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Saudi Consensus Report on Chronic Kidney Disease Management: Integrating the Latest Evidence and Clinical Practice Guidelines

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Abstract

Chronic Kidney Disease (CKD) poses a significant healthcare challenge in Saudi Arabia, necessitating a structured approach to management and treatment. Recent consensus guidelines in Saudi Arabia emphasize a comprehensive strategy for CKD management, tailored to local needs and healthcare resources. The guidelines advocate for early detection and stratified care to mitigate the progression of CKD and improve patient outcomes. Key recommendations include the routine assessment of albuminuria and estimated glomerular filtration rate (eGFR) for accurate diagnosis and staging of CKD. The consensus underscores the importance of utilizing updated tools like the CKD-EPI 2021 equation for eGFR calculation and incorporating cystatin C measurements for enhanced diagnostic accuracy. Management strategies focus on controlling underlying conditions such as diabetes and hypertension, which are prevalent risk factors in the Saudi population. Personalized treatment plans are recommended, incorporating lifestyle modifications, pharmacological interventions including SGLT-2 inhibitors and GLP 1 RA, and regular monitoring to manage CKD complications effectively. The guidelines also highlight the need for specialized care and referral pathways for advanced CKD stages, including the role of nephrologists in the comprehensive management of CKD patients. In addition, the consensus addresses the need for improving public awareness and education about CKD, emphasizing early screening and preventive measures, particularly in high-risk groups. The implementation of these guidelines aims to optimize CKD management across Saudi Arabia, reduce the burden of kidney disease, and enhance overall patient care in the region.

Keywords

Chronic Kidney Disease

1. Introduction

1.1. Definition of Chronic Kidney Disease

Chronic kidney disease (CKD) is a significant global health issue, affecting an estimated 800 million people worldwide. Characterized by the gradual loss of kidney function over time, CKD is more prevalent in older adults and often associated with chronic conditions such as diabetes (DM) and hypertension [1]. CKD is defined by abnormalities in kidney structure or function persisting for at least three months, with implications for the individual's health. These abnormalities include a decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73m^2 or an elevated urinary albumin-to-creatinine ratio (ACR) greater than 30 mg/g (3 mg/mmol), irrespective of the underlying cause [2].

The term "diabetes-related kidney disease" (DKD) has replaced the former term "diabetic nephropathy," which specifically referred to glomerular lesions such as nodular glomerulosclerosis and glomerular basement membrane thickening. This change reflects accumulating evidence of various types of DM-induced structural kidney impairments. DKD occurs in 20% - 40% of people with DM, typically developing after a duration of 10 years in type 1 diabetes (T1DM), but it may be present at the diagnosis of type 2 diabetes (T2DM) [3]-[7].

The terms DM with CKD, or CKD in DM, refer to DM that is accompanied by low eGFR and/or albuminuria/proteinuria with no known cause. This is the inclusion criterion utilized in most large outcome trials for diabetic renal disease. As a result, while any of the research subjects may have had DKD, others may have had CKD due to another cause in the context of DM [8].

1.2. Prevalence of CKD in KSA

Currently, over 20,000 patients in KSA are on dialysis, and 9810 patients are undergoing follow-up after kidney transplantation. The combined prevalence of renal replacement therapy is estimated at 294.3 per million. The age-standardized prevalence of CKD (stages 1 - 5, excluding renal replacement therapy) in KSA is estimated at 9892 per 100,000. Screening over 5000 first-degree relatives of Saudi patients on hemodialysis revealed a CKD prevalence of 13.8%, significantly higher than the general Saudi population of a similar age group [9].

1.3. Importance of Early Detection, Establishing Etiology and Management of CKD

Early detection and treatment of CKD are crucial for slowing disease progression, preventing complications and improving patient outcomes. However, only 9% of patients with CKD are aware of their condition. Because early stages of CKD are often asymptomatic, regular monitoring of at-risk individuals is essential. Early interventions can significantly slow CKD progression and reduce the risk of CVD. Effective early management includes monitoring and addressing issues such as anemia, mineral and bone disorders, and electrolyte imbalances, which can improve quality of life and reduce mortality. Identifying the underlying cause of CKD is critical for personalized treatment. Etiologies are categorized in various ways, including congenital, hereditary, systemic, and primary kidney disorders. While diagnostic approaches differ, determining the cause is essential for effective CKD management [10]-[12].

Therefore, a Saudi task force, including nephrologists, endocrinologists, diabetologists, and internal medicine experts, gathered to develop an explicit, evidence-based consensus on CKD management in the Kingdom of Saudi Arabia (KSA). This article has the recommendations of this expert panel.

2. Methods

Fourteen experts, including nephrologists, endocrinologists, diabetologists, internal medicine experts, clinical pharmacists from 14 centers with more than 15 years of experience, made up the task force. An initial concept proposal included the definition of CKD, population, scope, and prevalence in Saudi Arabia. The proposal was divided into several topics discussed in two meetings. The meetings panel approved that the consensus would include diagnosis, management, monitoring of CKD and special populations, and finally, among the entire Saudi population. An expert writer searched the literature based on their search strategies, and they determined their databases. Databases searched included PubMed, Embase, Scopus, and the Saudi Digital Library, covering publications from (2010) to (2024). Keywords such as "chronic kidney disease," "CKD management," "Saudi Arabia," "renal replacement therapy," and "diabetic nephropathy" were used. Local government reports were also reviewed to ensure comprehensive coverage. Most of the last updated literature, including guidelines, RCTs, consensus, and systematic reviews, were screened.

Consensus statements were selected based on relevance to CKD management in Saudi Arabia, regional context, and scientific rigor. Priority was given to guidelines tailored to the Middle East or addressing regional challenges, such as high CKD prevalence due to diabetes and hypertension. International guidelines were used but after localization. Documents were required to be recent (within the last 10 years), peer-reviewed, and developed through systematic methodologies like the Delphi process or expert panels. Screening involved independent review by two researchers, with discrepancies resolved by a third reviewer.

After the literature review, a panel of experts adapted recommendations to the Saudi context. This process considered regional epidemiology, healthcare infrastructure, and cultural factors. The final guidelines aim to address CKD prevention, diagnosis, and management while reflecting the unique needs and resources of the Saudi healthcare system.

A draft report was written and distributed electronically to the expert panel. Approval of the recommendations required consensus, defined as a majority approval using Delphi method. The recommendations were revised to accommodate any differences of opinion until a consensus was reached. Recommendations were finally formulated. Subsequently, the panel reviewed and discussed the revised recommendations and tried to develop a consensus statement to be valid for the Saudi society and health care professionals (HCPs).

The CKD guidelines will be disseminated through international publication, national conferences, workshops, webinars, and official publications, targeting healthcare professionals at all levels. Continuous feedback from healthcare providers and patients will support refinement and sustainability.

3. Epidemiology, Risk Factors and Disease Burden of CKD

3.1. Disease Burden Worldwide and in the Kingdom of Saudi Arabia

Chronic Kidney Disease is a global public health issue with a substantial disease burden. According to the Global Burden of Disease study, CKD is the 12th leading cause of death worldwide, and its prevalence is on the rise due to an aging population, increased prevalence of DM and hypertension, and lifestyle factors such as poor diet and physical inactivity. The economic impact on healthcare systems is significant, driven by the costs associated with dialysis, transplantation, and managing CKD-related complications [13] [14]. Worldwide, the vast majority of those who suffer from CKD are residing in low- and lower-middle-income countries. In these regions, many individuals lack access to essential diagnostic, preventive, and treatment services for CKD. This situation is exacerbated by inadequate primary care infrastructure, resulting in up to 90% of individuals with CKD being unaware of their condition and thus not seeking necessary treatment. The prevalence of CKD is projected to increase dramatically in the coming decades. Currently, CKD is the third fastest-growing cause of death globally. By 2040, it is expected to become the fifth leading cause of years of life lost worldwide [11].

Chronic kidney disease is a significant health issue in the KSA, with a substantial disease burden. One study found a higher prevalence of obesity (39.8%) among the screened relatives compared to the general Saudi population (28.7%), with a notable increase in CKD stages 2-5 (70.9%) compared to stages 0-1 (63.2%). Despite the high prevalence of DM in the general Saudi population (12.1%), the study reported a higher prevalence among relatives (23.4%), though only 9.5% showed glycosuria on the day of screening. Hypertension was also more prevalent among relatives with CKD, with 28.1% having systolic hypertension despite only 14.3% reporting a history of the condition. These findings indicate a high rate of undiagnosed hypertension (13.8%). The significant burden of CKD in KSA underscores the need for nationwide screening programs to manage the escalating healthcare costs and improve early detection and treatment of CKD [9].

3.2. Risk Factors

Chronic kidney disease has emerged as a prominent cause of mortality and morbidity in the 21st century, largely driven by escalating rates of key risk factors. CKD is associated with a range of risk conditions that include DM, hypertension, and CVD. Acute kidney injury (AKI) and a family history of kidney disease or genetic kidney disorders also elevate the risk. Obesity and social deprivation contribute significantly, as do age 50 years or older and urinary tract obstructions. Recurrent kidney stones, systemic infections like HIV and viral hepatitis, and malignancies further increase CKD risk. Autoimmune disorders and low birth weight are also notable risk factors, highlighting the multifaceted nature of CKD's etiology [15].

Obesity, DM, and hypertension are among the primary contributors to the increasing burden of CKD globally, with significant impact also observed within the KSA. In KSA, CKD has been recognized as a critical public health issue due to the growing incidence and prevalence of end-stage kidney disease (ESKD) among Saudi nationals. Recent epidemiological studies highlight the pervasive presence of CKD risk factors in the Saudi population, underscoring the substantial roles played by DM, hypertension, and obesity in exacerbating this health challenge [16]-[21].

3.2.1. Diabetes Mellitus

Diabetes mellitus stands out as the foremost risk factor for CKD in both developed and developing regions. Extensive research underscores the strong association between DM and CKD, with studies indicating a high prevalence of CKD among individuals diagnosed with DM. Diabetes exerts a profound impact on kidney function, often precipitating diabetic nephropathy, a primary cause of CKD. Importantly, many diabetic patients also contend with concurrent conditions like hypertension and vascular disease, further heightening their risk for CKD. This pattern is mirrored in Saudi Arabia, where DM is a predominant risk factor for CKD, aligning with global trends. Epidemiological studies conducted in KSA reveal a significant prevalence of DM, which markedly elevates the likelihood of developing CKD and contributes substantially to the burden of kidney disease, influencing both kidney function and progression to ESKD [16]-[20].

3.2.2. Hypertension

Hypertension stands as a significant risk factor for CKD, closely intertwined with its prevalence globally. The association between hypertension and CKD is well-documented, attributed to elevated blood pressure causing progressive damage to the kidney's blood vessels, thereby compromising kidney function over time. In

KSA, hypertension similarly emerges as a critical risk factor linked to the development and progression of CKD. High blood pressure contributes significantly to kidney damage, amplifying the risk of CKD in the population. The prevalent rates of hypertension in KSA underscore its pivotal role in the burden of CKD within the region [16]-[20].

3.2.3. Obesity

The rising global rates of obesity have had a profound impact on the incidence of CKD. Obesity is closely linked to the development of conditions such as DM and hypertension, which are primary risk factors for CKD. In KSA, where obesity rates are also on the rise, there has been a notable increase in CKD prevalence. Obesity not only predisposes individuals to DM and hypertension but also directly impairs kidney function. Research underscores the correlation between obesity and the risk of CKD, underscoring the urgency for targeted interventions to address these risks among the Saudi population. Additionally, similar to other populations, advancing age plays a significant role in determining the prevalence of CKD in KSA [16]-[20].

3.2.4. Age

Advancing age stands out as a crucial determinant of CKD prevalence. Age-related declines in glomerular filtration rate (GFR) can lead to CKD even without other risk factors present. Studies consistently reveal a higher prevalence of CKD in older age groups, with rates escalating significantly as age increases. For instance, in the United States, CKD stages 1 - 4 affected 5.6% of individuals aged 20 to 39, whereas it impacted 44% of those aged over 70. This underscores how age-related kidney function decline contributes substantially to CKD prevalence among older individuals, emphasizing age as a critical non-modifiable risk factor [16]-[20].

4. Pathophysiology and Etiology of CKD

4.1. Pathophysiology of CKD

Understanding the pathophysiological mechanisms and risk factors is crucial for developing effective prevention and treatment strategies to address this growing health challenge. Unlike AKI, which typically allows for complete functional recovery, CKD involves ongoing and sustained insults that result in progressive kidney fibrosis and the destruction of normal kidney architecture. This pathology affects all three compartments of the kidney: the glomeruli, the tubules, the interstitium, and the vessels, manifesting histologically as glomerulosclerosis, tubulointerstitial fibrosis, and vascular sclerosis [17] [22] [23].

The progression of CKD involves a complex, overlapping, and multistage sequence of events leading to kidney scarring and fibrosis. Initially, damaged kidneys are infiltrated by extrinsic inflammatory cells. That is followed by activation, proliferation, and loss of intrinsic renal cells through apoptosis, necrosis, mesangiolysis, and podocytopenia. Subsequently, extracellular matrix (ECM) producing cells, including myofibroblasts and fibroblasts, are activated and proliferate, leading to the deposition of ECM that replaces the normal kidney architecture. Several mechanisms can accelerate the progression of CKD, leading to a histological condition known as focal segmental glomerulosclerosis. These include systemic and intraglomerular hypertension, glomerular hypertrophy, intrarenal calcium phosphate precipitation, and altered prostanoid metabolism. Clinical risk factors associated with the accelerated progression of CKD include proteinuria, hypertension, black race, and hyperglycemia. Environmental exposures such as lead, smoking, metabolic syndrome, certain analgesic agents, and obesity have also been linked to the accelerated progression of CKD [17] [22] [23].

4.2. Etiology of CKD in Saudi Arabia

In KSA, DM is notably prevalent, with the country ranking among the highest globally for DM prevalence. Studies have identified DM as a primary risk factor for CKD, with a prevalence of 21.8% among diabetic patients in KSA. The duration of DM significantly influences the risk of developing CKD, with diabetic nephropathy affecting a notable percentage of patients. Hypertension also plays a critical role in CKD development and progression, with the prevalence of hypertension in KSA reaching as high as 30.2% in certain regions. Uncontrolled hypertension exacerbates kidney damage and increases the risk of CKD and subsequent cardiovascular events. Additionally, the prevalence of obesity and overweight in KSA is alarmingly high, contributing significantly to the burden of CKD. Obesity rates exceeding 63.6% in some regions underscore its role as a risk factor for CKD. Obesity not only predisposes individuals to DM and hypertension but also directly impacts kidney function, highlighting the need for targeted interventions to mitigate these risks [24].

Glomerulonephritis, including focal and segmental glomerulosclerosis (FSGS) and membranoproliferative glomerulonephritis (MPGN), represents a substantial portion of CKD cases in KSA. These conditions, identified through renal biopsies, contribute significantly to the burden of primary glomerular diseases and subsequent CKD progression. Hereditary cystic kidney diseases, such as autosomal dominant polycystic kidney disease, are also prevalent in KSA and contribute to a notable proportion of ESKD cases. Genetic factors play a significant role in these conditions, often leading to renal failure in childhood or adulthood. Various other conditions, including plasma cell dyscrasias, sickle cell nephropathy, and infections like tuberculosis and schistosomiasis, also contribute to CKD prevalence in KSA. These conditions collectively account for a significant percentage of CKD cases and necessitate further research to understand their impact fully [24].

5. Diagnosis and Staging

5.1. Assessment of Albuminuria

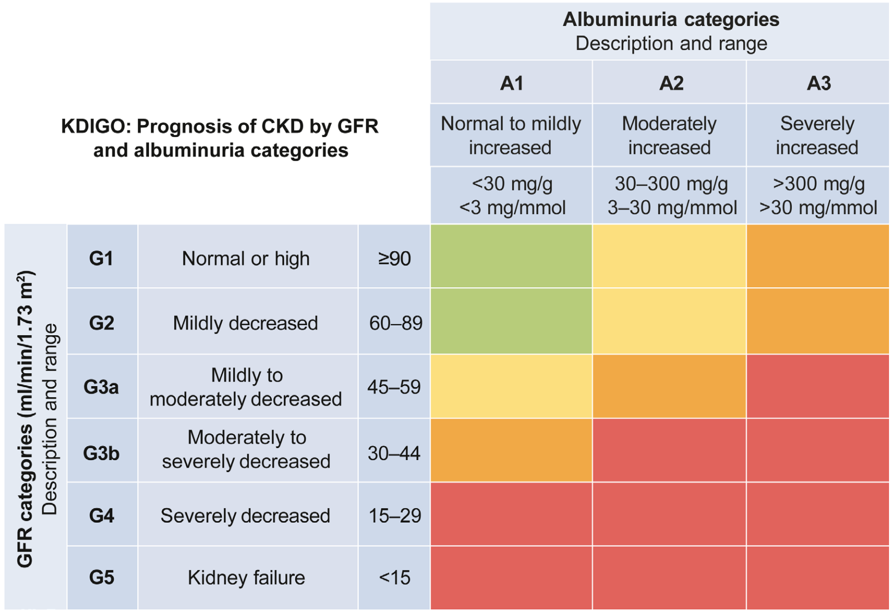
The KDIGO guidelines recommend that the term microalbuminuria be phased out and replaced with albuminuria [2]. Testing for ACR can readily screen for albuminuria in random spot urine collections. Timed or 24-hour collections contribute nothing to accuracy. Normal urine albumin excretion is <30 mg/g creatinine. Moderately increased albuminuria is ≥30 - 300 mg/g creatinine. Severe albuminuria is ≥300 mg/g creatinine. However, ACR is a continuous measurement, and deviations between the normal and pathological ranges are linked to kidney and cardiovascular outcomes. Furthermore, due to the substantial biological variability of >20% between measurements in urine albumin excretion, two of three ACR specimens collected within a 3- to 6-month period should be abnormal before classifying an individual as having moderately or severely increased albuminuria [6] [25]-[28]. ACR values more than 30mg/g indicate renal impairment and are also a measure of cardiovascular risk [29] [30]. ACR levels more than 300 mg/g indicate more damage and a higher chance of progression to renal failure and the development of CKD complications such as anemia, CVD, and infection. Sudden onset or fast-growing albuminuria should trigger additional tests to rule out other types of renal disease [2]. Increased urinary albumin may be seen in the setting of urinary tract or systemic infection, exercise within 24 h, fever, congestive heart failure, marked hyperglycemia, menstruation, and marked hypertension may elevate ACR independently of kidney damage. So, confirmation is necessary to establish the diagnosis of DKD or CKD in DM [2] [28].

5.2. Assessment of Estimated Glomerular Filtration Rate

The Chronic Kidney Disease Epidemiology Collaboration's CKD-EPI equation is more accurate for calculating eGFR over 60 mL/min/1.73m^2 than the previous Modification of Diet in Renal Disease equation, and it is now favored. Importantly, the CKD-EPI equation has been changed to a new, race-agnostic form known as CKD-EPI 2021. The American Society of Nephrology and the National Kidney Foundation have urged rapid implementation of CKD-EPI 2021 as a significant tool for improving CKD care and reducing health inequalities based on race. Furthermore, the use of cystatin C (another eGFR marker) in conjunction with serum creatinine is recommended because combining both filtration markers is more accurate and would support better clinical decisions than using either signal separately [2] [8] [28].

5.3. Chronic Kidney Disease Diagnosis

Chronic kidney disease is diagnosed when there is a glomerular filtration rate (GFR) of less than 60 ml/min/1.73m^2 or evidence of kidney damage for three or more months. Kidney damage is typically indicated by the presence of albuminuria, but can also include abnormalities in urine sediment, structural abnormalities observed in imaging, or specific findings from kidney biopsies. Upon identification, CKD is risk-stratified using the cause-GFR category-albuminuria category (C-G-A classification), as illustrated in the heat map in **Figure 1** [2] [28].



Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk. GFR, glomerular filtration rate.

Figure 1. CKD is risk-stratification.

5.4. Diabetic Kidney Disease

Diabetic kidney disease (DKD) is a clinical diagnosis based on the presence of albuminuria and/or reduced eGFR in the absence of signs or symptoms of other primary kidney injury. DKD is typically characterized by long-term DM, retinopathy, albuminuria without extensive hematuria, and progressive reduction in eGFR. However, DKD symptoms may be present at diagnosis or without retinopathy in T2DM. Reduced eGFR without albuminuria has been documented often in both T1DM and T2DM, and it is becoming more common as DM prevalence rises [5] [6] [28] [31].

An active urinary sediment (which includes red or white blood cells or cellular casts), rapidly increasing albuminuria or total proteinuria, nephrotic syndrome, a rapidly falling eGFR, or the absence of retinopathy (in T1DM) indicate alternative or additional causes of kidney disease. Individuals exhibiting these characteristics should be sent to a nephrologist for a more thorough diagnosis, which may include a kidney biopsy. People with T1DM rarely acquire renal damage without retinopathy. In T2DM, retinopathy is only marginally sensitive and selective for DM-induced CKD, as validated by kidney biopsy [28].

5.5. Chronic Kidney Disease Staging

Stage G1 and G2 CKD are defined by high albuminuria with an eGFR ≥60 mL/min/1.73m^2, while stages G3 to G5 are marked by progressively lower eGFR ranges. At any eGFR, the degree of albuminuria is closely linked to the risk of CVD, CKD progression, and mortality. Therefore, an additional subclassification based on urine albumin levels is used. The KDIGO guidelines recommend a comprehensive CKD staging system that includes albuminuria at all eGFR stages, which is more closely associated with risk. Both eGFR and albuminuria must be quantified to guide treatment decisions. Accurate eGFR measurement is essential for adjusting medication dosages, and the degree of albuminuria should influence the choice of antihypertensive and glucose-lowering medications. The history of eGFR decline and the cause of kidney damage, including non-diabetic causes, may also affect treatment decisions [2] [8] [28].

6. Screening for CKD

Screening for CKD is critical because of its serious health consequences and the potential for early management to avoid development to ESKD. Early detection by targeted screening identifies high-risk patients, such as those with DM, hypertension, or a family history of kidney disease, allowing for prompt medical intervention. This preventive strategy can delay or prevent serious consequences, decreasing the need for expensive treatments such as dialysis or kidney transplants. Early detection also allows for lifestyle adjustments and treatments that reduce the CVD risks linked with CKD. Focusing on high-risk populations improves screening cost-effectiveness while also ensuring efficient resource usage. As the global prevalence of CKD rises, particularly among aging populations and those with higher rates of DM and hypertension, effective screening measures become even more important. Therefore, that can reduce the burden of CKD on individuals and healthcare systems [2] [8] [12] [28].

Addressing CKD requires several essential components: educating health personnel and at-risk populations, implementing early detection programs, and integrating evidence-based treatments for CKD and associated conditions like hypertension and DM. The KDIGO Controversies Conference highlighted the potential benefits of early CKD identification in asymptomatic individuals at risk, especially when accompanied by risk stratification and timely treatment initiation. Effective programs should prioritize treatment for newly diagnosed high-risk CKD patients to justify early detection efforts, particularly in resource-constrained settings [32]-[34].

High-risk groups for CKD encompass individuals with hypertension, DM, cardiovascular disease (CVD), genetic predispositions, and exposure to environmental toxins or nephrotoxic medications. Despite these risks, global awareness of CKD remains disproportionately low, with only a small percentage of both the general and high-risk populations aware of their CKD status. Advocates stress the importance of earlier screening and diagnosis, coupled with comprehensive patient and family education to enhance healthcare access and adherence to lifestyle changes and prescribed medications [34]-[36].

In low- and middle-income countries (LMICs), significant disparities exist between the burden of CKD and the availability of adequate healthcare resources. Limited access to kidney replacement therapy, increasing rates of DM and hypertension, and disparities in CKD treatment access based on sex and gender underscore the urgent need for early identification and intervention in primary care settings. Most of the global CKD burden resides in LMICs, where challenges include insufficient diagnostic services, a shortage of skilled healthcare providers, and the affordability of essential medications. Efforts to mitigate CKD progression in LMICs have shown promise through care models supporting primary care providers and allied health workers. These models effectively slow the decline in eGFR, emphasizing the strategic allocation of resources to preventable, higher-risk stages. Slowing CKD progression early on not only yields economic benefits but also reduces the likelihood of kidney failure and cardiovascular complications, highlighting the critical role of early intervention strategies in global CKD management [37]-[39].

6.1. Screening Frequency

The American Diabetes Association, American Association of Clinical Endocrinology and KDIGO recommend annual CKD screening for people with DM, starting at diagnosis for T2DM and five years after diagnosis for T1DM. The frequency of screening should be guided by CKD risk, with risk equations available to estimate the interval risk of developing CKD and guide repeat testing intervals (**Figure 2**) [2] [8] [28].

CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)			Albuminuria categories Description and range		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
GFR categories (mL/min/1.73 m²) Description and range			<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	>300 mg/g >30 mg/mmol
G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
G4	Severely decreased	15–29	Treat and refer* 3	Treat and refer* 3	Treat and refer 4+
G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD)
High risk
Moderately increased risk
Very high risk

The numbers in the boxes are a guide to the frequency of screening or monitoring (number of times per year). Green reflects no evidence of CKD by estimated GFR or albuminuria, with screening indicated once per year. For monitoring of prevalent CKD, suggested monitoring varies from once per year (yellow) to four times or more per year (i.e., every 1 - 3 months, [deep red]) according to risks of CKD progression and CKD complications (e.g., cardiovascular disease, anemia, hyperparathyroidism). These are general parameters based only on expert opinion and underlying comorbid conditions, and disease state must be taken into account, as well as the likelihood of impacting a change in management for any individual. CKD, chronic kidney disease; GFR, glomerular filtration rate. Reprinted and adapted from de Boer *et al.* [7]

Figure 2. Risk of CKD progression, frequency of visits, and referral to nephrology according to GFR and albuminuria. [28]

Both albuminuria and eGFR should be measured on a yearly basis to enable timely CKD diagnosis, monitor CKD progression, detect superimposed renal illnesses such as AKI, assess the risk of CKD consequences, dose drugs appropriately, and determine whether nephrology referral is required. Albuminuria and eGFR in persons with pre-existing renal disease may vary due to CKD progression, the development of a different superimposed cause of kidney disease, AKI, or other medication-related consequences [2] [8] [28]. Individuals taking diuretics should also have their serum potassium levels checked since these drugs can produce hypokalemia, which is linked to an increased risk of heart disease and death [40]-[42]. Patients with eGFR <60 mL/min/1.73m^2 using ACE inhibitors, ARBs, or MRAs should have their serum potassium levels checked regularly. The prevalence of CKD complications correlates with eGFR. When eGFR is <60 mL/min/1.73m^2, screening for complications of CKD is indicated (**Table 1**). Furthermore, patients with this lower eGFR range should have their medication-dosing checked and their exposure to nephrotoxins reduced [28]. Elevated blood pressure and volume overload should be assessed at every clinical contact; laboratory evaluations are generally recommended every 6 - 12 months for stage G3 CKD, every 3 - 5 months for stage G4 CKD, and every 1 - 3 months for stage G5 CKD, or as needed to assess symptoms or changes in therapy [28].

6.2. Screening for Complications

Persons with CKD should undergo annual or more frequent assessment of electrolytes to assess potassium and acid-base status; blood counts to assess anemia status; and calcium, phosphorus, 25(OH) vitamin D, and parathyroid hormone (PTH) measurements to assess mineral metabolism (**Table 1**) [28].

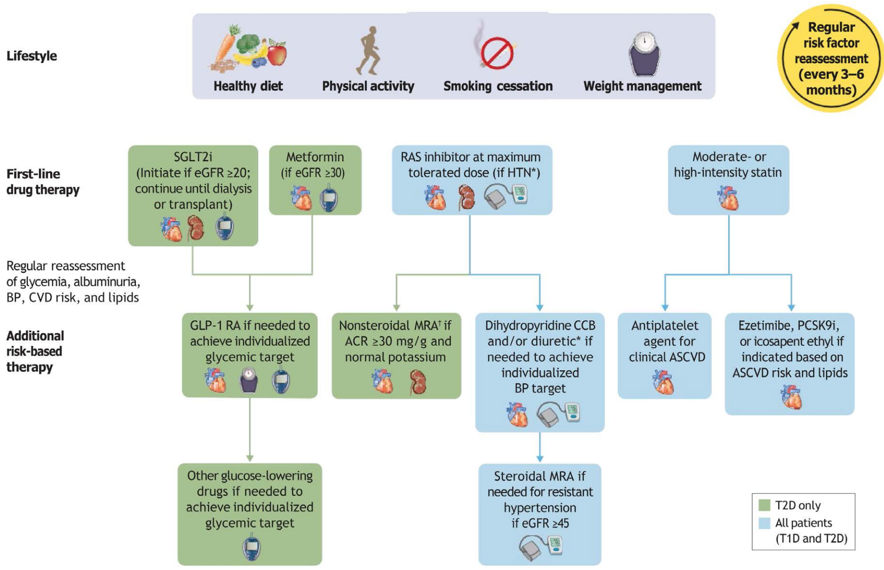
Table 1. Screening for selected complications of chronic kidney disease [28].

Complication	Physical and laboratory evaluation
Blood pressure > 130/80 mmHg	Blood pressure, weight, BMI
Volume overload	History, physical examination, weight
Electrolyte abnormalities	Serum electrolytes
Metabolic acidosis	Serum electrolytes
Anemia	Hemoglobin, iron, iron saturation, ferritin testing if indicated
Metabolic bone disease	Serum calcium, phosphate, PTH, vitamin 25(OH)D

PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D.

7. Prevention and Management

The KDIGO (kidney disease: Improving Global Outcomes) guidelines 2024 provide a comprehensive framework for the treatment and risk modification of CKD, emphasizing a holistic approach (**Figure 3**) that integrates medical, lifestyle, and psychosocial strategies. Recognizing CKD as a multifaceted condition that impacts various aspects of a patient's health and well-being, the KDIGO guidelines advocate for a multidisciplinary and patient-centered approach to care. This approach aims not only to slow the progression of the disease and manage its complications but also to enhance the overall quality of life for CKD patients. This integrated approach is similarly adopted by the American Diabetes Association (ADA) in their 2024 guidelines and the American Association of Clinical Endocrinology (AACE) in their 2022 guidelines, reflecting a consensus on the holistic management of CKD across major medical organizations [2] [8] [28].



Icons presented indicate the following benefits: BP cuff, BP lowering; glucometer, glucose lowering; heart, cardioprotection; kidney, kidney protection; scale, weight management. eGFR is presented in units of mL/min/1.73m^2. *ACEi or ARB (at maximal tolerated doses) should be first-line therapy for hypertension when albuminuria is present. Otherwise, dihydropyridine calcium channel blocker or diuretic can also be considered; all three classes are often needed to attain BP targets. †Finerenone is currently the only ns-MRA with proven clinical kidney and cardiovascular benefits. ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to creatinine ratio; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HTN, hypertension; MRA, mineralocorticoid receptor antagonist; ns-MRA, nonsteroidal mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SGLT2i, sodium–glucose cotransporter 2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes. Reprinted from de Boer *et al.* [7]

Figure 3. Holistic approach to chronic kidney disease [2].

Slowing down the progression of DKD or CKD in DM is crucial for lowering the risk of kidney failure and CVD, which includes HF, atherosclerotic events, and other causes of death. ACE inhibitors, ARBs, SGLT2is, GLP-1 RAs, and the nonsteroidal mineralocorticoid antagonist finerenone have all been reported to improve albuminuria and eGFR levels. According to ADA 2024, the only validated main preventative strategies for CKD in adults with DM are blood glucose (A1C goal of 7%) and blood pressure control (BP <130/80 mmHg). There is no evidence that RAAS inhibitors or other therapies prevent DKD in the absence of hypertension or albuminuria. As a result, the ADA does not suggest routine use of these drugs only to avoid the onset of DKD [2] [8] [28].

7.1. Treatment and Risk Modification

Risk factors associated with the progression of CKD, CVD, and other CKD complications are highly interrelated, necessitating an integrated approach to their management. The term "CKD treatment and risk modification" encompasses the goal of CKD treatment, which is to achieve meaningful beneficial effects on both "CKD manifestations" and "CKD outcomes." CKD manifestations include symptoms and clinical or laboratory abnormalities associated with CKD that have significant health implications. These manifestations encompass increased blood pressure, anemia, dyslipidemia, CKD-mineral and bone disorder (CKD-MBD), potassium imbalances, severe acidosis, decreased fertility, and heightened risk of pregnancy complications. CKD outcomes refer to the progression to kidney failure and the broader spectrum of CKD-associated morbidity and mortality. These outcomes include various CVDs, hospitalizations, infections, and gout. Targeting the underlying pathophysiology of CKD to reduce the risk of its progression can have beneficial effects across a range of CKD manifestations and associated outcomes. However, specific complications may still require targeted interventions to effectively manage their impact [2] [43].

To optimize possible benefits, healthcare practitioners should prioritize identifying persons at risk and initiating therapies early in the course of CKD. Early intervention can dramatically improve outcomes by addressing the underlying pathophysiology of CKD and limiting its progression, lowering the risk of consequences. This **proactive strategy** is critical for producing significant health gains and improving the quality of life for CKD patients [2].

7.2. Lifestyle Factors

A comprehensive and integrated approach to lifestyle modification is needed. There *is value in referring people to professionals or programs with expertise in lifestyle modification* (***LSM specialists***). We also appreciate that different healthcare systems and regions will have variable access to such specialized services or teams, and thus availability may be an issue.

7.2.1. Avoiding Use of Tobacco Products

The KDIGO advice to patients with DM and CKD who use tobacco to quit were expanded to all people with CKD who use tobacco products in order to lower the risk of CVD-related premature mortality, as well as the risk of respiratory disease and cancer. Special intensive programs (***Smoking cessation programs***) are helpful in promoting smoking cessation in addition to pharmacotherapy (e.g., nicotine replacement therapy using nicotine-receptor partial agonists) [44]-[47].

7.2.2. Physical Activity and Optimum Weight

While BMI is an imperfect measure of adiposity, it is important to remember that it is just one piece of the puzzle when it comes to assessing the health of CKD patients. A BMI of more than 25 kg/m^2 in adults (i.e., overweight or obese) is associated with an increased risk of numerous long-term illnesses, including the development of CKD. However, BMI can overestimate risk in those with high muscle mass, and risk varies by ethnicity. Therefore, it is critical to provide CKD patients with weight guidance based on BMI, but this guidance should be part of a comprehensive approach that also considers other factors such as ethnicity, food, comorbidities, physical activity levels, risk of falls, and laboratory values. This comprehensive approach will help healthcare professionals provide the best care for their CKD patients [48]-[52].

The KDIGO 2024 recommended the same practice points relating to physical activity for people with DM and CKD to those with CKD without DM [2].

7.3. Diet

A whole-food, plant-based diet (**Table 2**) low in animal-based and ultra-processed foods are helpful for slowing the progression of CKD and delay need for dialysis as they reduce the cardiometabolic risk factors such as hypertension, CVD, DM, and obesity [53]-[55].

The association of dietary patterns and kidney-related outcomes was evaluated in a systematic review. It has demonstrated that dietary patterns that include more plant-based unprocessed protein, slow the trajectory of eGFR decline, reduce the risk of kidney failure, reduce risk of mortality, and improve scores in some QoL domains (e.g., DASH and Mediterranean diet) [56] [57].

Table 2. Diet pattern in CKD.

Diet pattern	Definitions [53]-[55]
Dietary Approaches to Stop Hypertension (DASH)	rich in fruits, vegetables, whole grains, and low-fat dairy foods
Mediterranean	built around vegetables, fruits, herbs, nuts, beans, whole grains, and seafood but also includes moderate amounts of dairy, meat, and eggs
Vegan and vegetarian diets	plant-based
Ultra-processed foods	sugar-sweetened beverages, fast foods, frozen meals, chips, candy, and pastries are high in salt, sugar, and fat, and low in nutritional value, and they promote inflammation, which may contribute to worsening kidney function.
A plant-based diet	rich in anti-inflammatory nutrients, fiber, and phytochemicals, and has been shown to reduce proteinuria and decrease metabolic acidosis. The probiotic nature of plant-based foods may also support the microbiome and reduce inflammation and intestinal production of uremic toxins.

Dietary protein management may complement risk factor reduction and pharmacological treatments for CKD. In those with DKD or eGFR <30 mL/min/1.73m^2, KDIGO 2024 and ADA 2024 suggest restricting protein consumption to 0.8 g/kg per day. Dietary measures can also help manage elevated levels of potassium and phosphorus. People with DM who require antihypertensive drugs should limit their sodium intake to 2.3 g per day. These methods may be especially relevant for people with low eGFR, as their urinary sodium and potassium excretion may be impeded. Individuals on dialysis should consider increasing their dietary protein intake because malnutrition is a major issue for some dialysis patients. Individual sodium and potassium intake recommendations should take into account comorbid conditions, medication use, blood pressure, and laboratory findings. Obesity is a risk factor for hypertension and incident CKD, so people with DM should consider weight management, which includes nutrition, physical exercise, and various weight-loss methods (pharmacotherapy, bariatric surgery, GLP-1 RAs) [2] [28] [58] [59].

Diets with little to no protein are not recommended for those with unstable metabolisms or during times of metabolic instability. This covers ailments like sarcopenia, cachexia, active inflammatory or infectious diseases, hospital stays or the early postoperative period, poorly controlled DM, consumptive diseases like cancer, treatment with antibiotics or immunosuppressive drugs, and notable short-term weight loss that may increase the risk of malnutrition in the context of inadequate intake of proteins [2].

The KDIGO 2024, the AACE 2022 and the ADA 2024 guidelines recommend that patients with CKD limit their sodium intake to reduce hypertension and fluid retention. The guidelines suggest a dietary sodium intake of less than 2 grams per day (or less than 5 grams of sodium chloride) to help manage blood pressure and decrease the risk of cardiovascular events and disease progression. Reducing sodium intake can help alleviate symptoms such as edema and improve overall kidney health in CKD patients. Regular monitoring and individualized dietary counseling are advised to ensure adherence and effectiveness of sodium restriction in managing CKD [2] [8] [28].

7.4. Blood Pressure Control

Blood pressure control in CKD is crucial for managing disease progression and preventing cardiovascular complications. Although RCTs have not shown that aggressive BP-lowering reduces the risk of kidney failure, the RCT evidence suggesting significant cardiovascular benefits should encourage such an approach. Observationally, each 20 mmHg increase in SBP and 10 mmHg increase in diastolic BP is related with an estimated doubling of cardiovascular risk, with no lower limit below 115/75 mmHg [2].

Providing consistent blood pressure monitoring in clinics can be time-consuming. However, applying the suggested SBP target of <120 mm Hg to non-standardized measurements of blood pressure can be risky. Home-based monitoring (or telemonitoring) is a feasible option for identifying excessive blood pressure. Trials have demonstrated that two morning and evening blood pressure measures performed in the first week of each month can be used to titrate antihypertensive medication and lower blood pressure more effectively than "usual care" procedures [60] [61].

Individuals with frailty, short life expectancy, or a history of falls and fractures may have a higher risk of further occurrences if blood pressure targets of <120 are met. Postural hypotension is associated with negative outcomes in these persons, therefore when selecting particular targets, assess the benefits of some attenuation of eGFR drop against the life-changing impact of falls, fractures, and other occurrences. Therefore, individualized BP targets and use of agents according to age, coexistent CVD, and other comorbidities; risk of progression of CKD; and tolerance to treatments is highly encouraged [62].

According to the KDIGO 2024 guidelines, maintaining a systolic blood pressure (SBP) target of <120 mm Hg using standardized office BP measurement is recommended for adults with high BP and CKD to slow the progression of kidney damage. The ADA 2024 emphasizes a target BP of <130/70 mm Hg to reduce CVD mortality and slow CKD progression among all people with DM. The AACE 2022 guidelines align closely with the ADA, recommending a BP goal of <130/80 mm Hg for patients with DM and CKD, while also considering more stringent targets based on patient-specific factors [2] [8] [28].

7.5. Glycemic Control

The KDIGO 2024 guidelines recommend individualized glycemic targets to balance the benefits of glycemic control with the risk of hypoglycemia. For most patients with CKD and DM, an HbA1c target of around 7% is suggested, though less stringent targets may be appropriate for those with a high risk of hypoglycemia or limited life expectancy. The ADA 2024 guidelines similarly emphasize individualized HbA1c targets, advocating for an HbA1c goal of <7% for many non-pregnant adults to reduce the risk of DM complications. The AACE 2022 guidelines align with these recommendations, endorsing an HbA1c target of ≤6.5% for patients with a low risk of hypoglycemia, but allowing for higher targets in certain populations. All three guidelines stress the importance of using agents that have proven renal and cardiovascular benefits, such as SGLT2 inhibitors and GLP-1 receptor agonists, to optimize both glycemic control and kidney health [2] [8] [28].

7.6. Renin-Angiotensin System Inhibitors

Renin-angiotensin system (RAS) inhibitors are essential for managing CKD, as they lower blood pressure and slow kidney damage progression. The KDIGO 2024 guidelines emphasize their use, particularly ACE inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs), for patients with proteinuria to reduce CKD progression and cardiovascular risk. The ADA 2024 standards also recommend ACEIs or ARBs for patients with DM and hypertension with albuminuria, noting their renal protective effects beyond blood pressure reduction and advising regular monitoring of kidney function and potassium levels. Similarly, the AACE 2022 guidelines endorse RAS inhibitors for CKD patients, highlighting their benefits in hypertension control and renal protection, stressing individualized treatment plans, and careful monitoring of kidney function and electrolytes [2] [8] [28].

7.7. Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2i)

One of the most significant advances in CKD care over the last decade has been the finding that SGLT-2 inhibitors have strong protective effects on the heart and kidneys in individuals with and without DM. Recent trials show a 30% reduction in risk for various renal outcomes among patients with baseline estimated GFR values as low as 20 mL/min/1.73m^2 [63].

Most significantly, three trials designed with primary kidney outcomes (Canagliflozin and Renal Events in Diabetes and Established Nephropathy Clinical Evaluation (CREDENCE), Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD), and Study of Heart and Kidney Protection with Empagliflozin (EMPA-KIDNEY)) were stopped early because predetermined efficacy criteria have been met, with a follow-up time 2.0 - 2.6 years [64]-[68].

Subgroup analyses of the DAPA-CKD and EMPA-KIDNEY studies have revealed more information about the wide range of patients who may benefit from SGLT-2 inhibitors. In DAPA-CKD, dapagliflozin outperformed placebo in all predetermined subgroups by baseline age, sex, race, DM status, systolic blood pressure, estimated GFR, and ACR. In EMPA-KIDNEY, empagliflozin reduced the risk of the major composite outcome in comparison to placebo, regardless of baseline DM status or estimated GFR [64] [68].

The DAPA-CKD trial also demonstrated that kidney-specific protective effects of SGLT-2 inhibitors apply to patients with IgA nephropathy, and possibly those with focal segmental glomerulosclerosis [69] [70].

SGLT-2 inhibitors, which work at the proximal tubule level to prevent glucose and sodium reabsorption, are generally safe for use in CKD patients. Early warning signs of increased risks of volume depletion, major vaginal infections, bone fractures, and the need for limb amputation in the Canagliflozin Cardiovascular Assessment Study (CANVAS) were not shown in following studies—CREDENCE, DAPA-CKD, and EMPA-KIDNEY—tone down these concerns [63]-[65] [68] [71].

Therefore, sodium-glucose cotransporter-2 inhibitors (SGLT2i) have emerged as a significant advancement in the treatment of CKD, particularly for patients with T2DM. KDIGO 2024 guidelines recommend SGLT2 inhibitors as a standard part of treatment for CKD patients with T2DM due to their proven benefits in slowing kidney disease progression and reducing cardiovascular events. These inhibitors work by reducing glucose reabsorption in the kidneys, leading to glycosuria and, consequently, lower blood glucose levels. The guidelines underscore that SGLT2 inhibitors should be considered as part of the standard treatment for patients with T2D and CKD, regardless of baseline HbA1c levels, due to their renoprotective effects. The synthesis of evidence in the guidelines demonstrated that large trials, both individually and in meta-analyses, show that SGLT2i has clear net benefits, with net benefits being especially major in persons without DM because to the minimal risk of serious consequences from ketoacidosis or lower-limb amputation. However, evidence supporting improvements on CKD in patients without DM and low albuminuria is restricted to eGFR slope studies in heart failure trials and one CKD trial, all with short follow-up durations. However, extrapolating these eGFR slope data shows that long-term treatment would provide significant improvements to such persons [2].

The ADA 2024 guidelines advocate for the inclusion of SGLT2 inhibitors in the therapeutic regimen for patients with T2DM and CKD. The ADA highlights the dual benefits of SGLT2 inhibitors in managing hyperglycemia and providing significant renal and cardiovascular protection. The guidelines suggest that these agents should be initiated in patients with an eGFR ≥ 30 mL/min/1.73m^2, and continued until dialysis or kidney transplantation is necessary [28].

Similarly, the AACE 2022 guidelines support the use of SGLT2 inhibitors in managing CKD in patients with T2DM. AACE emphasizes the importance of these medications in improving renal outcomes and reducing cardiovascular risk. The guidelines recommend considering patient-specific factors such as existing CVD and kidney function when selecting an SGLT2 inhibitor and monitoring for potential side effects like genital infections and dehydration. AACE emphasizes the importance of these agents in reducing the risk of kidney disease progression and cardiovascular events. The guidelines advocate for the early initiation of SGLT2 inhibitors in eligible patients to maximize renal and cardiovascular benefits [8].

7.8. Mineralocorticoid Receptor Antagonists (MRA)

Several MRAs are available and can be effective additions to RAAS inhibitors, especially in populations with albuminuria and/or DM. Spironolactone and eplerenone are two common steroidal non-selective MRAs that reduce albuminuria [47]. In a meta-analysis of 372 patients from seven trials, combined therapy with a non-selective MRA and an ACE inhibitor and/or ARB resulted in a significant reduction in proteinuria, but at a higher risk of hyperkalemia [72].

Finerenone, a recently approved non-steroidal selective MRA, offers advantages over steroidal non-selective MRAs. It has stronger selectivity for the mineralocorticoid receptor, a shorter half-life, less impact on blood pressure, a more favorable side effect profile, and potentially greater anti-inflammatory and antifibrotic effects. The Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) trial and the Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) trial evaluated finerenone's kidney and cardiovascular benefits, respectively, in patients with T2DM and albuminuria levels ≥ 30 mg/g, all on maximally tolerated ACE inhibitors or ARBs. FIDELIO-DKD included participants with more severe baseline CKD. A pooled analysis of these trials showed that finerenone reduced the risk of kidney composite outcomes by 15-23% and lowered the mean change in albumin-to-creatinine ratio (ACR) by 32% from baseline to four months. Hyperkalemia was more common with finerenone (14%) compared to placebo (7%) [73]-[77].

Mineralocorticoid receptor antagonists (MRAs), such as spironolactone and eplerenone, are increasingly recognized for their role in managing CKD. The KDIGO 2024 guidelines highlight their benefits in reducing albuminuria and providing cardiovascular protection, particularly in patients with resistant hypertension or those intolerant to high doses of ACE inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs). The ADA 2024 guidelines also recommend MRAs as add-on therapy for DM and CKD patients with significant proteinuria or hypertension despite optimal RAS inhibitor therapy. Both KDIGO and ADA emphasize careful monitoring of serum potassium and renal function to mitigate hyperkalemia risk. Similarly, the AACE 2022 guidelines support the use of MRAs in patients with difficult-to-control blood pressure or proteinuria, stressing the importance of regular electrolyte and kidney function monitoring to ensure safety [2] [8] [28].

7.9. Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RA)

GLP-1 receptor agonists have demonstrated improved kidney outcomes in T2DM patients, primarily in trials targeting cardiac outcomes. These trials reported a 15% to 36% reduction in kidney outcomes, including albuminuria [78]-[89].

A meta-analysis of around 44,000 participants across six trials showed a 21% lower risk of developing composite kidney outcomes (new onset albuminuria >300 mg/g, serum creatinine doubling, ≥40% decline in eGFR, kidney replacement therapy, or kidney-related death) compared with placebo, driven mainly by reduced incident albuminuria. However, the associations with CKD progression and kidney failure were not statistically significant [89].

A Study Comparing Dulaglutide with Insulin Glargine on Glycemic Control in Participants with Type 2 Diabetes and Moderate or Severe Chronic Kidney Disease (AWARD-7) trial, focused on glycemic control, involved 577 adults with T2DM and CKD stages 3-4. Participants received dulaglutide (1.5 mg or 0.75 mg weekly) or daily insulin glargine. Both dulaglutide doses slowed eGFR decline more effectively than insulin glargine, with greater ACR reductions in those with baseline albuminuria >300 mg/g over one year [90].

Recently, the results of the FLOW (Evaluate Renal Function with Semaglutide Once Weekly) trial that investigated the efficacy of semaglutide in reducing the risks of kidney failure, cardiovascular events, and death in patients with T2DM and CKD, has been published. A total of 3533 patients were randomized to receive either weekly subcutaneous semaglutide (1.0 mg) or a placebo. CKD was defined by an estimated glomerular filtration rate (eGFR) of 50 to 75 ml/min/1.73m^2 with a urinary albumin-to-creatinine ratio (UACR) of >300 and <5000 mg/g, or an eGFR of 25 to <50 ml/min/1.73m^2 with a UACR of >100 and <5000 mg/g. The primary outcome was a composite of kidney failure, a 50% reduction in eGFR, or death from kidney-related or cardiovascular causes. After a median follow-up of

3.4 years, the semaglutide group had a 24% lower risk of primary outcome events compared to the placebo group (hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.66 to 0.88; P = 0.0003). Kidney-specific outcomes and cardiovascular deaths also favored semaglutide (HR, 0.79; 95% CI, 0.66 to 0.94 and HR, 0.71; 95% CI, 0.56 to 0.89, respectively). Secondary outcomes showed that semaglutide slowed the annual eGFR decline by 1.16 ml/min/1.73m^2 (P < 0.001), reduced major cardiovascular events by 18% (HR, 0.82; 95% CI, 0.68 to 0.98; P = 0.029), and lowered the risk of death from any cause by 20% (HR, 0.80; 95% CI, 0.67 to 0.95; P = 0.01). Serious adverse events were less frequent in the semaglutide group (49.6% vs. 53.8% in the placebo group). The findings suggest that semaglutide effectively reduces significant kidney and cardiovascular outcomes in this high-risk patient population [91].

Proposed mechanisms for these benefits include improved glycemic control, weight loss, increased natriuresis, and reduced inflammation and oxidative stress. Adverse effects noted include diarrhea, nausea, and vomiting [78] [81] [83] [84] [90] [92]-[95].

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are recommended for managing T2DM and have shown benefits in CKD management. The KDIGO 2024 guidelines suggest the use of GLP-1 RAs like liraglutide and semaglutide in patients with CKD and T2DM to improve glycemic control and provide cardiovascular and renal protection. These agents have been associated with a reduction in albuminuria and a slower progression of kidney disease in clinical trials [2].

The ADA 2024 guidelines also support the use of GLP-1 RAs in patients with T2DM and CKD. The ADA emphasizes that these agents not only help in achieving glycemic targets but also offer significant cardiovascular benefits, including reduced risk of major adverse cardiovascular events. Additionally, GLP-1 RAs have been shown to have favorable effects on weight and blood pressure, making them a valuable addition to the treatment regimen for patients with DM and CKD [28].

AACE 2022 guidelines advocate for the use of GLP-1 RAs in patients with T2DM and CKD, highlighting their multifaceted benefits. AACE notes that GLP-1 RAs can help manage hyperglycemia, promote weight loss, and provide cardiovascular and renal protection. The guidelines recommend considering GLP-1 RAs for patients who need additional glucose-lowering therapy, particularly those with a high risk of CVD [8].

7.10. Metabolic Acidosis

Metabolic acidosis is a common complication in CKD, contributing to disease progression and adverse outcomes. The KDIGO 2024 guidelines recommend maintaining normal serum bicarbonate levels through oral bicarbonate supplementation to slow CKD progression, improve nutritional status, and reduce risks of bone disease and muscle wasting. Similarly, the ADA 2024 guidelines advise regular monitoring of serum bicarbonate in CKD and DM patients, initiating supplementation when levels drop below 22 mmol/L, to enhance metabolic control and quality of life. The AACE 2022 guidelines also stress early identification and treatment of metabolic acidosis, highlighting the benefits of maintaining normal bicarbonate levels on kidney function and overall health, and recommending oral bicarbonate supplements with regular acid-base status monitoring [2] [8] [28].

7.11. Hyperkalemia in CKD

Hyperkalemia is a frequent and potentially life-threatening complication of CKD, often exacerbated by RAS inhibitors. The KDIGO 2024 guidelines recommend regular monitoring of serum potassium levels, dietary interventions, and potassium binders such as patiromer or sodium zirconium cyclosilicate for patients on RAS inhibitors experiencing hyperkalemia. Similarly, the ADA 2024 guidelines emphasize regular potassium monitoring and dietary modifications to reduce intake, with potassium binders as an additional measure to manage hyperkalemia while continuing RAS inhibitor therapy. The AACE 2022 guidelines also stress the importance of preventing and managing hyperkalemia in CKD patients through regular potassium monitoring, dietary adjustments, and the use of potassium binders, when necessary, along with medication adjustments to control potassium levels. Higher ACR and previous DM, hyperglycemia, constipation, RASi, and MRA were among the additional risk factors for hyperkalemia in addition to lower eGFR. Take note that SGLT2i do not seem to raise potassium levels in the serum [2] [8] [28].

7.12. Anemia

Anemia is a common complication in CKD and is associated with increased morbidity and mortality. The KDIGO 2024 guidelines recommend regular screening for anemia in CKD patients and the use of erythropoiesis-stimulating agents (ESAs) and iron supplementation to manage anemia. The guidelines suggest individualized treatment goals based on the severity of anemia and patient-specific factors, with the aim of improving quality of life and reducing the risk of cardiovascular complications. Iron, transferrin saturation, ferritin, vitamin B12, and folate levels should all be further examined in cases of anemia, which is defined as hemoglobin <13 g/dL in males and <12 g/dL in women. Regardless of ferritin level, deficiencies should be filled and a transferrin saturation target of >30% achieved. Intravenous administration of iron may yield superior outcomes compared to oral replacement. Moreover, both the ADA 2024 guidelines and the AACE 2022 guidelines also address anemia management in patients with CKD and DM. They recommend routine screening for anemia and treating with ESAs and iron supplementation as appropriate. The guidelines emphasize the importance of addressing underlying causes of anemia and monitoring for potential adverse effects of ESA therapy, such as increased risk of cardiovascular events. The guidelines suggest that treating anemia can improve symptoms, enhance quality of life, and potentially slow the progression of CKD [2] [8] [28].

7.13. CKD-Mineral Bone Disorder (CKD-MBD)

CKD-Mineral Bone Disorder (CKD-MBD) involves abnormalities in mineral metabolism, bone structure, and vascular calcification. The KDIGO 2024 guidelines recommend regular monitoring of serum calcium, phosphate, parathyroid hormone (PTH), and vitamin D in CKD patients, with treatments including dietary phosphate restriction, phosphate binders, vitamin D analogs, and calcimimetics. The ADA 2024 guidelines stress the importance of managing CKD-MBD in diabetic patients to reduce the risk of fractures, CVD, and other complications. The AACE 2022 guidelines also advocate for comprehensive management through regular monitoring and individualized treatment plans using dietary modifications, phosphate binders, vitamin D supplements, and calcimimetics to optimize outcomes. AACE recommends adequate calcium intake and achievement of 25(OH) vitamin D levels of >30 ng/dL in all persons [2] [8] [28].

7.14. Hyperuricemia

Hyperuricemia is common in CKD and linked to gout, CVD, and kidney disease progression. The KDIGO 2024 guidelines recommend monitoring serum uric acid levels and using urate-lowering therapies like allopurinol or febuxostat for symptomatic hyperuricemia to reduce gout flares and potentially slow CKD progression. The ADA 2024 guidelines similarly advocate for monitoring uric acid levels in CKD patients with DM, recommending urate-lowering therapy for those with gout or significant hyperuricemia to lower cardiovascular risk and prevent kidney disease progression. The AACE 2022 guidelines emphasize identifying and managing hyperuricemia in CKD patients through regular monitoring and urate-lowering therapies to prevent gout, reduce cardiovascular risk, and slow CKD progression [2] [8] [28].

7.15. Cardiovascular Disease (CVD) and Additional Specific Interventions to Modify Risk

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in CKD patients. The KDIGO 2024 guidelines recommend a comprehensive approach to managing cardiovascular risk, including lipid management with statins, antiplatelet therapy with aspirin for secondary prevention, and individualized decisions on invasive versus intensive medical therapy for coronary artery disease. Similarly, the ADA 2024 guidelines advocate for statin therapy for all DM and CKD patients, regardless of baseline lipid levels, and suggest antiplatelet therapy for those at high cardiovascular risk, balancing benefits against bleeding risks. The AACE 2022 guidelines emphasize a multifaceted approach, incorporating lipid-lowering therapies, blood pressure and glycemic control, and antiplatelet agents, with a focus on individualized treatment plans based on patient-specific factors and risks [2] [8] [28].

7.16. CKD and Atrial Fibrillation

Atrial fibrillation (AF) is prevalent in CKD patients, increasing their risk of stroke and cardiovascular events. The KDIGO 2024 guidelines recommend regular AF screening and anticoagulation therapy, favoring direct oral anticoagulants (DOACs) over warfarin due to better safety and ease of use. Similarly, the ADA 2024 guidelines advocate anticoagulation for AF patients with DM and CKD, preferring DOACs for those with suitable renal function and emphasizing regular renal function monitoring. The AACE 2022 guidelines also prefer DOACs over warfarin for AF management in CKD patients, highlighting their efficacy and lower bleeding risk, and stress the importance of individualized treatment plans and regular kidney function monitoring [2] [8] [28].

7.17. Drug Toxicities and AKI

Individuals with CKD or CKD in DM are at risk of AKI and different forms of medication toxicity (**Table 3**). It could be necessary to alter glucose-lowering medications in order to lessen hypoglycemia. When taken by someone with a low eGFR, several other medications should be avoided or used carefully. People with CKD should be made aware of their diagnosis and should refrain from dehydration, gadolinium-requiring imaging, high phosphate bowel preparations, and excessive dosages of iodinated contrast agents [2] [8] [28].

Table 3. Mitigation of side effects for newer agents to treat DKD (AACE) [8].

Side effects	Mitigation strategies
SGLT2 inhibitors	
Genital mycotic infections	Hygiene, topical antifungals
Volume depletion	Proactive dose reduction of diuretics in persons at risk for hypovolemia
	Hold SGLT2is during GI illness (nausea, vomiting, diarrhea)
	Improve glucose control to reduce glucosuria
Ketoacidosis	Educate persons with DM on early recognition.
	"STOP DKA" protocol (stop SGLT2i, test for ketones, maintain fluid and carbohydrate intake, use maintenance and supplemental insulin)
Hypoglycemia	Adjustment of background antihyperglycemic agents
GLP-1 receptor agonists	
Nausea/vomiting/diarrhea	Patient education on tolerability and symptom recognition
	Start at lowest dose and titrate slowly
Hypoglycemia	Adjustment of background antihyperglycemic agents
Finerenone	
Hyperkalemia	Dietary restriction of potassium
	Thiazide or loop diuretics
	SGLT2i
	Potassium-binding agents (patiromer or sodium zirconium cyclosilicate)

Abbreviations: DM: diabetes mellitus; GI: gastrointestinal; GLP-1: glucagon-like peptide 1; SGLT2i: sodium-glucose cotransporter 2 inhibitor.

7.18. Referral to a Nephrologist

If a diabetic patient's UACR is consistently rising or eGFR is declining, if the cause of their kidney disease is unknown, if managing their condition is difficult (anemia, secondary hyperparathyroidism, significant increases in albuminuria despite well-managed blood pressure, metabolic bone disease, resistant hypertension, electrolyte disturbances), or if their eGFR is less than 30 mL/min/1.73m^2, then a referral to a nephrologist should be considered by medical professionals. The frequency with which a health care provider sees patients with DM and renal disease will determine the appropriate threshold for referral. When stage 4 CKD manifests, consulting a nephrologist has been shown to lower costs, enhance care quality, and postpone dialysis. People with DM should also be informed by other experts and medical personnel on the progressive nature of CKD, the advantages of aggressively managing blood pressure and blood sugar, and the possibility of needing renal replacement therapy [2] [7] [8] [28] [96].

8. Addressing Culture Barriers to CKD Management in KSA

Cultural barriers to CKD management in Saudi Arabia, such as stigma, reliance on traditional remedies, and low health literacy, can be addressed through culturally sensitive strategies. Education programs using simple language, visual aids, and community engagement can improve awareness and understanding. Involving family members and incorporating religious principles into treatment plans, such as halal dietary guidance and Ramadan adjustments, can enhance trust and adherence. Mobile health tools in Arabic, along with outreach via community and religious leaders, can further empower patients to actively participate in their care while respecting cultural values [97] [98].

9. Recommendations

Statement 1: Use spot urinary albumin-to-creatinine ratio (ACR) and estimated glomerular filtration rate (eGFR) to diagnose and classify CKD.

Statement 2: Use the heat map (**Figure 1**) to risk-stratify people with CKD.

Statement 3: At least annually, urinary ACR and eGFR should be assessed in people with T1DM with duration of ≥5 years and in all people with T2DM regardless of treatment.

Statement 4: In people with established CKD, urinary albumin (e.g., spot urinary ACR) and eGFR should be monitored 1 - 4 times per year depending on the stage of the kidney disease (**Figure 2**).

Statement 5: Treat people with CKD with a comprehensive treatment strategy to reduce risks of progression of CKD and its associated complications.

Statement 6: Optimize glucose management to reduce the risk or slow the progression of CKD.

Statement 7: Optimize blood pressure control and reduce blood pressure variability to reduce the risk or slow the progression of CKD and reduce cardiovascular risk.

Statement 8: In nonpregnant people with DM and hypertension, either an ACE inhibitor or an angiotensin receptor blocker (ARB) is recommended for those with moderately increased albuminuria (UACR 30 - 299 mg/g creatinine) B and is strongly recommended for those with severely increased albuminuria (UACR ≥300 mg/g creatinine) and/or eGFR <60 mL/min//1.73m^2 to prevent the progression of kidney disease and reduce cardiovascular events. In the absence of albuminuria and with normal BP, ACE inhibitors or ARBs do not prevent DKD onset. ACE inhibitors and ARBs should not be used together due to increased risks of adverse effects, particularly hyperkalemia and AKI.

Statement 9: Periodically monitor for increased serum creatinine and potassium levels when ACE inhibitors, ARBs, and mineralocorticoid receptor antagonists are used, or for hypokalemia when diuretics are used.

Statement 10: An ACE inhibitor or an ARB is not recommended for the primary prevention of CKD in people with DM who have normal blood pressure, normal UACR (<30 mg/g creatinine), and normal eGFR.

Statement 11: Do not discontinue renin-angiotensin system blockade for mild to moderate increases in serum creatinine (≤30%) in the absence of signs of extracellular fluid volume depletion.

Statement 12: For people with T2DM and CKD, use of a sodium–glucose cotransporter 2 (SGLT2) inhibitor is recommended to reduce CKD progression and cardiovascular events in individuals with eGFR ≥20 mL/min//1.73m^2 and urinary albumin ≥200 mg/g creatinine.

Statement 13: For people with T2DM and CKD, use of an SGLT2 inhibitor is recommended to reduce CKD progression and cardiovascular events in individuals with eGFR ≥20 mL/min/1.73m^2 and urinary albumin ranging from normal to 200 mg/g creatinine.

Statement 14: For cardiovascular risk reduction in people with T2DM and CKD, consider use of an SGLT2 inhibitor (if eGFR is ≥20 mL/min/1.73m^2), a glucagon-like peptide 1 agonist, or a nonsteroidal mineralocorticoid receptor antagonist (if eGFR is ≥25 mL/min/1.73m^2).

Statement 15: As people with CKD and albuminuria are at increased risk for cardiovascular events and CKD progression, a nonsteroidal mineralocorticoid receptor antagonist that has been shown to be effective in clinical trials is recommended to reduce cardiovascular events and CKD progression (if eGFR is ≥25 mL/min/1.73m^2). Potassium levels should be monitored. Finerenone can be used for persistent albuminuria in addition to an ACE inhibitor or an ARB and SGLT2i, or in people with CKD in DM who cannot take an SGLT2i.

Statement 16: Measure ACR and eGFR after medication additions or adjustments (e.g., ACE inhibitors, ARBs, SGLT2is, finerenone, nonsteroidal anti-inflammatory drugs, proton pump inhibitors) or change in clinical status that may affect kidney function (e.g., iodinated contrast administration, acute illness).

Statement 17: Assess for complications of CKD, including anemia and bone and mineral metabolism disorders, in severe CKD (stages 4 to 5).

Statement 18: In people with CKD who have ≥300 mg/g urinary albumin, a reduction of 30% or greater in mg/g urinary albumin is recommended to slow CKD progression.

Statement 19: For people with non-dialysis-dependent stage G3 or higher CKD, dietary protein intake should be aimed to a target level of 0.8 g/kg body weight per day. A For individuals on dialysis, 1.0 - 1.2 g/kg/day of dietary protein intake should be considered since protein energy wasting is a major problem in some individuals on dialysis.

Statement 20: Individuals should be referred for evaluation by a nephrologist if they have continuously increased urinary albumin levels and/or continuously decreasing eGFR and/or if the eGFR is <30 mL/min/1.73m^2.

Statement 21: Promptly refer to a nephrologist for uncertainty about the etiology of kidney disease, difficult management issues, and rapidly progressing kidney disease, or complication management.

Statement 22: Healthcare providers should use culturally tailored strategies for CKD management in Saudi Arabia, including involving families in education, guiding safe CAM use, and framing advice within Islamic principles. These approaches build trust, enhance engagement, and improve adherence.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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