

# Diabetes and chronic kidney disease: the diagnostic imperative

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## About this article

This article, supported by Abbott and created by Economist Impact, serves as an educational resource to raise awareness of tests and international guidelines to be considered during clinical consultations. It aims to empower patients to engage in informed discussions with their doctors about diabetes.

The editorial team at Economist Impact would like to thank the following individuals (listed alphabetically) for generously contributing their time and insights, which have been critical to the creation of this article.

- **Professor Andrew Boulton**, President of the Worldwide Initiative for Diabetes Education, Chair of EURADIA (European Alliance for Diabetes Research), and former President of the International Diabetes Federation (IDF)
- **Professor Vivian Fonseca**, Professor of Medicine, Assistant Dean for Clinical Research, the Tullis-Tulane Alumni Chair in Diabetes, and Chief of the Section of Endocrinology at Tulane University Medical Center, and Past President (Medicine & Science) at the American Diabetes Association (ADA)

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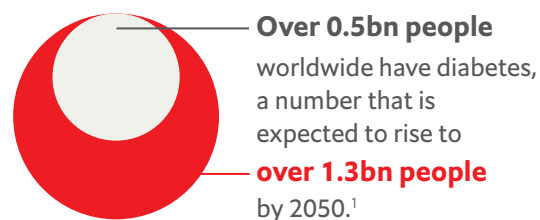
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## The diagnostic imperative

Diabetes mellitus (DM) or diabetes (hereafter used interchangeably), characterized by chronic hyperglycemia, can, over time, lead to irreversible damage to the heart, blood vessels, eyes, kidneys, and nerves. As a result, diabetes – a silent killer – is a leading cause of death and disability worldwide, affecting patients across ethnicities, age groups, and genders.<sup>1</sup> In the United States, more than 11% of the population (37m people) have diabetes and 96m people have prediabetes.<sup>2</sup> Prediabetes refers to the common and reversible condition where blood glucose levels are elevated but not high enough for a diagnosis of T2DM.<sup>3</sup> Similar trends are evident in Europe, where about 60m people have diabetes, equating to 10.3% of men and 9.6 % of women aged 25 years and above.<sup>4</sup>

Diabetes has been recognized as a global health challenge, and, in 2006, was identified as a threat to world health equivalent to that posed by infectious diseases such as tuberculosis and HIV.<sup>5</sup> Over half a billion people worldwide have DM, a number that is expected to rise to more than 1.31bn by 2050.<sup>1</sup> In 2004, it was estimated that

the number of people with DM globally would reach 382m by 2030, but this milestone was breached by 2013, suggesting an exponential increase in incidence.<sup>6</sup> An increase in prevalence in every region of the world is expected by 2045 (see Table 1).<sup>7</sup>



Worldwide, the mortality rate due to diabetes increased by 3% between 2000 and 2019; this increase was particularly significant given that the probability of dying from a disease like cancer or chronic respiratory diseases between the ages of 30 and 70 decreased by 22% in the same period.<sup>8</sup> The DM burden is growing more rapidly in low- and middle-income countries (LMICs), driven in part by a combination of population ageing, poor nutrition, and sedentary lifestyles.<sup>9</sup>

**Table 1: Age-adjusted comparative prevalence of diabetes** <sup>7</sup>

Percentage, by year

Region	2000	2011	2021	2030*	2045*
Africa	1.2	4.5	5.3	5.5	5.6
Europe	4.9	6.7	7.0	8.0	8.7
Middle East and North Africa	7.7	11.0	18.1	19.6	20.4
North America and Caribbean	7.8	10.7	11.9	13.3	14.2
South and Central America	3.7	9.2	8.2	9.2	9.9
South-East Asia	5.3	9.2	10.0	10.9	11.3
Western Pacific	3.6	8.3	9.9	10.9	11.5

\*Projections by the International Diabetes Federation

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DM is broadly classified into three types based on clinical presentation and etiology. These are Type 1 diabetes (T1DM), Type 2 diabetes (T2DM), and gestational diabetes (GDM). Monogenic and secondary diabetes also exist, but they are far less common. The most common is T2DM, which includes almost 90% of all diabetes cases.<sup>10</sup> It is most frequently seen in patients aged over 45, but it is increasingly evident in younger age groups due to rising levels of obesity, physical inactivity, and poor diets. T1DM is more common in children and adolescents but can develop at any age. It accounts for 5-10% of DM and results from an insulin deficiency caused by the body attacking and destroying the insulin-producing cells of the pancreas.<sup>11</sup> Unlike T2DM, which is a largely preventable lifestyle disease, T1DM is an autoimmune disorder.<sup>12,13</sup>

Affordable treatment is critical for the survival of patients living with diabetes. “Access to medications is crucial; it is about equity and ensuring that everyone has access to effective treatments,” said Professor Andrew Boulton, President of the Worldwide Initiative for Diabetes Education, Chair of EURADIA (European Alliance for Diabetes Research), and former President of the International Diabetes Federation (IDF). Those with T1DM require daily doses of insulin, while T2DM is treated with lifestyle changes, as well as medicine and insulin, depending on the severity of the disease.<sup>14,15</sup> Inadequately-controlled diabetes, such as chronic hyperglycemia, can impact several organ systems and potentially lead to fatal consequences.<sup>2,16-19</sup> Continuous Glucose Monitoring (CGM) can be an effective method to help patients increase awareness of their glucose levels, thus improving their quality of life.<sup>20,21</sup>

“The prevalence of diabetes is increasing rapidly, and this is concerning, but it is preventable with early screening and taking action early,” said Prof Boulton. To combat the rise of diabetes, patient education is critical to improve self-management and monitoring, as well as treatment compliance.<sup>22-24</sup>



### Associated costs of treating diabetes

Care for people diagnosed with diabetes costs 1 in 4 healthcare system dollars (2022) in the United States, and people diagnosed with diabetes spend on average 2.6 times more on their healthcare than people without diabetes.<sup>25</sup> Glucose-lowering medicines and other diabetes supplies contribute to direct medical costs, while contributors to indirect costs include reduced employment and lost productivity as a result of premature deaths that can impact the economy.<sup>25</sup>

In England and Wales, the National Health Service (NHS) spends 10% of its budget on diabetes, equivalent to over \$3.2m every hour.<sup>27,B</sup> That is nearly \$30.3bn spent annually on treating diabetes and its complications.<sup>27,28,B</sup> The NHS spends \$373m on supplies such as blood glucose meters, test strips, and needles for insulin pens.<sup>27,28,B</sup> According to the IDF's Global Diabetes Atlas, cost is expected to rise in almost every region of the world by 2045 (see Table 2).<sup>26</sup>

### Chronic kidney disease (CKD)

The importance of protecting the body from hyperglycemia (high levels of blood glucose) cannot be overstated; its effects are normally divided into macrovascular and microvascular complications. Macrovascular complications include "cardiovascular, cerebrovascular, and peripheral vascular disease," while microvascular complications include "retinopathy, neuropathy and nephropathy".<sup>29</sup>

Kidney diseases rank as the ninth leading cause of death in the United States, and research suggests that T2DM is the leading cause of CKD and end-stage kidney disease globally.<sup>30-32</sup> About 30-40% of those with T1DM will develop CKD with a high risk of cardiovascular events, renal insufficiency and kidney failure, whereas those with T2DM are at a major risk for end-stage renal disease.<sup>33,34</sup> Diabetic nephropathy is a significant cause of CKD, which often develops slowly and is asymptomatic until it is advanced.

**Table 2: Diabetes-related health expenditure per person**<sup>26,A</sup>  
US\$, by year

Region	2011	2021	2030*	2045*
Africa	883	633	2,183	1,661
Europe	1,493	3,573	6,373	6,521
Middle East and North Africa	684	539	1,882	1,467
North America and Caribbean	2,232	9,503	2,047	1,965
South and Central America	1,080	2,535	3,100	2,834
South-East Asia	No data	130	26,414	20,611
Western Pacific	1,354	1,394	35,786	36,926

\*Projections by the International Diabetes Federation

<sup>A</sup> Adapted from the International Diabetes Federation, with costs rounded to the nearest US\$ and transposed from the publication year of 2021 to 2024 US\$ with an average inflation rate of 5.03% and cumulative inflation of 15.76%.

<sup>B</sup> Costs transposed from 2012, the year the date was reported, with an average exchange rate of 1 US\$ to 0.78 Pounds£, and an average inflation rate of 2.65% and cumulative inflation of 36.63%.

CKD is clinically defined as a low estimated glomerular filtration rate (eGFR) or other signs of kidney damage and persistently elevated urinary albumin excretion present for three months or more.<sup>35</sup> The National Kidney Foundation reported that nearly 90% of adults living with CKD in the United States are unaware that they have it.<sup>36</sup> Of all the long-term complications of diabetes, CKD is the most expensive to treat and has a severe impact on daily life. “CKD can be a very expensive disorder if people don’t get diagnosed early and treated appropriately to prevent the need for dialysis,” explained Professor Vivian Fonseca, Professor of Medicine, Assistant Dean for Clinical Research, the Tullis-Tulane Alumni Chair in Diabetes, and Chief of the Section of Endocrinology at Tulane University Medical Center, and Past President (Medicine & Science) at the American Diabetes Association (ADA).

**“Chronic kidney disease can be a very expensive disorder if people don’t get diagnosed early and treated appropriately to prevent the need for dialysis.”**

Vivian Fonseca, Professor of Medicine, Tulane University Medical Center.

Treating CKD patients with dialysis in the United States can cost nearly three times as much as non-dialysis CKD Medicare patients.<sup>37</sup>

Dialysis or a kidney transplant may be required for patients with kidney failure. Diabetic dialysis patients are challenging to manage as they experience higher rates of cardiovascular events and mortality in comparison to non-diabetic patients on dialysis, although mortality rates have declined over the last century.<sup>38</sup> Despite this, reports suggest that excess mortality associated with both T1DM and T2DM is restricted to patients with CKD, making prevention and effective management key aims for managing these patients.<sup>39</sup>



**Nearly 90% of adults living with chronic kidney disease in the United States are unaware that they have it.**<sup>36</sup>

### Detecting diabetes early

Prevention of diabetes is the most effective way to minimize the impact of diabetic kidney disease.<sup>40</sup> “There needs to be an awareness about early recognition and the importance of it. This allows for early treatment to prevent disease progression,” said Prof Fonseca. Screening for prediabetes and T2DM is effective in preventing the progression from prediabetes to diabetes to CKD.

Prevention and effective management strategies for diabetes represent good value in terms of costs per quality-adjusted life year or QALY gained. Public health interventions, for example, are widely accepted as cost-effective prevention measures and cost less than \$50,000 per QALY.<sup>2</sup> Lifestyle modifications to prevent T2DM in those at high risk cost \$12,500 per QALY when compared to no such modifications.<sup>2</sup> “It is economically viable to screen high-risk groups but not the whole population,” explained Prof Boulton. “All complications of diabetes can be silent until it is too late. Screening picks them up before that,” he continued.

Aggressive interventions and regular follow-ups are important for those at very high risk based on their test results. Vigilance is key in primary care, where relevant patients are contacted annually about their screenings. Some countries perform better at this phase, Prof Boulton explained. “Scotland is a good example of a country that has trained primary-level care to ensure things [diabetes] are detected early. The Netherlands has done very well with its programs, and the Scandinavians are very good.

<sup>c</sup> Glomerular filtration rate (eGFR) less than 60 ml/min per 1.73 square meters.



It's about having the system to recall and review patients regularly," he said. In Europe, screening is recommended annually for patients with kidney disease and less frequently for non-diabetics, while the United States' recommendations are testing regularly, annually for cystic fibrosis-related diabetes and at least every three years if levels are normal.<sup>41,42</sup>

Regular review of patients includes checking average blood sugar levels, which can be used to monitor seemingly healthy individuals, those at high risk of developing diabetes, and those who already have diabetes. There are three recognized diagnostic tests for diabetes, but the test with the best diagnostic accuracy is rarely straightforward as each has its advantages and disadvantages.<sup>43</sup>

**"...(early detection is) about having the system to recall and review patients regularly..."**

Andrew Boulton, President of the Worldwide Initiative for Diabetes Education.



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## Diagnostic tests

Diabetes and prediabetes are detected by measuring fasting plasma glucose (FPG) levels, HbA1c (glycated hemoglobin), or with an oral glucose tolerance test (OGTT), including a 2-hour plasma glucose measurement during the oral glucose tolerance test. This section assesses the diagnostic options recommended by current guidelines in the United States and Europe (see Table 3).

### Fasting plasma glucose (FPG)

FPG is the fastest and simplest way to diagnose diabetes; it is inexpensive and sensitive. In patients presenting with classic symptoms such as hyperglycemia, the plasma glucose level is enough to diagnose diabetes, although some physicians may still test for HbA1c to determine how chronic the elevated glucose levels are. Studies comparing OGTT, FPG, and HbA1c and concluded that FPG has a higher level of accuracy than HbA1c

and is more convenient to use than OGTT.<sup>43,45</sup> However, FPG is not failure-proof; it is vulnerable to pre-analytical variables such as recent food intake, how well the sample is stored, acute stress and diurnal variations, and common drugs such as corticosteroids, which can influence glucose metabolism.<sup>46,47</sup>

### HbA1c

HbA1c has several advantages compared to other screening and diagnostic tests. It is more convenient as fasting is not required, and it has better pre-analytical stability as it is not affected by day-to-day fluctuations in plasma glucose levels due to illness or nutrition. The advantages of the HbA1c test may be offset by its higher cost, lower sensitivity, limited availability in some developing countries, and poor correlation between its value and average glucose levels in some patients.<sup>42</sup>

**Table 3: Guidelines for diabetes testing**<sup>41,42,44</sup>

United States		Europe	
Guidelines	Tests	Tests	Guideline
Standards of Care in Diabetes—2023 Abridged for Primary Care Providers	HbA1c	HbA1c	2019 European Society of Cardiology (ESC) Guidelines on diabetes, pre-diabetes, and cardiovascular diseases, developed in collaboration with the European Association for the Study of Diabetes (EASD)
	Fasting Plasma Glucose (FPG)		
	2-hour plasma glucose during 75-g (OGTT)	FPG	
	Random plasma glucose (RPG)		
Classification and Diagnosis of Diabetes: Standards of Care in Diabetes—2023	HbA1c	OGTT	
	FPG		
	OGTT	RPG	
	RPG		

See Appendix A for ranges and frequency

Anything affecting red blood cell turnover can also interfere with HbA1c results. Factors increasing HbA1c include vitamin B12 deficiency, decreased erythropoiesis and/or a splenectomy; on the other hand, chronic liver disease, some medicines, and rheumatoid arthritis can reduce HbA1c values.<sup>48</sup> Despite this, studies have shown a strong correlation between HbA1c and diabetes complications and lower HbA1c levels are associated with an increased risk of hypoglycemia in patients with both T1DM and T2DM.<sup>49</sup>

### **Alternative markers of glycemia**

Clinical guidelines strongly base diagnostic strategies on FPG and HbA1c. However, these tests are not always appropriate. Glycated albumin and fructosamine have evolved as alternative markers of glucose control, and can be used as an adjunct test to HbA1c or as a reliable measure when HbA1c is unsuitable. Despite this, no guideline currently supports the use of glycated albumin and fructosamine for the diagnosis of diabetes or prediabetes.<sup>50</sup>

The NHS Trust in England recommends that fructosamine testing be used for monitoring diabetes patients when HbA1c results are not available, as there is no established diagnostic threshold based on evidence.<sup>51</sup>

Fructosamine is made by the glycation of serum proteins, including albumin. Since albumin is abundant in plasma, fructosamine is principally glycated albumin.<sup>52</sup> Glycated albumin and fructosamine reflect short-term glycemic levels and are not influenced by conditions that affect HbA1c. HbA1c measures glycated hemoglobin over three months, while glycated albumin and fructosamine measure a shorter period of approximately two weeks, thus bridging the gap between HbA1c and continuous glucose monitoring and allowing for more effective monitoring of changes in blood glucose levels.<sup>53,54</sup> Testing for glycated albumin is more affordable than HbA1c, and can even be automated.

Prof Fonseca shared some insight into the various diagnostic methods used: “HbA1c is very important, but testing glucose is less important. Fructosamine (FRA) and glycated albumin (GA) are useful in certain situations, and while GA is a better test than FRA, FRA testing is done more,” he explained. He affirms that GA is a new test that is not widely available, so FRA is often used. Indeed, the diagnostic efficiency of glycated albumin is superior to that of fructosamine due to the changes that can occur in glycated serum proteins in response to systemic disorders. Glycated albumin can be reported as a ratio to total albumin, minimizing any interference from the presence of non-glycated albumin. Methods for measuring glycated albumin are also better standardized than those for fructosamine.<sup>47</sup>

### **Oral glucose tolerance test (OGTT)**

The OGTT was the gold standard for diagnosing diabetes and prediabetes but is now used infrequently due to several limitations.<sup>55</sup> The OGTT encounters issues with reproducibility, is sensitive to time of testing, and there are more acceptable alternatives in clinical settings.<sup>55</sup> There is also uncertainty about how well patients adhere to the preparation requirements.<sup>56</sup> The World Health Organization (WHO) has recommended using HbA1c to diagnose T2DM in the community, meaning the OGTT is now only performed on patients for whom HbA1c measurement would be inappropriate. Additionally, research suggests that the OGTT, which requires ingesting a syrupy solution and waiting two hours for testing, may be an inconvenient approach that is not entirely accepted by patients.<sup>57,58</sup> One study reported that approximately half of women experienced stress and nausea during the OGTT.<sup>59</sup>



### Preventing kidney disease in diabetes

Uncontrolled diabetes is well-known for its ability to cause damage to various tissues in the body, particularly the kidneys. This close relationship emphasizes the importance of not only regularly testing for diabetes but also for regular screening for CKD. It is crucial to note that approximately one in three adults with diabetes also has CKD, highlighting the direct connection between these conditions.<sup>31</sup> If diabetes progresses to CKD, the financial impact is significant as patients with CKD face nearly triple the medical expenses compared to those without CKD.<sup>37</sup> This underscores the urgent need for integrated monitoring of both diabetes and CKD to reduce risks and effectively manage costs.

For those living with diabetes, avoiding complications is extremely important. Daily self-monitoring of blood sugar levels, regular HbA1c tests, and attending annual screenings for renal complications are effective measures. Self-monitoring is often done with capillary blood glucose tests, which involve blood drop samples usually collected from a finger prick.<sup>60</sup>



**Only 47% of people living with diabetes in England received all their required checks in 2021-2022 (this statistic is likely linked to the Covid-19 pandemic).**<sup>63</sup>

Adherence to these finger prick tests is known to be poor; on the other hand, minimally invasive continuous glucose monitors (CGMs) are fast growing in popularity. CGMs measure real-time interstitial glucose values, providing information on variability in blood glucose levels.<sup>61,62</sup> “The general availability of continuous glucose monitoring has been a very significant change,” said Prof Fonseca concerning increased usage of CGMs. This is particularly important in diabetics with advanced kidney disease, where fluctuations in blood glucose are very common, and HbA1c is not a reliable test.

Prof Fonseca affirms that HbA1c and urine microalbuminuria tests are not only very important in the early detection of CKD, but they are not being done often enough. “We are not testing HbA1c enough,” he said. A recent report from England suggests that less than half (47%) of people living with diabetes received all their required checks in 2021-2022, a statistic likely linked to the Covid-19 pandemic.<sup>63</sup>

To prevent progression to kidney disease, pharmacologic interventions such as metformin therapy should be considered for adults at high risk of T2DM, including those with FPG levels  $\geq 110$  mg/dL.<sup>44</sup> The diagnosis of prediabetes or T2DM should be confirmed with repeat testing before starting interventions.<sup>64</sup>

Understanding the risk factors for kidney disease in diabetes patients can help with early identification and intervention. Prof Boulton explained that screening and early detection can reverse the incidence of CKD. “You can reverse it if you catch it early, it requires good blood pressure control with ACEi [angiotensin-converting enzyme inhibitors], ARBs [angiotensin receptor blockers],

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and SGLT2 [sodium-glucose cotransporter-2] inhibitors," he said. Kidney protective medicines, including ARBs and ACEi, that also lower blood pressure can be used to slow the decline in renal function.<sup>65,66</sup> Randomized controlled trials (RCTs) have shown that if microvascular complications are treated effectively from the point of diagnosis, it can reduce major cardiovascular complications.<sup>67</sup>

The ADA recommends that the urinary albumin-to-creatinine ratio (UACR) and eGFR should be assessed (at least) annually in patients with T1DM for more than five years, for all people with T2DM, and for all patients who have comorbid hypertension to check for kidney disease (see Table 4). The European Society of Cardiology (ESC)/European Association for the Study of Diabetes (EASD) guidelines further suggest that the serum creatinine test is also done annually, along with tight glucose and blood pressure control, while American guidelines

recommend periodic monitoring of serum creatinine.<sup>68,69</sup>

Measurement of eGFR is challenging as it depends on measurement of serum creatinine, which has limitations in terms of accuracy and sensitivity.<sup>70</sup> Cystatin C, however, is a protein that has emerged as an alternative marker for kidney function. Unlike creatinine, it is unaffected by muscle mass and has a stronger association with cardiovascular disease and mortality than creatinine.<sup>71</sup> In its 2012 guidelines, Kidney Disease Improving Global Outcomes (KDIGO) recommended using cystatin C to confirm diagnosis of CKD determined using creatinine-based GFR, as cystatin C is a more accurate marker of kidney function to inform clinical decision-making.<sup>72</sup> Cystatin C also removes race from the GFR equation, making CKD diagnosis more equitable.<sup>73</sup>

**Table 4: Guidelines for chronic kidney disease (CKD) testing**<sup>41,42,44</sup>

United States		Europe	
Guidelines	Tests	Tests	Guideline
Standards of Care in Diabetes—2023 Abridged for Primary Care Providers	Urinary Albumin Measurement (Spot UACR)	Urine Albumin-to-Creatinine Ratio (UACR)	2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD
	Estimated Glomerular Filtration Rate (eGFR)	Estimated Glomerular Filtration Rate (eGFR)	
	Serum Creatinine	Urine Protein Test	
Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes—2023	UACR	UACR	
	eGFR	eGFR	
	Serum Creatinine	Serum Creatinine	
	Serum Potassium	HbA1c	
	Urinary Sediment Analysis	Urine Protein Test	

See Appendix B for ranges and frequency

## Conclusion

Diabetes is a global challenge that causes significant morbidity and mortality. Prediabetes is a risk as it can progress to diabetes and its complications, including CKD, which affects approximately one-third of diabetes patients. Early detection and treatment of diabetes can also prevent or delay the development of CKD, which often leads to significant morbidity and mortality.

Outcomes can be significantly improved if both diabetes and CKD are caught early. Screening and diagnostic tests are recommended alongside interventions such as lifestyle changes to prevent progression. Screening is particularly important since diabetes and its complications can be silent until it is too late to treat effectively. Lifestyle modifications and public health interventions are cost-effective interventions when compared to the cost of inaction. Examples include community-based education programs, changing daily diets, and exercising, among others.<sup>74</sup>

Guidelines recommend tests for screening, diagnosis, and monitoring to prevent the progression of diabetes. These include regular testing of glycemia, blood pressure, and kidney function, alongside medication as required. There is a part for both patients and doctors to play. Research indicates that less than half of patients engage effectively with monitoring appointments. Patients need to be educated on the importance of attending screening and treatment appointments, as well as performing self-monitoring and care. Doctors need to remain vigilant and monitor patients who are at high risk of developing diabetes and its long-term complications. It is important that these very preventable diseases, T2DM and CKD, are caught early and managed effectively.



Appendix A: Guidelines for diabetes <sup>41,42,44</sup>

United States				
Guideline	Tests	Pre-diabetes	Diabetes	Frequency
Standards of Care in Diabetes—2023 Abridged for Primary Care Providers	HbA1c	5.7–6.4% (39–47 mmol/mol)	≥6.5% (48 mmol/mol)	At least annually for prediabetes; more frequently based on risk factors and initial results
	Fasting Plasma Glucose (FPG)	100–125 mg/dL (5.6–6.9 mmol/L)	≥126 mg/dL (7.0 mmol/L)	Annually for screening
	2-hour plasma glucose during 75-g (OGTT)	140–199 mg/dL (7.8–11.0 mmol/L)	≥200 mg/dL (11.1 mmol/L)	As needed based on risk factors or abnormal FPG/A1C results
	Random plasma glucose (RPG)	-	≥200 mg/dL (11.1 mmol/L)	As needed, especially if symptoms of diabetes are present
Classification and Diagnosis of Diabetes: Standards of Care in Diabetes—2023	HbA1c	5.7–6.4% (39–47 mmol/mol)	≥6.5% (48 mmol/mol)	At least every 3 years if normal; annually for prediabetes
	FPG	100–125 mg/dL (5.6–6.9 mmol/L)	≥126 mg/dL (7.0 mmol/L)	Annually for prediabetes; every 3 years if normal
	OGTT	2-h PG level of 140–199 mg/dL (7.8–11.0 mmol/L)	≥200 mg/dL (11.1 mmol/L)	As recommended by healthcare provider
	RPG	-	≥200 mg/dL (11.1 mmol/L) in patients with classic symptoms of hyperglycemia or hyperglycemic crisis	As needed
Europe				
Guideline	Tests	Pre-diabetes	Diabetes	Frequency
2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD	HbA1c	5.7–6.4% (39–47 mmol/mol)	≥6.5% (48 mmol/mol)	At least twice a year for diabetics; less frequently for non-diabetics
	FPG	5.6–6.9 mmol/L (100–125 mg/dL)	≥7.0 mmol/L (126 mg/dL)	Annually for those with pre-diabetes or more frequently based on medical advice
	OGTT	7.8 to <11.1 mmol/L (140–199 mg/dL)	≥11.1 mmol/L (≥200 mg/dL)	As needed
	RPG	-	Measures blood sugar at any time of day, regardless of when you last ate. Levels of ≥11.1 mmol/L (200 mg/dL), along with symptoms of diabetes, indicate diabetes	As needed

## Appendix B: Guidelines for chronic kidney disease (CKD) <sup>41,42,44</sup>

United States			
Guideline	Tests	Range	Frequency
Standards of Care in Diabetes—2023 Abridged for Primary Care Providers	Urinary Albumin Measurement (Spot UACR)	Normal: <30 mg/g creatinine Moderately Elevated: 30–300 mg/g creatinine Severely Elevated: ≥300 mg/g creatinine	At least annually for people with T1DM (≥5 years of duration) At least annually for all people with T2DM. More frequent monitoring (1–4 times per year) for people with established diabetic kidney disease depending on the disease stage
	Estimated Glomerular Filtration Rate (eGFR)	Varies based on the CKD stage	Regular monitoring for people with CKD; typically part of routine lab work
	Serum Creatinine	Normal reference range varies by laboratory	Regular monitoring for people on medications affecting kidney function
Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes—2023	UACR	Normal: <30 mg/g creatinine Moderately Elevated: 30–300 mg/g creatinine Severely Elevated: ≥300 mg/g creatinine	Annually for people with T1DM (≥5 years duration) and all people with T2DM 1–4 times per year for established diabetic kidney disease, depending on disease stage
	eGFR	Normal: >60 mL/min/1.73 m <sup>2</sup> Abnormal: <60 mL/min/1.73 m <sup>2</sup>	Annually or more frequently depending on CKD stage and patient status
	Serum Creatinine	Varies based on age, sex, muscle mass	Periodically monitor in patients on ACE inhibitors, ARBs, or MRAs; or when eGFR <60 mL/min/1.73 m <sup>2</sup>
	Serum Potassium	Normal range typically 3.5–5.0 mEq/L	Periodically in patients on diuretics, ACE inhibitors, ARBs, MRAs
	Urinary Sediment Analysis	Presence or absence of red/white blood cells, casts	As indicated in cases of rapidly changing kidney function or to differentiate CKD causes
Europe			
Guideline	Tests	Range	Frequency
2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD	Serum Creatinine Measurement	Varies based on age, sex, and muscle mass; normal range: 0.7–1.3 mg/dL for men, 0.6–1.1 mg/dL for women	Annually for patients with diabetes
	eGFR	Normal: ≥90 mL/min/1.73m <sup>2</sup> ; CKD: <60 mL/min/1.73m <sup>2</sup>	Annually for DM patients; more frequently if CKD is present
	UACR	Normal: <30 mg/g; Microalbuminuria: 30–300 mg/g; Macroalbuminuria: >300 mg/g	Annual
	Urine Protein Test	Normal <150 mg/day; persistent proteinuria indicated by higher values	Based on clinical suspicion or existing CKD
	HbA1c	Goal for DM patients <7%; individualized goals in CKD	At least twice a year in stable patients; quarterly in patients with treatment changes or not meeting glycemic goals



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## Diabetes and chronic kidney disease: the diagnostic imperative

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