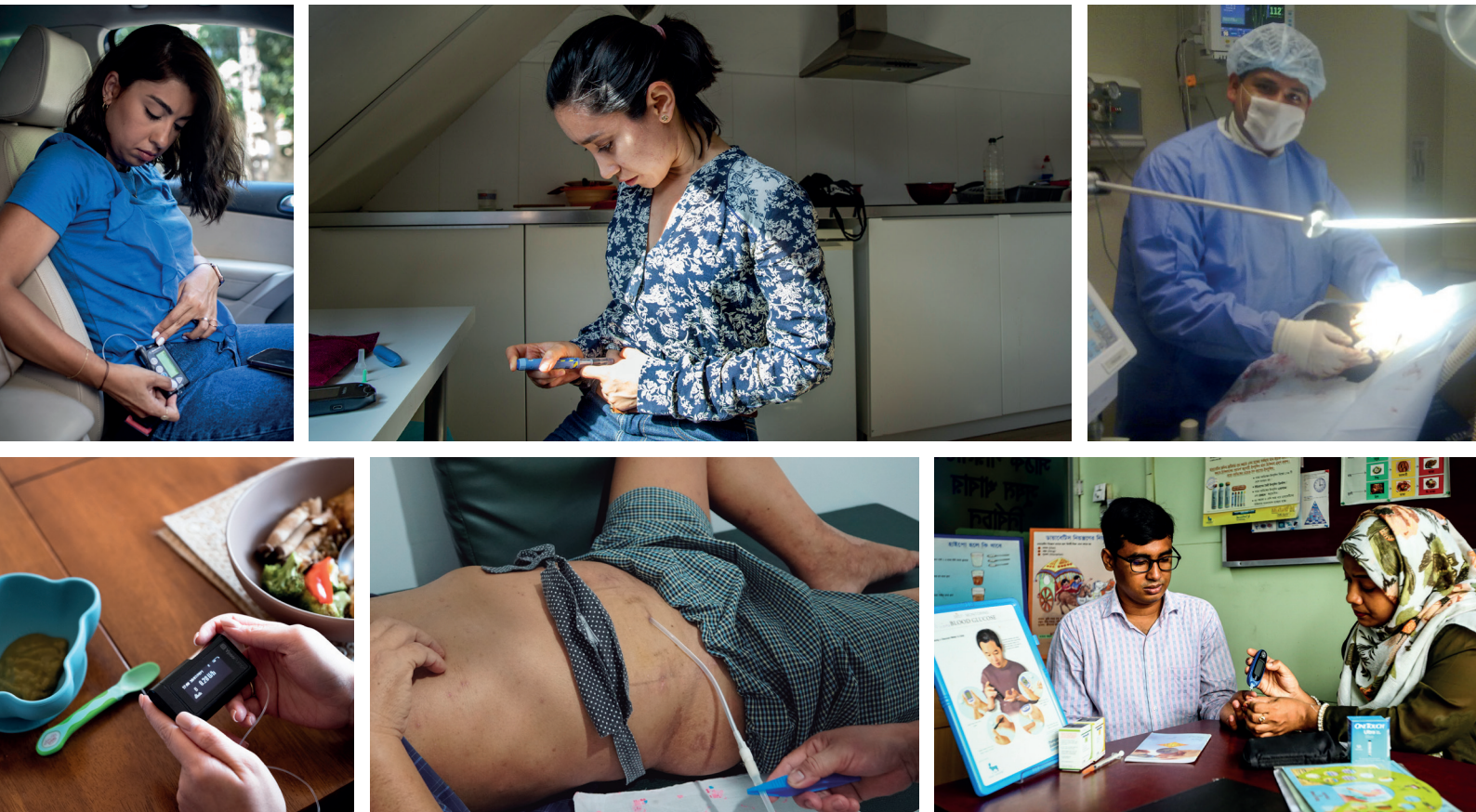


Renewing the Fight: A Call to Action for Diabetes and Chronic Kidney Disease

A policy brief by the International Diabetes Federation
and the International Society of Nephrology



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INTRODUCTION

About this Policy Brief

The International Diabetes Federation (IDF) and the International Society of Nephrology (ISN) have developed this policy brief to target advocates, healthcare professionals and policy makers in the area of kidney disease in people living with diabetes, with the aim of providing recommendations on actions required to prevent, manage and treat this condition effectively.

This policy brief:

- ❑ Highlights the links between diabetes and kidney disease, underscoring its impact and severity.
- ❑ Emphasises that we will only be able to address kidney disease in people with diabetes by developing a multisectoral approach to prevent and treat both conditions.
- ❑ Provides policy recommendations to improve prevention and care and ultimately improve the lives of people living with, or at risk of, kidney disease in people with diabetes.
- ❑ Shares life experiences of people living with both conditions and advocates for people-centred care and the inclusion of people living with diabetes and kidney disease in policy development.

About the International Diabetes Federation

The International Diabetes Federation (IDF) is the global voice of the diabetes community. We are a non-profit umbrella organisation of more than 240 national diabetes associations in 161 countries and territories, working together to improve and empower the lives of the 540 million people estimated to be living with diabetes and prevent diabetes in those at risk.

IDF activities aim to influence policy, increase public awareness and encourage health improvement.

Our work covers seven regions where we support national diabetes associations and promote collaboration between them.

We collect and share high-quality information about diabetes, advocate for the best possible standards of care and prevention, and provide education for people living with diabetes and their healthcare providers.

Our humanitarian activities prioritise the needs of people with diabetes affected by a natural or human-made disaster, particularly in low- and middle-income countries.

Learn more about IDF at www.idf.org.

About the International Society of Nephrology

The International Society of Nephrology (ISN) is a global professional association dedicated to advancing kidney health worldwide since 1960 through education, grants, research and advocacy. The ISN is advancing its mission by:

- **Bridging the Gaps** of available care through advocacy and collaborations with our global partners.
- **Building Capacity** in healthcare professionals via granting programs, education and research.
- **Connecting our Community** to develop a stronger understanding of the management of kidney disease.

The ISN, through its 8,500 individual members and in collaboration with national and regional societies, engages 30,000 health professionals in more than 160 countries to reduce the burden of kidney diseases and provide optimal health care for people affected.

Learn more about ISN at www.theisn.org.

THE GLOBAL IMPACT OF DIABETES AND KIDNEY DISEASE

What is Diabetes ^[1]

Diabetes is a metabolic disorder characterised by high blood glucose (sugar) levels. Insulin, a hormone secreted by the pancreas, facilitates the uptake of glucose that arrives in the bloodstream from the food we consume into the body's cells to produce energy. However, in people with diabetes, the body either does not produce enough insulin or the cells fail to normally respond to it, both leading to elevated blood glucose levels, known as hyperglycaemia. If left untreated, these high blood glucose levels can over time cause damage to different organs and tissues, increasing the risk of developing severe comorbidities, including hypertension, cardiovascular events such as myocardial infarction, stroke and heart failure, eye disease and chronic kidney disease (CKD).

IDF estimates that 537 million adults aged 20-79 are currently living with diabetes, a number that is predicted to rise to 784 million by 2045. There are two main types of diabetes: type 1 and type 2. People with type 1 diabetes often have little to no insulin production and are commonly diagnosed in childhood or early adulthood. Because of the body's inability to produce sufficient insulin, people with type 1 diabetes rely on daily insulin injections to maintain blood glucose levels within the normal range. A far more common form of diabetes is type 2 diabetes, accounting for approximately 90% of all cases. In people with type 2 diabetes, the body is unable to use insulin properly because of insulin resistance. This can eventually lead to a chain reaction in which the pancreas can no longer produce sufficient insulin to manage the elevated glucose levels in the blood. Lifestyle changes, including increased physical activity and a healthy diet, are the mainstay of treatment. However, over time, most people with type 2 diabetes will require oral drugs, insulin, or both to control their blood glucose levels^[2].

Key diabetes statistics (2021)^[1]:

- ❑ 537 million adults live with diabetes; and 90% live with type 2 diabetes
- ❑ 45% of diabetes cases in adults (240 million) are undiagnosed
- ❑ Diabetes is responsible for 6.7 million deaths annually (excluding the mortality risks associated with COVID-19)
- ❑ Diabetes accounts for US\$ 966 billion of healthcare expenditure (11.5% of the total healthcare spent on adult healthcare worldwide)
- ❑ 541 million adults have impaired glucose tolerance and 319 million have impaired fasting glucose, significantly increasing their risk of developing type 2 diabetes



What is Chronic Kidney Disease

Chronic kidney disease (CKD) is a progressive condition characterised by a gradual loss of kidney function. Because the kidneys play a critical role in filtering waste and excess fluids from the blood, malfunction can lead to serious illness and kidney disease. High blood glucose levels can damage the blood vessels in the kidneys, increasing the risk of developing CKD. It is a serious complication that can lead to kidney failure ^[3].

CKD is currently one of the most prominent causes of death and suffering as well as a major contributor to cardiovascular disease and heart failure. Due in part to the rise in risk factors, such as obesity and diabetes, the number of people affected by CKD has also been increasing, affecting an estimated 850 million individuals worldwide. The Global Burden of Disease (GBD) studies have shown that CKD has emerged as a leading cause of mortality worldwide^[4]. In its advanced stages, CKD can lead to kidney failure, while treatment with dialysis and kidney transplant associated with a high burden to healthcare systems.

The non-profit organisation “Kidney Disease: Improving Global Outcomes (KDIGO)” defines CKD as “abnormalities of kidney structure or function present for more than 3 months, with implications for health^[5].” Besides the cause, two measures are used to classify CKD into five stages that reflect the disease progression and severity. The first measure, described as the estimated glomerular filtration rate (eGFR), indicates how well the kidneys are filtering blood. The second measure assesses the amount of the albumin (a specific type of protein) in the urine, reported as the albumin-to-creatinine ratio (ACR), derived by dividing the urine albumin concentration by the urine creatinine concentration. In case the kidneys are not properly functioning, the eGFR may be reduced, albumin levels in the urine may be elevated (a state known as albuminuria) or both may occur.

Key CKD statistics:

- ❑ An estimated 850 million people live with chronic kidney disease (2017)
- ❑ The death rate in CKD has increased by 42% in 17 years
- ❑ CKD is the 12th most common cause of death in 2017 and it is estimated to become the 5th most common cause 2040
- ❑ The burden of CKD in LMICs is very large and is among the top 10 causes of death
- ❑ A higher risk of premature mortality, cardiovascular events and kidney failure are associated with CKD ^[6]
- ❑ CKD in people living with diabetes was found in over 58% of people screened at random for albuminuria and eGFR ^[7]

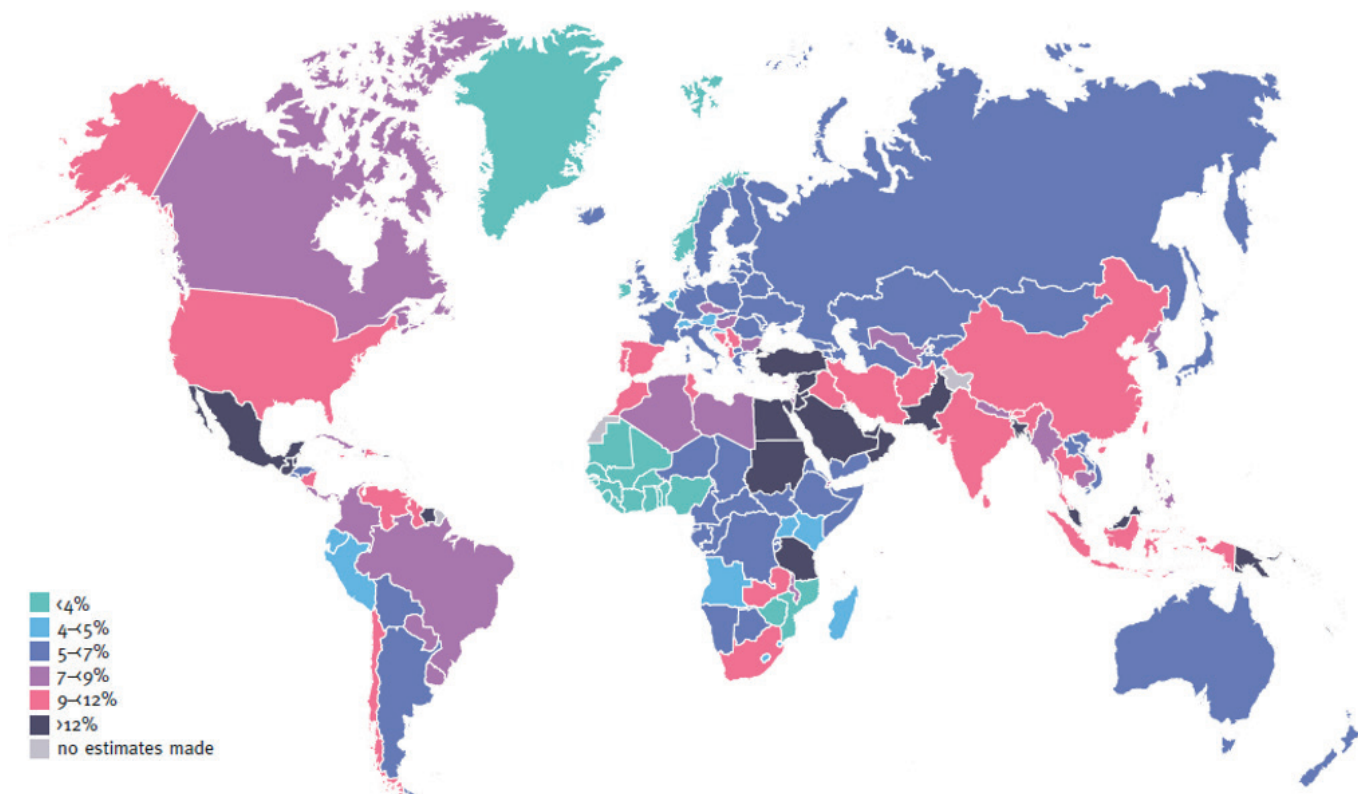


CHRONIC KIDNEY DISEASE IN PEOPLE LIVING WITH DIABETES

People with prolonged uncontrolled blood glucose could develop a progressive kidney disease leading to kidney function impairment and failure. CKD is a common complication of diabetes and diabetes is one of the leading causes of kidney failure. The gold standard for diagnosis of diabetic kidney disease would be based on a kidney biopsy indicating kidney disease caused by diabetes. But, in people living with diabetes, CKD is rarely confirmed by histology and the cause of CKD in diabetes can be multifactorial and may present with various pathophysiological feature. Thus, “CKD in people living with diabetes” is a more realistic representation as compared to the term “diabetic kidney disease”.

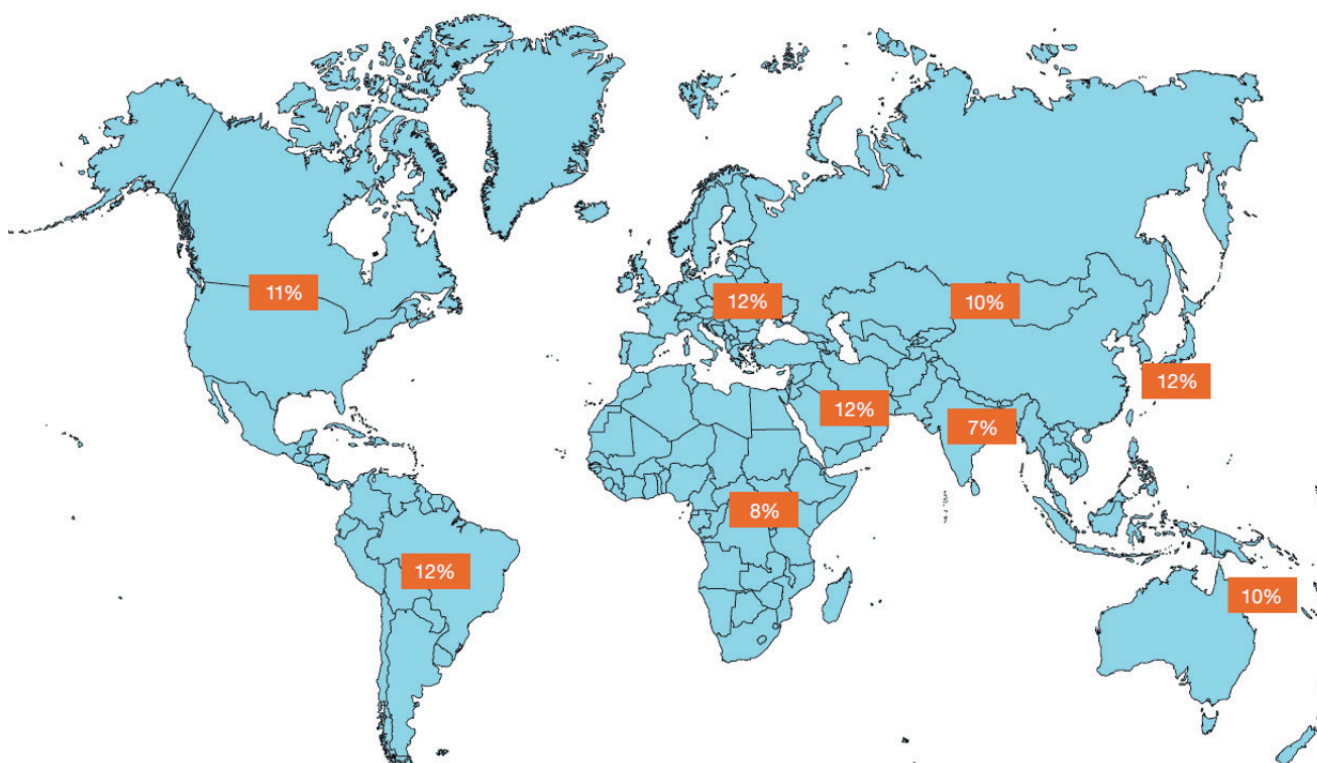


Diabetes and Kidney Disease Prevalence Worldwide^[1, 8]



Map 1. Estimated age-adjusted comparative prevalence of diabetes in adults (20-19 years) in 2021

6



Map 2. Estimated global prevalence of CKD
Geographic regional structure not based on ISN regional framework

Anita Sabidi (Indonesia), living with type 1 diabetes and chronic kidney disease



“ I was diagnosed with type 1 diabetes in 1997. When I was pregnant with my second baby in 2015, I experienced pre-eclampsia and nearly had a stroke. I learned of my kidney disease when I was admitted to the ICU. I had heard of nephropathy before, but my doctor had never explained my risk of developing CKD.

Upon my kidney disease diagnosis, I received information on CKD and screenings for diabetes-related complications. It was difficult, considering I had a newborn son and was also processing my diagnosis. There were psychological effects, and I had to work through them alone. I had no outside professional support. Thankfully, I had my family. My mother and husband offered their kidney for a transplant, but I prefer to follow my nephrologist's plan to keep my kidneys as long as possible. I am also lucky to have an amazing team of doctors led by my endocrinologist and nephrologist. We communicate via WhatsApp, which makes consultations easy.

Of course, my daily routine changed completely, especially at mealtimes. I now limit my protein intake. In addition to counting carbs, I monitor minerals and avoid processed foods and bottled drinks. I take medications to control protein leaks. One medication was out of stock recently, so my kidney function was off target for several months until my nephrologist prescribed a substitute.

Governments should act to improve diabetes education and awareness. People living with diabetes would have a much better quality of life if they had proper healthcare access, availability of medicines and blood glucose monitoring across the country. Talking about complications is very delicate. However, through targeted education, we can learn to manage them. Society also needs to be educated to provide support and not stigmatise people with diabetes complications.

Diabetes and Chronic Kidney Disease on the Political Agenda

Globally, non-communicable diseases (NCDs), such as diabetes, heart disease and kidney disease are leading causes of mortality, with the prevalence of diabetes approaching epidemic proportions. Because of the increasing prevalence and global impact of NCDs on healthcare, various international commitments are aiming to address their burden and halt their rise.

In 2013, Member States adopted the World Health Organisation (WHO) overarching goal of 25% reduction of premature mortality from NCDs by 25% by 2025. Member States further aligned on nine voluntary targets on NCDs, including one aiming for 0% increase in obesity and type 2 diabetes prevalence and another on achieving 80% access to essential medicines and devices by 2025.

At the United Nations (UN) level, the Sustainable Development Goal (SDG) 3.4 target primarily aims to prevent and treat NCDs and promote mental health and well-being^[9]. This sets a precedence for various other policies to meet the overarching goal of the SDG to reduce premature mortality from NCDs by one third by 2030.

In alignment with these goals, in April 2021 WHO launched the Global Diabetes Compact, a global initiative with a vision of reducing the risk of diabetes and ensuring that all who are diagnosed with diabetes have access to equitable, comprehensive, affordable and quality treatment and care.

In May 2021, Member States adopted a Resolution on reducing the burden of NCDs through strengthening diabetes prevention and control. This resolution called for urgent coordinated global action on diabetes and tasked WHO with developing clear diabetes recommendations and a set of diabetes targets to address the gaps in diagnosis and access to care. As a result, Member States adopted new global coverage targets for diabetes in May 2022 – focusing on ensuring access to equitable, comprehensive, affordable and quality treatment for all.

Despite its prevalence and impact on premature mortality, CKD is not featured as an indicator for any NCD target at the UN or WHO level. Although CKD was estimated to cause 1.2 million deaths in 2017^[10], the WHO NCD Action Plan mentions kidney disease only as a comorbidity or risk factor for diabetes and cardiovascular disease. This could be due to a variety of factors, such as kidney disease being considered

a component of a broader health issue or simply because the targets were developed before kidney disease received increased attention as a public health concern. Because of the close association between CKD and other NCDs, initiatives to prevent the risk of and reduce premature mortality from NCDs, including diabetes, will indirectly reduce premature mortality from CKD. However, CKD management would benefit from the development of global strategic action plans specifically directed to tackling the condition. Kidney disease needs targeted health interventions because it is a complex and multifaceted condition that requires

specialised care and management. While kidney disease may co-occur with other chronic conditions, it is a distinct condition with unique clinical features, risk factors and treatment considerations. By including kidney disease specifically in UN and WHO targets, for example in the political declaration on the upcoming 2025 UN High Level meeting on NCDs, policymakers and stakeholders can increase awareness about the importance of kidney health and improve the allocation of resources to prevent, detect and manage kidney disease.

WHO GLOBAL DIABETES COMPACT ^[11]

Why do we need to act?

- ❑ Although premature mortality in other major non-communicable diseases (NCDs) has seen a downward trend, premature deaths due to diabetes have risen by 5% between 2000-2016.
- ❑ In May 2022, Member States recognised the urgent need to act and adopted five historic global coverage targets for diabetes

What is the WHO Global Diabetes Compact?

In response to the increased burden of diabetes, the WHO Global Diabetes Compact (GDC) was launched on the 100th anniversary of the discovery of insulin in April 2021. This global initiative has the vision of reducing the risk of diabetes and ensuring that all who are diagnosed with diabetes have access to equitable, comprehensive, affordable and quality treatment and care. It also aims to support Member States in achieving the global coverage targets for diabetes and contribute to Sustainable Development Goal 3.4 (reducing premature mortality due to NCDs by one-third by 2030).

The WHO Global Diabetes Compact works through six workstreams:

1. Access to essential diabetes medicine and associated health technologies
2. Technical products
3. Prevention, health promotion and health literacy
4. Country support
5. Research and innovation
6. Governance and partnerships



Michael Donohoe (USA), living with type 2 diabetes and chronic kidney disease



“ I was diagnosed with type 2 diabetes in August 1996 and in November 2019 with diabetes-related kidney disease. Before my diagnosis, I had heard about nephropathy because my father and paternal grandmother had the condition. However, I received very little information from my doctor on my risk of developing diabetes-related kidney disease.

After two and a half years, my primary care physician (PCP) referred me to a nephrologist, who diagnosed me with Stage 3A chronic kidney disease (CKD). At that point, I requested an appointment with a nutritionist who specialised in diabetes and kidney issues. The nutritional advice, along with a change in medication, stabilised my condition. In addition, the diagnosis caused me to change my diet, work even harder on blood sugar control, and do light cardio exercise like walking.

I was also highly impacted psychologically. Kidney failure had killed my father and my grandmother. Unfortunately, I did not receive any specific psychological support. My healthcare team, however, has been supportive overall.

I feel that the government and organisations representing the interests of people with diabetes in my country need to do more to prevent and treat diabetes-related kidney disease and improve the quality of life of people affected.

LINKS BETWEEN DIABETES AND KIDNEY DISEASE

The root causes of diabetes and CKD can be multifactorial, as various genetic, environmental and physiological factors influence their development and progression. It is therefore important to understand this complexity and develop a holistic management approach to reduce the global disease burden of both conditions.

Causes of Diabetes

Overweight, obesity and physical inactivity

Overweight and obesity can cause beta cell dysfunction in the pancreas, which is responsible for the production and secretion of insulin. People living with overweight and obesity are prone to developing insulin resistance, putting them at risk of developing type 2 diabetes. A sedentary lifestyle with physical inactivity, often resulting in higher body fat accumulation, further increases the risk of developing overweight, obesity and diabetes among other NCDs, such as heart disease, stroke and cancer^[12].

Genes and family history

Besides environmental and physiological factors, both type 1 and type 2 diabetes have a hereditary component, increasing a person's risk of developing the condition. Studies indicate that type 2 diabetes tends to cluster in families, with its prevalence varying widely among populations. Some populations, such as Asian Americans, African Americans and Native Americans, have a higher probability of developing type 2 diabetes compared to others. This genetic predisposition to diabetes based on family history or ethnicity can have a significant impact on the development and progression of the disease.

Genetic mutations

In addition to type 1 and type 2 diabetes, rare forms of diabetes can result from mutations in a single gene (i.e. monogenic) that are usually inherited from one or both parents, though in some cases the mutations happen spontaneously. Examples of such rare forms of diabetes include maturity-onset diabetes of the young (MODY) and neonatal diabetes. In most of these cases, the mutation renders the pancreas less capable of producing insulin. MODY is the most common form of monogenic diabetes, typically diagnosed during adolescence, whereas neonatal diabetes occurs in the

first 6 months of life and can be either permanent or transient^[13].

Diabetes can also result from other genetic disorders. One of these is cystic fibrosis in which thick mucus can cause scar tissue in the pancreas, preventing it from producing insulin. Another condition, called haemochromatosis, similarly increases the risk of developing diabetes because of iron accumulation that can damage the pancreas and other organs, if left untreated^[14, 15].

Other endocrine diseases

Generally, endocrine diseases affect the glands that secrete various hormones in the body, resulting in a hormonal dysfunction or disorder. While diabetes itself is an endocrine condition affecting the pancreas, abnormal function of the endocrine system induced by endocrine conditions other than diabetes can lead to insulin resistance because of the overproduction of certain hormones, such as cortisol in Cushing's disease, growth hormone in acromegaly and thyroid hormone in hyperthyroidism^[16].

Damage to or removal of the pancreas

Damage to the pancreas and consequently the beta cells that produce insulin can occur due to pancreatitis, pancreatic cancer or trauma, while removal of the damaged pancreas can also lead to diabetes because of the loss of beta cells^[17].

Drugs

Drug-induced diabetes can be caused by various mechanisms, including damage to the beta cells, inhibition of insulin function, insulin resistance, decreased insulin production and glucose intolerance. Steroids, antipsychotics, antiretrovirals, chemotherapy, diuretics, transplant immune-suppressants, among others, and can all be associated with hyperglycaemia due to drug-induced diabetes^[18].

Causes of Chronic Kidney Disease

CKD is a common comorbidity of other diseases, with diabetes and hypertension being responsible for two-thirds of CKD cases worldwide^[19]. Both high glucose levels from uncontrolled diabetes and hypertension can cause damage to the blood vessels in the kidneys, affecting their ability to filter blood, leading to kidney

malfunction. In addition, the inability of the kidneys to filter blood effectively can exacerbate hypertension. As a result, CKD, diabetes and hypertension are highly interrelated comorbidities, worsening each other.

Obesity is a growing concern as a major risk factor for developing CKD. The association between obesity and CKD is bidirectional and can be explained by the pathophysiological pathways, risk factors and comorbidities that both these diseases have in common^[20]. Obesity is also linked to the risk of CKD in diabetes, specifically in type 1 diabetes, obesity and CKD in people with diabetes share a causal relationship^[21].

Besides diabetes, hypertension and obesity there are a few other conditions that can cause CKD. Diseases affecting the kidneys such as glomerulonephritis, congenital kidney and urinary tract abnormalities, polycystic kidney disease and autoimmune diseases can contribute to CKD. It can also be a consequence of physical obstruction in the kidneys, due to stones or a tumour, an enlarged prostate or recurrent urinary tract infections.



Causes of CKD in People Living with Diabetes

CKD commonly occurs in people with both type 1 and type 2 diabetes. It is characterised by progressively impaired kidney function and ultimately kidney failure contributing to high morbidity and mortality in

Salih Hendricks (South Africa), living with diabetes and chronic kidney disease



“ In 1978, at the age of 12, I was diagnosed with diabetes insipidus, a rare disorder that causes the body to make too much urine because of a hormone imbalance. Before then, I had never heard of kidney disease. My doctor at that moment, who was a diabetes-kidney specialist, explained my risk of developing kidney disease.

In 1983, I had diabetic ketoacidosis (DKA) and was diagnosed with type 1 diabetes and kidney disease. Before then, I had many kidney disease symptoms. My blood pressure was high. I also had protein and blood in my urine and an increased need to urinate. My feet, ankles and hands were swollen, and I had shortness of breath. I lost weight because my appetite was gone. Lastly, I had difficulty focusing and concentrating in school.

After my diagnosis, my daily life as a teenager changed at school and home, including my eating habits and the sports I played. No psychological support was available, which as a boy of 12, made my condition even more challenging to accept. From then until today, I have been dealing with the psychological impact of my diagnosis and trying to cope.

Since my diagnosis, I have taken hypertension medication. My kidney function has improved because of better circulation due to controlled insulin intake and a partial leg amputation.

My family has been very supportive, especially since I come from a “diabetes family” who understands the complications and issues related to the condition. In addition, the team at my diabetes clinic has been equally wonderful and supportive.

Access to new technology has improved the control and care management of my diabetes and kidney disease. I think governments must do more for prevention and access to improve the quality of life of people with these conditions.



diabetes. Although kidney damage could result from long-term exposure to high blood glucose levels in diabetes, kidney disease in people living with diabetes can often be multifactorial. Kidney disease in diabetes is characterised by impairment of metabolism and hence can present with various pathophysiological features that may be related and also unrelated to diabetes.

CKD in People Living with Diabetes: Implications for Cardiovascular Risk and Total Mortality

Cardiovascular disease represents the leading cause of death and disability among people with diabetes in whom the incidence of stroke, coronary artery disease and peripheral artery disease is higher compared to the general population^[19]. Evidence to suggests a link between high blood glucose levels and atherosclerosis, the hardening and narrowing the arteries, which reduces blood flow. Nevertheless, besides uncontrolled blood glucose levels, many other

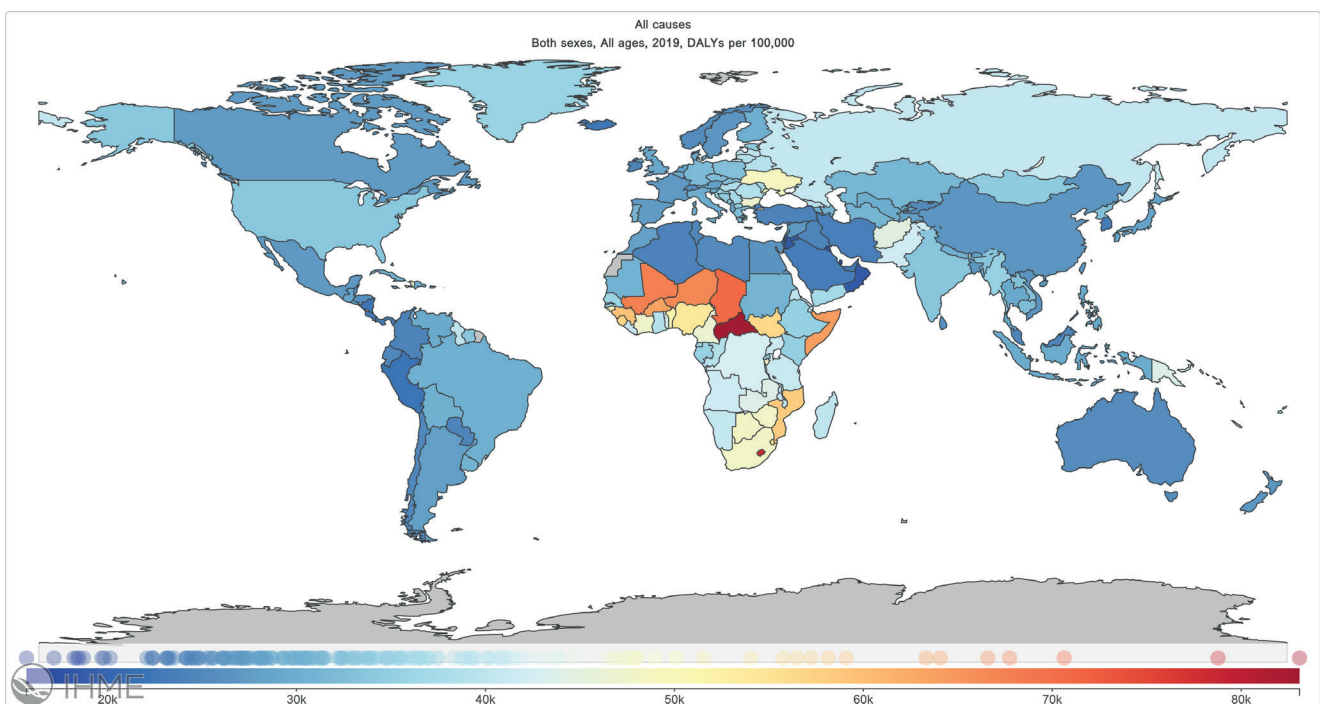
factors, including genetics, ethnicity, gender, obesity, age, lifestyle habits, blood pressure and blood lipids, influence the risk of developing cardiovascular disease.

The cardiovascular risk in people with diabetes further increases in the presence of CKD, which in itself represents a well-known cardiovascular risk predictor. A reduction in kidney function together with an increase in urine albumin excretion results in a three- to five- fold increased risk of developing cardiovascular complications, negatively affecting the prognosis and life expectancy of people with diabetes and kidney disease versus those with normal kidney function. Diabetes, occurrence of cardiovascular disease and development of early CKD are associated with a reduction in life-expectancy of an individual by 6, 12 and 16 years respectively.

Kidney disease in people living with diabetes, exponentially increases the risk of experiencing a macrovascular event and premature death. Hence, most people affected die prematurely before progression to kidney failure and before requiring kidney replacement therapy, either through dialysis

or kidney transplantation. Clinical research therefore prioritises the prevention and treatment of CKD to reduce the burden of cardiovascular diseases and improve the life expectancy of people with diabetes.

Given the substantial morbidity and mortality of cardiovascular disease in people with diabetes, it is not surprising that treatment is generally not limited to blood glucose lowering drugs, but instead also consists of non-pharmacological measures and pharmacotherapy to prevent and treat cardiovascular disease and its risk factors. Pharmacological strategies aim to reduce cardiovascular complications by focussing on controlling blood pressure, reducing blood lipids and preventing atherosclerosis with anti-thrombotic agents to eventually improve the quality of life and life expectancy of people with living diabetes and CKD. More recently, encouraging results have also been described with anti-inflammatory drugs to manage cardiovascular disease.



Map 3: Incidence of deaths due to diabetes and kidney disease^[22]

The Impact of CKD for People Living with Diabetes and Healthcare Budgets

As described above, diabetes, hypertension and CKD are frequent comorbidities contributing to about 80% of end-stage kidney disease globally. In addition, these conditions often lead to the development of cardiovascular diseases, reducing a person's quality of life and life expectancy ^[23].

Because of the morbidity and mortality, CKD in people living with diabetes substantially increases the health expenditure. In the United States, healthcare costs of people with diabetes and CKD were reported to be about 50% higher than those of people with diabetes but no CKD ^[24]. In addition, for people progressing to kidney failure, the costs for dialysis and kidney transplant create a significant economic burden to healthcare. Hence, the most effective strategies to reduce the economic impact of diabetes and its comorbidities are those focussing on prevention. In case people are already affected by diabetes, it is essential to screen, diagnose and treat CKD in its early stages to prevent further complications and reduce the impact on healthcare budgets ^[23, 25].



Perseus Propere (Saint Lucia), living with type 1 diabetes and chronic kidney disease



“ I was diagnosed with type 1 diabetes in 1991, when I was seven. In 2008, after 17 years living with diabetes, I was diagnosed with stage 2 kidney disease.

Before my diagnosis, my doctor explained that I was at risk of CKD. But I was young and did not think I was at risk, so I never paid much attention.

My entire life changed. Every day, my swollen feet and ankles and shortness of breath made physical activity more and more difficult. In addition, my diet and eating habits completely changed. I had to drink fewer liquids and reduce sodium, potassium and phosphorus in my meals. I was 25 and felt like an elderly person. To make things worse, I was made redundant because I had to take time off for medical care.

The diagnoses of retinopathy and kidney disease affected me psychologically. Because of my age, it really impacted my mental health. I had suicidal thoughts, depression and anxiety, so I met with a counsellor to talk through my feelings. Thankfully I had my family and friends, who were my biggest support team!

If more information had been available about diabetes, I wouldn't have the health issues I have today. There should be more sustainable and affordable diabetes prevention and management programmes. This includes more dialysis centres, a viable government transplant system, increasing access to healthcare and essential medications, and diabetes education and awareness.

ADDRESSING DIABETES AND CKD IN PEOPLE LIVING WITH DIABETES

Diabetes Prevention

Prevention of type 2 diabetes is a key strategy in reducing the diabetes burden. Several clinical trials have demonstrated that lifestyle intervention, consisting of an individualised reduced-calorie meal plan and appropriate physical activity, are highly effective in preventing or delaying type 2 diabetes and in improving other cardiometabolic markers, such as blood pressure, blood lipids and inflammation [26, 27,28]. In agreement with the outcomes of these studies, the American Diabetes Association (ADA) recommends that adults living with overweight and obesity at high risk of developing type 2 diabetes achieve weight loss by decreasing their caloric intake and implementing moderate intensity exercise regimens. Although type 1 diabetes cannot be prevented, strategies to avoid the onset or progression of chronic diabetes complications can improve quality of life and lower the economic burden over time[18]. It is important to emphasise that many cases of type 2 diabetes are due to genetic factors and cannot be prevented through lifestyle interventions.

Screening for CKD in People Living with Diabetes

In many countries, screening for diabetes in adulthood has been proposed as a public health policy. Evidence

suggests that screening for diabetes is cost-effective, with screening strategies reducing the incidence of developing complications, such as cardiovascular disease[29]. For example, the ADA recommends repeated screening of asymptomatic adults from 35 years onwards for prediabetes and type 2 diabetes with a minimum of three years intervals along with an assessment of risk factors, including overweight and obesity[18].

In addition, for people diagnosed with type 2 diabetes, current guidelines recommend that all should be screened annually for kidney disease from diagnosis onwards, whereas, in type 1 diabetes, annual screening should begin no later than five years from initial diagnosis. As described above, kidney function is assessed by measuring the amount of albumin in the urine and estimating the glomerular filtration rate of the kidneys, two markers associated with mortality, cardiovascular disease, heart failure and progression to kidney failure[30]. Despite a strong recommendation to screen for CKD the screening remains suboptimal [31]

Addressing the Different Causes of Kidney Disease in People Living with Diabetes

Although the causes of CKD in people living with diabetes can be multifactorial, the most important risk factors remain hyperglycaemia, obesity and hypertension and blood lipid abnormalities. These factors can all be improved through optimised and intensive diabetes management, significantly reducing the cumulative incidence of albuminuria, kidney impairment and kidney failure.



Therapeutic Approach to CKD in People Living with Diabetes – Lifestyle Modification and Treatment Targets

A comprehensive treatment plan, involving both the person affected and physician, should be outlined for the treatment of CKD in people with diabetes. Lifestyle modifications represent the cornerstone of treatment but can be supplemented with pharmacological interventions if needed to preserve organ function and maintain control over blood glucose levels, lipids and blood pressure.

The most common approaches for pharmacological management of CKD in people living with diabetes include:

- **Blood pressure control:** Reducing blood pressure in people with diabetes is essential in controlling the progression to kidney disease. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) are recommended drug classes for people with type 1 and type 2 diabetes who have hypertension and albuminuria, titrated to the maximum antihypertensive or highest tolerated dose.
- **Lipid control:** To reduce the risk of developing cardiovascular disease from blood lipid abnormalities, statins are recommended for people with both type 1 and type 2 diabetes. Statins act by controlling cholesterol levels, preventing the development of atherosclerotic cardiovascular disease in those with known atherosclerotic cardiovascular disease and in those at risk.
- **Blood glucose control:** Long-term glycaemic control reduces the risk of organ damage and associated comorbidities in people with diabetes. Blood glucose-lowering drugs, along with lifestyle changes, are recommended for people with type 2 diabetes to improve glycaemic control.

Disease Modifying Therapies for CKD in People Living with Diabetes

Apart from the lifestyle modifications and treatment targets for managing CKD in people living with diabetes, several intervention strategies, both well-established and recently introduced disease modifying therapies have emerged over the years. First, renin-angiotensin-aldosterone system (RAAS) inhibition has been the cornerstone of treatment for people with CKD for nearly 30 years. More recently, a range of added treatment options offers healthcare providers more possibilities for preventing and delaying the progression of CKD in people living with diabetes.

Some of these new therapeutics include^[32]:

- A sodium–glucose cotransporter 2 inhibitor (SGLT2i) promotes the renal excretion of glucose, lowering glucose levels in the blood. Because of its proven kidney and cardiovascular benefit, SGLT2i is recommended in people with type 2 diabetes and CKD.
- A glucagon-like peptide 1 (GLP-1) receptor agonist can be considered in people who do not achieve optimal glycaemic control with metformin and/or an SGLT2i or for those with contraindications to these drugs. GLP-1 acts by facilitating insulin secretion and has proven cardiovascular benefit as well as reduces albuminuria. It is therefore recommended for people with type 2 diabetes and CKD.
- A nonsteroidal mineralocorticoid receptor antagonist (ns-MRA) is known to prevent inflammation and fibrosis of the kidney and heart, providing kidney and cardiovascular benefit and being a possible add-on therapy for CKD in people living with diabetes.



CASE STUDIES

Singapore's 'War on Diabetes'

A great initiative to bring global targets and recommendations into practice was undertaken by the Singapore Government. In 2016, The Singapore Government declared the “War on Diabetes”, mobilising citizens to raise awareness of diabetes by generating community-based recommendations on diabetes prevention and management. These engagement models are based on the belief that citizens can contribute meaningfully to the co-creation and co-delivery of approaches on issues of significance to them and the community [33].

Screening and Managing People with Diabetes and CKD – The Uruguay Experience

Although Latin America is a heterogenous region with inequities in access to healthcare between different countries, in Uruguay, policy interventions have resulted in positive health impacts. Since 2009, a decree by the Department of Health includes screening for CKD in high-risk populations (“case-finding”) as part of the mandatory health check-ups of the working population. These health check-ups consist of a mandatory twice-yearly urine exam and serum creatinine tests in people with diabetes and hypertension. If the tests are abnormal, the person affected is referred to a general physician to confirm the findings, determine the treatment regimen and decide if a referral to nephrology is needed. In addition to this screening approach, dialysis has been a part of universal health coverage since 1981. Both these measures have resulted in an improvement in the quality of care along with a reduction in the incidence of CKD [34].

According to the guidelines for diabetes in Uruguay, attention should be given to control both blood pressure and albuminuria [34]. Although this can be achieved by using drugs that act on the renin-angiotensin-aldosterone system, diabetes care would benefit from universal and affordable access to other add-on treatments, such as SGLT2 inhibitors, that are currently not available (for all the people affected who will benefit of their use) in Uruguay and most other Latin American countries.

World Kidney Day

World Kidney Day is an annual global campaign that raises awareness about kidney health and the impact of kidney disease worldwide. The campaign was first launched in 2006 by the International Society of Nephrology (ISN) and the International Federation of Kidney Foundations (IFKF). Each year, World Kidney Day has a specific theme that highlights a different aspect of kidney health, such as prevention, detection, or management of kidney disease. The campaign has grown significantly since its inception, with events and activities now taking place in more than 100 countries around the world.

While it is difficult to determine the direct impact of World Kidney Day on the prevalence of kidney disease globally, the campaign has had a significant impact on increasing awareness and advocacy efforts for kidney health, which can help to improve prevention, diagnosis, and management of kidney disease. It is common for Ministries of Health to be involved in World Kidney Day activities, as they are responsible for promoting public health and ensuring that adequate resources are allocated to address the burden of kidney disease in their respective countries. Ministries of Health may participate in a variety of World Kidney Day activities, such as organising health screenings, promoting awareness campaigns, or hosting educational seminars.



RECOMMENDATIONS

CKD in people living with diabetes is common, the consequences are grim and we need to take action. IDF and ISN recommendations:

1. Ensure intersectoral and multisectoral collaboration in the development of comprehensive policies and investments to prevent and treat diabetes and CKD
2. Collaborate with WHO to implement the Global Diabetes Compact at the national level, to improve diabetes prevention and care
3. Develop and implement interventions to facilitate diabetes screening across the entire population, according to recommendations
4. Provide universal coverage to glycaemia and glycated haemoglobin tests, glucose lowering drugs and antihypertensive treatment drugs, in line with the WHO diabetes coverage targets to be achieved by 2030
5. Develop and implement programmes for CKD screening, risk stratification and monitoring in people with diabetes
6. Provide universal coverage for drugs that reduce CKD progression in people living with diabetes: ACE inhibitors/ARB, SGLT2 inhibitors and MRA
7. Provide universal coverage for CKD care, including dialysis and transplantation, which are critical components of the treatment and management of end-stage kidney disease and must be included in any comprehensive universal health coverage programme
8. Include kidney disease specifically in UN and WHO targets, for example in the political declaration on the upcoming 2025 UN High Level meeting on NCDs, to increase awareness about the importance of kidney health and improve the allocation of resources to prevent, detect and manage kidney disease
9. Advocate for people-centred care and ensure that people living with diabetes and CKD are included in the development and evaluation of interventions and guidelines



RELEVANT RESOURCES

- A single number for advocacy and communication—worldwide more than 850 million individuals have kidney diseases: <https://www.theisn.org/blog/2019/09/30/a-single-number-for-advocacy-and-communication-worldwide-more-than-850-million-individuals-have-kidney-diseases/>; 2019 KI_ASN_ERA-EDTA_ISN_Kidney Disease.pdf
- Global Kidney Health Atlas: <https://www.theisn.org/initiatives/the-isn-closing-the-gaps-ckd-initiative/>
- 10 Recommendations To Global Kidney Health: <https://www.theisn.org/in-action/advocacy/advocacy-activities/10-recommendations-for-global-kidney-health/>
- Diabetes basics: <https://idf.org/about-diabetes/introduction/>
- Data portal of the IDF Diabetes Atlas 2021: <https://diabetesatlas.org/data/en/>
- IDF guide to data-driven advocacy: <https://idf.org/media/uploads/2023/05/attachments-27.pdf>
- Map 2 Source: Hill et al., Global prevalence of chronic kidney disease- a systematic review and meta-analysis.
- Global Coalition for Circulatory Health White papers: <https://www.theisn.org/in-action/advocacy/policies-campaigns/#gcch>



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