide, with the greatest increases occurring in low- and middle-income countries. In most developed countries, type 2 diabetes is presently the leading cause of end-stage renal disease and also contributes substantially to cardiovascular disease. In countries with weaker economies type 2 diabetes is rapidly replacing communicable diseases as a leading cause of kidney disease and is increasingly competing for scarce health care resources. Here, we present a narrative review of the prevalence and incidence of diabetes-related kidney disease worldwide. Mortality among those with diabetes and kidney disease will also be explored. Given the high morbidity and mortality associated with chronic kidney disease, we will also examine the level of awareness of this disease among people who have it.

Keywords

Epidemiology; Prevalence; Incidence; Chronic kidney disease; Diabetes

INTRODUCTION

Diabetes mellitus is a major public health challenge, both in developed and developing nations.[1] In 2015, an estimated 8.8% or 415 million people were living with diabetes worldwide, nearly double the 4.6% (151 million) estimated in 2000, and this number is expected to increase to 10.4% (642 million) by 2040.[2] The most commonly diagnosed forms

Address correspondence to Meda E. Pavkov, Centers for Disease Control and Prevention, 4770 Buford Highway, NE MS-F75, Atlanta, GA 30341-3724. mpavkov@cdc.gov.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

of diabetes are type 2 and type 1. Other types of diabetes, including gestational diabetes, monogenic diabetes, and secondary forms of diabetes, are much less common.

Type 2 diabetes accounts for 87% to 91% of the global burden of diabetes and is the most frequent cause of kidney complications.[3] The onset of type 2 diabetes, unlike that of type 1 diabetes, often goes undetected and therefore both prevalence and incidence rates are generally under-reported. The age-adjusted prevalence of type 2 diabetes is highest in North America, the Caribbean, Western Pacific, Middle East, and North Africa and lowest in sub-Saharan Africa.[2,4] Most people with type 2 diabetes live in urban areas and in low- and middle-income countries, which are also projected to experience the highest increase in national prevalence of type 2 diabetes over the coming decades.[2] The highest rates of type 2 diabetes are reported in certain ethnic groups across the globe, including the indigenous people of Nauru, American Indians in the United States, First Nations people in Canada, and indigenous people in Australia and New Zealand.[4-6]

Type 1 diabetes accounts for 7% to 12% of the global burden of diabetes,[2,3,7] its incidence varying substantially by geography,[8] from around 60 cases per 100,000 people/y in Finland[9] and 40 cases per 100,000 people/y in Sardinia[10] to about 0.1 cases per 100,000 people/y in China, India, and Venezuela.[10] Half a million children aged <14 years lived with type 1 diabetes worldwide in 2015, with the highest number residing in Europe, North America, and South-East Asia.[2] In the United States, 1.25 million children and adults have type 1 diabetes[11] and this number continues to increase.[12]

Although the latest estimate from the International Diabetes Federation shows that prevalence of diabetes is increasing,[2] reports have emerged indicating that prevalence may be stabilizing in some populations. A recent study on adults in the United States,[13] using the National Health Interview Survey (NHIS), showed a doubling in the prevalence and incidence of diagnosed diabetes during 1990 to 2008 followed by a plateauing between 2008 and 2012. The age-adjusted prevalence of diabetes was 3.5% in 1990, 7.9% in 2008, and 8.3% in 2012. The age-adjusted incidence per 1000 persons was 3.2 in 1990, 8.8 in 2008, and 7.1 in 2012. The study also reported that both prevalence and incidence of diabetes continue to increase in non-Hispanic black and Hispanic subpopulations and those with less than high school education. Similarly, a study using a large US claims database reported that the overall prevalence of type 2 diabetes in adults remained stable from 2007 (1.24 million cases/15.07 million enrolled; 8.2%) to 2012 (2.04 million cases/24.52 million enrolled; 8.3%), whereas the percentage of newly diagnosed cases fell dramatically from 2007 (152,252 cases; 1.1%) to 2012 (147,011 cases; 0.65%).[14] In Laxa, central Sweden, the prevalence of diabetes has not increased since 1988, and the incidence rate was relatively stable for both type 1 and type 2 diabetes since the 1970s.[15] In Scotland, the incidence of type 2 diabetes remained stable between 2004 and 2013.[16] By contrast, in Taiwan the total population with diabetes increased by more than 70% between 2000 and 2009, representing a 35% increase in age-standardized prevalence rate, whereas the age-standardized incidence rate was nearly constant from 2000 to 2009.[17,18] Nonetheless, incidence rates of type 2 diabetes are increasing rapidly in persons aged <35 years, which may be of particular relevance with regard to personal and societal cost of long-term complications, and in those older than 75 years, in part because of greater longevity in developed countries.

People with diabetes are at increased risk of developing a number of disabling and life-threatening complications, including cardiovascular disease (CVD), kidney disease, blindness, and lower-limb amputations.[2] In this review, we will summarize the current evidence on the epidemiology of one of the most common complications associated with diabetes–CKD. Furthermore, we will explore trends in the incidence and prevalence of CKD in diabetes, mortality among those with CKD, and the level of awareness about kidney disease among patients with CKD.

Search Strategy

We searched PubMed and Medline for published articles with the following search terms “diabetes” AND “kidney disease” or “renal disease” or “ESRD” or ESKD” or “diabetic nephropathies” AND “epidemiology” or “prevalence” or “incidence” or “mortality” or “awareness.” The search was limited to articles that are published. We also searched the reference lists of articles identified by this search strategy and selected those we judged relevant.

EPIDEMIOLOGY OF CKD IN DIABETES

Risk Factors for CKD in Diabetes

CKD in patients with diabetes, like in other diseases, is clinically defined by the presence of persistent albuminuria (albumin-to-creatinine ratio [ACR] ≥30 mg/g for at least 3 months) and/or persistent low estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m^2) regardless of etiology.[19]

Certain risk factors for diabetic kidney disease are important targets in the prevention or delay of CKD and for personalizing treatment strategies. Genetic factors, male sex, age, and duration of diabetes, are among the nonmodifiable risk factors associated both with onset and progression of kidney disease. The modifiable risk factors include poor glycemic control, hypertension, lipid abnormalities, smoking, obesity, insulin resistance, low intensity of physical activity, high salt intake, birth weight, exposure to diabetes in utero, and periodontal disease (Box 1).[20-23] Many of the listed risk factors prevail in disadvantaged and displaced populations across the globe, predisposing to more frequent and earlier onset of diabetes and CKD.[24,25]

Prevalence of CKD in Diabetes

People with diabetes have nearly 2-fold higher odds of CKD than those without diabetes. The odds ratios for CKD vary between 1.3 and 4.6, depending on the region of the world, and this risk is compounded by the presence of hypertension.[26] Among those with diabetes, CKD prevalence varies widely between countries (Table 1),[27-43] with estimates ranging from 27.1% in Shanghai, China to 83.6% in Tanzania.[36,41] In the US National Health and Nutrition Examination Survey (NHANES) 2009 to 2014, CKD prevalence was 26.2% among adults with diabetes, taken into account albuminuria persistence. In those aged ≥65 years low eGFR was significantly more prevalent than among younger age groups, whereas persistent albuminuria prevalence was comparable.[44] A similar type of survey in Shanghai, China, reports a CKD prevalence of 33.5% among patients with diagnosed diabetes in

2008.[34] Information about diabetes duration was not collected in this study, however, the age-, sex-, body mass index–, and hypertension-adjusted prevalence of CKD was similar among participants with previously diagnosed and undiagnosed diabetes, 24.5% and 23.3%, respectively (median age 59 and 57 years, respectively), suggesting a relatively short duration of diagnosed disease; CKD prevalence was significantly lower without diabetes: 12.1% in participants with prediabetes and 9.8% in those with normal glycemia ($P <$ .001 for trend).[34] In contrast, in Singapore, CKD prevalence was 53% in 2011 to 2013 among a multiethnic group of primary care patients with type 2 diabetes[40]; 21% had eGFR–Modification of Diet in Renal Disease <60 mL/min/1.73 m^2, 48% had ACR ≥30 mg/g, and 28% had diabetic retinopathy, a marker of diabetes-related CKD. Patients at high risk of CKD were older, of Malay ethnicity, with longer duration of diabetes, higher body mass index, A1c, blood pressure, and lipid levels. Different from the Chinese survey, this was an ethnically diverse, urban, clinic referred population. Unlike the US survey mentioned previously,[44] the Asian studies used single spot urine ACR measurements to define CKD, which may in part explain the higher CKD prevalence in these Asian populations.

In Europe, where health care is universally subsidized by governments, CKD prevalence is 2 to 5 times higher in those with type 2 diabetes than in those without diabetes and age- and sex-adjusted values vary between 15.4% in the Netherlands and 41.5% in Germany.[45] Factors accounting for the variation may include differences in diabetes prevalence across the European Union, and local factors that may additionally impact risk of CKD, such as differences in access to nephrology care, genetic predisposition, public health policies, and environmental exposures.

In low- and middle-income countries around the world, access to screening and availability of treatment, including renal replacement therapy, vary widely and are affected both by the level of economic development, the relative prioritization of health care, and the distribution of existing resources toward more prevalent and equally severe diseases, such as HIV, tuberculosis, and CVD. A meta-analysis examining CKD epidemiology in 21 mostly sub-Saharan African countries found a substantial overlap of communicable and noncommunicable diseases increasing the risk of CKD.[46] In high-risk populations, including those with diabetes, hypertension, or HIV, CKD prevalence varied widely between 3% and 38%; the pool of higher quality studies indicated an overall prevalence of 14%. In another systematic review of diabetes-related CKD from 16 countries in Africa, the prevalence of CKD ranged from 11% to 84%, with proteinuria being almost exclusively used (96%) as the sole diagnostic marker.[47] Furthermore, a high usage of herbal and traditional medicines in this region may be related to the higher rate of hospital admissions with a diagnosis of acute kidney injury than in developed countries (4.5%-35% vs 2.5% in the United States).[48] With less than 1 nephrologist per million population in many of the sub-Saharan countries and a limited public health infrastructure, detection, prevention, and treatment of CKD remain substandard,[49] even as Africa, like the rest of the world, is experiencing an increasing trend in noncommunicable diseases.

In Central America and South Asia, the high prevalence of diabetes interacts with environmental exposures to increase the burden of CKD. For example, exposure to polychlorinated biphenyls and persistent pesticides, agrochemicals that have been used around the globe for decades and persist in the environment for long periods of time, increase the risk of diabetes-related ESRD.[50]

Much of the variation in CKD epidemiology reflects true regional differences; however, considerable variation is caused by using different equations and thresholds for estimating GFR, differences in the timing, frequency, and method of albuminuria measurement, and study design.[51] Most studies used primary care–based populations, and few others are true population-based studies. Prevalence estimates also differ with regard to duration of diabetes, ascertainment method, and type of diabetes. Ohta and colleagues[31] reported that patients with type 2 diabetes are more than twice as likely as those with type 1 diabetes to have CKD because of an age-independent higher prevalence of albuminuria and age-dependent decreased eGFR.

Prevalence of Nonalbuminuric Kidney Disease in Diabetes

Albuminuria is considered an early indicator of diabetic kidney disease. However, a number of studies have documented that nonalbuminuric CKD (eGFR <60 mL/min/1.73 m^2 in the absence of albuminuria) occurs relatively frequent in persons with diabetes and its prevalence is increasing.[44,52,53] In NHANES 1988 to 1994,[54] 30% of participants 40 years and older with type 2 diabetes and low eGFR had no albuminuria or retinopathy. In more recent years, the National Evaluation of the Frequency of Renal impairment cO-existing with NIDDM (NEFRON) survey of primary care patients with type 2 diabetes found that 55% of those with low eGFR were persistently nonalbuminuric. This percentage was lower in Indigenous (17%) or Polynesian (<20%) patients.[55] Although specific treatments were not explored in this study, the authors indicate that medicines known to reduce urinary albumin excretion (UAE) were commonly used in the care of these patients. Among 109 patients with type 2 diabetes attending a single tertiary referral center, nonalbuminuric CKD was reported in 39% of them.[56] After excluding those patients whose normoalbuminuric status was possibly related to treatment with renin-angiotensin-aldosterone system (RAAS) inhibitors, the prevalence of nonalbuminuric CKD was 23%.[56] This phenotype has also been reported in clinical trials. In the UK Prospective Diabetes Study, of the 1132 patients with type 2 diabetes and incident kidney dysfunction (Cockcroft-Gault estimated creatinine clearance <60 mL/min or doubling of plasma creatinine), 575 (51%) were found not to have preceding albuminuria.[57] Although albuminuria and low kidney function shared many of the same risk factors, certain nondiabetes-related factors specifically contributed to loss of kidney function (high systolic blood pressure, central obesity, female sex). Similarly, in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study, 24% of the 89 patients with type 1 diabetes who had sustained low eGFR did not have albuminuria.[58] Those with initial albuminuria had significantly longer diabetes duration and experienced a steeper decline in kidney function than those without albuminuria.

The Developing Education on Microalbuminuria for Awareness of renal and cardiovascular risk in Diabetes (DEMAND) study, a multinational cross-sectional clinic-based study conducted in 2003, found that 21% of the patients with an average duration of type 2 diabetes of 7.6 years had kidney dysfunction (assessed by the Cockcroft-Gault equation) with normal albuminuria.[59,60] Overall, 12% of this cohort had diabetic retinopathy. In a 2007 cross-sectional survey of primary care patients in Catalonia, Spain, with 7 years of diabetes duration, 15% of the patients had nonalbuminuric CKD.[33] These patients had better metabolic control, lower prevalence of smoking and macrovascular disease, and were more obese than those with albuminuria. On the other hand, CKD may be due to other causes than diabetes per se, particularly when diabetic retinopathy is absent. Few studies, however, include information on retinal examination, a simple, noninvasive, ambulatory screening test that may help identify persons most likely to have kidney disease because of diabetes.

Incidence of CKD in Diabetes

Generally, the annual incidence of albuminuria is about 8% in type 2 diabetes or mixed diabetes type populations, and approximately 2% to 3% in type 1 diabetes.[61] The incidence of low eGFR is approximately 2% to 4% per year regardless of type of diabetes; however, pooled incidence rates for CKD are not feasible because of substantial heterogeneity in population estimates.[61]

The UK Prospective Diabetes Study reported that 38% of persons with newly diagnosed type 2 diabetes developed albuminuria during a median follow-up of 15 years,[57] 29% developed renal impairment (Cockroft-Gault estimated creatinine clearance <60 mL/min or doubling of plasma creatinine), and 14% developed both conditions. The risk of these outcomes increased with longer duration of diabetes, and the risk of developing albuminuria was higher among men than women. In the DCCT, the cumulative incidence of persistent moderate albuminuria (ACR 30-300 mg/g) was 14%, 33%, and 38% at 10, 20, and 30 years duration of type 1 diabetes, respectively, among persons with conventional hypoglycemic treatment (mean A1c 9.6% [81 mmol/mol]). However, the incidence was lower, 10%, 21%, and 25%, respectively, with intensive diabetes treatment (mean A1c 8.9% [74 mmol/mol]).[62] Eighteen years after the end of randomization in DCCT, those formerly assigned to intensive treatment had a 57% lower adjusted risk for moderate albuminuria and 84% lower risk for severe albuminuria (ACR ≥300 mg/g) compared with those who never received intensive therapy, suggesting a long lasting beneficial effect of tight glycemic control on the development of kidney damage.[63] A long-term postrandomization effect was also observed with regard to kidney function, those in the intensive treatment arm having a 44% reduction in persistently low eGFR when compared with those who were treated conventionally. Other studies have shown that improving bodyweight, A1c, and systolic blood pressure reduces the incidence of advanced CKD (defined as eGFR <30 mL/min/1.73 m^2 regardless of ACR; eGFR <45 mL/min/1.73 m^2 and ACR ≥30 mg/g; eGFR <60 mL/min/1.73 m^2 and ACR >300 mg/g; or onset of dialysis) after a median follow-up of 8 years. An overall improvement in healthy lifestyle has a favorable effect on incidence of albuminuria over a short time period.[64,65]

Population-based data on incidence of albuminuria, low eGFR, or both are virtually inexistent in other parts of the world. In sub-Saharan Africa, a study enrolling 4815 participants from Ghana, Kenya, and Nigeria found that the adjusted odds of low GFR were twice as high in those with that without type 2 diabetes, and the risk was highest among those with both diabetes and hypertension.[66] A study comparing South-Asian migrants with type 2 diabetes from the Indian subcontinent with matched European Dutch counterparts found that more South-Asians had albuminuria after 5 years of follow-up (26% vs 14%, adjusted relative risk = 2.8; 95% CI, 1.08-4.9) and kidney function declined at a faster rate, although at baseline the South-Asian group was younger, had fewer cardiovascular risk factors, and lower blood pressure than the European group.[67] In Chennai, India, of the 2630 patients newly diagnosed type 2 diabetes without albuminuria, 44% had >500 mg/d urinary protein excretion after a median follow-up of 11 years; the presence of diabetic retinopathy and high A1c being the strongest predictors of this outcome.[68]

In general, the residual lifetime incidence of CKD is estimated to be 54% for an individual aged 30 to 49 years and no CKD at baseline; the probability of developing CKD declines with age and is 42% after 65 years.[69] Incidence of diabetes has an unfavorable impact mostly on those with advanced CKD. Approximately half of all patients with type 2 diabetes and one-third of those with type 1 diabetes will develop CKD over the course of their lifetime.[70-73] This difference is mostly because patients with type 1 diabetes are younger and healthier at diagnosis and carry fewer comorbid condition than those with type 2 diabetes.[21]

Secular Trends in CKD in Diabetes

A secular decline in the incidence of diabetes-related CKD has been described for type 1 diabetes but not for type 2 diabetes. The trends in type 1 diabetes coincide with a trend for earlier initiation of antihypertensive treatment after the onset of diabetes, expansion of RAAS inhibitor usage, and sustained improvements in glycemic and blood pressure control.[70,72,74-76]

In type 2 diabetes, Afkarian and colleagues[44] reported that overall prevalence of diabetes-related CKD based on NHANES data has not changed significantly from 1988 to 2014. The prevalence was 28.4% in 1988 to 1994 and 26.2% in 2009 to 2014 (age-, sex-, and race/ethnicity-adjusted prevalence ratio = 0.95; 95% CI, 0.86-1.06; $P = .39$ for trend). Specifically, the prevalence of albuminuria declined from 20.8% to 15.9% (adjusted prevalence ratio = 0.76; 95% CI, 0.65-0.89; $P < .001$ for trend), largely because of declines among adults <65 years and non-Hispanic Whites. The prevalence of low eGFR, however, increased from 9.2% to 14.1% (adjusted prevalence ratio = 1.61; 95% CI, 1.33-1.95; $P < .001$ for trend), without differences in age or race/ethnicity–specific eGFR trends. This increase in the prevalence of low eGFR was despite increased use of glucose-lowering medications and RAAS inhibitors in people with diabetes. The SUrveillance, PREvention, and ManagEment of Diabetes Mellitus (SUPREME-DM) Data Link study in the United States, including 879,312 persons with diabetes,[77] found that age- and sex-standardized prevalence of CKD diagnosis codes increased from 10.7% in 2005 to 14.3% in 2011 (an average relative increase of 4.1% per year, $P < .001$). However, ascertainment of low eGFR declined from 9.7% in 2005 to 8.6% in 2011 (an average relative decrease of 2.3% per year, $P < .001$). The discrepancy with the NHANES results likely reflects the poor concordance between laboratory measurements and diagnosis codes for CKD.

ESRD in Diabetes

Globally, 80% of ESRD cases are caused by diabetes, hypertension, or a combination of the both. Compared with adults without diabetes, the incidence of ESRD is up to 10 times as high in those with diabetes. Even so, only a limited number of patients with diabetes-related CKD will ever receive renal replacement therapy, as 78% of these people are living in low- and middle-income countries where resources, coverage, and access to dialysis and kidney transplantation are limited. The proportion of diabetes-related ESRD varies greatly between countries around the world. In 2014, between 5% and 66% of new ESRD cases were primarily caused by diabetes,[78] the highest proportion being reported in Singapore, Malaysia, and the Jalisco region of Mexico, and the lowest in Norway, Romania, and Iceland. Most countries at the upper end of this distribution experienced a steep increase in diabetes-related ESRD incidence over the past decade; between 2001 and 2015 top increases were by 1448% in Thailand, 981% in Russia, and 378% in the Philippines. Because these rates are reported for the overall country-specific populations, they essentially reflect the increasing prevalence of diabetes in those populations, in part as a consequence of disease burdens moving away from infections toward chronic lifestyle-related diseases and increased life expectancy. Treated ESRD prevalence was highest, ranging from 1568 to 3219 per million population, in the Asian countries of Taiwan, Japan, Singapore, and the Republic of Korea, as well as the United States, Portugal, and the Jalisco region of Mexico.[78] Although treated ESRD incidence rates have been quite stable or have declined in many countries during recent years, the prevalence has steadily increased in all 32 countries that provided data from 2001 to 2014.

In the United states, 44% of new cases of ESRD is attributed to diabetes (either type 1 or type 2), with non-Hispanic Black people having the highest and non-Hispanic White people the lowest rates.[71,72,78,79] Detailed quantitative information on the trend in diabetes-related ESRD and how it relates to other diabetes complications in the United States comes from the analysis of several nationally representative databases (NHIS, National Hospital Discharge Survey, US Renal Data System, and National Vital Statistics System) between 1990 and 2010.[80] In the population with diabetes (largely type 2 diabetes), rates of myocardial infarction, stroke, amputations, ESRD, and death from hypoglycemia have declined, with the largest decline in cardiovascular events and the smallest in ESRD. In the 1990s, diabetes-related ESRD incidence was low, as cardiovascular morbidity and mortality represented important competing events. The reduction in these competing causes over the following decade allowed people with diabetes to live long enough to progress to ESRD, which explains why the decline in ESRD is more limited. Even so, after the year 2000 the study found a statistically significant decline in diabetes-related ESRD across all age groups, paralleling considerable advances in adoption of renoprotective treatments nationwide.[44,81] Similar declining trends have been reported in Denmark and Catalonia.[82,83]

In Australia, diabetes has surpassed other causes of ESRD over the past 2 decades, to become the single leading cause of ESRD. In 2012, 38% of new ESRD cases had a primary diagnosis of diabetes, compared with 13% in 1991, representing an annual incidence rate of 1 case/1000 in 2012.[84] The prevalence of diabetes-related ESRD was 208 per million population at the end of 2012, a 130% increase since the 1990s, and one of the largest among high-income countries.[84] This growth in diabetes-related ESRD is predominantly due to the increased prevalence of type 2 diabetes in the Australian population, improved survival among those with diabetes, and a greater willingness to treat older and sicker patients with ESRD.

Diabetic Kidney Disease and Mortality

People with type 1 or type 2 diabetes[16,85,86] experience higher risk of premature death compared with the general population, and the presence of CKD further increases this risk.[21,78,87-90] For example, in the US adult population, age-standardized 10-year cumulative all-cause mortality was 7.7% among persons without diabetes or CKD (ACR ≥30 mg/g and/or eGFR ≤60 mL/min/1.73 m^2), 11.5% among persons with diabetes but without CKD, and 31.1% in the population with both diabetes and CKD.[91]

In the FinnDiane study, a cohort representing 16% of the population with type 1 diabetes in Finland, the presence and severity of CKD was a major predictor of all-cause mortality.[92] The presence of moderate albuminuria (UAE = 20-200 μg/min) was associated with a nearly 3 times higher risk of death than in the general Finnish population (adjusted standardized mortality ratio (SMR) 2.8; 95% CI, 2.0-4.2), CVD representing 56% of these deaths; severe albuminuria (UAE ≥200 μg/min) was associated with 9 times the death rate observed in the age- and sex-matched general population (adjusted SMR 9.2; 95% CI, 8.1-10.5), 45% of these being caused by CVD. Other major causes of death with severe albuminuria included infections and cancer. Among persons with ESRD, the SMR was 18.3 times as high as in the general population, with the same leading causes of death.[92] In contrast, persons without albuminuria had similar mortality as the general population, regardless of the duration of diabetes (adjusted SMR 0.8;, 95% CI, 0.5-1.1), indicating that kidney disease is a major driver of excess mortality in diabetes. Irrespective of the albuminuria level, the eGFR was independently associated with mortality, but in a U-shaped fashion, possibly reflecting confounding from other comorbid conditions unrelated to kidney disease at high eGFR levels. The Pittsburgh Epidemiology of Diabetes Complications Study in patients with type 1 diabetes showed similar findings.[93] SMR was 2.0 (95% CI, 1.2-2.8) without albuminuria; 6.4 (95% CI, 4.4-8.4) for patients with moderate albuminuria; 12.5 (95% CI, 9.5-15.4) for those with severe albuminuria, and 29.8 (95% CI, 16.8-42.9) for ESRD.

The global burden of disease study showed that age-standardized death and disability-adjusted life year (DALY) rates associated with noncommunicable diseases have been declining globally. However, such favorable trends were not found for CKD.[94] For the 51 countries studied, CKD ranked among the top 10 causes of years of life lost, DALYs, or both in 2013. Specifically, age-standardized death rate for CKD due to diabetes increased from 1.4 to 2.9 per 100,000 people from 1990 to 2013, a 107% change. Similarly, the age-standardized DALY rate for CKD due to diabetes increased from 59.3 to 90.9 per 100,000 people from 1990 to 2013, a 53% increase.[94]

Awareness of CKD

One in 3 adults with diabetes are estimated to have CKD and most of them are not aware of having kidney disease.[95] Moreover, claims data indicate that testing for urine albumin, an early marker of kidney disease in diabetes, is being done in less than half of patients.[96] Early detection and better management of CKD can slow its progression, prevent complications, and reduce cardiovascular outcomes.[97] However, early kidney disease is asymptomatic and consequently most patients with CKD are unaware of their condition.[98-100]

Globally, the level of CKD awareness is less than 10% in the general population of CKD patients.[29,41,101-105] The NHANES[101] collected data on the level of awareness among US patients with CKD by asking participants whether they had ever been told they had “weak or failing kidneys.” From 1999 to 2004, in the general population of CKD patients, only 6% reported being told that they had weak or failing kidneys (3.7%, 3.5%, 7.8%, and 41.8% for Stage 1, 2, 3, and 4, respectively). Participants at high risk of CKD reported better awareness: 17.8% of those with diabetes were aware of having CKD compared with 5.9% of those without diabetes.[99]

Among 7853 participants with diabetes and CKD in the US Kidney Early Evaluation Program (KEEP), 9.4% were aware of their CKD; awareness level was 6% in those with CKD Stages 1 and 2 and 10.9% in those with later-stage CKD.[102,103] In line with this study, the ADD-CKD study (Awareness, Detection and Drug Therapy in Type 2 Diabetes and Chronic Kidney Disease) in the United States reported that although more than half of participants with type 2 diabetes had CKD as manifested by changes in the urine protein excretion, a decreased eGFR, or both, only 12% had their CKD identified by the primary care practitioners. It also reported that clinicians were more likely to identify advanced than early CKD.[106] Although regular physician visits were not associated with greater awareness in a Canadian study,[107] they were in other studies from the United States and Canada.[100,108] Studies in other populations reported similar CKD awareness, between 5% and 10%, with lowest values among people with low socioeconomic and educational statuses.[104,105] In a single center study in Tanzania, mostly in patients with type 2 diabetes, more than three-quarters (83.7%) had CKD and 80% had significant albuminuria, however, none of them was aware of their illness.[36]

CONCLUSION

Increasing prevalence of diabetes around the world and changes in clinical practice have influenced the epidemiology of CKD in recent years. In many countries, including the United States, diabetes is responsible for over 40% of new cases of ESRD, surpassing other causes to become the single leading driver of incident kidney failure. Persons with diabetes-related CKD have lower survival relative to those without CKD, primarily because of the excessive risk of coexistent morbidity, particularly CVD, associated with CKD. Nonetheless, wide variation was observed in the epidemiology of CKD among populations with diabetes globally, largely because of the lack of high quality population-based studies with validated measures of CKD. Although considerable research is under way in search for better diagnostic means and more effective treatments, outside the research community and the realm of health care professionals, awareness of CKD has remained very low even among patients with diabetes.

Support:

D.N.K. is supported by a Monash University Postgraduate Research Scholarship and a Baker Bright Sparks Scholarship. D.J.M. is supported by a National Health and Medical Research Council Senior Research Fellowship. This work is partially supported by the Victorian Government's Operational Infrastructure Support Program.

REFERENCES

1. Zimmet PZ, Magliano DJ, Herman WH, Shaw JE. Diabetes: a 21st century challenge. Lancet Diabetes Endocrinol. 2014;2(1):56–64. [PubMed: 24622669]
2. International Diabetes Federation. IDF Diabetes Atlas. 7th ed. Brussels, Belgium: International Diabetes Federation; 2015.
3. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010;87(1):4–14. [PubMed: 19896746]
4. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants. Lancet. 2016;387(10027):1513–1530. [PubMed: 27061677]
5. Forouhi NG, Wareham NJ. Epidemiology of diabetes. Medicine (Abingdon). 2014;42(12):698–702. [PubMed: 25568613]
6. Minges KE, Zimmet P, Magliano DJ, Dunstan DW, Brown A, Shaw JE. Diabetes prevalence and determinants in Indigenous Australian populations: a systematic review. Diabetes Res Clin Pract. 2011;93(2):139–149. [PubMed: 21742398]
7. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. Lancet (London, England). 2014;383(9911):69–82. [PubMed: 23890997]
8. Maahs DM, West NA, Lawrence JM, Mayer-Davis EJ. Epidemiology of type 1 diabetes. Endocrinol Metab Clin North Am. 2010;39(3):481–497. [PubMed: 20723815]
9. Harjutsalo V, Sund R, Knip M, Groop P-H. Incidence of type 1 diabetes in Finland. JAMA. 2013;310(4):427–428. [PubMed: 23917294]
10. DIAMOND Project Group. Incidence and trends of childhood type 1 diabetes worldwide 1990-1999. Diabet Med. 2006;23(8):857–866. [PubMed: 16911623]
11. American Diabetes Association. Statistics About Diabetes. American Diabetes Association. Available at: http://www.diabetes.org/diabetes-basics/statistics/. Accessed May 15, 2017.
12. Mayer-Davis EJ, Lawrence JM, Dabelea D, et al. Incidence trends of type 1 and type 2 diabetes among youths, 2002-2012. N Engl J Med. 2017;376(15):1419–1429. [PubMed: 28402773]
13. Geiss LS, Wang J, Cheng YJ, et al. Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980-2012. JAMA. 2014;312(12):1218–1226. [PubMed: 25247518]
14. Weng W, Liang Y, Kimball ES, et al. Decreasing incidence of type 2 diabetes mellitus in the United States, 2007–2012: epidemiologic findings from a large US claims database. Diabetes Res Clin Pract. 2016;117(7):111–118. [PubMed: 27267430]
15. Jansson SPO, Andersson DKG, Svärdsudd K. Prevalence and incidence rate of diabetes mellitus in a Swedish community during 30 years of follow-up. Diabetologia. 2007;50(4):703–710. [PubMed: 17268796]
16. Read SH, Kerssens JJ, McAllister DA, et al. Trends in type 2 diabetes incidence and mortality in Scotland between 2004 and 2013. Diabetologia. 2016;59(10):2106–2113. [PubMed: 27465219]
17. Jiang Y-D, Chang C-H, Tai T-Y, Chen J-F, Chuang L-M. Incidence and prevalence rates of diabetes mellitus in Taiwan: analysis of the 2000-2009 Nationwide Health Insurance database. J Formos Med Assoc. 2012;111(11):599–604. [PubMed: 23217595]
18. Tseng CH, Tseng CP, Chong CK, et al. Increasing incidence of diagnosed type 2 diabetes in Taiwan: analysis of data from a national cohort. Diabetologia. 2006;49(8):1755–1760. [PubMed: 16788802]
19. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1–150.

20. Harjutsalo V, Groop PH. Epidemiology and risk factors for diabetic kidney disease. Adv Chronic Kidney Dis. 2014;21(3):260–266. [PubMed: 24780453]
21. Thomas MC, Brownlee M, Susztak K, et al. Diabetic kidney disease. Nat Rev Dis Primers. 2015;1(7):15018. [PubMed: 27188921]
22. Nelson RG, Morgenstem H, Bennett PH. Birth weight and renal disease in Pima Indians with type 2 diabetes mellitus. Am J Epidemiol. 1998;148(7):650–656. [PubMed: 9778171]
23. Shultis WA, Weil EJ, Looker HC, et al. Effect of periodontitis on overt nephropathy and end-stage renal disease in type 2 diabetes. Diabetes Care. 2007;30(2):306–311. [PubMed: 17259499]
24. Thomas MC, Cooper ME, Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. Nat Rev Nephrol. 2016;12(2):73–81. [PubMed: 26553517]
25. Weil EJ, Curtis JM, Hanson RL, Knowler WC, Nelson RG. The impact of disadvantage on the development and progression of diabetic kidney disease. Clin Nephrol. 2010;74(suppl 1):S32–S38. [PubMed: 20979961]
26. Ene-Iordache B, Perico N, Bikbov B, et al. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. Lancet Glob Health. 2016;4(5):e307–e319. [PubMed: 27102194]
27. Lu B, Song X, Dong X, et al. High prevalence of chronic kidney disease in population-based patients diagnosed with type 2 diabetes in downtown Shanghai. J Diabet Complications. 2008;22(2):96–103.
28. Jia W, Gao X, Pang C, et al. Prevalence and risk factors of albuminuria and chronic kidney disease in Chinese population with type 2 diabetes and impaired glucose regulation: Shanghai diabetic complications study (SHDCS). Nephrol Dial Transplant. 2009;24(12):3724–3731. [PubMed: 19617258]
29. Collins AJ, Vassalotti JA, Wang C, et al. Who should be targeted for CKD screening? Impact of diabetes, hypertension, and cardiovascular disease. Am J Kidney Dis. 2009;53(3 suppl 3):S71–S77. [PubMed: 19231764]
30. Plantinga LC, Crews DC, Coresh J, et al. Prevalence of chronic kidney disease in US adults with undiagnosed diabetes or prediabetes. Clin J Am Soc Nephrol. 2010;5(4):673–682. [PubMed: 20338960]
31. Ohta M, Babazono T, Uchigata Y, Iwamoto Y. Comparison of the prevalence of chronic kidney disease in Japanese patients with type 1 and type 2 diabetes. Diabet Med. 2010;27(9):1017–1023. [PubMed: 20722675]
32. Assogba GF, Couchoud C, Roudier C, et al. Prevalence, screening and treatment of chronic kidney disease in people with type 2 diabetes in France: the ENTRED surveys (2001 and 2007). Diabetes Metab. 2012;38(6):558–566. [PubMed: 23036461]
33. Coll-de-Tuero G, Mata-Cases M, Rodriguez-Poncelas A, et al. Chronic kidney disease in the type 2 diabetic patients: prevalence and associated variables in a random sample of 2642 patients of a Mediterranean area. BMC Nephrol. 2012;13(8):87. [PubMed: 22905926]
34. Zhou Y, Echouffo-Tcheugui JB, Gu JJ, et al. Prevalence of chronic kidney disease across levels of glycemia among adults in Pudong New Area, Shanghai, China. BMC Nephrol. 2013;14(11):253. [PubMed: 24238578]
35. Rodriguez-Poncelas A, Garre-Olmo J, Franch-Nadal J, et al. Prevalence of chronic kidney disease in patients with type 2 diabetes in Spain: PERCEDIME2 study. BMC Nephrol. 2013;14(2):46. [PubMed: 23433046]
36. Janmohamed MN, Kalluvya SE, Mueller A, et al. Prevalence of chronic kidney disease in diabetic adult out-patients in Tanzania. BMC Nephrol. 2013;14(8):183. [PubMed: 24228774]
37. Ahn JH, Yu JH, Ko S-H, et al. Prevalence and determinants of diabetic nephropathy in Korea: Korea national health and nutrition examination survey. Diabetes Metab J. 2014;38(2):109–119. [PubMed: 24851205]
38. Bailey RA, Wang Y, Zhu V, Rupnow MF. Chronic kidney disease in US adults with type 2 diabetes: an updated national estimate of prevalence based on Kidney Disease: Improving Global Outcomes (KDIGO) staging. BMC Res Notes. 2014;7(7):415. [PubMed: 24990184]

39. Metsarinne K, Broijersen A, Kantola I, et al. High prevalence of chronic kidney disease in Finnish patients with type 2 diabetes treated in primary care. Prim Care Diabetes. 2015;9(1):31–38. [PubMed: 25066820]
40. Low SK, Sum CF, Yeoh LY, et al. Prevalence of chronic kidney disease in adults with type 2 diabetes mellitus. Ann Acad Med Singapore. 2015;44(5):164–171. [PubMed: 26198322]
41. Guo K, Zhang L, Zhao F, et al. Prevalence of chronic kidney disease and associated factors in Chinese individuals with type 2 diabetes:cross-sectional study. J Diabet Complications. 2016;30(5):803–810.
42. Laranjinha I, Matias P, Mateus S, et al. Diabetic kidney disease: is there a non-albuminuric phenotype in type 2 diabetic patients? Nefrologia. 2016;36(5):503–509. [PubMed: 27445098]
43. Chadban SJ, Briganti EM, Kerr PG, et al. Prevalence of kidney damage in Australian adults: the AusDiab Kidney Study. J Am Soc Nephrol. 2003;14(suppl 2):S131–S138. [PubMed: 12819318]
44. Afkarian M, Zelnick LR, Hall YN, et al. Clinical manifestations of kidney disease among US adults with diabetes, 1988-2014. JAMA. 2016;316(6):602–610. [PubMed: 27532915]
45. Brück K, Stel VS, Gambaro G, et al. CKD prevalence varies across the European general population. J Am Soc Nephrol. 2016;27(7):2135–2147. [PubMed: 26701975]
46. Stanifer JW, Jing B, Tolan S, et al. The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Glob Health. 2014;2(3):e174–e181. [PubMed: 25102850]
47. Noubiap JJN, Naidoo J, Kengne AP. Diabetic nephropathy in Africa: a systematic review. World J Diabetes. 2015;6(5):759–773. [PubMed: 26069725]
48. Swanepoel CR, Wearne N, Okpechi IG. Nephrology in Africa—not yet uhuru. Nat Rev Nephrol. 2013;9(10):610–622. [PubMed: 23958719]
49. Sharif MU, Elsayed ME, Stack AG. The global nephrology work-force: emerging threats and potential solutions! Clin Kidney J. 2016;9(1):11–22. [PubMed: 26798456]
50. Grice BA, Nelson RG, Williams DE, et al. Associations between persistent organic pollutants, type 2 diabetes, diabetic nephropathy and mortality. Occup Environ Med. 2017;74(7):521–527. [PubMed: 28438788]
51. Glassock RJ, Warnock DG, Delanaye P. The global burden of chronic kidney disease: estimates, variability and pitfalls. Nat Rev Nephrol. 2017;13(2):104–114. [PubMed: 27941934]
52. Pavkov ME, Mason CC, Bennett PH, Curtis JM, Knowler WC, Nelson RG. Change in the distribution of albuminuria according to estimated glomerular filtration rate in Pima Indians with type 2 diabetes. Diabetes Care. 2009;32(10):1845–1850. [PubMed: 19592626]
53. Perkins BA, Ficociello LH, Silva KH, Finkelstein DM, Warram JH, Krolewski AS. Regression of microalbuminuria in type 1 diabetes. N Engl J Med. 2003;348(23):2285–2293. [PubMed: 12788992]
54. Kramer HJ, Nguyen QD, Curhan G, Hsu C-Y. Renal insufficiency in the absence of albuminuria and retinopathy among adults with type 2 diabetes mellitus. JAMA. 2003;289(24):3273–3277. [PubMed: 12824208]
55. Thomas MC, Macisaac RJ, Jerums G, et al. Nonalbuminuric renal impairment in type 2 diabetic patients and in the general population (national evaluation of the frequency of renal impairment cO-existing with NIDDM [NEFRON] 11). Diabetes Care. 2009;32(8):1497–1502. [PubMed: 19470839]
56. MacIsaac RJ, Tsalamandris C, Panagiotopoulos S, Smith TJ, McNeil KJ, Jerums G. Nonalbuminuric renal insufficiency in type 2 diabetes. Diabetes Care. 2004;27(1):195–200. [PubMed: 14693989]
57. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR, Group US. Risk factors for renal dysfunction in type 2 diabetes: U.K. Prospective Diabetes Study 74. Diabetes. 2006;55(6):1832–1839. [PubMed: 16731850]
58. Molitch ME, Steffes M, Sun W, et al. Development and progression of renal insufficiency with and without albuminuria in adults with type 1 diabetes in the diabetes control and complications trial and the epidemiology of diabetes interventions and complications study. Diabetes Care. 2010;33(7):1536–1543. [PubMed: 20413518]

59. Dwyer JP, Parving H-H, Hunsicker LG, Ravid M, Remuzzi G, Lewis JB. Renal dysfunction in the presence of normoalbuminuria in type 2 diabetes: results from the DEMAND study. Cardiorenal Med. 2012;2(1):1–10. [PubMed: 22493597]

60. Parving HH, Lewis JB, Ravid M, Remuzzi G, Hunsicker LG, DEMAND investigators. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. Kidney Int. 2006;69(11):2057–2063. [PubMed: 16612330]

61. Koye DN, Shaw JE, Reid CM, Atkins RC, Reutens AT, Magliano DJ. Incidence of chronic kidney disease among people with diabetes: a systematic review of observational studies. Diabet Med. 2017;34(7):887–901. [PubMed: 28164387]

62. Boer IH, Rue TC, Cleary PA, et al. Long-term renal outcomes of patients with type 1 diabetes mellitus and microalbuminuria: an analysis of the diabetes control and complications trial/epidemiology of diabetes interventions and complications cohort. Arch Intern Med. 2011;171(5):412–420. [PubMed: 21403038]

63. DCCT/EDIC research group. Effect of intensive diabetes treatment on albuminuria in type 1 diabetes: long-term follow-up of the Diabetes Control and Complications Trial and Epidemiology of Diabetes Interventions and Complications study. Lancet Diabetes Endocrinol. 2014;2(10):793–800. [PubMed: 25043685]

64. Look ARG. Effect of a long-term behavioural weight loss intervention on nephropathy in overweight or obese adults with type 2 diabetes: a secondary analysis of the Look AHEAD randomised clinical trial. Lancet Diabetes Endocrinol. 2014;2(10):801–809. [PubMed: 25127483]

65. Wakasugi M, Kazama J, Narita I, et al. Association between overall lifestyle changes and the incidence of proteinuria: a population-based, cohort study. Intern Med. 2017;56(12):1475–1484. [PubMed: 28626171]

66. Adebamowo SN, Adeyemo AA, Tekola-Ayele F, et al. Impact of type 2 diabetes on impaired kidney function in sub-Saharan African populations. Front Endocrinol (Lausanne). 2016;7(5):50. [PubMed: 27303364]

67. Chandie Shaw PK, Baboe F, van Es LA, et al. South-Asian type 2 diabetic patients have higher incidence and faster progression of renal disease compared with Dutch-European diabetic patients. Diabetes Care. 2006;29(6):1383–1385. [PubMed: 16732026]

68. Viswanathan V, Tilak P, Kumpatla S. Risk factors associated with the development of overt nephropathy in type 2 diabetes patients: a 12 years observational study Indian J Med Res. 2012;136(1):46–53. [PubMed: 22885263]

69. Hoerger TJ, Simpson SA, Yarnoff BO, et al. The future burden of CKD in the United States: a simulation model for the CDC CKD Initiative. Am J Kidney Dis. 2015;65(3):403–411. [PubMed: 25468386]

70. Hovind P, Tarnow L, Rossing K, et al. Decreasing incidence of severe diabetic microangiopathy in type 1 diabetes. Diabetes Care. 2003;26(4):1258–1264. [PubMed: 12663607]

71. Krolewski AS, Warram JH, Christlieb AR, Busick EJ, Kahn CR. The changing natural history of nephropathy in type I diabetes. Am J Med. 1985;78(5):785–794. [PubMed: 3993659]

72. Pambianco G, Costacou T, Ellis D, Becker DJ, Klein R, Orchard TJ. The 30-year natural history of type 1 diabetes complications: the Pittsburgh Epidemiology of Diabetes Complications Study experience. Diabetes. 2006;55(5):1463–1469. [PubMed: 16644706]

73. Rossing P, Rossing K, Jacobsen P, Parving HH. Unchanged incidence of diabetic nephropathy in IDDM patients. Diabetes. 1995;44(7):739–743. [PubMed: 7789641]

74. Bojestig M, Arnqvist HJ, Hermansson G, Karlberg BE, Ludvigsson J. Declining incidence of nephropathy in insulin-dependent diabetes mellitus. N Engl J Med. 1994;330(1):15–18. [PubMed: 8259139]

75. Kofoed-Enevoldsen A, Borch-Johnsen K, Kreiner S, Nerup J, Deckert T. Declining incidence of persistent proteinuria in type I (insulin-dependent) diabetic patients in Denmark. Diabetes. 1987;36(2):205–209. [PubMed: 3803732]

76. Rossing P. The changing epidemiology of diabetic microangiopathy in type 1 diabetes. Diabetologia. 2005;48(8):1439–1444. [PubMed: 15986235]

77. Schroeder EB, Powers JD, O'Connor PJ, et al. Prevalence of chronic kidney disease among individuals with diabetes in the SUPREME-DM Project, 2005-2011. J Diabetes Complications. 2015;29(5):637–643. [PubMed: 25936953]
78. United States Renal Data System. 2016 USRDS annual data report: epidemiology of kidney disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Disease; 2016.
79. Burrows NR, Li Y, Geiss LS. Incidence of treatment for end-stage renal disease among individuals with diabetes in the U.S. continues to decline. Diabetes Care. 2010;33(1):73–77. [PubMed: 20040673]
80. Gregg EW, Li Y, Wang J, et al. Changes in diabetes-related complications in the United States, 1990-2010. N Engl J Med. 2014;370(16):1514–1523. [PubMed: 24738668]
81. Murphy D, McCulloch CE, Lin F, et al. Trends in prevalence of chronic kidney disease in the United States. Ann Intern Med. 2016;165(7):473–481. [PubMed: 27479614]
82. Heaf JG, Wehberg S. Reduced incidence of end stage renal disease among the elderly in Denmark: an observational study. BMC Nephrol. 2012;13(10):131. [PubMed: 23033904]
83. Comas J, Arcos E, Castell C, et al. Evolution of the incidence of chronic kidney disease Stage 5 requiring renal replacement therapy in the diabetic population of Catalonia. Nephrol Dial Transplant. 2013;28(5):1191–1198. [PubMed: 23147160]
84. White S, Chadban S. Diabetic kidney disease in Australia: current burden and future projections. Nephrology (Carlton). 2014;19(8):450–458. [PubMed: 24888506]
85. Tancredi M, Rosengren A, Svensson A-M, et al. Excess mortality among persons with type 2 diabetes. N Engl J Med. 2015;373(18):1720–1732. [PubMed: 26510021]
86. Emerging Risk Factors Collaboration, Seshasai SRK, Kaptoge S, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med. 2011;364(9):829–841. [PubMed: 21366474]
87. Tonelli M, Wiebe N, Culleton B, et al. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol. 2006;17(7):2034–2047. [PubMed: 16738019]
88. Wen CP, Cheng TYD, Tsai MK, et al. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. Lancet (London, England). 2008;371(9631):2173–2182. [PubMed: 18586172]
89. Svensson MK, Cederholm J, Eliasson B, Zethelius B, Gudbjörnsdottir S, Swedish National Diabetes R. Albuminuria and renal function as predictors of cardiovascular events and mortality in a general population of patients with type 2 diabetes: a nationwide observational study from the Swedish National Diabetes Register. Diab Vasc Dis Res. 2013;10(6):520–529. [PubMed: 24002670]
90. Weiner DE, Tighiouart H, Amin MG, et al. Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. J Am Soc Nephrol. 2004;15(5):1307–1315. [PubMed: 15100371]
91. Afkarian M, Sachs MC, Kestenbaum B, et al. Kidney disease and increased mortality risk in type 2 diabetes. J Am Soc Nephrol. 2013;24(2):302–308. [PubMed: 23362314]
92. Groop P-H, Thomas MC, Moran JL, et al. The presence and severity of chronic kidney disease predicts all-cause mortality in type 1 diabetes. Diabetes. 2009;58(7):1651–1658. [PubMed: 19401416]
93. Orchard TJ, Secrest AM, Miller RG, Costacou T. In the absence of renal disease, 20 year mortality risk in type 1 diabetes is comparable to that of the general population: a report from the Pittsburgh Epidemiology of Diabetes Complications Study. Diabetologia. 2010;53(11):2312–2319. [PubMed: 20665208]
94. Jager KJ, Fraser SDS. The ascending rank of chronic kidney disease in the global burden of disease study. Nephrol Dial Transplant. 2017;32(suppl_2):ii121–ii128. [PubMed: 28201666]
95. Centers for Disease Control and Prevention. National Chronic Kidney Disease Fact Sheet, 2017. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention;2017.
96. 2017 USRDS Annual Data Report: Executive Summary. Chapter 2: Identification and Care of Patients With CKD. Am J Kidney Dis. 2018;71(3):S31–S46.

97. Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on kidney in cardiovascular disease, high blood pressure research, clinical cardiology, and epidemiology and prevention. Hypertension. 2003;42(5):1050–1065. [PubMed: 14604997]

98. Brown WW, Peters RM, Ohmit SE, et al. Early detection of kidney disease in community settings: the Kidney Early Evaluation Program (KEEP). Am J Kidney Dis. 2003;42(1):22–35. [PubMed: 12830453]

99. Plantinga LC, Boulware LE, Coresh J, et al. Patient awareness of chronic kidney disease: trends and predictors. Arch Intern Med. 2008;168(20):2268–2275. [PubMed: 19001205]

100. Saab G, Whaley-Connell AT, McCullough PA, Bakris GL. CKD awareness in the United States: the Kidney Early Evaluation Program (KEEP). Am J Kidney Dis. 2008;52(2):382–383. [PubMed: 18640489]

101. Nickolas TL, Frisch GD, Opotowsky AR, Arons R, Radhakrishnan J. Awareness of kidney disease in the US population: findings from the National Health and Nutrition Examination Survey (NHANES) 1999 to 2000. Am J Kidney Dis. 2004;44(2):185–197. [PubMed: 15264176]

102. Whaley-Connell A, Bomback AS, McFarlane SI, et al. Diabetic cardiovascular disease predicts chronic kidney disease awareness in the Kidney Early Evaluation Program. Cardiorenal Med. 2011;1(1):45–52. [PubMed: 22258465]

103. Whaley-Connell A, Sowers JR, McCullough PA, et al. Diabetes mellitus and CKD awareness: the Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES). Am J Kidney Dis. 2009;53(4 suppl 4):S11–S21.

104. Cirillo M, Laurenzi M, Mancini M, Zanchetti A, Lombardi C, De Santo NG. Low glomerular filtration in the population: prevalence, associated disorders, and awareness. Kidney Int. 2006;70(4):800–806. [PubMed: 16820784]

105. Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. Lancet (London, England). 2013;382(9888):260–272. [PubMed: 23727169]

106. Szczech LA, Stewart RC, Su H-L, et al. Primary care detection of chronic kidney disease in adults with type-2 diabetes: the ADD-CKD Study (awareness, detection and drug therapy in type 2 diabetes and chronic kidney disease). PLoS ONE. 2014;9(11):e110535. [PubMed: 25427285]

107. Verhave JC, Troyanov S, Mongeau F, et al. Prevalence, awareness, and management of CKD and cardiovascular risk factors in publicly funded health care. Clin J Am Soc Nephrol. 2014;9(4):713–719. [PubMed: 24458079]

108. Hemmelgarn BR, Manns BJ, Lloyd A, et al. Relation between kidney function, proteinuria, and adverse outcomes. JAMA. 2010;303(5):423–429. [PubMed: 20124537]

CLINICAL SUMMARY

- The prevalence of diabetes is increasing in most parts of the world.
- The prevalence and incidence of end-stage renal disease remain high, driven largely by the high prevalence of diabetes and better survival among those with diabetes.
- Chronic kidney disease is associated with most of the excess all-cause and cardiovascular mortality in patients with diabetes.
- The level of chronic kidney disease awareness around the world is very low.

Box 1

Risk Factors for CKD in Diabetes

Nonmodifiable

- Genetic factors
- Male sex
- Age at onset of diabetes between 5 and 15 years
- Long duration of diabetes
- Increasing age
- Family history of diabetic kidney disease, type 2 diabetes, hypertension, and insulin resistance
- Ethnicity

Modifiable

- Poor glycemic control
- Hypertension
- Lipid abnormalities
- Smoking
- Obesity
- Socioeconomic disadvantage
- Sedentary lifestyle or low intensity of physical activity
- Maternal gestational diabetes or developmental glucose exposure
- Metabolic syndrome
- Insulin resistance
- Low-grade inflammation
- Endotoxins
- Advanced glycation end products
- Recurrent or chronic infections
- Episodes of acute kidney injury
- Salt intake
- Vitamin D deficiency
- Periodontal disease
- Birth weight

Table 1.

Studies Reporting Prevalence of Diabetic Kidney Disease

Author, Year	Country	Data Sources, Number with Diabetes	Diabetes Diagnosis	Definition of CKD	Prevalence of CKD
Lu and colleagues, 2008[27]	Downtown Shanghai, China	Community-based randomized cluster sampling, 2004 *N* = 1009	Self-reported	eGFR <60 mL/min/1.73 m^2 (Cockcroft-Gault) or ACR ≥30 mg/g (2 of 3 within 3 months should be abnormal)	32.8% eGFR <60; of those with GFR >60, 46.3% had albuminuria; CKD (Stages 1-5) prevalence was 63.9%; 8.8% had CKD Stage 1, 22.3% had CKD Stage 2, and 32.8% had CKD Stages 3-5
Jia and colleagues, 2009[28]	Shanghai, China	Shanghai Diabetic Complications Study urban community-based sample, 1998-2007 *N* = 930	Diabetes by ADA 1997 criteria, all had T2DM	eGFR-MDRD <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	Prevalence of moderate albuminuria, severe albuminuria, and CKD in subjects with diabetes was 22.8%, 3.4%, and 29.6%, respectively
Collins and colleagues, 2009[29]	United States	NHANES 1999-2004 *N* = 1277 adults	Self-reported diabetes	eGFR-MDRD <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	For ages 20-59 years, CKD prevalence was greater for participants with diabetes (33.8%) than for those without diabetes (8.2%); 44.4% overall prevalence of CKD in diabetes
Plantinga and colleagues, 2010[30]	United States	NHANES 1999-2006 *N* = 1125 adults with diabetes *N* = 2272 with prediabetes	Self-reported or FPG ≥126 mg/dL Prediabetes: FPG ≥100 and < 126 mg/dL	eGFR (MDRD or CKD-EPI) <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	39.6% of people with diagnosed and 41.7% with undiagnosed diabetes (FPG ≥126 mg/dL) had CKD; 17.7% with prediabetes and 10.6% without diabetes had CKD
Ohta and colleagues, 2010[31]	Japan	Diabetes Center consecutive patients in 2004 *N* = 3575 (504 T1DM and 3071 T2DM)	Diabetes diagnosis according to ADA 2010	eGFR (Japanese MDRD) < 60 mL/min/1.73 m^2 or ACR ≥30 mg/g (morning urine)	Albuminuria prevalence was higher in diabetic patients with type 2 than with type 1 (36.1 vs 15.9%); low eGFR prevalence was higher in diabetic patients with type 2 than with type 1 (25.2 vs 7.9%); CKD prevalence was also higher in diabetic patients with type 2 (46.0 vs 19.1%)
Assogba and colleagues, 2012[32]	France	French medical insurance fund databases (2001 and 2007) *N* = 3894	Adults reimbursed at least 3 times over the previous 12 months for oral hypoglycemic agents or insulin	eGFR-MDRD or albuminuria, proteinuria or dipstick microalbuminuria/proteinuria	CKD prevalence was 47% (women, 50%; men, 44%). CKD Stages 1-5 prevalence: 6%, 10%, 29%, 2%, and 0.4%, respectively
Coll-de-Tuero and colleagues, 2012[33]	Catalonia, Spain	Primary care cross-sectional random sample in 2007 *N* = 2642	Records review of doctor diagnosis	eGFR-MDRD <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	34.1% CKD, 22.9% low eGFR, 19.5%albuminuria. The prevalence of albuminuria low eGFR (13.5%) and nonalbuminuric low eGFR (14.7%) was similar
Zhou and colleagues, 2013[34]	Pudong New Area, Shanghai, China	Multistage random sampling survey in 2008	Self-reported *n* = 346 (diagnosed), FPG ≥126 mg/dL *n* = 274 (undiagnosed)	eGFR (MDRD or CKD-EPI) <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	CKD prevalence was 30.9%, 28.5%, 14.1%, and 9.2% in those with diagnosed diabetes, undiagnosed diabetes, prediabetes, and normoglycemia, respectively. The corresponding age-, gender-, and hypertension-adjusted CKD prevalence were 25.8%, 25.0%, 12.3%, and 9.1%, respectively. With the CKD-EPI equation, the unadjusted CKD prevalence was somewhat higher (33.6%, 29.2%, 15.2%, and 9.8% for diagnosed, undiagnosed diabetes, prediabetes, and normoglycemia, respectively).
Rodriguez-Poncelas and colleagues, 2013[35]	Spain	Primary care consults, 2011 *N* = 1145	FPG ≥126 mg/dL, nonfasting glucose	eGFR-MDRD <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	CKD prevalence was 27.9%: 3.5% with Stage 1; 6.4% with Stage 2; 16.8% with Stage 3, including 11.6% with Stage 3A and 5.2% with Stage 3B; and 1.2% with Stages 4 and 5

Author, Year	Country	Data Sources, Number with Diabetes	Diabetes Diagnosis	Definition of CKD	Prevalence of CKD
			≥200 mg/dL, or use of glucose-lowering drugs		
Janmohamed and colleagues, 2013[36]	Tanzania	Single center clinic-based study enrolling consecutive patients in 2011-2012 *N* = 309	Self-reported	eGFR-Cockroft-Gault <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	83.7% had CKD; 80.0% had significant albuminuria, and 24.7% had low eGFR <60 mL/min. None of these patients were aware of their kidney disease, and only 5 (1.3%) had a diagnosis of diabetic stages of kidney disease recorded in their file. Older age was significantly associated with CKD in this population
Ahn and colleagues, 2014[37]	Korea	KNHANES 2011 *N* = 660	FPG ≥126 mg/dL or HbA1c ≥ 6.5%, current use of hypoglycemic medicines, or self-report	eGFR-MDRD <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	26.7% had albuminuria (22% moderate and 4.6% severe albuminuria); 8.6% had CKD
Bailey and colleagues, 2014[38]	United States	NHANES 1999-2012 *N* = 2915	Self-report	eGFR (CKD-EPI) <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	Prevalence of CKD was 43.5% in the T2DM population overall, and 61.0% in those aged ≥65 years. The prevalence of eGFR <60/mL/min/1.73 m^2 was 22.0% overall and 43.1% in those aged ≥65 years. The prevalence of ACR ≥30 mg/g was 32.2% overall and 39.1% in those aged ≥65 years
Metsärinne and colleagues, 2015[39]	Finland	42 Primary care centers *N* = 625	Clinical diagnosis	eGFR (CKD-EPI) <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	Prevalence of CKD was 68.6%. 16.2% of patients had eGFR <60 mL/min/1.72 m^2. Albuminuria was present in 24.3% of patients, with moderate albuminuria in 17.1% and severe albuminuria in 7.2%
Low and colleagues, 2015[40]	Singapore	Primary care polyclinic in the northern region of Singapore, 2011-2013 *N* = 1861	Diagnosed diabetes patients	eGFR-MDRD <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	53% had CKD, 21.4% had GFR <60 mL/min/1.73 m^2, and 48% had ACR ≥30 mg/g
Guo and colleagues, 2016[41]	Shanghai, China	Diabetes Center, 2005-2012 *N* = 3301	WHO, 1999	eGFR-MDRD <60 mL/min/1.73 m^2 or ACR ≥30 mg/g	CKD prevalence = 27%; CKD 1 = 14%; CKD 2 = 7.1%; CKD 3-5 = 6% Low ACR (10-30 mg/g) = 29.5%, moderate albuminuria = 18.9%, and severe albuminuria = 6.2%
Laranjinha and colleagues, 2016[42]	Portugal	Single center outpatient clinic, 2012-2013 *N* = 146 T2DM and eGFR (CKD-EPI) <75 mL/min/1.73 m^2	Clinical diagnosis	ACR ≥30 mg/g	46.6% without albuminuria

Abbreviations: ACR, albumin-to-creatinine ratio; ADA, American Diabetes Association; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; KNHANES, Korean National Health and Nutrition Examination Survey; MDRD, Modification of Diet in Renal Disease; NHANES, National Health and Nutrition Examination Survey; T1DM, type 1 diabetes; T2DM, type 2 diabetes; WHO, World Health Organization.